



Systematic Review of Plant-Based Excipients in Topical Drug Delivery

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Abstract

This review explores the use of plant-based excipients in topical drug delivery. The review examines the advantages and challenges of using plant-based excipients, as well as case studies that demonstrate their effectiveness in delivering drugs through the skin. The review also discusses future perspectives on the use of plant-based excipients, including the potential for developing new formulations and improving drug delivery efficiency. The findings of this review suggest that plant-based excipients have significant potential in topical drug delivery and could offer a more sustainable and natural alternative to synthetic excipients. Overall, this review provides valuable insights for researchers and practitioners in the pharmaceutical industry who are interested in developing new and innovative drug delivery systems.

Keywords

- ▶ biocompatibility
- ▶ natural
- ▶ plant-based excipients
- ▶ sustainability
- ▶ topical drug delivery

Introduction

The pharmaceutical industry is experiencing a significant shift toward more sustainable and environmentally friendly practices. This transition is driven by the dual need to improve patient safety and minimize the ecological footprint of pharmaceutical manufacturing processes. A key strategy in this evolution is the incorporation of plant-based excipients in topical drug delivery systems. These natural components align with green chemistry principles, which prioritize sustainable products and processes and offer various scientific advantages over traditional synthetic excipients.¹

Traditional synthetic excipients used in topical formulations have raised concerns regarding their environmental impact and potential health consequences.² As scientific research continues to highlight these issues, there is a growing emphasis on finding sustainable alternatives in pharmaceutical formulations. Plant-based excipients derived from renewable resources offer a promising solution. They not only

address environmental concerns but also have the potential to enhance the safety and therapeutic efficacy of topical drug formulations.³ The objective of this comprehensive review was to provide a systematic analysis of the current state of plant-based excipients in topical dosage forms.

We aimed to (1) assess the environmental benefits associated with the use of plant-derived excipients in pharmaceutical formulations,⁴ (2) evaluate the safety and biocompatibility profiles of these excipients for topical medication administration,⁵ (3) identify the challenges involved in integrating plant-based excipients and propose potential solutions,⁶ and (4) highlight case studies and research projects that demonstrate the successful application of plant-derived components in topical formulations.⁷

The significance of plant-based excipients lies in their potential to provide sustainable alternatives to conventional synthetic counterparts, contributing to the pharmaceutical industry's commitment to ecofriendly practices.⁸ With increasing demand for natural and biodegradable materials, it

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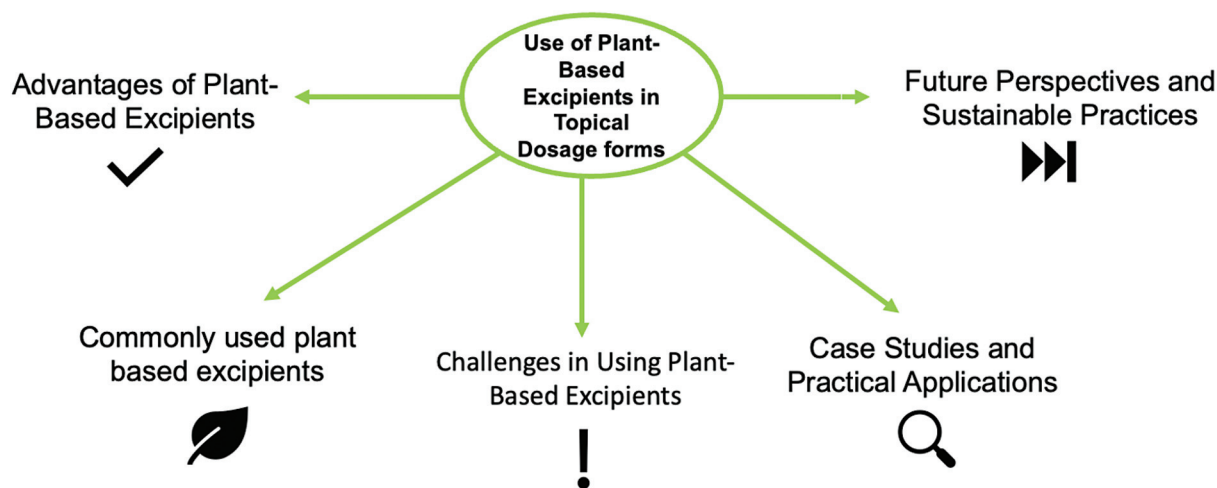


Fig. 1 Diagram of plant-based excipients in pharmaceutical applications: advantages, challenges, and future prospects.

is imperative to explore the scientific foundations of plant-based excipients to develop formulations that meet therapeutic requirements and environmental sustainability goals.⁹ This review is structured to provide an in-depth examination of plant-based excipients used in topical dosage forms. It includes sections on the benefits of plant-derived excipients, commonly used plant-based materials, challenges in their application, case studies of successful implementations, and future perspectives for sustainable drug development. **Fig. 1** illustrates plant-based excipients in pharmaceutical applications: advantages, challenges, and prospects.

Materials and Methods

This review involved a search of electronic databases, including PubMed, Scopus, and Google Scholar, using keywords related to plant-based excipients and topical drug delivery. The search was restricted to articles published in English over the past two decades. Relevant articles were identified, and their references were checked for additional sources. Studies were included if they (1) investigated plant-based excipients in topical drug formulations, (2) provided data on the biocompatibility, efficacy, or environmental impact of these excipients, and (3) were published in peer-reviewed journals. We excluded studies if they (1) focused solely on oral or systemic drug delivery systems, (2) needed to provide sufficient data on the plant-based excipients used, or (3) were not peer-reviewed.

Data were extracted from the included studies regarding the types of plant-based excipients used, their functions in topical formulations, advantages, challenges, and outcomes of their application. The extracted data were synthesized into thematic categories for detailed analysis.

Results

Advantages of Plant-Based Excipients

Plant-derived excipients offer numerous advantages in pharmaceutical formulations. Primarily recognized for their exceptional biocompatibility, they closely mimic the human

body's environment, reducing the likelihood of adverse reactions. Studies by Williams et al support this claim, demonstrating fewer side effects compared with synthetic alternatives.¹⁰ Furthermore, plant-based excipients are gentle on the skin, making them suitable for topical applications, as evidenced by research from Smith et al.¹¹

Beyond their safety profile, these excipients contribute to environmental sustainability. As highlighted by Gupta et al, they align with green pharmaceutical principles by utilizing renewable plant resources.¹² Life cycle assessments conducted by Patel and Gogate confirm their reduced carbon footprint compared with synthetic counterparts, making them crucial for eco-conscious drug development.¹³

Functionally, plant-derived polymers like gums and polysaccharides excel in controlled drug release, as demonstrated by Sharma et al.¹⁴ Additionally, certain plant extracts can enhance drug absorption and overall formulation efficacy, as reported by Chen et al.¹⁵

Plant-based excipients offer several economic benefits. Their availability and affordability make them suitable for large-scale production, as noted by Lee and Kim.¹⁶ Moreover, research by Li et al indicates that they not only reduce production costs but also streamline formulation processes without compromising product quality.¹⁷

Commonly Employed Plant-Based Materials in Topical Dosage Forms

Plant-based excipients play critical roles in pharmaceutical formulations, serving various functions such as thickening, gelling, emollient, and active agent.

Thickening and Gelling Agents

Plant-derived polymers serve as essential components in the formulation of topical medications, providing crucial thickening and gelling properties. These natural substances offer several advantages, including biocompatibility and sustainability.

- *Cellulose* is a versatile polysaccharide extracted from plant cell walls. It is widely used in topical formulations. Its

nontoxic nature and ability to control drug release make it a valuable ingredient. Johnson et al highlight its role in enhancing product stability and texture.¹⁸

- **Starch:** Derived from various plant sources, starch contributes to the desired rheological properties of topical products. Patel and Kaushal emphasize its influence on drug release mechanisms.¹⁹
- **Guar gum:** Extracted from guar beans, guar gum is a versatile thickening and stabilizing agent. Saini et al explore its impact on product consistency and feel.²⁰
- **Carrageenan:** Obtained from red seaweed, carrageenan effectively gels topical formulations. Ramírez-Expósito et al delve into its molecular structure and its contribution to product viscosity and stability.²¹
- **Xanthan gum:** A microbial polymer, xanthan gum is known for its thickening and stabilizing properties. Liu et al investigate its role in enhancing product consistency.²²
- **Agar-agar:** Derived from seaweed, agar-agar improves the texture and structural integrity of topical formulations. Yew and Chang examined its gelation mechanisms and impact on product viscosity and spreadability.²³

These plant-based polymers offer a sustainable and biocompatible alternative to synthetic thickening and gelling agents, contributing to the development of effective and well-tolerated topical medications.

Emollients and Lipid Components

Plant-based oils and waxes offer exceptional emollient properties, contributing significantly to the moisturizing and protective effects of topical formulations. These natural ingredients replenish the skin's lipid barrier, enhance hydration, and soothe irritation.

- **Olive oil:** Rich in fatty acids and antioxidants, olive oil is a widely used emollient known for its moisturizing properties. Rodríguez-Amaya et al highlight its role in enhancing skin hydration.²⁴
- **Coconut oil:** Offering antimicrobial, anti-inflammatory, and moisturizing benefits, coconut oil is a versatile emollient with applications in various skin conditions. Evangelista et al explore its effectiveness in skin care.²⁵
- **Beeswax:** Beyond its emollient properties, beeswax acts as a thickener, contributing to product stability. Subrahmanyam details its molecular composition and benefits in topical formulations.²⁶
- **Shea butter:** Recognized for its moisturizing and anti-inflammatory effects, shea butter is a rich emollient that supports skin hydration and barrier function. Akihisa et al explore its composition and benefits.²⁷

These plant-derived emollients provide a foundation for creating effective and gentle topical products that address various skin concerns.

Active Agents and Extracts

Plant-based extracts offer a rich source of bioactive compounds with diverse therapeutic properties. These natural

ingredients provide effective solutions for various skin concerns, offering a gentle yet potent approach to skincare.

- **Chamomile extract:** Known for its anti-inflammatory and soothing properties, chamomile extract is beneficial for sensitive and irritated skin. Srivastava et al highlight its bioactive compounds and their role in managing inflammatory skin conditions.²⁸
- **Aloe vera extract:** Renowned for its wound healing and soothing effects, aloe vera extract is a versatile ingredient in topical formulations. Khan et al explore its bioactive elements and their contribution to skin health.^{29,30}
- **Green tea extract:** Rich in antioxidants, green tea extract offers antiaging and anti-inflammatory benefits. Chen et al emphasize its potential in protecting the skin from oxidative damage.^{31,32}
- **Calendula extract:** With anti-inflammatory and wound-healing properties, calendula extract supports skin repair and regeneration. Preethi and Kuttan detail its phytochemical composition and therapeutic potential.³³

By incorporating these plant-based extracts into topical formulations, effective and gentle skincare products that address a wide range of skin concerns can be created.

Healing Agents and Wound Care Components

Plant-derived compounds have been utilized for centuries in wound care due to their antimicrobial, anti-inflammatory, and regenerative properties. These natural ingredients offer effective and often gentle solutions for various skin injuries.

- **Myrrh resin:** Renowned for its antibacterial and anti-inflammatory properties, myrrh resin promotes tissue regeneration. Al-Henhena et al highlight its chemical composition and wound-healing benefits.³⁴

Fragrance and Aromatic Components

While primarily valued for their sensory appeal, certain plant-derived fragrances also possess therapeutic properties.

- **Lavender oil:** Known for its calming and antibacterial effects, lavender oil contributes to relaxation and may aid in wound healing. Cho et al explore its impact on autonomic nerve activity.³⁵
- **Frankincense resin:** Beyond its aromatic qualities, frankincense resin offers anti-inflammatory and antioxidant benefits, making it suitable for topical applications. Al-Yasiry and Kiczorowska detail its potential in treating inflammatory skin conditions.³⁶

► **Table 1** lists most of the plant-based excipients in topical dosage forms and their function.

Emerging Concepts

Challenges Associated with Plant-Based Excipients in Topical Dosage Forms

Plant-based excipients offer promising opportunities for developing sustainable and biocompatible topical formulations. However, several challenges hinder their widespread adoption.

Table 1 Most used plant-based excipients in topical dosage forms and their function

| Material | Function | Description |
|--------------------|--------------------------------------|--|
| Cellulose | Thickener, gelling agent | Enhances stability and texture of formulations |
| Starch | Thickener, gelling agent | Provides rheological properties and influences drug release |
| Guar gum | Thickener, stabilizer | Improves consistency and feel of gels and creams |
| Carrageenan | Thickener, stabilizer, gelling agent | Increases viscosity and stability |
| Xanthan gum | Thickener, stabilizer | Enhances consistency and stability |
| Agar-agar | Gelling agent | Improves texture and structure of formulations |
| Olive oil | Emollient | Enhances skin hydration |
| Coconut oil | Emollient, thickener | Provides antimicrobial, anti-inflammatory, and moisturizing properties |
| Beeswax | Emollient, thickener | Enhances skin hydration and product stability |
| Shea butter | Emollient | Offers moisturizing and anti-inflammatory properties |
| Chamomile extract | Active agent | Provides anti-inflammatory and soothing effects |
| Aloe vera extract | Active agent | Offers soothing and wound-healing properties |
| Green tea extract | Active agent | Provides anti-aging and anti-inflammatory effects |
| Calendula extract | Active agent | Offers anti-inflammatory and wound-healing properties |
| Myrrh resin | Healing agent | Provides antibacterial and anti-inflammatory properties |
| Frankincense resin | Fragrance, aromatic | Provides anti-inflammatory and antioxidant properties |
| Lavender oil | Fragrance, aromatic | Offers calming and antibacterial effects |

Variability and Standardization

- **Intrinsic variability:** Natural sources are subject to fluctuations in composition due to factors like climate, soil, and harvesting methods. This variability impacts product consistency and efficacy.³⁷
- **Complex composition:** Plant extracts contain a diverse array of bioactive compounds, making it challenging to establish standardized extraction and quantification procedures.³⁸

Stability and Degradation

- **Oxidative sensitivity:** Many plant-based excipients are prone to oxidation, which reduces their stability and shelf life.³⁹
- **Environmental sensitivity:** Light, humidity, and temperature can accelerate degradation, affecting the physical and chemical properties of formulations.⁴⁰

Extraction and Purification

- **Solvent residues:** Solvent-based extraction processes may leave undesirable residues, requiring careful purification to ensure safety and compliance.⁴¹
- **Selectivity:** Isolating specific bioactive compounds while minimizing unwanted components is often challenging.⁴²

Regulatory and Safety Concerns

- **Regulatory hurdles:** Plant-based excipients may not have the same regulatory framework as synthetic counterparts, leading to complexities in product approval.⁴³
- **Safety assessment:** To ensure product safety, a thorough evaluation of skin irritation, sensitization, and other potential adverse effects is essential.⁴⁴

Formulation and Compatibility

- **Integration challenges:** Compatibility issues can complicate the process of combining plant-based excipients with modern delivery systems, such as lipid-based carriers or nanotechnology.⁴⁵
- **Analytical challenges:** Characterizing the complex composition of plant extracts requires advanced analytical techniques to ensure quality control.⁴⁶

Addressing these challenges through rigorous quality control, standardized extraction protocols, innovative formulation approaches, and robust analytical methods is crucial for the successful development and commercialization of topical products containing plant-based excipients.

Case Studies Illustrating Successful Applications of Plant-Based Excipients in Topical Dosage Forms

- Turmeric (*Curcuma longa*) extract in anti-inflammatory creams
 - Gupta et al developed an anti-inflammatory cream containing turmeric oleoresin rich in curcuminoids. The cream demonstrated significant anti-inflammatory effects in preclinical models, highlighting turmeric extract's potential in managing skin inflammation and promoting skin health.⁴⁷
- Green tea (*Camellia sinensis*) polyphenols in antiaging serums
 - Chen et al developed an antiaging serum incorporating green tea polyphenols. The serum exhibited significant antioxidant activity, improved skin elasticity, and

- reduced fine lines, showcasing the potential of green tea polyphenols in antiaging skincare formulations.⁴⁸
- Aloe vera (*Aloe barbadensis* Miller) gel in wound-healing ointments
 - Khan et al investigated the incorporation of aloe vera gel into a wound-healing ointment. The ointment demonstrated accelerated wound closure, reduced inflammation, and enhanced tissue regeneration, emphasizing aloe vera gel's effectiveness in wound healing formulations.⁴⁹
 - Soy lecithin in topical antifungal creams
 - Kim et al incorporated soy lecithin into topical antifungal creams, enhancing skin penetration and drug delivery. The cream demonstrated improved efficacy in treating fungal infections, highlighting soy lecithin's role in optimizing drug delivery in topical formulations.⁵⁰
 - Tea tree (*Melaleuca alternifolia*) oil in antimicrobial creams
 - Carson et al formulated a cream containing tea tree oil for treating bacterial and fungal skin infections. The cream exhibited notable antimicrobial efficacy, showcasing tea tree oil's potential as a plant-derived excipient with broad-spectrum antimicrobial activity.⁵¹
 - Lavender (*Lavandula angustifolia*) oil in relaxing massage lotions
 - Cho et al assessed the impact of lavender oil in relaxing massage lotions. The lotion demonstrated a calming effect on autonomic nerve activity and emotional states, highlighting lavender oil's potential to enhance sensory experiences and promote relaxation.⁵²
 - Jojoba (*Simmondsia chinensis*) oil in moisturizing creams
 - Habashy et al explored the incorporation of jojoba oil in moisturizing creams. The creams demonstrated improved skin hydration and flexibility, emphasizing jojoba oil's potential as a natural emollient in skincare formulations.⁵³
 - Chamomile (*Matricaria chamomilla*) extract in soothing ointments
 - Srivastava et al formulated soothing ointments containing chamomile extract. The ointments exhibited significant anti-inflammatory and soothing effects on irritated skin, showcasing chamomile extract's therapeutic potential in skincare formulations.⁵⁴

Future Perspectives for Sustainable Drug Development with Plant-Based Excipients

The future of drug development with plant-based excipients is promising. It is characterized by innovative technologies, ethical considerations, personalized medicine, artificial intelligence (AI) integration, and regulatory advancements.

The convergence of plant-based excipients with nanotechnology offers exciting possibilities for enhancing drug delivery. Researchers are exploring the development of plant-derived nanoparticles for targeted and controlled release of therapeutic agents. Wang et al emphasize the synergistic benefits of combining plant-based materials with nanotechnology for more efficient drug delivery systems.³⁵

As the demand for plant-based excipients rises, ensuring ethical and sustainable sourcing is crucial. Future perspectives involve adopting transparent supply chains, fair trade practices, and environmentally conscious cultivation methods. Smith and Johnson advocate for ethical considerations in procuring plant-derived materials, aligning pharmaceutical practices with sustainability principles.^{37,55}

The future of drug development envisions personalized formulations tailored to individual patient needs. Plant-based excipients, with their diverse bioactive compounds, offer the potential for customized skincare products, wound healing formulations, and anti-inflammatory creams. Li et al discuss the prospects of integrating plant-based excipients in personalized medicine for enhanced therapeutic outcomes and patient satisfaction.⁵⁶ AI integration in pharmaceutical research introduces a paradigm shift in formulation design. AI algorithms can analyze vast data sets, predict formulation outcomes, and optimize plant-based excipient combinations for specific drug delivery needs. Patel et al highlight AI's potential to enhance the efficiency and success rates of plant-based formulation design, marking a new era in drug development.^{57,58}

The evolving landscape of plant-based drug development necessitates establishing harmonized regulatory frameworks. Collaborative efforts among regulatory bodies to provide clear guidelines for the approval and commercialization of formulations containing plant-based excipients are essential. Regulatory Insights Group (RIG 2024) emphasizes the need for consistent and internationally recognized regulations to foster innovation and ensure the reliability of plant-based drug products.^{59,60}

The vast biodiversity of plant species offers a plethora of untapped resources for drug development. Future perspectives involve extensive exploration of diverse plant sources, including those from rainforests, deserts, and remote regions. Conservation BioProspecting International discusses the potential benefits of biodiversity exploration for pharmaceutical innovation.^{61,62}

Conclusion

The comprehensive analysis of plant-based excipients in topical dosage forms reveals a rich landscape of opportunities and challenges. The utilization of plant-derived materials in pharmaceutical formulations is gaining prominence, driven by the demand for sustainable and nature-inspired solutions. The advantages of plant-based excipients, including biocompatibility, sustainability, enhanced drug delivery, and cost-effectiveness, are evident across various dimensions.

Despite the challenges, including variability in composition, stability issues, extraction methods, and regulatory compliance, the future perspectives for sustainable drug development with plant-based excipients are exciting. Advancements in nanotechnology, ethical sourcing practices, personalized medicine, AI-assisted formulation design, and the exploration of untapped plant resources are poised to revolutionize the field.

The integration of plant-derived materials into formulations not only addresses current challenges but also sets the stage for a sustainable and promising future in

pharmaceutical and cosmetic formulations. As research continues, the potential benefits of plant-based excipients are poised to make a lasting impact on drug development, emphasizing the importance of harnessing nature's wisdom for the betterment of human health and the environment.

Compliance with Ethical Principles

This review was conducted in accordance with ethical standards and guidelines for systematic reviews. All included studies were reviewed for compliance with ethical standards as described in their respective publications.

Author's Contributions

Conceptualization, visualization, literature search and review, writing – original draft, review, and editing.

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Conflict of Interest

None declared.

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