REVIEW PAPER

Emerging Film-Forming Topical Spray Systems for Inflammatory Fungal Infections: Formulation Challenges and Future Perspectives

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ABSTRACT
Inflammatory fungal infections of the skin represent a widespread clinical challenge, characterized by persistent inflammation, high recurrence rates, and reduced patient quality of life. Although topical antifungal therapy remains the first-line treatment for superficial mycoses, conventional dosage forms such as creams, ointments, and gels are often limited by poor patient adherence, inadequate residence time on the skin, and suboptimal therapeutic efficacy. In this context, film-forming topical spray systems have emerged as a promising alternative, offering improved drug retention, uniform application, and sustained release at the site of infection. Upon application, these systems form a thin, continuous polymeric film that adheres to the skin surface, creating a localized drug reservoir capable of prolonged antifungal and anti-inflammatory action. This review critically examines the pathophysiology of inflammatory fungal infections and provides a comprehensive overview of film-forming topical spray systems, including formulation principles, key components, and design considerations. Furthermore, major formulation challenges such as drug solubility, film integrity, skin permeation, and safety concerns are discussed in detail. Current evaluation and characterization strategies, along with regulatory and translational considerations, are also highlighted. Finally, emerging research trends and future perspectives, including smart and nanotechnology-enabled film-forming systems, are explored to underscore the potential of this advanced topical delivery platform in improving the management of inflammatory fungal infections.

Keywords: *Film-forming spray, Topical antifungal delivery, Inflammatory, Polymeric films, Skin drug permeation*
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INTRODUCTION

Fungal infections are becoming a bigger threat to health and agriculture around the world, and the chemical antifungals we have now may cause different side effects [1] [2]. According to the most recent report, fungal infections affect millions of people and kill about 3.8 million people each year [3]. Traditional dosage forms for topical use have problems with poor delivery, not enough permeation through the skin, and low effectiveness because they don't reach the therapeutic level in the deeper layer of the skin [3]. These diseases are becoming more prevalent and fatal because to the microorganism's significant ability to develop resistance to existing treatments. The primary resistance factors are the introduction of novel strains and the indiscriminate use of antifungals. Consequently, it is essential to devise novel strategies that aid in the management of fungal infections in clinical settings [4]. Fungal infections can be categorized according to the infection site, the mode of pathogen acquisition, and the virulence displayed by the fungus. In humans, fungal infections can impact multiple organs, including the skin, nails, and hair. Among the several pathogenic fungi that cause infections, Candida albicans is the most common human fungal pathogen, leading to a spectrum of disorders from mucosal infections to systemic problems [5]. Film coating agent is a novel kind of topical formulation introduced in recent years. A film coating agent is a topical liquid formulation in which a medicine is either dissolved or dispersed in a solvent that contains a film-forming substance, resulting in the formation of a thin film upon application to the afflicted area. Upon application to the affected region, the organic solvent rapidly volatilizes, creating a protective layer while progressively releasing the encapsulated medicine to exert a therapeutic effect. Furthermore, the formulation of the coating ingredient is straightforward, thereby circumventing the issue of typical creams soiling garments [6]. It is frequently utilized as an alternative to traditional topical and transdermal medication formulations. delivering accurate performance at a specific location on the skin, extending/modifying medication release and hence enhancing therapeutic efficacy [7]. Inflammation caused by mycotic infections of the dermis occurs in many people around the globe and can create symptoms

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such as redness, itching, pain, and flaking skin that cause a great deal of negative impact on quality of life for people suffering from these conditions [8] . Current topical antifungal therapies are standard treatment for inflammatory mycotic infections of the dermis because they allow high concentrations of active drug to be delivered directly to the location of the infection while worsening little or no adverse systematic effects; but, traditional topical medications in the form of creams, ointments, or gels typically have poor cosmetic characteristics, do not remain on the dermis for long enough to allow consistent and effective absorption of the drug into the body, and require individuals to frequently apply these medications to achieve uniform therapeutic results. Film-forming topical spray systems are being studied as potential alternatives to the issues of traditional topical medication. [9]. Film-forming topical spray systems create a thin polymeric film that forms over areas of application that are treated to maintain a constant level of the antifungal agent (AF) in contact with the dermis, thus providing a longer pharmacologic retention time and a steady state of pharmacologic absorption. Ease of use, quick drying, and non-greasy composition of these new formulations improve patient compliance and effectiveness of antifungal therapies [10].

Inflammatory Fungal Infections: Pathophysiology and Clinical Significance

Dermatophytes, yeasts, and molds cause inflammatory fungal infections of the skin by invading and reproducing in keratinized tissues. The interaction between the host and the pathogen is complicated and results in activation of both the innate and adaptive immune systems. The fungi, such as Trichophyton, Candida, and Malassezia species, release enzymes that break down the stratum corneum allowing them to multiply and invade deeper layers of the skin [11][12]. These enzymes also cause keratinocytes and immune cells to produce pro-inflammatory cytokines and chemokines. The combination of these two processes creates an inflammatory response which causes symptoms such as redness, itchiness, swelling, and pain. At present, the burden of disease and discomfort associated with inflammatory fungal infections is substantial [13]. The persistence of an inflammatory response can lead to damage to the skin's barrier function and increase the risk of developing chronic forms of inflammatory fungal infections and of experiencing recurrent episodes, especially among people with weakened immune systems or metabolic disorders. Because both antifungal activity and the regulation of inflammatory responses play a critical role in determining the course of disease, effective management strategies for inflammatory fungal infections should include both antifungal and immune-modulatory therapy to optimize long-term therapeutic outcomes [14][15]. In Figure 1 Describe (A) Routes of fungal entry via inhalation or skin tissue invasion leading to localized and systemic invasive infections affecting multiple organs. (B) Recognition of fungal pathogen-associated molecular patterns (PAMPs), including chitin and β-1,3-glucans, by host pattern recognition receptors (PRRs) such as Toll-like receptors (TLRs) and C-type lectin receptors (Dectins), triggering innate immune signaling and cytokine-mediated activation of immune effector cells. (C) Key fungal virulence and immune evasion mechanisms, including polysaccharide shielding, formation of asteroidal bodies and titan cells, biofilm development, polysaccharide capsule-mediated immune suppression, and morphological switching, which collectively enhance survival, tissue invasion, and resistance to host defenses and antifungal therapies [16].

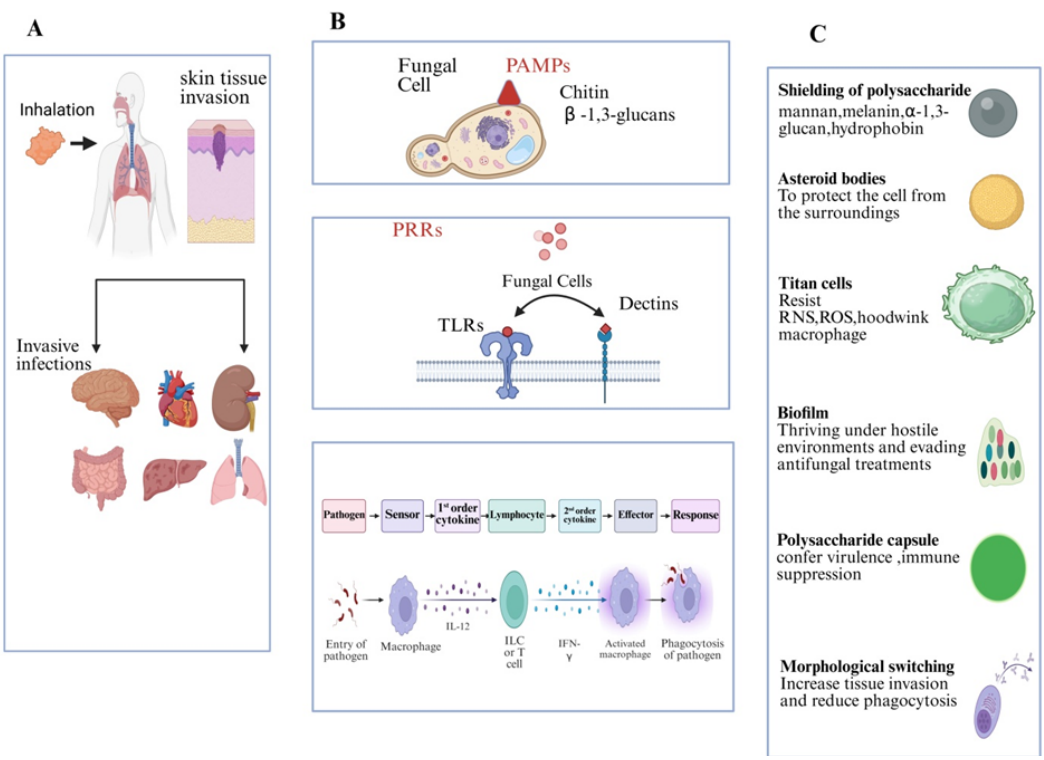

Figure 1. Host-fungal interactions during infection, immune recognition, and fungal immune evasion strategies.

Etiology and Common Fungal Pathogens

The primary cause of dermal fungal infection based on the viral nature of the pathogen, is the colonization of skin by a fungus, followed by an increase in amount of this type fungus to the point where it overgrows, which is caused by a number of factors. Compromised or weakened barrier function of the skin; excessive humidity; poor hygiene; immunosuppression; and certain metabolic diseases, all contribute to the cause of these types of infections [17]. The dermatophyte group of fungi, including species of Trichophyton, Microsporum and Epidermophyton, account for the majority of the fungal pathogens responsible for infection of keratinized tissues, which include hair, nails and skin. In addition to their virulence factors, the chitin component of fungal cell walls, leads to tissue invasion and persistence, resulting in the inflammatory nature of fungal skin infections and their recurrent and chronic nature [18].

Inflammatory Responses Associated with Fungal Infections

Fungal pathogens cause inflammation by activating immunity to prevent the spread of fungal pathogens, as well as to protect the skin from being penetrated by them. When a fungal infection occurs, keratinocytes and other cells in the body respond by activating Pattern Recognition Receptors (PRRs) to produce a number of proteins called pro-inflammatory mediators, including cytokines, chemokines, and antimicrobial peptides. Pro-inflammatory mediators recruit white blood cells to the area of the infection and produce inflammatory symptoms [19]. Although this inflammatory response is necessary for clearing the fungus from the skin, excessive or prolonged inflammation disrupts skin barrier function and hinders the healing process. Chronic inflammation from a persistent fungal infection leads to both increased damage to the skin and an increased chance of recurrence, thus creating a need for antifungal therapies and anti-inflammatory strategies that work together [20].

Limitations of Conventional Topical Therapies

Topical applications such as creams, ointments, lotions and gels are an established method for the treatment of inflammatory fungal disorders but are limited by formulation and patient variability. Formulations typically have short skin residence due to loss through sweating, washing and physical gas, leading to variability in the medication delivered to the affected area. In addition, greasiness, stickiness and poor sensory experience may lead to poor patient compliance, especially during prolonged use of the product [21]. Further, unpredictable drug placement and the requirement for frequent re-application contribute to decreased success of the therapy. In many instances, the use of standard topicals may cause skin irritation or occlusion, which can increase inflammation and discomfort. These limitations of current topical formulations indicate the need for improved topical delivery systems which may improve drug retention, enhance patient compliance and provide durability of therapeutic activity [22].

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Film-Forming Topical Spray Systems: An Overview

By utilizing film-forming topical spray systems, users can overcome many of the limitations associated with conventional semi-solid formulations and utilise this as an alternative means of delivering medications. Generally speaking, film-forming topical spray systems consist of an active ingredient dissolved in or suspended within a volatile solvent system containing film-forming polymers that evaporate rapidly upon application to the skin. A thin, even layer of polymer then remains behind on the skin. Polymer provides a reservoir for the active ingredient in that it prolongs the time the active ingredient stays at the application site; additionally, polymers allow for controlled release of the active ingredient at the application site over time [23]. There are various advantages to using film-forming topical spray systems, such as no need for direct contact with the skin, rapid drying time, better appearance from a cosmetic standpoint; and a uniform distribution of the active ingredient within the polymer. These advantages have made film-forming topical spray systems increasingly popular for use in the treatment of inflammatory fungal infections, where providing sustained antifungal action and increasing patient compliance is paramount to achieving successful therapy of an individual [24].

Principles of Film Formation on the Skin

The formation of films on the skin via topical spray products is accomplished through deposition and joining together of long chains of polymers from the rapid evaporation of volatile components after application. The liquid formulation is able to cover the skin area uniformly upon spraying, and as the solvents evaporate, the concentration of the polymers is increased. Increased concentration results in interactions between adjacent polymer chains that create a continuous flexible film [25]. The properties of the polymer such as molecular weight, glass transition temperature, and hydrophilicity are very important in determining how strong and well the film adheres to the skin as well as how durable and flexible the film will be. Additionally, the interaction between the polymeric film and the stratum corneum plays a major role in how well the film adheres to the application site as well as in retaining the active drug within the area where it was applied. Successful film creation on the application site allows for even and uniform coverage of the area, long-lasting durability, and a slow and sustained release of the active drug. All of these features together are essential to maximize the benefit of topical treatments for inflammatory fungal infections[26].Figure 2 illustrates the key elements of film-forming topical systems, including (1) formulation components such as polymers, solvents, drug/API, plasticizers, and excipients; (2) the mechanism of action involving spray application to the skin, solvent evaporation, polymer coalescence, and formation of a flexible film; (3) major advantages, including targeted drug delivery, sustained release, protection, and ease of use; and (4) critical challenges related to adhesion and flexibility, stability and sterility, development cost, and skin permeation–efficacy balance.

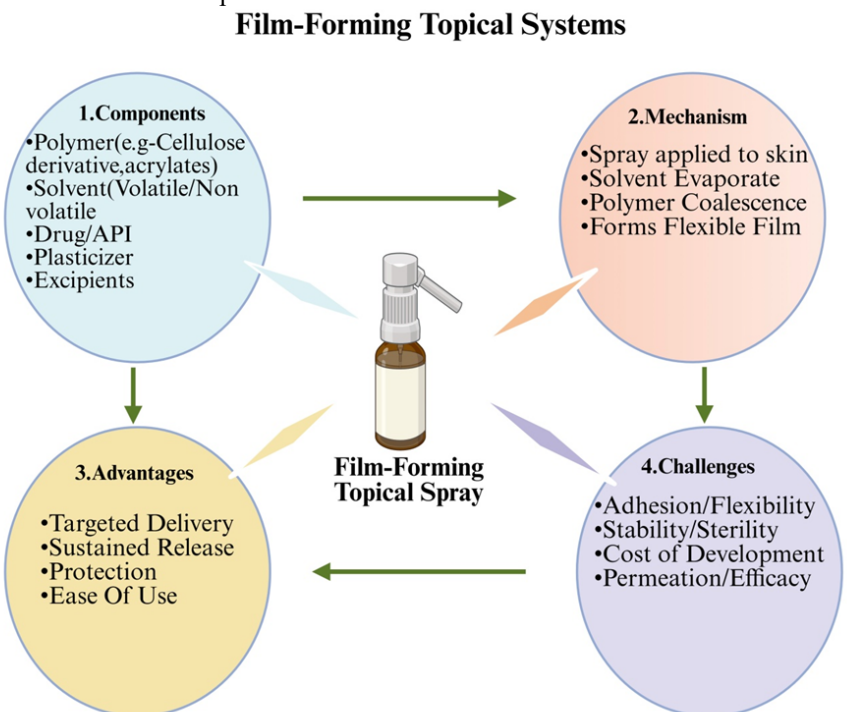

Figure2. Schematic representation of film-forming topical spray systems.

Classification of Film-Forming Sprays

Film-forming sprays can be classified based on formulation composition, film-forming mechanism, and the nature of the delivery system. Broadly, they are categorized into solution-based, suspension-based, and emulsion-based sprays, depending on whether the drug

is molecularly dispersed, suspended, or emulsified within the formulation. Based on the type of film-forming polymer, these systems may be further classified into natural polymer–based, synthetic polymer–based, and hybrid polymer systems, each offering distinct advantages in terms of biocompatibility, mechanical strength, and drug release behavior. Additionally, film-forming sprays can be classified according to solvent characteristics as volatile or non-volatile solvent systems, which influence drying time, film integrity, and patient comfort. This multifaceted classification aids in rational formulation design by aligning polymer selection, drug properties, and therapeutic requirements. Classification of film-forming sprays are shown in Table 1.

Table1. Classification of film-forming sprays based on polymer type, solvent system, film formation mechanism, dosage form, therapeutic application, and functional properties for topical drug delivery.

Classification Basis	Category	Description	Representative Examples / Applications	Reference
Type of Film-Forming Polymer	Synthetic polymers	Polymers manufactured through chemical synthesis that provide reproducible mechanical strength and controlled drug release	Polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Eudragit® RL/RS; antifungal and anti-inflammatory sprays	[27]
	Natural polymers	Biocompatible and biodegradable polymers derived from natural sources, offering enhanced skin compatibility	Chitosan, Alginate, Gelatin, Cellulose derivatives; wound healing and dermatological applications	[28]
	Semi-synthetic polymers	Chemically modified natural polymers with improved solubility and film-forming ability	Hydroxypropyl methylcellulose (HPMC), Ethyl cellulose; sustained topical delivery	[29]
Solvent System	Organic solvent-based systems	Utilize volatile organic solvents to facilitate rapid drying and film formation	Ethanol, Isopropanol-based sprays; antifungal and antiseptic formulations	[30]
	Aqueous-based systems	Employ water as the primary solvent, minimizing skin irritation and toxicity	Hydrogels and polymer dispersions; pediatric and sensitive skin applications	[31]
	Hydroalcoholic systems	Combination of water and alcohol to balance film integrity and evaporation rate	Anti-inflammatory and analgesic topical sprays	[32]
Film Formation Mechanism	Solvent evaporation-induced films	Film forms upon solvent evaporation after application on skin	Most topical film-forming sprays for dermal drug delivery	[33]
	Cross-linking-induced films	Film formation occurs through chemical or ionic cross-linking reactions	Wound dressings and bioadhesive protective films	[34]
	Temperature- or pH-responsive films	Films formed or stabilized in response to physiological conditions	Smart drug delivery and controlled-release systems	[35]
Dosage Form Type	Solution-based sprays	Drug and polymer dissolved completely in solvent	Rapid-acting dermatological treatments	[36]
	Suspension-based sprays	Insoluble drug dispersed within polymeric solution	Prolonged drug release and enhanced stability	[37]

	Emulsion-based sprays	Oil-in-water or water-in-oil systems providing moisturization and controlled delivery	Anti-inflammatory and cosmetic dermatology formulations	[38]
Therapeutic Application	Dermatological sprays	Intended for skin disorders including fungal infections and inflammation	Antifungal, corticosteroid, and antibacterial sprays	[39]
	Wound healing sprays	Provide protective barrier and controlled drug release for wounds	Diabetic ulcers, burns, post-surgical care	[40]
	Transdermal delivery systems	Designed to deliver drugs systemically through skin	Analgesic and hormone delivery	[41]
Functional Property	Bioadhesive films	Enhance residence time at the application site	Chronic dermatological and mucosal conditions	[42]
	Occlusive/semi-occlusive films	Reduce transepidermal water loss and protect affected area	Psoriasis, eczema, and wound management	[43]
	Drug-loaded protective films	Provide mechanical protection along with therapeutic effect	Infected wounds and inflammatory skin disorders	[44]

There are various ways to classify film-forming topical sprays; they can be categorized by polymer type, solvent system and film-forming mechanism. In terms of polymer composition, film-forming topical sprays can be divided into two main categories: synthetic polymersand natural polymers which are beneficial because they are considered both biocompatible and biodegradable. In terms of the solvent system, film-forming topical sprays can be classified into aqueous, organic or mixed solvent systems; selecting the appropriate solvent system will affect drying time, uniformity of the film and the solubility of the drug within the film once it is formed [32]. In terms of the film-forming mechanism, film-forming topical sprays can be classified according to one of the following mechanisms: solvent evaporation, coalescence of polymer particles, or in-situ cross-linking; each mechanism plays a role in determining how the film is formed and drug release profiles from the film as well as the adhesion properties of the film to the skin. Therefore, it is essential to understand how film-forming topical sprays are classified in order to develop an optimized formulation to treat inflammatory fungal infections [45].

Advantages over Conventional Dosage Forms

Film-forming topical spray systems offer several distinct advantages over conventional dosage forms such as creams, ointments, and lotions in the management of inflammatory fungal infections. Upon application, these systems form a thin, uniform, and adherent film on the skin, enabling prolonged residence time and sustained drug release at the site of infection, thereby reducing dosing frequency. Unlike semi-solid formulations, film-forming sprays are non-greasy, rapidly drying, and provide enhanced patient comfort and ease of application, particularly on inflamed, sensitive, or hard-to-reach areas. Additionally, the occlusive yet breathable nature of the formed film protects the affected site from external contaminants while improving drug penetration and minimizing systemic exposure, collectively leading to improved therapeutic efficacy and patient adherence. Comparative Overview of Conventional Topical Formulations vs. Film-Forming Sprays are shown in Table 2.

Table2. Comparative Overview of Conventional Topical Formulations vs. Film-Forming Sprays

Formulation Type	Advantages	Limitations	Patient Compliance	Drug Retention/Residence Time	Reference
Creams	Easy to apply; suitable for moist or exudative lesions	Greasy; short residence time; frequent application required	Moderate; often inconvenient due to texture and frequency	Low; removed easily by washing or friction	[46]
Ointments	Occlusive; good for dry lesions; prolonged	Greasy, sticky, cosmetically unacceptable	Low; poor patient acceptability	Moderate; better than creams but still affected by friction	[47]

	hydration				
Lotions	Lightweight; spreads easily over large areas	Low drug retention; rapid evaporation	Moderate to high; easy to apply	Low; short duration due to quick absorption or washing	[48]
Gels	Non-greasy; transparent; suitable for hairy areas	May dry quickly or peel; limited mechanical strength	High; cosmetically acceptable	Moderate; limited by brittleness or flaking	[49]
Film-Forming Sprays	Forms thin, continuous, non-greasy film; sustained drug release; uniform coverage; easy application without hand contact	Requires optimization of polymer and solvent system; potential irritation if formulation not well-designed	High; user-friendly and cosmetically acceptable	High; prolonged residence time and controlled release, resistant to washing and friction	[50]

Topical spray systems that create a polymeric film on the skin have multiple benefits as compared with more established semisolid formulations. The creation of a continuous, thin film on the skin surface promotes retention of the drug at the application site, resulting in prolonged drug release and improved local bioavailability. A rapid drying time combined with a non-greasy and clear product increases the product's cosmetic acceptability, leading to increased patient adherence, especially for chronic conditions [51]. The even distribution of the drug on the skin minimizes differences between dosages, leading to a more consistent therapeutic effect than with older semisolid formulations. Additionally, the method of applying the product without directly contacting it with one's hands decreases the chance of contamination and allows for greater convenience to patients. Therefore, taken as a whole, the benefits of film-forming topical spray systems surpass the many limitations of topical treatment options available today for managing inflammatory fungal infections.Formulation Components and design Considerations [52] .

Selection of Polymers for Film Formation

The selection of an appropriate polymer is a critical determinant of performance in film-forming topical spray systems intended for inflammatory fungal infections (Table 3). Polymers must exhibit rapid film formation upon solvent evaporation, strong yet flexible adhesion to the skin, and adequate mechanical integrity to withstand movement and moisture exposure. Both natural and synthetic polymers, such as cellulose derivatives, acrylates, and polyurethanes, are commonly explored due to their favorable film-forming ability, biocompatibility, and tunable drug release profiles. Importantly, the polymer should be non-irritant and compatible with antifungal agents, particularly in inflamed or sensitive skin conditions, while also facilitating optimal drug permeation and sustained therapeutic action.

Table 3. Key Polymers, Excipients, and Functional Roles in Film-Forming Sprays

Component	Exampl	Functional Role	Impact on Film Properties	Safety/Regulatory Notes	Reference
Polymers	Polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Eudragit, Hydroxypropyl methylcellulose (HPMC), Chitosan	Provide structural matrix; form continuous film; control drug release	Determines film adhesion, flexibility, mechanical strength, and drying time	Generally recognized as safe (GRAS) or pharmaceutically acceptable; synthetic polymers widely approved; natural polymers biocompatible	[53]
Plasticizers	Glycerol, Propylene glycol, Polyethylene glycol (PEG)	Enhance film flexibility; reduce brittleness	Improves elasticity and prevents cracking of the film	Safe at low to moderate concentrations; avoid high concentrations that	[54]

				may cause stickiness or irritation	
Solvents	Ethanol, Isopropyl alcohol, Water, Acetone, Mixtures	Dissolve polymers and drug; enable spraying; control drying rate	Affects sprayability, drying time, film uniformity, and drug distribution	Volatile organic solvents must comply with ICH residual solvent limits; water is safe and non-irritant	[55]
Penetration Enhancers	Oleic acid, Menthol, Isopropyl myristate, Surfactants	Improve drug permeation through stratum corneum	Enhances bioavailability and therapeutic efficacy	Selection based on skin tolerance; may cause irritation if overused	[56]
Active Pharmaceutical Ingredient (API)	Clotrimazole, Ketoconazole, Miconazole, Terbinafine	Provide antifungal activity	Drug solubility and stability influence uniformity, crystallization, and release	Must be compatible with excipients; chemically and physically stable in formulation	[57]

The choice of polymers will impact the performance of the film-forming systems intended for topical applications; suitable polymers will not only be free from toxicity and biocompatibility but also have the capability of producing a continuous, flexible, and firmly adhered film to the skin. Synthetic polymers like polyvinyl alcohol, polyvinylpyrrolidone, and many acrylic derivatives have been recommended because of their reproducibility and ease of obtaining selected polymer types for further studies [58]. Natural polymers have also been suggested as they possess useful properties such as biodegradability, built-in antimicrobial properties and compatibility with sensitive skin. The molecular weight of the polymer, its solubility, glass transition temperature, and the interaction of the polymer with other components in the formulation all influence the film thickness, mechanical properties, drying time, and drug release rates of the formulation. Thus, it is critical to carefully choose the appropriate type and level of polymer for optimal film formation, prolonged drug release, and comfortable use in controlling inflammatory fungal infections [59].

Role of Plasticizers, Solvents, and Penetration Enhancers

Plasticizers, solvents, and penetration enhancers are essential excipients that directly influence the activity, stability and effectiveness of topical film forming sprays. Plasticizers such as glycerol, propylene glycol and polyethylene glycol enhance flexibility through lessened brittleness and enhanced mechanical strength ensuring the resultant films remain intact throughout the wear of normal skin. Solvents, which may be an aqueous, organic or a combination thereof, solubilize or disperse polymers and drugs for controlled drying times and offer uniformity and smoothness of resultant films [60]. Penetrating enhancers increase drug permeation through the stratum corneum, resulting in improved local bio-availability and thus therapeutic effect. A careful selection and optimization of these components is required to generate a stable, uniform and effective film-forming spray with prolonged antifungal activity and that is safe for the skin and acceptable to the patient [56].

Drug Excipient Compatibility and Stability

Effective drug formulations, it is essential that the developmental process provides for a thorough examination of possible compatibility and stability issues regarding the drug and excipients used in the formulations. Most commonly, incompatible interactions between the active pharmaceutical ingredient (API) and excipients will lead to a breakdown of the API. Failure to resolve any product incompatibility will ultimately lead to product failure with respect to uniformity, efficacy, and safety [61]. Some of the most critical areas of consideration when evaluating stability are the chemical stability of the API across many different storage conditions, the physical stability of the polymeric film, and how well the mechanical and adhesive characteristics of the film will remain stable over time. common methods used to assess excipient compatibility and identify potential incompatibilities include differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FTIR), and X-ray diffraction/X-ray powder diffraction (XRD/XPD). The optimization of the excipient selection process and the assessment of long-term stability via accelerated and real-time stability testing are both critical steps in ensuring the formulation retains its therapeutic effectiveness

throughout its intended shelf life and remains acceptable for use by patients [62].

Formulation Challenges in Antifungal Film-Forming Sprays

The development of antifungal topical spray systems with film-forming capabilities has brought about several formulation obstacles/disadvantages that may affect both the safety and acceptability of the product and its effectiveness. One major challenge to overcome is the limited soluble form of most antifungal compounds in water-based systems. Due to this characteristic, antifungals are susceptible to forming crystals in a film system and uneven distribution throughout the polymer film, which can reduce the overall therapeutic efficacy. In order to optimize film integrity, it is important to determine the optimal levels of adhesion, flexibility, mechanical strength, of the films [63]. Some additional formulation considerations are the selection of polymers, solvents and excipients that provide for the best physical/chemical properties of the formulation, while providing for the best biocompatibility; long-term stability of the formulation under various environmental conditions; and a thorough/complete pre-clinical evaluation of the formulation and the use of advanced analytical techniques for characterization [64]. highlights major limitations encountered during the development of antifungal film-forming spray systems, including poor solubility of antifungal agents, compromised film integrity and durability leading to cracking, peeling, and inadequate adhesion, susceptibility to moisture and water exposure resulting in erosion during sweating or washing, and the risk of skin irritation or sensitization, particularly on inflamed or sensitive skin in Figure 3.

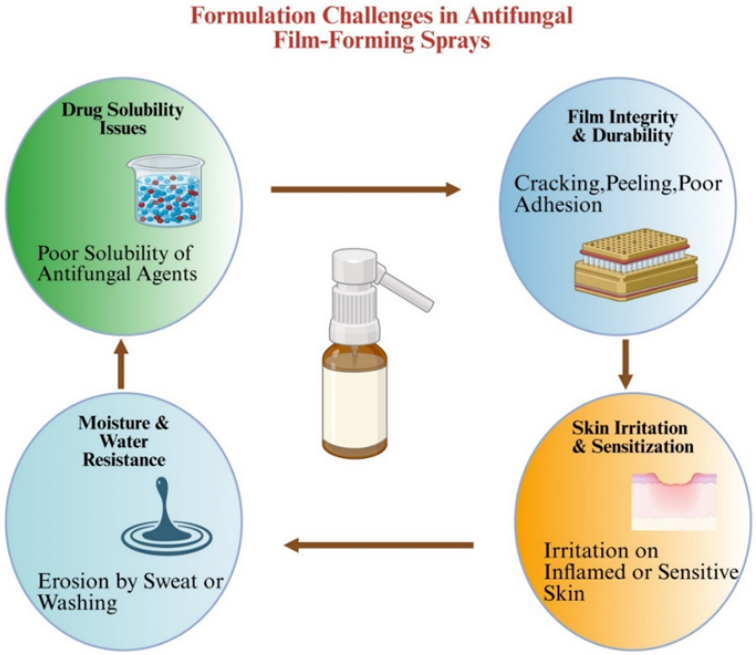

Figure 3. Key formulation challenges associated with antifungal film-forming sprays

Drug Solubility and Crystallization Issues

The difficulty of developing antifungal film-forming sprays is attributed to antifungal agent's limited solubility; during or following the creation of the film, antifungal agents may precipitate as crystals. Precipitation will give rise to an uneven distribution of the antifungals in the polymer matrix, which decrease the localized bioavailability, thereby adversely affecting their clinical usefulness [65]. Lipophilic antifungals are especially susceptible to crystallization because of their poor solubilization in common solvent mixtures. Strategies for overcoming antifungal agent solubility and crystallization problems include co-solvents, solubilizing agents, emulsifying agents, and amorphous drug solutions [66].

Film Integrity, Adhesion, and Mechanical Properties

The polymeric film must be adequately adhered to skin, but have sufficient flexibility to accommodate normal skin movement without cracking. Brittle films will crack resulting in uneven drug distribution and reduced residence time; conversely, overly soft films may not stay on, interrupting an effective sustained release of drug. Mechanical properties of films, including tensile strength, elasticity, and elongation at break, are determined by the type of polymer used and its concentration, level of plasticizer, and solvent system [67]. The interaction of the polymeric film with the skin's stratum corneum also plays a role in adhesion and retention of the drug. Properly optimizing these parameters is vital to generate even coverage of skin, maintain prolonged residence time, and achieve consistent therapeutic effectiveness when treating inflammatory fungal infections [68].

Skin Permeation, Retention, and Irritation Potential

Sufficient penetration is needed so that the antifungal agent can effectively penetrate the stratum corneum and upper layers of the epidermis, where the fungus is typically localized; however, excessive penetration through the epidermis may cause systemic absorption, resulting in the potential for adverse effects on the individual. In addition to adequate penetration, the retention of the antifungal agent within the polymeric film and at the site of application is necessary for continuous therapeutic activity, as premature removal of the film due to washing, sweating, or friction may impair the efficacy of the product [69]. Furthermore, with respect to the formulation, the type of solvent, penetration enhancer, and some of the polymers used can cause skin irritation, skin sensitivity, or allergic reaction when applied to areas that are already inflamed, irritated, or damaged [70].

Evaluation and Characterization of Film-Forming Sprays

Skin permeation testing to determine kinetic drug release rates and skin absorption/recovery velocities. In vitro antifungal activity assays and, when applicable, anti-inflammatory drug models will also verify the therapeutic activity of these products. Stability evaluations will provide data to determine shelf-life based on various environmental conditions. Safety evaluations will focus on skin irritation sand product compatibility [71].

Physicochemical and Mechanical Characterization

To ensure suitability for film-forming topical spray systems, it is important to characterize the physicochemical and to assess how they affect application performance, integrity of the formed film, and compliance by patients with the product. These properties will determine how easy it is to apply, how well it spreads out uniformly, and how it behaves when being applied. Key physicochemical values include viscosity, pH, surface tension, and spray pattern.[72]. The mechanical properties of the film will determine whether or not it remains attached to the skin and prevents the film from cracking or peeling when in use. Other quality parameters, such as moisture content, water vapor transmission rate, and transparency, should also be assessed to verify that the film is non-occlusive, appears good from a cosmetic standpoint, and is comfortable for the patient [73].

In Vitro and Ex Vivo Skin Permeation Studies

Drug release, penetration and retention characteristics of a film-forming topical spray system, in vitro and ex vivo skin permeation studies are necessary. Franz diffusion cells and other diffusion apparatuses utilize human or animal skin that has been excised and serves as a model barrier for these types of tests. An in vitro study will give the initial kinetics for the antifungal agent's release from the polymer film; the ex vivo study will provide the most physiologically relevant information about how much drug can penetrate through stratum corneum and epidermis [74]. The parameters measured in these two types of tests include, but are not limited to, cumulative drug permeated, flux, permeability coefficients, and skin retention, which when taken together, provide the best indication of how the formulation will perform in vivo. In addition to determining the formulation's effectiveness at delivering local antifungal activity, these studies will help determine how polymer type and content, plasticizer content and solvent system, as well as penetration enhancers impact drug delivery, thus allowing us to optimize the formulation for sustained local delivery and low systemic absorption. Therefore, in vitro and ex vivo skin permeation studies are integral components in the development of safe, effective and clinically relevant film-forming topical sprays [75].

Antifungal and Anti-Inflammatory Efficacy Assessment

Antifungal efficacy is typically determined using in vitro microbiological assays such as disk diffusion, broth microdilution, or time-kill studies against relevant fungal pathogens, including *Trichophyton*, *Candida*, and *Malassezia* species. These studies provide quantitative measures of the formulation’s ability to inhibit fungal growth and ensure uniform drug distribution within the polymeric film [76]. Anti-inflammatory activity is assessed using in vitro or in vivo models that measure the reduction of pro-inflammatory mediators, cytokine expression, or edema in response to inflammatory stimuli. Together, these evaluations confirm that the film-forming spray not only delivers effective antifungal therapy but also modulates inflammation at the site of infection, thereby enhancing overall clinical outcomes. Incorporating both assessments ensures that the formulation provides comprehensive therapeutic benefits while maintaining safety and patient acceptability [77][78].

Regulatory, Safety, and Translational Considerations

Careful attention must be paid to regulatory, safety and translational factors during the clinical translation and development of film-forming topical spray products in order to ensure that the products will be effective and provide maximum safety to patients while remaining within the requirements of the governing regulatory agencies. Specifically, the regulatory framework for topical drug products has been established by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and other global agencies, and defines the various requirements with respect to quality control, stability, and excipient safety [79]. Safety evaluations include determining whether or not the spray product causes skin irritation or sensitization, as well as establishing its general toxicity and allergenic potential. Any of the components used in a formulation might contribute to interactions with an area of skin that is inflamed or compromised. [80].

Future Perspectives and Emerging Research Trends

Future advancements in film-forming topical spray systems that treat inflammatory fungal infections will focus on developing new technologies and formulations to increase therapeutic effectiveness and support compliance by patients, but most importantly; continue to uphold safety. One emerging trend for such systems is the creation of smart, or responsive, polymer films that release antifungal compounds in response to certain environmental situations. For instance, the use of nanocarriers contained within the film matrix can potentially allow for improved solubility, stability and controlled release of the antifungal compound. Biodegradable and/or naturally derived polymers have become a popular choice among consumers due to their greater biocompatibility, lessen impact to the environment, and that they typically contain either antimicrobial or anti-inflammatory properties. Recent advances in 3D printing and precision spray technology has allowed for the creation of personalized dosages through optimal thickness of the film of the system based on therapeutic indication and the anatomy of the end user. Additionally, functional agents that exhibit combined antifungal, anti-inflammatory, and skin barrier-restoring effects represent an attractive strategy for promising next-generation topical therapies. For effective translation into clinically-relevant and commercially-viable products, ongoing interdisciplinary collaboration between the fields of pharmaceutical sciences, material science and dermatology.

CONCLUSION

Topical sprays made from film-forming materials will continue to demonstrate advantages over traditional formulations in treating fungal diseases. Topically applied sprays form a single, thin, continuous film over the skin, which allows greater drug retention than the conventional formulations, provides better overall drug coverage to the affected area, and can provide sustained release of the drug to maintain prolonged antifungal therapeutic effect at the site of application and encourage more compliant patients. The formulation of topical sprays will depend heavily upon the careful selection of the polymers, plasticizers, solvents, and penetration enhancers, including the evaluation of the physicochemical, mechanical, and biological properties of the selected constituents, to ensure that the sprays are stable and safe to apply and provide effective treatment. The current formulations utilizing these materials will continue to create challenges such as obtaining drugs dissolved in a physical state that allows them to retain film structure upon drying, as well as creating products that are non-irritating to the skin. Continued innovations in product formulation, including the invention of "stimuli responsive" systems, as well as new methods to produce nanocarriers and biodegradable polymers for the formulation of topical sprays will open the door to more effective therapies and better patient treatment outcomes. The potential of topical sprays based upon film-forming materials to serve as a versatile and effective platform for localized treatment of inflammatory fungal disease is high, as the ability to both provide better clinical efficacy and be less disruptive to patients with user-friendly application provides significant advantages.

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