Journal of Pharmaceutical Sciences and Computational Chemistry
2025, Volume 1, Issue 3

Review Article

Herbal Emulgel Delivery Systems for Proctological Applications: Current Trends, Mechanisms, and Clinical Perspectives

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Citation V. Prasanth, V. Rangarao, V. N. D. Deeshitha, G. Veerla, P. Jahnavi, Herbal Emulgel Delivery Systems for Proctological Applications: Current Trends, Mechanisms, and Clinical Perspectives. *J. Pharm. Sci. Comput. Chem.* **2025**, 1 [3], 174-188.

https://doi.org/10.48309/jpscc.2025.535219.1019

Article info:
Submitted: 2025-07-17
Revised: 2025-08-02
Accepted: 2025-08-09
Published: 2025-08-23
ID: JPSCC-2507-1019

Keywords:
Anti-inflammatory herbs, Herbal emulgel, Proctological disorders, Rectal drug delivery, Sustained release.

ABSTRACT

Proctological disorders, including haemorrhoids, anal fissures, and proctitis, are common anorectal conditions marked by inflammation, bleeding, and mucosal damage that significantly impact patients' quality of life. Conventional treatments often present challenges such as poor mucosal retention, frequent dosing, irritation, and systemic side effects. Herbal emulgels—hybrid drug delivery systems combining emulsions and gels—offer a promising alternative by enabling localized, non-invasive, and sustained delivery of herbal bioactives. These formulations enhance drug penetration and retention, improving therapeutic efficacy. This review highlights the phytotherapeutic potential of key herbal ingredients such as *Hamamelis virginiana* (witch hazel), *Calendula officinalis*, *Aloe vera*, *Curcuma longa* (turmeric), *Melaleuca alternifolia* (tea tree oil), *Matricaria chamomilla* (chamomile), and *Azadirachta indica* (neem), known for their anti-inflammatory, antimicrobial, analgesic, and wound-healing properties. The manuscript further discusses formulation strategies, including emulsification techniques, selection of gelling agents, penetration enhancers, and preservatives. Critical evaluation parameters—such as pH, viscosity, spreadability, drug content uniformity, *in vitro* release, antimicrobial activity, and skin compatibility—are outlined. Advances in nanoemulgels, phytosome-based formulations, and patient-centric attributes (*e.g.,* non-irritant and odourless designs) are addressed alongside regulatory considerations and standardization challenges. While preclinical studies support the efficacy of herbal emulgels in managing anorectal conditions, robust clinical trials and regulatory validation are essential to ensure their safety, efficacy, and broader therapeutic adoption. The integration of modern drug delivery technologies with traditional herbal medicine offers a patient-friendly, effective solution for chronic proctological therapy.

Introduction

Proctological disorders encompass a range of anorectal conditions, primarily including haemorrhoids, anal fissures, and proctitis. These conditions are prevalent across diverse age groups and are associated with symptoms such as pain, itching, bleeding, and discomfort. Haemorrhoids, resulting from the engorgement and prolapse of vascular cushions in the anal canal, are considered the most common of these disorders, affecting up to 55% of adults at some point in their lives [1]. Anal fissures are longitudinal tears in the anoderm, often induced by trauma during bowel movements and associated with internal sphincter hypertonia. Proctitis, on the other hand, is characterized by inflammation of the rectal mucosa due to infections, inflammatory bowel disease, or radiation exposure. Collectively, these conditions pose a

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significant health burden, not only due to their high prevalence, but also due to their detrimental effect on patient quality of life, productivity, and psychological well-being. Despite their non-life-threatening nature, the chronic and recurring nature of these disorders warrants improved therapeutic strategies.

Conventional therapeutic interventions for proctological disorders include topical corticosteroids, vasoconstrictors, local anaesthetics, and nitric oxide donors. While these treatments offer symptomatic relief, they are often associated with several limitations. First, rectal mucosa presents challenges related to drug retention and absorption, leading to reduced contact time and necessitating frequent reapplication. Furthermore, prolonged use of topical corticosteroids can cause mucosal thinning, perianal dermatitis, and skin atrophy. Vasoconstrictors such as phenylephrine may relieve swelling temporarily but risk systemic absorption and cardiovascular effects. Nitroglycerin and calcium channel blockers, often used to relax the anal sphincter in fissures, frequently cause systemic side effects such as hypotension and headaches, limiting patient compliance. Additionally, conventional dosage forms such as ointments and suppositories are often greasy, difficult to retain, or uncomfortable, particularly in inflamed anorectal tissues. These challenges highlight the need for patient-friendly, localized, and efficient drug delivery systems capable of maintaining prolonged therapeutic action with minimal systemic absorption [2].

Given the anatomical and physiological complexities of the rectal region, there is a strong clinical need for delivery systems that can provide prolonged retention, targeted drug release, and enhanced mucosal adherence. A localized delivery strategy offers the advantage of minimizing systemic drug exposure, thereby reducing the risk of adverse effects. Moreover, sustained-release delivery platforms can ensure continuous drug action, improve treatment efficacy, and reduce the frequency of administration, which is crucial for managing chronic and recurring anorectal conditions [3]. Non-invasive delivery forms with good spreadability and bioadhesion are particularly valuable in ensuring better patient compliance and comfort. These systems are especially important in managing hemorrhoidal bleeding, chronic fissures, and inflamed rectal mucosa, where tissue sensitivity and pain often prevent repeated application of conventional agents.

Emulgels represent an innovative class of semi-solid dosage forms that combine the benefits of emulsions and gels. Structurally, they consist of an oil-in-water emulsion base incorporated into a gel matrix, allowing for the delivery of both hydrophilic and lipophilic drugs. The inclusion of emulsifying agents (Span 20, Tween 80) facilitates the formation of stable emulsion systems, while gelling agents such as Carbopol 934 or sodium carboxymethyl cellulose (NaCMC) provide the desired rheological properties and bioadhesion [4]. The hybrid nature of emulgels offers multiple advantages, including improved drug stability, enhanced skin penetration, better patient acceptability due to non-greasy texture, and controlled drug release. Moreover, their high-water content enhances hydration of the skin or mucosal surface, promoting better drug diffusion. These properties make emulgels highly suitable for rectal applications where mucosal integrity is compromised and long-term contact is required. Their mucoadhesive nature further contributes to prolonged retention at the site of action, making them an ideal platform for treating haemorrhoids, fissures, and rectal inflammation [5].

Herbal extracts are gaining increasing attention in proctological therapy due to their wide range of pharmacological effects, safety profiles, and historical use in traditional medicine. Natural agents such as witch hazel (*Hamamelis virginiana*) possess astringent and vasoconstrictive properties, making them effective in reducing hemorrhoidal swelling and inflammation. Calendula officinalis (marigold) is well-known for its ability to stimulate tissue regeneration, collagen synthesis, and wound healing, and is commonly used in treating skin and mucosal injuries. Tea tree oil (Melaleuca alternifolia) exhibits broad-spectrum antimicrobial activity, aiding in the prevention of secondary infections in the anorectal area. Other botanicals such as Aloe vera, turmeric (*Curcuma longa*), and chamomile (*Matricaria chamomilla*) provide additional anti-inflammatory, antioxidant, and soothing

benefits. Many of these herbs are rich in flavonoids, polyphenols, terpenoids, and essential oils that modulate inflammatory cytokines, improve vascular tone, and accelerate epithelial repair. When incorporated into emulgel bases, these herbal ingredients not only enhance the therapeutic profile of the formulation, but also contribute to improved patient acceptability due to their natural origin, mildness, and synergistic actions. The integration of phytochemicals into emulgel systems represents a promising direction for the development of safe and effective topical treatments for proctological disorders [6].

Emulgels as Drug Delivery Systems

Definition and Composition

Emulgels are a novel class of semisolid formulations that combine the structural advantages of emulsions and gels into a single, efficient drug delivery platform. Typically, these systems involve the dispersion of an oil-in-water (o/w) or water-in-oil (w/o) emulsion within a hydrophilic gel matrix. This dual-phase architecture allows for the simultaneous incorporation of both hydrophilic and lipophilic drugs, addressing the limitations of conventional single-phase topical systems. The gel base provides structural integrity, mucoadhesive properties, and enhanced spreadability, while the emulsified phase improves drug solubilization and penetration into deeper tissues. This structural synergy makes emulgels highly versatile for localized drug delivery, particularly in conditions requiring mucosal adhesion and prolonged contact time [7].

Advantages Over Conventional Gels and Ointments

Compared to traditional gels, creams, or ointments, emulgels offer several significant therapeutic and pharmaceutical advantages. One of the most important benefits is enhanced drug penetration. The presence of oil droplets in emulgels facilitates the delivery of lipophilic drugs through skin or mucosal barriers, while the gel matrix allows for the controlled and sustained release of hydrophilic compounds. This dual mechanism enhances the overall bioavailability and therapeutic efficacy of the drug. Furthermore, emulgels exhibit superior physical stability, as the gel network inhibits emulsion breakdown and phase separation, thereby prolonging shelf life. Their non-greasy, non-staining, and easily spreadable nature ensures better patient compliance, especially for long-term use in sensitive areas such as the anorectal region [8]. These advantages collectively position emulgels as a superior alternative to conventional topical formulations.

Mechanism of Drug Release

Drug release from emulgels typically follows a two-phase mechanism. Initially, the drug diffuses from the internal oil phase (in the case of o/w emulsion) into the surrounding gel matrix. From there, the drug continues to diffuse outward into the skin or mucosal tissue. This biphasic release system enables both immediate and sustained drug delivery, with the emulsion droplets providing rapid onset and the gel matrix ensuring extended action. Factors affecting the release rate include the type of emulsifier used, droplet size, viscosity of the gel base, and concentration of drug within each phase. This mechanism is particularly advantageous for treating chronic proctological disorders, where a consistent local drug level is desired to manage inflammation, pain, and tissue repair (Figure 1).

Following application, the drug release from emulgels at the rectal site involves a multi-step mechanism governed by diffusion dynamics, mucosal interaction, and physicochemical properties of both the formulation and the rectal environment. Initially, the drug molecules are released from the dispersed oil phase into the gel matrix (in the case of o/w emulgels). From the gel, the drug diffuses toward the mucosal epithelium, driven by concentration gradients. The rectal mucosa, composed of a single-layer columnar epithelium and mucus-secreting goblet cells, presents both a barrier and a conduit for drug transport. Mucoadhesive agents (*e.g.,* Carbopol and NaCMC) within the gel matrix facilitate intimate contact with the mucosal surface, ensuring prolonged residence time and allowing sufficient diffusion across the mucus layer.

Once in contact with the mucosa, the drug permeates through the mucus gel layer via passive diffusion, aided by penetration enhancers like isopropyl myristate and ethanol that transiently disrupt mucin structures or lipid bilayers, lowering barrier resistance. The high hydration levels at the rectal site can swell the gel matrix, further modulating drug release by forming aqueous channels for hydrophilic compounds and enhancing solubilization for lipophilic drugs. Eventually, the drug reaches the epithelial cells and enters the lamina propria through paracellular or transcellular pathways, depending on molecular size, lipophilicity, and ionization. This sustained and localized delivery minimizes first-pass metabolism and systemic side effects, enabling effective treatment of anorectal disorders by maintaining therapeutic levels at the site of inflammation or injury.

Role of Excipients

The performance of an emulgel largely depends on the choice and functionality of its excipients, which include gelling agents, emulsifiers, penetration enhancers, preservatives, and pH modifiers.

Gelling agents, such as Carbopol 934/940, Hydroxypropyl Methylcellulose, sodium carboxymethyl cellulose (NaCMC), and xanthan gum, provide a gel-like consistency and control the viscosity, spreadability, and mucoadhesive properties of the formulation. These agents also play a vital role in stabilizing the emulsion phase and modulating drug release kinetics.

Emulsifiers, such as Span 20, Tween 80, and Pemulen, reduce the interfacial tension between the oil and water phases, leading to the formation of a stable emulsion with fine droplets that aids in improved drug dispersion and absorption.

Penetration enhancers, including ethanol, propylene glycol, oleic acid, and isopropyl myristate, disrupt the lipid structure of the stratum corneum or mucosal surface, facilitating deeper drug permeation and improved therapeutic outcomes.

Preservatives such as parabens, benzyl alcohol, or phenoxyethanol are essential for maintaining microbial stability during storage, while pH adjusters such as triethanolamine ensure the formulation remains within an acceptable pH range (typically 4.5-6.5) to prevent irritation and ensure compatibility with mucosal tissues [9].

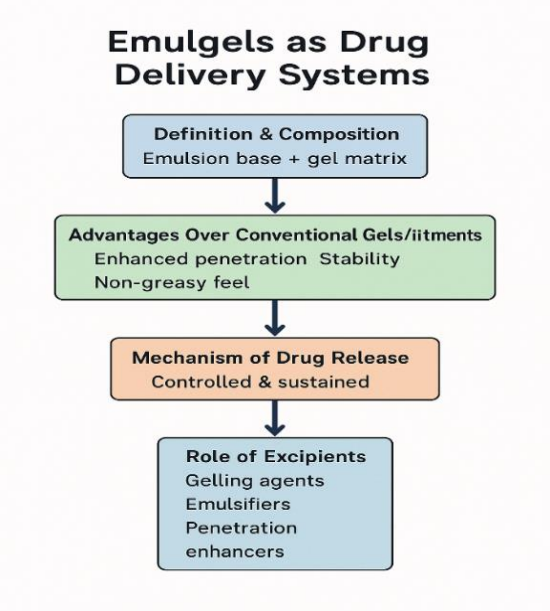


Figure 1: Structural representation of an emulgel showing dual-phase architecture (oil-in-water emulsion in gel matrix), drug release pathway, and mucosal penetration mechanisms

Herbal Extracts Used in Emulgel Formulations

Herbal therapies have gained renewed attention in modern pharmaceutics due to their wide therapeutic spectrum,

biocompatibility, and minimal systemic side effects. In the treatment of proctological disorders—such as haemorrhoids, anal fissures, and proctitis—plant-based extracts offer targeted relief through multiple mechanisms, including anti-inflammatory, analgesic, astringent, antimicrobial, and wound-healing actions. However, delivering these herbal actives in a stable, effective, and patient-compliant dosage form remains a challenge. The emulgel system serves as a strategic platform by allowing sustained release, improved mucosal adhesion, and enhanced skin permeation of these bioactives (Table 1 and Figure 2). The following subsections elaborate on key herbal extracts used in emulgel formulations, along with their phytochemical profiles, mechanisms of action, and relevance in anorectal therapy [10-12].

Witch Hazel (Hamamelis Virginiana)

Witch hazel is a time-tested botanical known for its astringent and vasoconstrictive properties, making it particularly effective in managing early-stage haemorrhoids. The key phytoconstituents—primarily tannins such as hamamelitannin—bind to proteins on the mucosal surface, forming a protective barrier that reduces vascular permeability, inflammation, and local irritation. Additionally, flavonoids (quercetin and kaempferol) and gallic acid derivatives provide potent antioxidant action, which helps mitigate oxidative stress-induced mucosal damage. These properties contribute to its clinical use in reducing perianal swelling, itching, and mild bleeding.

Calendula (Calendula Officinalis)

Calendula has long been recognized for its wound-healing capabilities and is widely used in dermatological and mucosal formulations. The flower extract contains a complex blend of triterpenoids (faradiol esters), carotenoids, flavonoids (rutin, quercetin), and volatile oils, all contributing to tissue regeneration. Calendula promotes fibroblast activation, angiogenesis, and granulation tissue formation, which are critical for healing fissures and rectal ulcerations. Its anti-inflammatory activity is linked to the suppression of prostaglandin synthesis and the inhibition of nitric oxide production. Moreover, its antimicrobial potential protects against secondary infections that may exacerbate proctological conditions.

Tea Tree Oil (Melaleuca Alternifolia)

Tea tree oil is an essential oil with broad-spectrum antimicrobial and anti-inflammatory properties. Its primary active, terpinen-4-ol, disrupts microbial membranes, making it effective against bacteria, fungi, and viruses. It also downregulates pro-inflammatory cytokines like TNF-α and IL-1β, reducing edema and tissue sensitivity. In the context of anorectal disorders, tea tree oil not only prevents bacterial colonization in fissures and inflamed hemorrhoidal tissue but also provides a soothing and analgesic effect, improving patient comfort.

Aloe Vera (Aloe Barbadensis Miller)

Aloe vera is a well-established mucosal protectant and healer, particularly valued for its high content of acemannan—a polysaccharide with immunomodulatory and wound-healing properties. Aloe also contains vitamins (A, C, and E), amino acids, enzymes (bradykinase), and minerals that work synergistically to accelerate fibroblast proliferation, collagen deposition, and epithelialization. Its anti-inflammatory effects stem from the inhibition of prostaglandin E2 and thromboxane B2, both key mediators of inflammation. Furthermore, its cooling and soothing properties provide symptomatic relief in conditions marked by burning and rectal discomfort.

Turmeric (Curcuma longa)

Turmeric is revered in both traditional and modern medicine for its potent anti-inflammatory and antioxidant activity, largely due to the polyphenol curcumin. *In vitro* and *in vivo* studies have demonstrated curcumin's ability to inhibit NF-κB signalling, COX-2 expression, and cytokine release (TNF-α and IL-6), which are hallmarks of inflammatory processes. Its free radical scavenging ability helps protect against oxidative damage in rectal tissues, while its pro-healing effects support epithelial regeneration. This makes

turmeric especially useful in chronic inflammatory anorectal disorders, such as proctitis and recurrent fissures.

Chamomile (Matricaria Chamomilla)

Chamomile is known for its calming, anti-inflammatory, and antispasmodic effects. Its active constituents include apigenin, bisabolol, chamazulene, and flavonoids, which contribute to inhibition of leukotriene and prostaglandin synthesis. Apigenin, in particular, has shown strong affinity for benzodiazepine receptors, offering both anti-anxiety and local analgesic effects. In the context of anorectal applications, chamomile helps relieve spasms of the internal anal sphincter and reduces mucosal inflammation, which can accelerate healing and improve comfort, particularly in sensitive or paediatric patients.

Neem (Azadirachta Indica)

Neem is a cornerstone of Ayurvedic medicine and offers multifaceted benefits relevant to proctological therapy. It contains azadirachtin, nimbolide, quercetin, and nimbin, compounds known for their antimicrobial, anti-inflammatory, and tissue-regenerating effects. Neem promotes keratinocyte proliferation and collagen synthesis while reducing local microbial burden, making it ideal for formulations intended to treat anorectal infections, fissures, and inflamed hemorrhoidal tissue. Its antipruritic properties also help manage anal itching (pruritus ani), a common complaint in patients with rectal inflammation.

In polyherbal formulations, synergistic or antagonistic interactions may affect bioavailability and therapeutic efficacy. For instance, flavonoids in *chamomile* may interact with the phenolic components of *turmeric*, potentially altering their solubility or stability. Similarly, volatile oils from *tea tree oil* may interfere with polymeric gels, affecting drug release kinetics. Understanding these interactions is critical for optimizing the safety and efficacy of the emulgel.

Herb–excipient compatibility also warrants attention. Carbopol and HPMC, while excellent for mucoadhesion, may hinder the penetration of certain hydrophobic actives unless used with permeation enhancers such as propylene glycol. Potential incompatibilities—such as precipitation, pH sensitivity, or degradation—must be screened during formulation development through FTIR, DSC, or HPLC profiling. Addressing these issues in the manuscript improves formulation robustness and guides future development strategies.

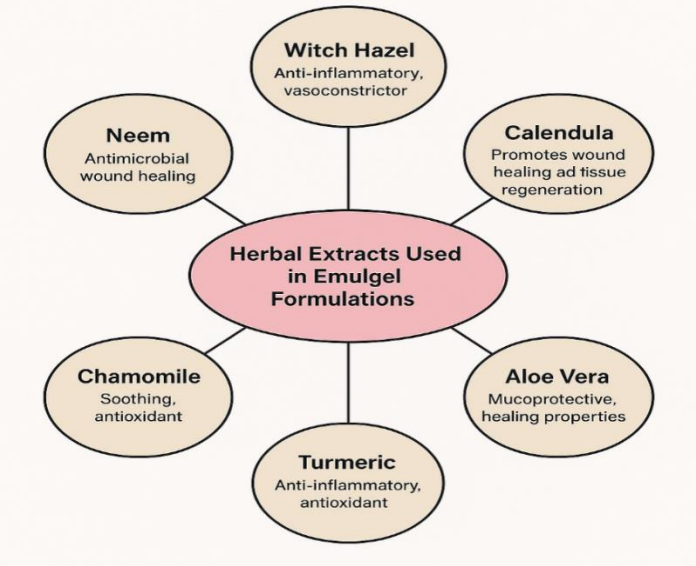


Figure 2: Key herbal extracts used in emulgel formulations with corresponding mechanisms of action for treating proctological disorders—includes antimicrobial, anti-inflammatory, vasoconstrictive, and wound-healing effects

Table 1: Herbal extracts used in emulgel formulations for proctological disorders

Herbal Name	Botanical Name	Key Phytoconstituents	Mechanism of Action
Witch Hazel	*Hamamelis virginiana*	Tannins, flavonoids, and gallic acid	Vasoconstriction, antioxidant, and anti-inflammatory
Calendula	*Calendula officinalis*	Triterpenoids, flavonoids (rutin), and carotenoids	Enhances collagen synthesis, promotes angiogenesis, anti-inflammatory, and antimicrobial
Tea Tree Oil	*Melaleuca alternifolia*	Terpinen-4-ol, cineole, and α-terpineol	Broad-spectrum antimicrobial, reduces cytokines, and analgesic
Aloe Vera	*Aloe barbadensis miller*	Acemannan, vitamins (A, C, and E), and enzymes	Stimulates fibroblast activity, collagen deposition, and anti-inflammatory
Turmeric	*Curcuma longa*	Curcumin	Inhibits COX-2 and NF-κB, antioxidant, and cytokine suppression
Chamomile	*Matricaria chamomilla*	Apigenin, bisabolol, and chamazulene	Inhibits prostaglandins/leukotrienes, antispasmodic, and antioxidant
Neem	*Azadirachta indica*	Azadirachtin, nimbin, quercetin, nimbolide	Antimicrobial, keratinocyte proliferation, and epithelial regeneration

Formulation Approaches and Evaluation Parameters

Formulating herbal emulgels involves a series of optimized steps, starting with the appropriate selection of the oil phase based on the solubility profile of herbal actives—commonly used oils include isopropyl myristate, olive oil, or castor oil, which support skin penetration and drug solubilization. The emulsification process typically employs high-shear homogenization or magnetic stirring, using non-ionic emulsifiers such as Span 20 and Tween 80 to form a stable oil-in-water emulsion. This is then incorporated into a pre-prepared gel base, usually composed of Carbopol 934 or hydroxypropyl methylcellulose, neutralized with triethanolamine to achieve the desired consistency and pH. The resultant emulgel is evaluated using critical parameters: pH (to ensure compatibility with skin/mucosal pH), viscosity (to assess flow and spreadability), and drug content uniformity (to ensure consistent therapeutic efficacy). Spreadability determines the ease of application, while *in vitro* drug release studies assess sustained release potential using Franz diffusion cells or dialysis bag methods. Additionally, antimicrobial and anti-inflammatory activities of herbal-loaded emulgels are assessed through agar diffusion assays and protein denaturation inhibition tests (Table 2). Finally, skin irritation and biocompatibility are evaluated using patch testing on animal or human models to confirm formulation safety and tolerance for rectal or dermal application [13].

Table 2: Formulation approaches and evaluation parameters of herbal emulgels

Parameter	Details	Purpose
Oil Phase Selection	Isopropyl myristate, castor oil, and sesame oil	Solubilizes lipophilic herbal actives and enhances permeation.
Emulsification Technique	High-shear homogenization or magnetic stirring with Span/Tween	Forms stable emulsion with uniform droplet size
Gelling Agent	Carbopol 934, hydroxypropyl methylcellulose, and NaCMC	Provides viscosity, bioadhesion, and controlled drug release.
pH	Maintained between 5.0 and 6.5	Ensures mucosal/skin compatibility.
Viscosity	Measured using Brookfield viscometer	Indicates flow, spreadability, and retention.
Spreadability	Measured in g·cm/sec (slip and drag method)	Determines ease of application.

Drug Content Uniformity	Analyzed spectrophotometrically (UV/HPLC)	Ensures homogeneity and dosage consistency.
***In Vitro* Drug Release**	Franz diffusion cell and dialysis bag method	Evaluates sustained release behaviour.
Antimicrobial Activity	Agar well diffusion assay (zone of inhibition)	Confirms herbal extract efficacy against microbial strains
Anti-inflammatory Activity	Bovine serum albumin protein denaturation method and membrane stabilization assay	Assesses inflammation control potential.
Skin Irritation Testing	Patch test on animal/human models	Evaluates formulation safety and tolerability.

Mechanisms of Action in Proctological Conditions

Proctological conditions such as hemorrhoids, anal fissures, and proctitis are associated with a complex interplay of pathophysiological events, including venous hypertension, mucosal damage, inflammatory mediator release, and oxidative stress. These lead to hallmark symptoms like pain, bleeding, swelling, and discomfort during defecation. The inflammation is typically driven by the overexpression of cyclooxygenase (COX) enzymes and pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which contribute to vasodilation, capillary permeability, and local tissue breakdown.

Herbal emulgels offer a multifaceted therapeutic approach to these conditions. The bioactive constituents in medicinal plants—such as curcumin, apigenin, acemannan, and flavonoids—exert anti-inflammatory, antioxidant, and wound-healing effects by downregulating inflammatory pathways, scavenging free radicals, and stimulating fibroblast activity and collagen synthesis. These actions help control edema, reduce pain, and accelerate mucosal regeneration.

To provide a mechanistically structured understanding of herbal emulgel therapy for proctological disorders, it is beneficial to classify herbal agents based on their predominant pharmacodynamic actions. Anti-inflammatory herbs such as *Curcuma longa* (curcumin), *Calendula officinalis*, and *Matricaria chamomilla* exert effects primarily through the inhibition of cyclooxygenase (COX) enzymes, downregulation of NF-κB signalling, and suppression of pro-inflammatory cytokines such as TNF-α and IL-6. Curcumin, in particular, has been shown to block multiple inflammation-related pathways, thereby reducing mucosal edema and pain. Analgesic activity is evident in herbs such as *Chamomile* (due to apigenin and bisabolol) and *Melaleuca alternifolia* (tea tree oil), which influence peripheral nociceptive responses and exhibit antispasmodic properties. Their ability to modulate neuronal ion channels and inflammatory mediators contributes to relief from rectal discomfort. Antimicrobial activity, critical in preventing secondary infections in anorectal wounds and fissures, is prominently demonstrated by *tea tree oil*, *Neem* (*Azadirachta indica*), and *Calendula*, which disrupt bacterial membranes and biofilms through their terpenoid and flavonoid content. By grouping herbal actives according to these pharmacological categories, formulators and clinicians can better design combination therapies that target multiple symptoms—such as pain, infection, and inflammation—simultaneously, while minimizing adverse interactions and optimizing therapeutic outcomes.

Importantly, the emulgel's semi-solid and mucoadhesive matrix facilitates localized delivery of these phytoconstituents directly to the rectal mucosa. This not only enhances drug concentration at the site of action, but also limits systemic absorption, reducing the risk of side effects. The gel's viscosity enables prolonged contact with the inflamed tissues, allowing for sustained release and deeper penetration of active compounds. Together, these properties make herbal emulgels highly effective for targeted, symptom-specific, and long-acting therapy in the management of chronic anorectal disorders [14-16].

Recent advancements in clinical and pharmacokinetic evaluation have substantiated the utility of mucoadhesive

emulgel formulations for rectal drug delivery, particularly those incorporating herbal bioactives. For instance, a 2023 randomized study on Aloe vera and curcumin-based rectal gels reported statistically significant improvements in hemorrhoidal symptom scores and mucosal healing rates compared to traditional corticosteroid suppositories. From a pharmacokinetic perspective, studies utilizing nanoemulgel matrices demonstrated enhanced bioavailability of lipophilic herbal compounds such as curcumin and boswellic acid, showing a 2- to 3-fold increase in AUC and C_{max} following rectal application versus oral delivery. These findings are attributed to the prolonged mucosal residence time and bypassing of hepatic first-pass metabolism. Notably, bioadhesive polymers such as Carbopol and HPMC, incorporated into these formulations, were shown to significantly increase drug retention at the rectal site, maintaining therapeutic concentrations for up to 6-8 hours. *In vivo* animal studies corroborate these results with improved drug permeation across the rectal mucosa and reduced systemic exposure, further supporting the feasibility of such delivery systems for chronic inflammatory anorectal conditions. These data not only validate the pharmacological relevance of herbal emulgels but also underscore their translational potential in human therapy, provided robust clinical trials and standardized testing protocols are implemented.

Physicochemical Characterization

Comprehensive physicochemical characterization is pivotal for ensuring the performance, stability, and efficacy of herbal emulgel formulations. Among the most critical parameters is zeta potential, which reflects the surface charge of emulsion droplets and predicts colloidal stability; values above ±30 mV are generally considered optimal, as they prevent aggregation and phase separation during storage. Another essential parameter is droplet size distribution, particularly for nanoemulgels where smaller droplets (<200 nm) increase the surface area available for drug diffusion and enhance penetration across rectal mucosa. Dynamic light scattering (DLS) and transmission electron microscopy (TEM) are commonly used techniques to evaluate this feature. Rheological properties, such as viscosity and flow behaviour, are equally important. Herbal emulgels are typically designed to exhibit non-Newtonian, shear-thinning behaviour—where viscosity decreases with shear rate—allowing for ease of application and spreading upon rectal administration, followed by structural recovery for optimal retention. These properties are measured using a Brookfield viscometer or oscillatory rheometer. Collectively, these physicochemical parameters not only influence the formulation's therapeutic performance, but also dictate patient compliance, shelf-life stability, and regulatory acceptability. Therefore, systematic optimization and standardization of these attributes are integral to product development and quality assurance [17].

Herb–Herb or Herb–Excipient Interactions in Multi-Component Systems

Multi-component herbal emulgel systems present unique formulation challenges due to the potential for complex herb–herb and herb–excipient interactions that can affect efficacy, safety, and stability. Herbal extracts often contain a diverse array of phytoconstituents—such as alkaloids, flavonoids, saponins, and terpenes—that may synergize or antagonize one another when co-administered. For example, while *Curcuma longa* and *Melaleuca alternifolia* each exhibit anti-inflammatory properties, their concurrent use may enhance local irritation due to overlapping terpenoid content unless buffered by soothing agents like Aloe vera. Similarly, the pH sensitivity of flavonoids may interact unfavourably with acidic gelling agents like Carbopol, leading to precipitation or reduced bioavailability. Furthermore, surfactants like Tween 80, though essential for emulsification, can alter the solubility or stability of herbal actives, potentially leading to degradation or reduced activity. These interactions may also impact drug release kinetics or permeability profiles, necessitating pre-formulation compatibility testing using FTIR, DSC, or HPLC-based stability studies. A strategic formulation approach—including controlled component ratios, pH buffering, and incorporation of stabilizing agents—is

thus essential for optimizing therapeutic synergy while minimizing degradation, toxicity, or antagonistic effects in multi-herb emulgel preparations.

Compare Herbal Emulgels with Synthetic Formulations on Retention Time or Permeation

Herbal emulgels offer a distinct advantage over synthetic formulations such as corticosteroid suppositories or anaesthetic creams in terms of mucosal retention time and permeation efficiency. Synthetic agents, although potent, often suffer from rapid clearance from the rectal site due to peristalsis and mucosal secretions, leading to reduced efficacy and the need for repeated applications. In contrast, herbal emulgels—particularly those formulated with mucoadhesive polymers like Carbopol or NaCMC—adhere strongly to the mucosal lining, significantly increasing the residence time. In comparative studies using excised rectal tissue, formulations containing *Aloe vera*, *Neem*, or *Calendula officinalis* demonstrated superior permeation coefficients (Kp) and retention of drug content at the target site, often maintaining therapeutic levels for over six hours. The biphasic release kinetics of emulgels enable an initial burst release followed by sustained delivery, ensuring continuous therapeutic effect. Additionally, herbal formulations are less likely to induce local irritation or rebound symptoms, a common issue with long-term use of steroids. Thus, in terms of local pharmacodynamics, user comfort, and long-term tolerability, herbal emulgels exhibit favourable performance characteristics that justify their use over conventional synthetic rectal therapies in suitable clinical contexts [18].

Mechanism of Mucoadhesive Polymer Interaction with Rectal Mucosa

The effectiveness of rectal emulgels is largely attributed to the presence of mucoadhesive polymers, which facilitate prolonged residence and intimate contact with the rectal mucosa. Polymers such as Carbopol 934, NaCMC, and HPMC interact with mucosal surfaces through a combination of physical entanglement and chemical bonding mechanisms. The rectal mucosa is coated with a mucus layer rich in glycoproteins (mucins), which possess carboxyl, hydroxyl, and amino groups. Mucoadhesive polymers form hydrogen bonds and electrostatic interactions with these mucins, creating a cohesive and adhesive matrix. Upon application, the hydrated polymer network swells and interpenetrates the mucus layer, enhancing adhesion. This not only prevents premature expulsion due to peristalsis, but also creates a depot for sustained drug diffusion. The viscoelastic properties of the gel matrix help resist mechanical shear forces, thereby improving formulation retention under dynamic physiological conditions. This mechanism is particularly valuable in treating chronic anorectal conditions, where sustained local drug levels are required without systemic absorption. Optimization of polymer concentration, molecular weight, and degree of crosslinking is essential to balance bioadhesion, spreadability, and patient comfort [19,20].

Pharmacokinetic Advantages of Rectal Emulgel Delivery

Rectal emulgel delivery offers several pharmacokinetic advantages over conventional routes, particularly for drugs with poor oral bioavailability or high hepatic first-pass metabolism. The rectal mucosa is highly vascularized, allowing for partial systemic absorption while bypassing significant portions of the hepatic portal system. Herbal emulgels exploit this route by combining the advantages of localized therapy and systemic sparing. When formulated with mucoadhesive polymers, these systems ensure sustained contact with the absorption site, allowing for prolonged drug release and enhanced absorption of lipophilic and hydrophilic phytoconstituents. For instance, nanoemulgel-based rectal delivery of curcumin has shown a three-fold increase in relative bioavailability compared to oral administration in preclinical models, along with higher Tmax and extended half-life (t½). Furthermore, emulgel formulations reduce the dosing frequency required for symptom control, enhancing patient compliance and reducing the likelihood of dose-dependent side effects. They also minimize

gastrointestinal degradation and enzymatic hydrolysis, which are common issues with orally administered plant compounds. This combination of targeted action, reduced systemic exposure, and prolonged efficacy underscores the pharmacokinetic superiority of emulgel-based rectal drug delivery systems [21].

Potential Immunological or Allergenic Risks of Chronic Herbal Use

While herbal emulgels are generally perceived as safer alternatives to synthetic drugs, their long-term use may pose immunological and allergenic risks that warrant careful consideration. Chronic rectal application of certain herbal components—such as *tea tree oil* (rich in terpenes), *Neem* (containing azadirachtin), or *Calendula* (with sesquiterpene lactones)—can lead to contact dermatitis, hypersensitivity reactions, or delayed-type immune responses, especially in individuals with pre-existing sensitivities. Furthermore, the immunomodulatory properties of some herbs, while beneficial in inflammatory conditions, may interfere with host immune responses if used without regulation. For example, high concentrations of Aloe vera polysaccharides may stimulate immune cell activation or alter mucosal immune tolerance. There is also a potential for cumulative toxicity or metabolic interference if these phytochemicals are used in high doses or in combination with immunosuppressive medications. Therefore, thorough dermatotoxicity studies, patch testing, and chronic exposure models should be incorporated into product development pipelines. Additionally, labelling regulations should mandate the listing of potential allergens and contraindications, especially for sensitive or paediatric populations [22].

In Vitro and Ex Vivo Permeability Studies

To validate the therapeutic efficacy and bioavailability of herbal emulgel formulations, it is imperative to conduct *in vitro* and *ex vivo* permeability studies using standardized models. Franz diffusion cells are widely used for *in vitro* assessments, where rectal or synthetic membranes simulate drug permeation dynamics. These setups enable quantification of permeation rate, flux, lag time, and drug deposition across membranes. *Ex vivo* studies using excised animal rectal tissues (*e.g.,* porcine or goat) provide more physiologically relevant data, particularly regarding mucosal integrity, enzymatic interaction, and drug retention. These studies help compare the penetration profiles of herbal emulgels against synthetic benchmarks and assess the impact of formulation variables such as polymer concentration, pH, and emulsifier type. Furthermore, mucoadhesion testing, using detachment force or residence time measurements, can complement permeability data by confirming retention efficacy. These evaluations are critical in preclinical formulation optimization and regulatory submission packages, as they establish proof-of-concept and predict *in vivo* performance. Incorporating such data into early-phase development can enhance the translational success of herbal emulgel therapies [23].

Current Trends and Advances

Recent advancements in herbal emulgel technology reflect a growing focus on improving bioavailability, patient compliance, and formulation efficiency. One significant trend is the emergence of nanoemulgels and phytosome-based systems, which offer enhanced solubility, deeper tissue penetration, and controlled release of herbal actives. These nano-sized carriers increase surface area, improving drug absorption and therapeutic outcomes in proctological disorders. Additionally, the incorporation of essential oils (*e.g.,* tea tree oil, eucalyptus, lavender) and standardized herbal extracts ensures consistency in potency, broad-spectrum antimicrobial action, and improved stability of formulations.

There is also a strong shift towards patient-centred product design, with emphasis on odourless, irritating, and easily spreadable formulations that cater to sensitive anorectal tissues. These enhancements improve user acceptability and long-term adherence, particularly for chronic use. Furthermore, regulatory frameworks are evolving to address the quality control, standardization, and safety evaluation of herbal rectal formulations. Agencies now emphasize Good

Manufacturing Practices (GMP), stability testing, and toxicological assessments to ensure that these novel delivery systems meet acceptable pharmaceutical standards. For example, under the US FDA's Botanical Drug Development Guidance, herbal rectal preparations require evidence of safety through Phase I/II trials and can proceed through the CDER division with an Investigational New Drug (IND) application. Similarly, the EMA (European Medicines Agency) mandates a well-defined monograph and consistent quality profile according to the HMPC guidelines.

These innovations collectively pave the way for safer, more effective, and user-friendly herbal emulgels, aligning with both modern therapeutic goals and traditional medicine principles [17].

Clinical Perspectives and Challenges

Herbal emulgels for proctological applications have shown promising results in preclinical studies, demonstrating significant anti-inflammatory, antimicrobial, wound-healing, and analgesic effects. *In vitro* and animal studies using herbal extracts like *Curcuma longa*, *Calendula officinalis*, and *Aloe vera* in emulgel matrices have reported enhanced mucosal healing and symptom relief in induced rectal inflammation or wound models. However, clinical data remain limited and largely anecdotal, with few well-designed randomized controlled trials (RCTs) conducted to validate their therapeutic equivalence or superiority to conventional allopathic treatments (Table 3). A few randomized controlled clinical trials, such as those involving Calendula-based rectal gels and Aloe vera ointments for haemorrhoids, have shown symptomatic relief, improved mucosal healing, and patient satisfaction, although sample sizes and methodological limitations constrain definitive conclusions

In terms of safety and tolerability, herbal emulgels are generally well-accepted due to their natural origin, lower risk of systemic side effects, and soothing properties. Compared to corticosteroid or nitrate-based conventional therapies, they exhibit fewer adverse reactions such as mucosal thinning, rebound symptoms, or systemic hypotension, making them a safer long-term option, especially for sensitive or paediatric populations.

From a market perspective, the demand for herbal and plant-based rectal formulations is growing, driven by increasing consumer preference for natural, non-invasive, and self-care therapies. The trend is reinforced by the popularity of ayurvedic and complementary medicine systems globally, especially in gastrointestinal and anorectal care.

Despite these advantages, several challenges persist. One major limitation is the lack of standardization in herbal actives, as variability in plant sources, extraction methods, and bioactive concentrations can affect reproducibility and efficacy. Additionally, stability concerns arise due to the sensitivity of herbal compounds to temperature, light, and microbial contamination. Furthermore, regulatory barriers for herbal rectal preparations—especially in Western countries—require extensive toxicological evaluations, clinical substantiation, and manufacturing consistency, which are often resource-intensive [24].

Table 3: Clinical perspectives and key challenges of herbal emulgels in proctological therapy

Aspect	Details
Preclinical and Clinical Evidence	Positive *in vitro* and animal studies showing anti-inflammatory, antimicrobial, and healing effects; limited clinical trials available
Safety & Tolerability	Generally well-tolerated; fewer side effects than corticosteroids or vasodilators
Efficacy vs. Conventional Therapy	Effective in mild-to-moderate conditions; may offer sustained relief with fewer relapses
Market Potential	High consumer demand for natural rectal formulations; aligns with trends in herbal and ayurvedic care
Standardization Issues	Variability in phytochemical content affects consistency and reproducibility

Stability Concerns	Herbal extracts are sensitive to oxidation, microbial degradation, and environmental conditions
Regulatory Barriers	Requires thorough validation, GMP compliance, stability testing, and safety profiling for approval

Conclusion and Future Perspectives

Herbal emulgels present a promising therapeutic platform for the effective management of proctological disorders such as haemorrhoids, anal fissures, and proctitis. By combining the pharmacological benefits of traditional herbal medicine with the functional advantages of emulgel drug delivery systems, these formulations offer localized, sustained, and patient-friendly treatment options. Emulgels enhance mucosal retention and reduce systemic side effects, while the inclusion of bioactive plant extracts—such as *Curcuma longa*, *Hamamelis virginiana, Calendula officinalis*, and *Aloe vera*—exhibits anti-inflammatory, wound-healing, and antimicrobial effects with a generally favourable safety profile. Despite promising preclinical data, the clinical translation of herbal emulgels remains limited due to a lack of large-scale, controlled human trials. Regulatory standardization also remains a key bottleneck, underscoring the need for rigorous quality control and reproducibility of herbal actives. To overcome these challenges, future efforts should focus on the optimization of formulation parameters and the integration of advanced drug delivery strategies—such as nanoemulsions, phytosomes, and bioadhesive polymers—to further improve therapeutic performance and stability. A multidisciplinary approach combining phytopharmacology, pharmaceutical technology, and clinical research will be essential to fully harness the potential of herbal emulgels. With appropriate scientific validation and regulatory support, these formulations could emerge as safer, more effective natural alternatives or adjuncts to conventional rectal therapies.

Acknowledgements

None

Ethical issues

None

Competing interests

Author declared that there is no conflict of interest exists.

Authors' contributions

Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review and editing by VP, VR, VNDD, GV, and PJ.

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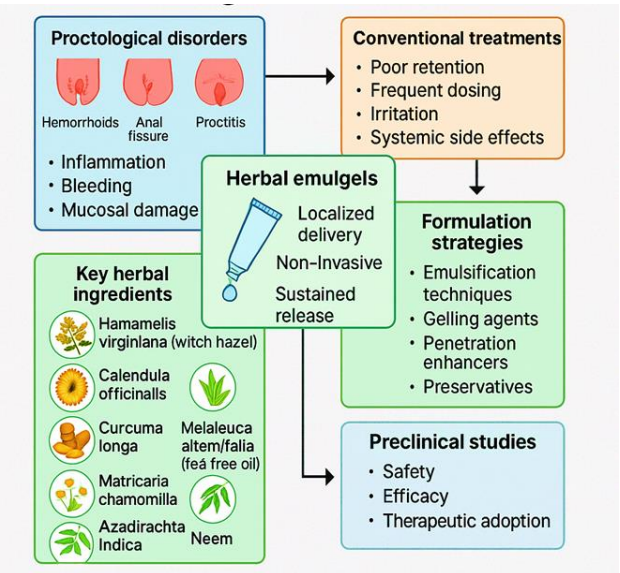
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