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FILM-FORMING SYSTEMS AS NEXT-GENERATION PLATFORMS FOR WOUND HEALING AND TOPICAL DRUG DELIVERY

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ABSTRACT

Wound healing is a complex biological process that requires an optimal microenvironment to facilitate tissue repair, prevent infection, and maintain appropriate moisture balance. Conventional topical formulations and wound dressings often face challenges such as poor adhesion, limited drug retention, frequent reapplication, and reduced patient compliance. Film-forming systems (FFSs) have emerged as innovative platforms for wound management and topical drug delivery, offering significant advantages over traditional dosage forms. These systems are applied as liquid solutions, gels, or emulsions that undergo solvent evaporation upon application, forming a thin, transparent, flexible, and adherent polymeric film directly on the skin. The resulting film provides prolonged residence time, enhanced drug retention, sustained and controlled drug release, barrier protection, and improved patient comfort while maintaining cosmetic acceptability. This review provides a comprehensive overview of film-forming systems, its principle, composition, classification, and therapeutic applications of film-forming systems (FFSs). Their roles in wound healing, topical and transdermal drug delivery, dermatological therapy, and cosmetic applications are highlighted. Recent advances, including nanoparticle-loaded films, bioactive polymers, stimuli-responsive systems, and growth factor-based formulations, are discussed along with current challenges, commercial products, and future prospects. Overall, film-forming systems represent a versatile, and patient-friendly and innovative approach for localized and controlled drug delivery, offering significant potential to improve wound care outcomes and expand the scope of advanced topical therapeutic strategies

Keywords: Film-forming systems; Wound healing; Transdermal delivery; Controlled release; bioactive, stimuli-responsive.

1. INTRODUCTION:

The skin serves as the body's primary protective barrier against physical, chemical, and microbial insults. Any disruption to its integrity due to injury, burns, surgical procedures, or chronic diseases can result in wound formation. Effective wound management is essential to prevent infection, reduce healing time, and restore normal tissue function. Wound healing is a highly coordinated biological process that plays a vital role in re-establishing the structural and functional integrity of injured tissues. Although substantial progress has been made in wound care strategies, chronic and infected wounds remain a significant global healthcare concern because of impaired healing, a higher likelihood of complications, and considerable economic burden associated with treatment [1]. Traditional wound care modalities, such as gauze dressings, creams, ointments, and topical solutions, frequently suffer from drawbacks including limited retention at the application site, insufficient drug residence, and the requirement for repeated administration, which can adversely affect therapeutic efficacy and patient adherence [2].

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To address these challenges, growing research efforts have focused on advanced topical drug delivery platforms capable of ensuring sustained wound coverage and controlled therapeutic release. Among the various approaches explored, film-forming systems (FFSs) have gained considerable recognition as effective carriers for wound healing and localized drug delivery applications [3]. Typically, these formulations are administered as liquids, sprays, or gels that transform into a thin polymeric film on the skin surface after solvent evaporation at the site of application [4]. The favorable properties of film-forming systems, such as convenient application, transparency, flexibility, and extended residence on the skin, have increased their appeal for wound care and site-specific drug delivery. In addition, advancements in polymer technology, biomaterials engineering, and nanotechnology have further enhanced their capability to incorporate bioactive agents and improve therapeutic performance [5].

This review presents an overview of recent progress in film-forming systems, with special focus on liquid-, spray-, and gel-based formulations designed for wound healing and drug delivery. Key aspects including formulation strategies, underlying mechanisms, therapeutic potential, existing limitations, and future opportunities associated with these emerging systems are critically examined.

2. WOUND HEALING:

Wound healing is a complex and highly regulated biological process that restores the structural and functional integrity of damaged tissues following injury. It involves the coordinated interaction of various cell types, extracellular matrix components, cytokines, and growth factors to achieve tissue repair and regeneration [2]

It is essential for maintaining skin integrity and protecting the body from microbial invasion, fluid loss, and environmental hazards. Wounds may arise from various causes, including trauma, burns, surgical procedures, infections, and chronic diseases such as diabetes. Effective wound healing is crucial for minimizing complications, preventing infection, reducing scarring, and restoring normal tissue functionality. Despite the remarkable regenerative capacity of the skin, several factors such as age, nutritional status, underlying medical conditions, and wound type can influence the healing outcome. Therefore, the development of advanced wound care strategies and drug delivery systems has become increasingly important to promote faster and more efficient healing [6].

2.1 Wound Healing Process: It involves a series of overlapping phases, including hemostasis, inflammation, proliferation, and remodeling, which are regulated by complex cellular interactions, cytokines, and growth factors [7]. Immediately after injury, hemostasis occurs through vasoconstriction and clot formation to prevent blood loss and provide a temporary extracellular matrix for cell migration. This is followed by the inflammatory phase, where neutrophils and macrophages eliminate debris and microbial contamination to prevent infection [8]. During the proliferative phase, fibroblasts, endothelial cells, and keratinocytes actively participate in granulation tissue formation, angiogenesis, and re-epithelialization, leading to partial restoration of the wound surface [9]. Finally, the remodeling phase strengthens the repaired tissue through collagen maturation and reorganization, resulting in improved tensile strength of the healed skin. Any disruption in these stages may lead to chronic or non-healing wounds, which remain a significant clinical challenge worldwide [7].

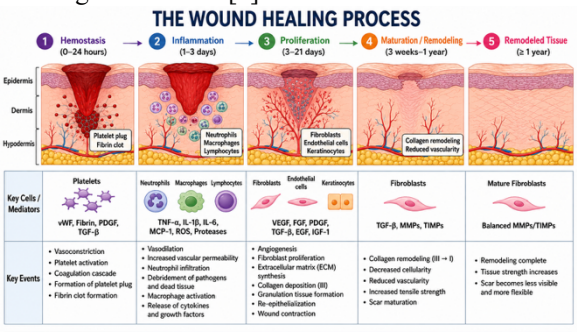

Figure 1. Key mediators and cellular events involved in the phases of wound healing.

The **hemostasis phase** involves von Willebrand factor (vWF), platelet-derived growth factor (PDGF), and transforming growth factor beta (TGF-β), which initiate clot formation and early signaling for tissue repair. The **inflammatory phase** is characterized by the release of tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), and reactive oxygen species (ROS), which coordinate immune cell recruitment and defense responses. During the **proliferative phase**, vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), PDGF, TGF-β, epidermal growth factor (EGF), and insulin-like growth factor-1 (IGF-1) promote angiogenesis, fibroblast activation, re-epithelialization, and extracellular matrix (ECM) formation. The **remodeling phase** is regulated by matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs), leading to extracellular matrix reorganization and the transition of type III collagen to type I collagen. The process involves key cellular participants including endothelial cells (ECs), keratinocytes (KCs), fibroblasts, macrophages, neutrophils, and lymphocytes, which collectively orchestrate tissue repair and regeneration.

2.2 Ideal Wound Dressing Requirements:

An ideal wound dressing should provide a favorable environment that promotes rapid and effective wound healing while protecting the wound from external contamination. It should maintain optimal moisture levels, allow adequate oxygen permeability, absorb excess exudates, and provide a barrier against microbial infection. Additionally, the dressing should be biocompatible, non-toxic, non-allergenic, easy to apply and remove, and capable of minimizing pain and tissue trauma during dressing changes. Appropriate mechanical strength, thermal insulation, and cost-effectiveness are also

important characteristics of an ideal wound dressing. These properties collectively contribute to enhanced tissue regeneration, reduced healing time, and improved patient comfort and compliance [1,10].

Table 1: Properties of an Ideal Wound Dressing [11]

S. NO.	FEATURE	DESCRIPTION
1	**No toxic component**	Free of harmful substances that can harm and have disastrous effects.
2	**Bacterial infection prevention**	Avoiding bacterial infections that may impair and prolong healing of wound.
3	**Adhesiveness**	Supplying the wound region with the right amount of adhesive substance (too much adhesive results in damage).
4	**Moisture**	Maintaining the optimal moisture amount to encourage cell migration & proliferation.
5	**Thermal insulation**	To reduce pain, keep the wound site at its optimal temperature.
6	**Absorption of excessive exudates**	Controlling the amount of exudates produced in the wound.
7	**Permeability of oxygen**	Allow oxygen diffusion into the wound area to accelerate cell activity.
8	**Physical & Mechanical properties**	Similar to native skin's structure.
9	**Minimum tissue-trauma (pain)**	Reducing patient's pain at the time of application & removal.
10	**Cost-effectiveness**	Offering a reasonable wound-dressing.
11	**Free-availability**	Accessible to all medical care centers or patients.

3. FILM-FORMING SYSTEMS:

Film-forming systems (FFSs) are advanced topical drug delivery platforms designed to generate a thin, continuous film on the skin or other biological surfaces following application. These systems are generally formulated as solutions, gels, emulsions, or sprays containing film-forming polymers, volatile solvents, plasticizers, and active pharmaceutical ingredients. Upon application, evaporation of the volatile components leads to the formation of a transparent and adherent film that remains in close contact with the application site, enabling sustained drug release and improved therapeutic efficacy [3,12].

Conventional topical dosage forms such as creams, ointments, and lotions often suffer from drawbacks including poor residence time, easy removal by clothing or washing, frequent reapplication requirements, and reduced patient compliance. Film-forming systems have emerged as a promising alternative because they combine the advantages of semisolid formulations with the prolonged skin retention characteristics of transdermal patches while maintaining superior cosmetic acceptability [13]. The formed film acts as a drug reservoir and provides controlled release of the incorporated therapeutic agent, thereby enhancing local or systemic drug delivery depending on the formulation design [3,14].

The performance of an FFS is largely influenced by the type of polymer, solvent system, and plasticizer employed. An ideal film should exhibit rapid drying, flexibility, transparency, adequate adhesion, non-irritancy, and resistance to mechanical abrasion. Both water-soluble and water-insoluble polymers have been investigated to achieve optimal film properties and drug-release behavior [13]. Recent advances in polymer science and formulation technologies have further expanded the application of FFSs in wound healing, antimicrobial therapy, pain management, dermatological disorders, and transdermal drug delivery [4,15].

Particularly in wound management, film-forming systems provide a protective barrier against microbial contamination while maintaining a moist environment favorable for tissue repair. Their ability to conform to irregular wound surfaces, reduce cross-contamination, and prolong drug residence time has attracted considerable attention for the development of next-generation wound care products [15]. Owing to these advantages, film-forming systems are increasingly recognized as a

versatile and patient-friendly platform for topical and transdermal drug administration.

3.1 Mechanism of Film-Forming System for Topical Drug Delivery

Film-forming systems in the form of solutions, gels, or emulsions are applied directly to the skin as liquid or semi-solid formulations. Upon application, the volatile solvent evaporates, leading to the formation of a thin, continuous polymeric film on the skin surface. The formed film adheres closely to the skin and acts as a reservoir for the incorporated drug. The drug is then released in a controlled manner and penetrates into the skin layers, providing prolonged therapeutic action. This mechanism enhances drug retention at the application site, improves bioavailability, and reduces the frequency of application [16]. Figure 2. showing application and spreading of the liquid formulation, solvent evaporation, and formation of a continuous polymeric film on the skin for sustained drug release.

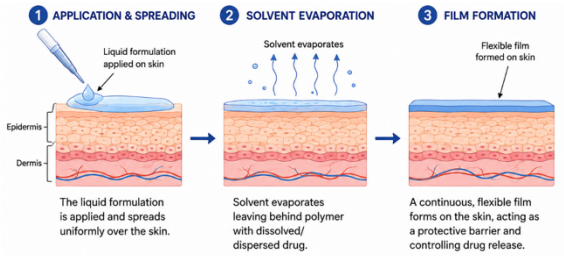

Figure 2. Mechanism of Film-Forming System (FFS) for topical drug delivery

3.2 Benefits of film-forming systems:

Film-forming systems offer several advantages over conventional topical formulations. Upon application, they form a thin, transparent, and flexible film that adheres closely to the skin, resulting in prolonged residence time and improved drug retention. These systems provide controlled and sustained drug release, reducing the frequency of application and enhancing patient compliance. Additionally, the formed film acts as a protective barrier against external contaminants while maintaining good cosmetic acceptability due to its non-greasy and invisible nature. Their ability to conform to irregular skin surfaces further makes them suitable for wound healing and localized drug delivery applications [3].

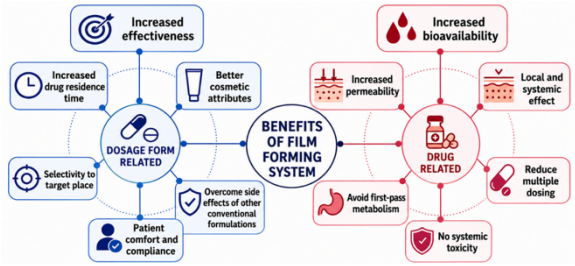

Figure 3: Benefits of film forming system related to dosage form and drug

3.3 Advantages of Film-Forming Systems over Conventional Topical Formulations

A comparative assessment of film-forming systems and conventional topical formulations provides valuable insight into their formulation characteristics and performance attributes. The accompanying tabular comparison presents differences across various parameters, while the schematic illustration offers a visual representation of these distinctions. Together, they facilitate a clearer understanding of how the two approaches differ in terms of their behavior after application and overall delivery performance. This combined presentation enables readers to interpret comparative features more effectively and comprehensively [15,17].

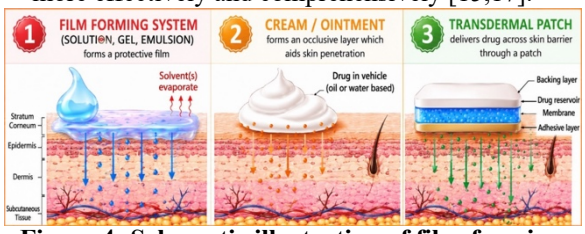

Figure 4: Schematic illustration of film-forming system & conventional topical formulations

Table 2: Comparison of Film-Forming systems with Conventional Topical Formulations

PARAMETERS	FILM FORMING SYSTEMS	CREAM/ OINTMENT	TRANSDERMAL PATCH
Cosmetic Appearance	Smooth, invisible, transparent layer	Thick, Visible, Shiny/oily layer	Visible patch stuck to skin
Application	Easy spreading, non-greasy, thin film	Greasy, uneven layer	Fixed size, Bulky, sometime sticky, Require adhesive

Adhesion	Strong adhesion, long-lasting	Easily wiped off	Adhesive may loosen/irritate
Drug Release	Sustained release	Mostly immediate release	Sustained but limited drug loading
Occlusive property	Semi occlusive film	Variable Occlusiveness	Occlusive film, Risk of maceration
Comfort	Breathable and flexible	Greasy and uncomfortable	Rigid, sometimes uncomfortable
Dose Frequency & Flexibility	Less Frequent, Adjustable dosage	Frequent, Adjustable dosage	Infrequent, Fixed dosage
Side effects	Minimal	Local irritation	Irritation/Maceration
Water Resistance	Resistant to wash-off	Washes off easily	Adhesive weakens with moisture
Compliance	High patient compliance	Moderate patient compliance	Moderate patient compliance

3.4 Types of Film-Forming Systems

Film-forming systems (FFSs) are topical formulations that undergo transformation into a thin, continuous film upon application to the skin or wound surface. Depending on their physical state and formulation composition, FFSs are generally classified into film-forming solutions, film-forming gels, and film-forming emulsions. Each type possesses distinct characteristics that influence drug release, film formation, patient acceptability, and therapeutic performance.

3.4.1 Film-Forming Solutions

Film-forming solutions are homogeneous liquid preparations in which film-forming polymers and active pharmaceutical ingredients are dissolved in volatile solvents or solvent mixtures. Upon application, the solvent evaporates rapidly, resulting in the formation of a transparent and flexible polymeric film on the skin. The formed film acts as a protective barrier and serves as a reservoir for sustained drug release [12].

Film-forming solutions offer several advantages, including ease of application, rapid drying, uniform film formation, and improved cosmetic appearance. These systems are particularly suitable for delivering antimicrobial, anti-inflammatory, and analgesic agents to wounds and skin disorders. The selection of an appropriate polymer and solvent system is critical for achieving desirable film properties such as adhesion, flexibility, and durability.

3.4.2 Film-Forming Gels

Film-forming gels are semi-solid formulations in which film-forming polymers are dispersed or dissolved within a gel matrix. These systems combine the advantages of conventional gels with the film-forming capability of polymeric formulations. Following application, solvent evaporation leads to the formation of a thin adherent film while maintaining the ease of spreading associated with gels.

Compared with film-forming solutions, film-forming gels generally exhibit higher viscosity, allowing better retention at the application site and reducing formulation runoff. They are particularly beneficial for irregular wound surfaces and moist wound environments where prolonged contact between the formulation and the tissue is desirable. In addition, film-forming gels can improve patient comfort by providing a cooling sensation and reducing the frequency of application [18].

3.4.3 Film-Forming Emulsions

Film-forming emulsions are biphasic systems consisting of oil and aqueous phases stabilized by emulsifying agents and incorporated with film-forming polymers. After application, evaporation of the volatile components results in the formation of a continuous film on the skin

surface while simultaneously providing emollient and moisturizing effects.

These systems are particularly useful for the delivery of lipophilic drugs and bioactive compounds with limited aqueous solubility. The presence of an oil phase enhances skin hydration and can improve drug permeation through the stratum corneum. Film-forming emulsions also offer good spreadability, patient acceptability, and the ability to combine protective film formation with moisturization. Consequently, they have gained increasing attention for wound healing, dermatological therapy, and cosmetic applications [19].

3.5 Composition of Film-Forming Systems

Film-forming systems (FFSs) are composed of several functional ingredients that work together to produce a stable formulation capable of forming a thin, flexible, and adherent film upon application to the skin or wound surface. The composition typically includes film-forming polymers, solvents, plasticizers, active pharmaceutical ingredients, penetration enhancers, preservatives, and other auxiliary excipients. Each component plays a specific role in determining the film-forming ability, mechanical properties, drug release behavior, skin adhesion, and therapeutic performance of the final formulation. The selection and concentration of these ingredients are carefully optimized to achieve rapid film formation, adequate flexibility, prolonged residence time, and enhanced wound-healing or drug-delivery efficacy [3,14]. The typical composition of film-forming systems used for wound healing and topical drug delivery is summarized in Table 1. The major components commonly incorporated into film-forming systems are discussed below.

3.5.1 Active Pharmaceutical Ingredients

Active pharmaceutical ingredients are the therapeutic agents incorporated within the film-forming matrix. Following film formation, the resulting polymeric film serves as a reservoir that allows localized and sustained drug release at the site of application. The selection of a suitable active ingredient depends on the intended therapeutic purpose, desired release profile, and compatibility with other formulation components.[12]

The selection of an appropriate drug is essential for the successful development of film-forming systems (FFSs). An ideal drug should have a low molecular weight (<500 Da), moderate lipophilicity (Log P 1–4), and high potency with a low dose requirement to ensure effective incorporation and skin permeation. Adequate aqueous and lipid solubility is also important for formulation development and drug release. The drug should be physiochemically stable, compatible with the polymer matrix and excipients, and cause minimal skin irritation or sensitization. Drugs with a short to moderate half-life and those undergoing extensive first-pass metabolism are particularly suitable, as topical or transdermal film-forming systems can provide sustained drug release, reduce dosing frequency, and improve bioavailability and patient compliance [20].

3.5.2 Polymers

Polymers constitute the backbone of film-forming systems and are primarily responsible for the formation of a continuous film upon solvent evaporation. They determine critical film characteristics such as mechanical strength, flexibility, adhesion, permeability, and drug-release behavior. The physicochemical properties of the polymer significantly influence the quality and performance of the final film. Therefore, selecting a suitable polymer is essential for achieving optimal therapeutic outcomes and patient compliance.[21]

3.5.3 Solvents

Solvents provide a medium for dissolving or dispersing formulation ingredients and facilitate uniform application to the skin or wound surface. Following application, solvent evaporation triggers film formation by depositing the polymeric matrix onto the target site. The choice of solvent affects drying time, drug solubility, spreadability, and overall film appearance. An ideal solvent system should ensure efficient film formation while minimizing irritation and maintaining formulation stability[22].

3.5.4 Plasticizers

Plasticizers are incorporated to improve the flexibility and elasticity of the formed film. They reduce intermolecular interactions within the polymer matrix, thereby enhancing polymer chain mobility and preventing film brittleness. The presence of an appropriate amount of plasticizer contributes to improved mechanical properties and patient comfort, particularly in formulations intended for application on flexible body surfaces.

3.5.5 Penetration Enhancers

Penetration enhancers are included to improve the transport of active substances across the skin barrier. These agents temporarily modify the

structure or permeability of the stratum corneum, thereby facilitating drug diffusion into deeper skin layers. Their incorporation can improve local drug availability and therapeutic efficacy, especially in formulations intended for dermal or transdermal drug delivery.[23]

3.5.6 Other Excipients

In addition to the primary formulation components, various auxiliary excipients may be incorporated to enhance product stability, performance, and patient acceptability. These excipients contribute to maintaining physicochemical stability, preventing microbial contamination, improving aesthetic properties, and optimizing formulation functionality. Their selection should ensure compatibility with the active ingredient and the overall formulation while maintaining safety and efficacy [23].

Table 3. Typical Composition of Film-Forming Systems [17,24,25]

Component Category	Type/Class	Common Examples	Concentration Range (% w/w)	Function
Film-forming polymers	Synthetic polymers	Eudragit® RS100, Eudragit® RL100, Polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP)	2–20	Formation of a continuous, flexible film after solvent evaporation
	Semi-synthetic polymers	Hydroxypropyl methylcellulose (HPMC), Hydroxypropyl cellulose (HPC), Ethyl cellulose (EC), Sodium carboxymethyl cellulose (NaCMC)	2–15	Film formation, viscosity modification, controlled drug release
	Natural polymers	Chitosan, Sodium alginate, Gelatin, Hyaluronic acid, Pullulan, Pectin	1–10	Biocompatibility, bioadhesion, wound healing enhancement
Gelling agents	Synthetic gelling agents	Carbopol 934, Carbopol 940, Poloxamer 407	0.5–5	Provide gel consistency and improve spreadability
	Natural gelling agents	Xanthan gum, Sodium alginate, Guar gum	0.5–5	Increase viscosity and improve wound residence time
Plasticizers	Hydrophilic plasticizers	Propylene glycol, Polyethylene glycol (PEG 400), Glycerol	1–15	Improve film flexibility and reduce brittleness
	Hydrophobic plasticizers	Triethyl citrate, Dibutyl sebacate, Tributyl citrate	1–10	Enhance elasticity and mechanical strength
Volatile solvents	Alcohols	Ethanol, Isopropyl alcohol	20–80	Rapid evaporation and film formation

	Organic solvents	Acetone, Ethyl acetate	10–60	Polymer solubilization and quick drying
Non-volatile solvents / Co-solvents	Hydrophilic co-solvents	Propylene glycol, PEG 400, Glycerol	5–30	Improve drug solubility and film integrity
	Permeation-enhancing co-solvents	Transcutol® P, N-Methyl-2-pyrrolidone (NMP)	2–20	Improve drug diffusion through skin
Penetration enhancers	Fatty acids and esters	Oleic acid, Isopropyl myristate (IPM)	1–10	Disrupt stratum corneum lipids and increase permeation
	Sulfoxides	Dimethyl sulfoxide (DMSO)	1–10	Enhance transdermal transport
	Terpenes	Menthol, Limonene	0.5–5	Improve drug penetration
	Solvent enhancers	Transcutol® P	1–10	Increase drug partitioning into skin
Preservatives	Parabens	Methyl paraben, Propyl paraben	0.01–0.2	Prevent microbial contamination
	Quaternary ammonium compounds	Benzalkonium chloride	0.01–0.1	Antimicrobial preservation
	Others	Phenoxyethanol, Sodium benzoate	0.1–1.0	Product stabilization
Vehicle	Aqueous vehicle	Purified water	q.s. to 100%	Formulation medium and solvent

3.6 EVALUATION OF FILM-FORMING SYSTEMS

The successful development of film-forming systems requires systematic evaluation of their physicochemical, mechanical, and pharmaceutical characteristics to ensure optimal performance and reproducibility. Characterization of FFSs provides valuable information regarding formulation quality, film integrity, drying behavior, adhesion, flexibility, drug content, release profile, stability, and skin compatibility. These parameters collectively determine the suitability of the formulation for clinical application and regulatory acceptance. Commonly employed evaluation and characterization methods for film-forming systems are presented in following table 4.

Table 4: Evaluation & Characterization Parameters of Film-Forming Systems [14,26,20,27]

Evaluation Category	Parameter	Purpose/Significance	Common Evaluation Method	Desired Characteristics
Physicochemical Properties	**Appearance and Clarity**	Determines aesthetic acceptability and formulation homogeneity.	Visual inspection against light and dark backgrounds.	Clear, uniform, and free from particulate matter.

	pH	Ensures compatibility with skin and minimizes irritation.	Digital pH meter.	Skin-friendly pH (4.5–6.5) for topical application.
	Viscosity	Influences spreadability, film formation, and residence time.	Brookfield viscometer or rheometer.	Adequate viscosity for easy application without runoff.
	Drying Time	Indicates the time required for solvent evaporation and film formation.	Stopwatch method on skin or glass surface.	Rapid drying (typically <5 min).
Mechanical Properties	**Film Thickness**	Affects drug release, flexibility, and patient comfort.	Digital micrometer or thickness gauge.	Uniform thickness throughout the film.
	Tensile Strength	Measures resistance to mechanical stress during use.	Universal Testing Machine (UTM).	High strength without brittleness.
	Percent Elongation	Assesses flexibility and elasticity of the formed film.	UTM stretching test.	Adequate flexibility to withstand skin movement.
	Folding Endurance	Evaluates resistance to repeated bending and cracking.	Repeated manual folding until breakage.	High endurance with no cracking.
Surface Characteristics	**Stickiness/ Tackiness**	Determines patient comfort and tendency to attract dust or clothing.	Texture analyzer or thumb-tack test.	Low residual tack after drying.
	Surface Morphology	Evaluates smoothness and uniformity of the film surface.	Scanning Electron Microscopy (SEM).	Smooth, homogeneous surface.
Adhesion Properties	**Bioadhesive Strength**	Measures the ability of the film to adhere to skin or mucosal tissue.	Texture analyzer or detachment force test.	Sufficient adhesion without causing discomfort.
	Peel Strength	Determines force required to remove the film.	Peel adhesion test.	Strong adhesion with painless removal.
Drug Delivery Performance	**Drug Content Uniformity**	Ensures uniform distribution of drug throughout the formulation.	UV-Visible spectroscopy or HPLC.	Drug content within pharmacopeial limits.
	In Vitro Drug Release	Evaluates release kinetics and therapeutic availability.	Franz diffusion cell or dissolution apparatus.	Controlled and reproducible drug release.
	Ex Vivo Skin Permeation	Predicts drug penetration through biological	Franz diffusion cell using excised skin.	Desired permeation profile and flux.

		membranes.		
Safety Evaluation	**Skin Irritation Test**	Determines potential for erythema, edema, or irritation.	In vivo or reconstructed human epidermis models.	Non-irritant and non-sensitizing.
	Cytotoxicity Assessment	Evaluates cellular compatibility of formulation components.	MTT assay or cell viability studies.	High cell viability and biocompatibility.
Microbiological Evaluation	**Antimicrobial Activity** (if applicable)	Assesses efficacy against wound pathogens.	Agar diffusion or broth dilution methods.	Effective inhibition of microbial growth.

3.7 Applications of Film-Forming Systems

Film-forming systems (FFSs) are innovative drug delivery platforms that form a thin, flexible, and adherent film at the site of application following solvent evaporation. The resulting polymeric film acts as a drug reservoir, providing prolonged residence time, controlled drug release, enhanced stability, and improved patient compliance compared with conventional topical formulations [3,28]. FFSs are widely explored for topical treatment of dermatological disorders, wound healing, fungal infections, inflammatory skin diseases, and localized pain, where they maintain therapeutic drug concentrations while minimizing systemic exposure [4,12]. They also show considerable potential in transdermal delivery by enhancing skin contact, drug permeation, and bioavailability for sustained systemic administration. [48]

Recent advancements include the incorporation of nanocarriers, liposomes, nanoemulsions, nanoparticles, and nanostructured lipid carriers to improve drug solubility, stability, skin penetration, and controlled release. Furthermore, bioactive compounds, peptides, and growth factors have expanded the application of FFSs in regenerative medicine. Their versatility in topical, transdermal, mucosal, and wound-healing applications makes FFSs promising candidates for next-generation pharmaceutical drug delivery systems [29].

Table 5. Major Drug Delivery Applications of Film-Forming Systems [20,30]

Application Area	Examples of Drugs/Bioactives	Therapeutic Purpose
Wound healing	Mupirocin, Silver sulfadiazine, Curcumin, Hyaluronic acid	Infection control and tissue regeneration
Anti-inflammatory therapy	Diclofenac, Ketoprofen, Ibuprofen, Naproxen	Pain and inflammation management
Local anesthesia	Lidocaine, Benzocaine	Local pain relief
Antifungal therapy	Clotrimazole, Ketoconazole, Amorolfine	Fungal skin infections
Antiviral therapy	Acyclovir	Viral skin disorders
Transdermal delivery	Nicotine, Estradiol, Testosterone, Clonidine	Systemic drug delivery
Dermatological therapy	Corticosteroids, Tacrolimus	Skin disorders and inflammation
Cosmetic and cosmeceutical delivery	Vitamins, Retinoids, Antioxidants	Skin care and rejuvenation

4. ADVANTAGES OF FILM-FORMING SYSTEMS OVER TRADITIONAL WOUND DRESSINGS

Film-forming systems (FFSs) offer several advantages over conventional wound dressings such as gauze, bandages, creams, and ointments. Upon application, these systems transform into a thin, transparent, and flexible film that conforms closely to the wound surface, providing intimate

contact and prolonged residence time. Unlike traditional dressings that may require frequent replacement, film-forming systems create a protective barrier that remains adherent to the skin, thereby reducing the need for repeated applications and minimizing patient discomfort [31,32].

The formed film protects the wound from external contaminants, microbial invasion, and mechanical irritation while maintaining a moist microenvironment that promotes tissue regeneration and accelerates wound healing. In contrast to conventional gauze dressings, which may adhere to the wound bed and cause trauma during removal, film-forming systems can provide non-invasive wound protection with minimal disruption to newly formed tissue [33].

Another significant advantage is their ability to serve as localized drug reservoirs. Therapeutic agents incorporated within the film can be released in a controlled and sustained manner, resulting in prolonged drug action, reduced dosing frequency, and improved therapeutic outcomes. Traditional topical formulations such as creams and ointments often exhibit poor retention at the application site due to rubbing, washing, or sweating, leading to reduced efficacy [34].

Film-forming systems also demonstrate superior cosmetic acceptability because the resulting film is generally transparent, non-greasy, and aesthetically pleasing. This characteristic enhances patient compliance, [46,47]particularly for long-term treatment of chronic wounds and dermatological conditions. Furthermore, modern film-forming systems can be formulated with bioactive compounds, nanoparticles, and wound-healing agents to provide antimicrobial, anti-inflammatory, and regenerative effects, thereby offering multifunctional wound care capabilities beyond simple physical protection [34,35].

5. RECENT ADVANCES IN FILM-FORMING SYSTEMS FOR WOUND HEALING

Recent advancements in film-forming systems (FFSs) have transformed them from simple protective wound coverings into multifunctional therapeutic platforms capable of promoting tissue regeneration, preventing infection, and delivering bioactive agents in a controlled manner. The integration of nanotechnology, natural biomaterials, smart responsive polymers, and regenerative medicine approaches has significantly enhanced the wound-healing potential of these systems. Modern FFSs are designed not only to provide a favorable healing environment but also to actively participate in tissue repair through targeted therapeutic interventions [34,36].

5.1 Nanoparticle-Based Film-Forming Systems

Nanoparticle-loaded film-forming systems have gained considerable attention owing to their ability to improve drug stability, skin penetration, antimicrobial efficacy, and sustained drug release. Various nanoparticles, including silver nanoparticles, zinc oxide nanoparticles, polymeric nanoparticles, lipid nanoparticles, and nanoemulsions, have been incorporated into film-forming matrices to enhance therapeutic outcomes. Silver nanoparticle-containing films exhibit potent broad-spectrum antimicrobial activity and have demonstrated accelerated wound closure in infected wounds. Similarly, curcumin-loaded nanoparticles incorporated into film-forming systems improve antioxidant activity and overcome the poor aqueous solubility of curcumin, thereby enhancing wound repair and tissue regeneration [37].

5.2 Bioactive and Natural Polymer-Based Systems

Natural polymers such as chitosan, alginate, hyaluronic acid, gelatin, collagen, pectin, and pullulan are increasingly being employed in film-forming wound dressings due to their biocompatibility, biodegradability, and intrinsic biological activities. Chitosan-based films possess antimicrobial and hemostatic properties, while hyaluronic acid promotes cell migration and angiogenesis. Collagen- and gelatin-based systems provide structural support for cellular attachment and extracellular matrix formation. The incorporation of natural bioactive compounds, including curcumin, aloe vera, honey, and plant-derived polyphenols, further enhances anti-inflammatory and antioxidant activities, contributing to improved wound healing performance [38,39].

5.3 Smart/Stimuli-Responsive Systems

Smart film-forming systems capable of responding to environmental stimuli represent an emerging area of wound-care research. These systems can modulate drug release in response to changes in pH, temperature, moisture, enzyme activity, or bacterial infection. pH-responsive films are particularly attractive for chronic

wounds because wound pH changes during different stages of healing and infection. Temperature-sensitive polymers and moisture-responsive materials can further optimize drug delivery according to wound conditions. Such adaptive systems enable on-demand therapeutic release, minimize unnecessary drug exposure, and improve treatment efficiency [40].

5.4 Growth Factor and Cell-Based Approaches

Recent research has explored the incorporation of growth factors, stem-cell-derived products, and extracellular vesicles into film-forming systems to stimulate tissue regeneration. Growth factors such as epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF) play crucial roles in angiogenesis, collagen synthesis, and re-epithelialization. Furthermore, stem-cell-derived exosomes have emerged as promising bioactive agents capable of modulating inflammation and enhancing tissue repair. Film-forming systems provide a protective matrix that facilitates the sustained delivery and stabilization of these sensitive biological therapeutics, thereby improving their regenerative efficacy in chronic and difficult-to-heal wounds [41,42].

6. CRITICAL CHALLENGES IN CURRENT RESEARCH

Despite their immense potential, current research highlights several systemic bottlenecks:

1. Formulation Complexity and Drug Loading

There is an inherent conflict between polymer concentration, viscosity, and drug loading. High drug concentrations often inhibit solvent evaporation and compromise film flexibility. Conversely, lowering the polymer concentration to achieve a faster drying time reduces the sustained-release capacity of the film (26,43).

2. Exudate Management

Wounds inherently produce fluid (exudate). Hydrophobic films, while possessing high mechanical strength and water resistance, trap excess moisture. This can lead to maceration at the wound bed. Conversely, highly hydrophilic hydrocolloid networks may dissolve or disintegrate prematurely in the presence of heavy exudate (44).

3. Cytotoxicity and Degradation Rates

Many synthetic polymers or organic solvent systems require rigorous testing to ensure they do not induce local cytotoxicity. The degradation rate of the film must perfectly sync with tissue regeneration to prevent the need for mechanical removal, which can damage newly formed granulation tissue.

5. Clinical Translation

Despite considerable progress in the development of film-forming systems, their evaluation has predominantly been limited to in vitro, ex vivo, and animal studies, while evidence from human clinical trials remains scarce. Successful clinical translation requires thorough assessment of critical formulation attributes, such as drying time, tackiness, adhesion, flexibility, and mechanical strength, under diverse patient and wound conditions. In addition, the large-scale production of these systems presents significant challenges, particularly in maintaining formulation stability, supersaturation, and consistent product quality across manufacturing batches, thereby hindering their widespread commercial application [45].

7. COMMERCIALLY AVAILABLE FILM-FORMING PRODUCTS [4, 12, 20, 35]

Table 6. Commercially Available Film-Forming Products for Wound Healing and Skin Protection

Brand Name	Manufacturer	Indication	Dosage Form
Opsite® Spray	Smith & Nephew	Minor wounds, surgical sites, dressing fixation	Film-forming spray
Cavilon™ No Sting Barrier Film	3M Health Care	Skin protection, pressure injury prevention	Barrier film spray/applicator
Nobecutan®	B. Braun	Wound protection and dressing fixation	Film-forming spray

New-Skin® Liquid Bandage	New-Skin Products	Minor cuts, abrasions, skin cracks	Liquid bandage
Urgo Filmogel® Wounds	Urgo Medical	Superficial wounds and abrasions	Film-forming gel
Hansaplast® Spray Plaster	Beiersdorf AG	Minor cuts and abrasions	Spray plaster
Elastoplast® Spray Plaster	Beiersdorf AG	Small wounds and skin injuries	Film-forming spray
Nexcare™ Liquid Bandage	3M Health Care	Minor cuts and skin protection	Liquid bandage
Askina® Barrier Film Spray	B. Braun	Peri wound skin protection	Barrier film spray
Secura™ Protective Barrier	Medline Industries	Moisture-associated skin damage prevention	Barrier film
Cutimed® Protect Spray	Essity	Peri wound and fragile skin protection	Film-forming spray

8. CONCLUSION: Film-forming systems represent a promising next-generation approach for wound healing and topical drug delivery by combining sustained drug release, enhanced skin adhesion, improved patient compliance, and localized therapeutic action. Their versatility allows the incorporation of a wide range of therapeutic agents, including conventional drugs, nanocarriers, and bioactive molecules, thereby expanding their clinical potential. Ongoing advancements in polymer science and formulation technologies are expected to further improve their performance, making film-forming systems valuable alternatives to conventional topical dosage forms for future pharmaceutical and wound care applications.

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