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# A Review on Novel Film Forming Systems for Topical and Transdermal Drug Delivery

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**ABSTRACT**

Conventional formulations intended for topical and dermatological administration of drugs such as creams, foams, gels, and lotions are considered to reside for a relatively short duration in the targeted region. Sweating, clothing, movements, and susceptibility to being rapidly washed away upon contact with water are among the issues that have limited the effectiveness and duration of traditional topical formulations. For efficient treatment of local tissues, diseases, or wounds, the specific pharmacological component must remain at the treatment site for an appropriate period of time. Film-forming formulations represent a distinctive form of sustained-release dermatic products. They are applied to the skin as a liquid or semi-solid formulation. By evaporating the volatile solvent on the skin, the polymer contained in the formulation provides a solid layer. They can be used as an alternative to patch systems to administer a variety of drugs, either topically or systemically. It is a unique technique useful in offering a sustained-release drug delivery system with enhanced resistance time, decreased skin irritation, decreased dosing frequency, improved skin adhesion properties, increased drug release, and improved patient comfortability. This review briefly describes the dermal system, transdermal system, film forming system, advantages and disadvantages, formulation components of the Film Forming System (FFS), formulations, comparison of topical drug delivery systems, evaluation, commercialized of film-forming products, application devices and applications.

## INTRODUCTION

For several decades, most of the drug delivery for the treatment of acute or chronic illnesses has been achieved using various pharmaceutical dosage forms, such as tablets, capsules, creams, gels, ointments, suppositories, aerosols, injectables, etc., as drug carriers. Recent advances in pharmaceutical research have led to various unique drug delivery breakthroughs, which have made it possible to target the distribution of a medicine to a specific tissue and control the rate of drug delivery. Delivering a therapeutic dose of the drug to the site of action and maintaining the appropriate drug level in the tissue or body to elicit the desired pharmacological effect without major side reactions is the aim of any drug delivery system.

The skin is a particularly attractive organ for the application of pharmaceutically active substances due to its considerable size and easy access. The goal of drug administration through the skin might be either local therapy for dermatological illnesses or transdermal drug distribution to underlying tissues or systemic circulation. The topical drug delivery method can deliver drugs to the skin, skeletal muscle, and systemic circulation. Local target tissue can receive higher drug concentrations than systemic circulation.[1]

### Dermal System

Dermal treatments are mainly designed to have only a local effect. They are used for the treatment of acute skin infections and chronic skin diseases. At regular intervals, a liquid or semi-solid form is utilized. The formulation should be constructed in such a manner that the active substance present can permeate into the epidermis and maximize its action. To minimize a systemic impact, penetration into the dermis should be limited to a minimum. Especially in the case of antibiotics and immunosuppressants such as cortisone, a sufficiently high therapeutic value can be reached by topical administration without burdening the body with the substance. The risk-benefit profile can be positively changed.

Conventional topical remedies can be washed or rubbed off. The therapy is consequently sometimes unsuccessful since the active substance is not available in the epidermis in sufficient and required amounts. Using a larger concentration of the medication is not an option for this disadvantage because the concentration changes would simply expand, increasing the possibility of the drug getting into the dermis. A more elegant approach is supplied by formulations with a high degree of substantiality. The substantivity is described

as the capacity of the active ingredient to be stored at the place of action, on the surface, or as a reservoir in the stratum corneum.

Patches and plasters for dermal treatment of skin problems can be utilized to develop an alternative. They operate as a physical barrier between the product and the environment, protecting it from deterioration. This physical barrier tends to cause an occlusion of the skin, which, in addition to the affections of an unappealing appearance and a poor wearing experience, is adverse to patient compliance. In most situations, the patches cannot be cut to the required size, which often makes them unsuitable for individualized therapy. Skin damage can occur when the patches are taken off, which makes them inappropriate for use in diseases with a disturbed skin barrier. Allergies to the matrix adhesives are another concern; therefore, these solutions are not necessarily the best.[2]

**Transdermal System**

In transdermal systems, an active component incorporated into a liquid or semi-solid formulation is applied to the skin, or the active ingredient is delivered via a patch. In contrast to dermal systems, the purpose is to transport the active ingredient to the systemic circulation. Compared to other forms of delivery, transdermal systems provide several advantages. They are one technique to avoid the first-pass effect. Compared to injections or intravenous applications during the delivery of medications, the skin is not injured by needles or incisions. [3]

With patches, which are the most popular therapy, the sustained release of the drug is typically straightforward. The drug is incorporated into its formulation in the membrane of the patch and may be released through a control membrane or regulated by diffusion in the adhesive. Patches are typically straightforward to apply since they are simply applied at the correct time intervals to undamaged, hairless parts of the body surface. When appropriately administered, the drug release is continuous, such that the plasma level is steady. The active component is well protected from extraneous effects in the formulation by the backing layer. In the case of insufficient penetration, in addition to penetration enhancers, technologies such as microneedles or iontophoresis can also be utilized to increase penetration. The drawbacks of patches for transdermal usage are the same as in the use of dermal distribution, namely the beauty element. Currently, mostly opiates and hormones are given transdermally. However,

transdermal application is a possibility for several medications with a low therapeutic range and pharmaceuticals with stability problems.[4]

The development of topical formulations that can stay in contact with the skin for a longer period and, consequently, reduce the need for reapplication is of greater dermatological interest.[5]

## FILM FORMING SYSTEM

Pharmaceutical research faces the major challenge of developing novel technologies to give formulations different features that overcome the therapeutic limitations of conventional dosage forms, including adjustable release profiles, flexibility of use, the ability to carry more than one active ingredient, and enhanced patient compliance. [6]

The film-forming system (FFS) is a novel approach that can be used as an alternative to conventional topical and transdermal formulations. It is defined as a non-solid dosage form that produces a film in situ, i.e., after application on the skin or any other body surface. These systems contain the drug and film-forming excipients in a vehicle that, upon contact with the skin, leaves behind a film of excipients along with the drug upon solvent evaporation.[7]

FFS rapidly creates supersaturated systems upon skin application, thereby overcoming the issue of instability. Consequently, it enhances the penetration of drugs via the skin in comparison to alternative transdermal formulations.[8]

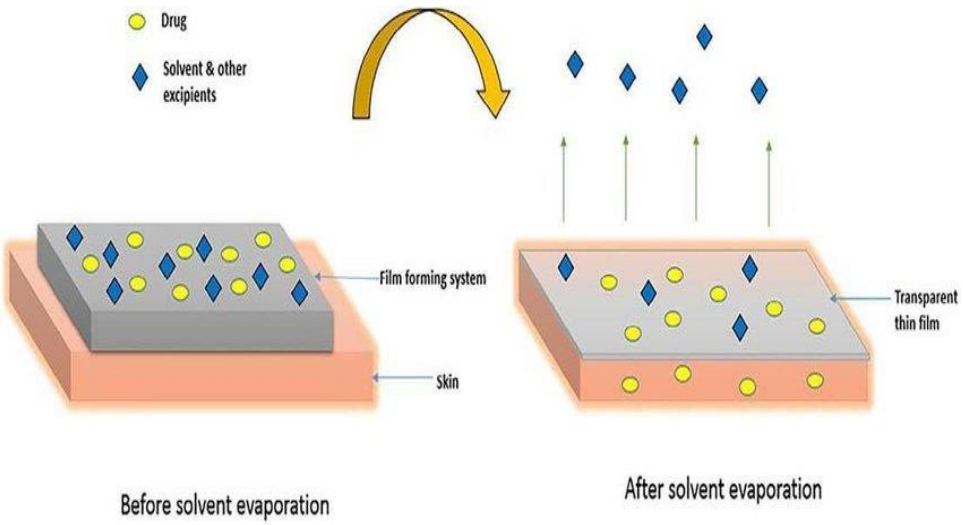


**Figure-1. Film formation after application**

These film-forming systems (FFS) are particularly promising formulations in the dermatological field because they overcome the limitations described above, and systems have also been studied for transdermal delivery of steroid hormones, analgesics, the development of mucoadhesive systems for stomach retention, and as an alternative to patching, aiming to increase drug safety and efficacy.

In the field of dermatological illnesses, there are also numerous uses such as antifungal administration, and treatment of burns and wounds, and also play a role in the prevention of transepidermal water loss, therefore assisting in skin hydration and other applications of skin care products.[5]

**Advantages of Film Forming System.**

- Film forming systems are simple and offer the advantages of transparency, non-greasy and lower skin irritation.
- Greater enhanced dose flexibility, greater patient compliance and aesthetic appearance.
- Preferred in early patients/patients receiving multiple medication to avoid drug interaction.
- The film-forming gel formulation has prolonged contact time with the applied nail surface and has a controlled release of the drug.

**Disadvantages of Film Forming System.**

- The formed film may detach from the applied site if it is not protected properly.
- These formulations have local side effects such as periungual erythema and proximal nail fold erythema.
- The therapy is longer, it takes a longer time to cure the disease of nail. [9]

## FORMULATION COMPONENTS FOR FILM FORMING SYSTEM

### ➢ Drug

For a transdermal application, appropriate drug must fulfill specific criteria that are independent of the dosage form. Due to the reality that the skin is a very powerful protective barrier for the whole body, not merely against physical or microbiological but also against medications, only powerful drugs are appropriate for this application method with a daily dose of less than 10mg.The size of the molecule is necessary to be small to offer a sufficient mobility in the skin structures (molecular weight < 500 Da). As the drug has to pass through lipophilic as well as hydrophilic areas of the skin on its way into the systemic circulation, it is helpful if the drug is neither very hydrophilic nor excessively lipophilic (log P between 1 and 3). Therefore, molecules with a pH value between 5 and 9 in an aqueous condition are preferred for transdermal application.

Further criteria that are favorable for the transdermal delivery of a medicine are a limited number of hydrogen bonding groups (<2) and a low melting point (less than 200 °C). The reservoir size of the dosage form is comparatively small due to the excessive thinness of the films (approximately 5–25 μm). Taking this into account, it seems evident that the film-forming solutions will be especially attractive for drugs that have,

- A high potency (example: the progestin Nestorone)
- A high skin permeability (example: nicotine)
- A high solubility in the solvent

A high potency is useful since it results in the lowest required daily doses for medical care. High skin permeability promotes high exploitation of the thin reservoir, provided an appropriate polymeric matrix is available. A high solubility in the formulation, lastly, allows substantial drug loadings and the creation of a high gradient between formulation and skin.[8]

### ➢ Polymer

The choice of film-forming polymer has the greatest effect on the substantivity of the formulation. The polymer is required to form films at the skin surface temperature (28 °C-32 °C) and should have a certain inherent flexibility and affinity to the skin to avoid the usage of

excessive amounts of plasticizer.[7] Polymers can be used individually or in combination. It is important that they can form a flexible, thin, transparent, and resistant film. Essentially, a distinction is made between water-soluble and water-insoluble film forms. Water-soluble polymers have a hydrophilic property, and most of them are not appropriate for substantivity increases in conventional formulations on the skin surface but are ideal for formulations from which the drug quickly permeates the stratum corneum to form a drug reservoir there. Some, such as methylcellulose, are suitable for improving the substantivity of thermo-emulsions via thermal gelation. In film-forming formulations, the aim is to develop a drug reservoir in the formulation itself, for which the hydrophilic polymers alone are not suitable.

Water-insoluble polymers provide water-resistant films with high substantivity but are generally brittle and inflexible, which makes adhesion to the skin difficult and causes the film-forming formulations to collapse. To enhance the homogeneity of the film and its flexibility, plasticizers are frequently added to the formulation, or the polymer is combined with a water-soluble polymer. Small polymers with a low molecular weight are usually better suited to film-forming systems.[10]

The viscosity of the formulation increases during the solvent evaporation process, especially more so for polymers with a high molecular weight. Furthermore, smaller polymers with shorter chain lengths can generally organize themselves better in space, so that the distance for the interaction of the polymer chains is closer to the ideal condition for gel formation. After the evaporation of the volatile solvent, the produced film adheres evenly to the skin, such that no major variances in film thickness result. This is particularly significant for the penetration of the active component into the skin since the concentration gradient between the film and the stratum corneum is thus also constant over a longer duration of time on all parts of the skin.[11]

- **Solvent**

The utilized solvent must be compatible with the skin, even if the skin barrier is damaged or affected. It should not irritate the skin during the evaporation process. The film-forming polymer must be adequately dispersed or dissolved in the solvent. The polymer layer should develop within less than one minute following the application of the formulation; hence, the solvent must evaporate quickly at skin surface temperature.

At the same time, this must proceed consistently and slowly enough on the skin surface that, despite the ensuing rise in the viscosity of the formulation, the polymers are still sufficiently mobile for contact and homogeneous film development. Ethanol and isopropanol are especially excellent solvents for film-forming compositions. Propylene glycol and isopropyl myristate have the advantage of further penetration-enhancing properties but do not evaporate.[12][13]

- **Plasticizer**

The primary challenge faced in the process of developing film-forming formulations is the brittle nature of numerous polymer films. When the film is excessively inflexible, it becomes incapable of accommodating the movements of the skin, particularly in areas of application such as the elbows. Consequently, the film's adherence to the skin is decreased. To reduce this issue, a combination of different polymers within a single formulation can be used to take advantage of the distinct properties of each polymer. However, the inclusion of a plasticizer is typically required. Plasticizers can infiltrate the spaces between the polymer chains of the film-forming polymer to interact with the functional group. The intermolecular forces between the polymer chains decrease, resulting in weaker bonds and increased flexibility of the film. Research has found that the optimal concentration of plasticizers is between 5% and 20% of the total dry weight. Utilizing the combination of several plasticizers might also be advantageous.[14][15]

- **Further excipients**

In addition to the basic components of a film-forming polymeric solution (polymer, solvent, and plasticizer), it may be appropriate to include additional excipients in the formulation. In the case of some polymers, such as the acrylate Eudragit E 100, it is advantageous to incorporate a crosslinker (such as succinic acid) into the formulation to enhance the stability of the film. For some drugs, a solubilizer or co-solvent can be necessary to improve the drug loading of the formulation and the drug flux. Further examples of supplemental excipients are antioxidants to stabilize oxidation-sensitive medications in the formulation during storage, sunscreens for the protection of photosensitive drugs, or dyes to ease the localization of the produced film for the patient.[8]

## FILM FORMING FORMULATIONS

- **Solutions / Spray**

The utilization of film-forming solutions and sprays is a popular approach in the development of transdermal dosage forms. The polymeric solution is applied to the skin in a liquid state or sprayed onto the skin. Through the process of solvent evaporation, it then forms an almost transparent layer [16]. The film-forming sprays and solutions consist of four primary constituents: the drug, solvent systems (including volatile and non-volatile vehicles), polymers, and penetration enhancers. The presence of a non-volatile component in the solvent system prevents the drugs from becoming solid particles when the volatile solvent component evaporates.

It is essential that the non-volatile component rapidly partition into the stratum corneum and help the drug partition into the stratum corneum. Additionally, the non-volatile component should increase drug diffusivity by disturbing the ordered intercellular lipids and enhancing penetration. The invisible drug depot building in the stratum corneum allows for slow absorption into the systemic circulation; this is the mechanism by which this delivery strategy works. Thus, a longer and improved penetration of medicine over the skin can be achieved following a once-a-day application.[17] Film-forming spray is manufactured as a metered dosage pump dispenser to supply a fixed amount of medicine, and it is sprayed on the topical location to produce a transparent film.[18]

Misra et al. were one of the first to make a liquid film-forming solution for the transdermal administration of testosterone. For that purpose, testosterone was dissolved in isopropyl alcohol. As film-forming polymers, polyvinyl alcohol, and polyvinylpyrrolidone were utilized in varied quantities. Liquid paraffin and polysorbate 20 were added. The *ex-vivo* permeation studies revealed a constant release of testosterone from the polymer film, following a burst release at the beginning. The retarded impact increased with increasing polymer concentration. The concept of transdermal administration of hormone derivatives using film-forming solutions was taken up by Schroeder et al., who developed new formulations for the delivery of ethinyl oestradiol.[19]

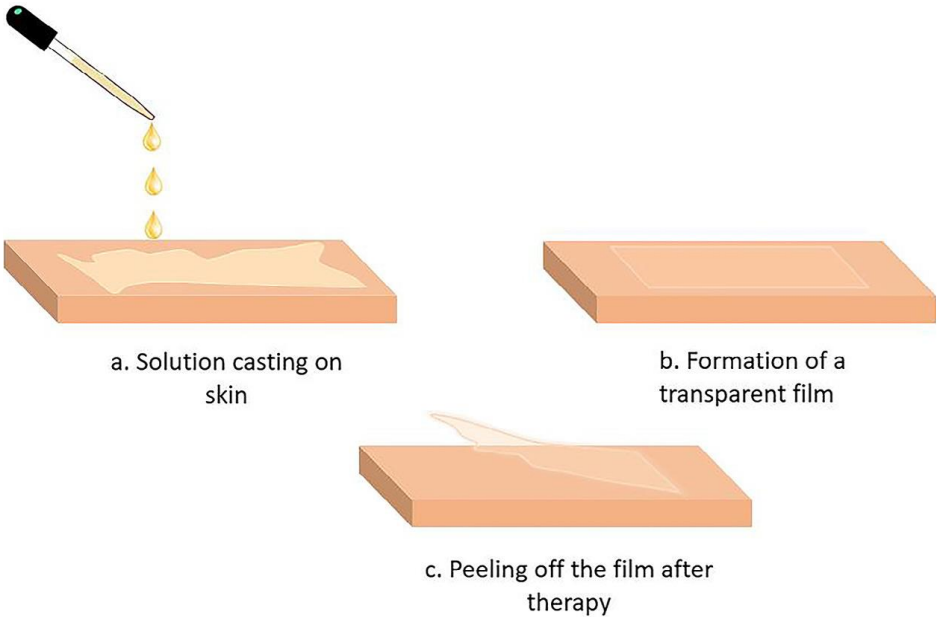


**Figure-2. Application of film-forming solution to skin.**

One application area of film-forming solutions is the cutaneous application of anti-infectives. Antiseptics and antibiotics need a sufficiently high and continuous concentration to effectively decrease or kill microorganisms. As the side effect profile rises with larger concentrations, it is particularly desirable here to transfer the active substance to the site of action by the shortest route and to prevent systematic administration in cases of dermal or underlying tissue infection. To achieve a steady drug concentration, conventional formulations must be administered at regular intervals. Retardation of the dermal system is a promising method for effective therapy and increased compliance.[20]

For the treatment of dermal fungal infections, Mori et al. effectively developed a transdermal spray containing voriconazole. The medication was dissolved in a solution of ethanol and acetone. In each formulation, a mixture of camphor and menthol was used as penetration enhancers, and polyethylene glycol 400 was added. Several mixtures of the film formers Eudragit® and Ethyl cellulose were compared to one another. A film-forming spray combining Eudragit® RLPO 10.05% and 5.02% ethyl cellulose proved to be effective for drug delivery.[21]

The topical delivery of local anesthetics is another field of application for film forming systems. For topical analgesia, Ranade et al. created a film-forming spray using the non-steroidal anti-inflammatory drug ropivacaine. The formulations were constructed of the

needed drug and various concentrations of Eudragit EPO®, which were both dispersed in ethanol and isopropyl alcohol. The analgesic impact of this spray is equal to that of a conventional lidocaine gel, but it may be administered more readily and less often, which enhances patient compliance.[22]

- **Gels**

Gels are defined as semisolid dosage forms incorporating both solid and liquid components. The liquid component may be hydrophobic or hydrophilic in nature, immobilized in a three-dimensional network of the linked solid components. Hydrogels are aqueous gels containing hydrophilic polymers that produce a three-dimensional network in water. The development of transdermal formulations is focused on utilizing various polymers as film-forming agents and gelling agents. The administration of film-forming gel involves applying a dose to the arms, shoulders, and internal areas of the thighs or abdomen to generate a thin bio-adhesive film on the skin [23]. The drug substance is dissolved in the film-producing vehicle and is thus incorporated into the film created on the skin. The film can function as an external reservoir or limit the delivery of drug substances to the skin, regulating the release of drugs. Complete skin contact across the whole application is essential; therefore, the formulation requires great flexibility to adapt to the movement of the skin, high substantivity, and strong adhesion to the skin for constant distribution and absorption of the drug. Hence, gelling agents, film-forming agents, plasticizers, preservatives, etc. are added to the formulation. Compared to previous forms, these systems offer easier usage and application, appropriate consistency and adhesiveness, good flexibility and elasticity, and simplicity of manufacture.[24]

In the state of wound healing, Kin et al. produced film-forming hydrogels with polyvinyl alcohol and polyvinylpyrrolidone as film-forming polymers, propylene glycol, ethanol, and water. The gel exhibited high adhesion to the skin and effective protection of the wound from external effects. The gel can also act as a base for the topical application of drugs.[25]

Vij and Saudagar created a film-forming gel for prolonged delivery of terbinafine hydrochloride. The polymers used were eudragit and hydroxypropyl cellulose in conjunction to provide a matrix film that would facilitate the release of terbinafine for an extended period. The formulas were prepared using 32 complete factorial designs. Li et al. created a film-forming gel formulation for prolonged release of rotigotine with hydroxypropyl cellulose and

carbomer 934. To optimize this formulation, the response surface analysis approach was applied.[24]

➢ **Emulsion**

Emulsions are semisolid or liquid preparations that can solubilize both lipophilic and hydrophilic drugs. Pharmaceutical emulsions consist of combinations of aqueous and oily phases stabilized by appropriate emulsifying agents. These can be oil-in-water (O/W) emulsions (the oil phase is dispersed in the water phase) or water-in-oil (W/O) emulsions (the water phase is dispersed in an oily continuous phase). The type of emulsion formed depends mostly on the type of emulsifiers, which is defined by the hydrophilic-lipophilic balance (HLB). An emulsifying agent is a substance that stabilizes the emulsion. There are different types of emulsifying agents, including surfactants, polymers, proteins (gelatin), and finely divided solid particles (bentonite).[26]

In the case of film-forming emulsions, the used polymers serve not only as film-forming agents but also as thermodynamic stabilizers of the emulsion, which may minimize the quantity of emulsifier needed to stabilize the emulsion and therefore the risk of skin irritation. Emulsions generally show great compliance with the patient, as they are comfortable to apply due to their usually lower viscosity and, in contrast to gels, still have a lipophilic phase without occluding properties.

The advantage of film-forming emulsions over semisolid formulations is that they permit the treatment of wider regions of damaged skin with prolonged contact time and acceptable substantivity, thus allowing continuous dermal therapy for chronic conditions.[27]

Lunter et al. developed film-forming emulsions for sustained dermal administration of nonivamide with Eudragit NE and RS 30D as film formers. In another investigation by Lunter et al., the in vitro skin permeability and penetration of nonivamide from the produced film-forming emulsions were studied. It was revealed that the rate of penetration of the active material is governed by diffusion through the polymeric matrix in which the droplets were embedded. Thereby, constant penetration rates and efficient API concentrations in the skin could be maintained for a duration of 12 hours.[28]

Padula et al. formulated transdermal films and a microemulsion for the transdermal application of levothyroxine. For the microemulsion, isopropyl myristate and isobutanol are mixed, and polysorbate, sorbitan monolaurate, and water are mixed. The levothyroxine was incorporated into the microemulsion and stayed in the oily outer phase. The permeated amount of levothyroxine from the microemulsion was the same regardless of the concentrations. In later phases, the microemulsions were loaded into the transdermal films, which improved the skin retention of levothyroxine, which made the concentration scalable, and the use of this microemulsion as a continuous-release formulation possible.[29]

## COMPARISON OF TOPICAL DRUG DELIVERY SYSTEM [12]

Film-forming systems (FFS) serve as an intermediary between transdermal patches and semisolid dosage forms, providing the advantages of both. Table 1 provides a summary of the benefits of FFS compared to patches and ointments. Figure 3 illustrates the drug permeation pattern of all three systems.

In the case of transdermal patches, the drug is stored in a reservoir and released slowly. It is then absorbed into the capillaries and transported to the systemic circulation. Alternatively, the drug can be formulated as a topical patch to penetrate the skin and target specific tissues for localized action. When drugs are included in semisolids, they may act on the surface of the skin or penetrate deeper into the layers of the skin to reach their intended target. However, the transport of pharmaceuticals throughout the body is restricted owing to a variety of circumstances. Film-forming technologies may serve as both semisolids and patches and can provide topical as well as transdermal delivery as needed.

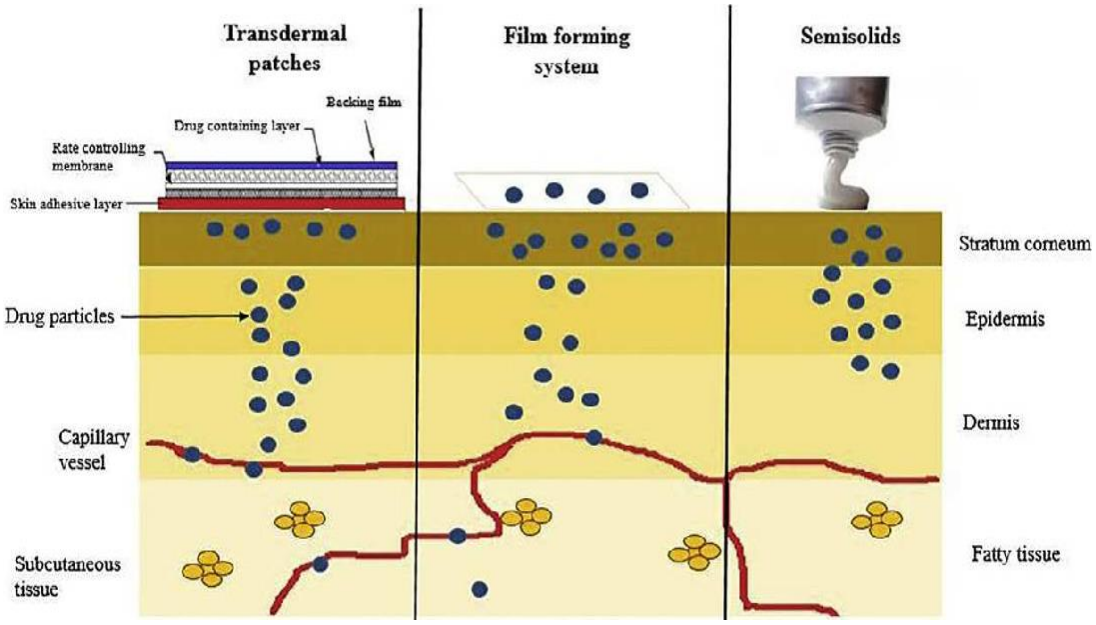


**Figure-3. Topical and transdermal drug release profile**

| Table-1. Comparison of Topical Drug Delivery System | | | |
|---|---|---|---|
| | **Patch** | **Film Forming System** | **Semisolids** |
| **Visual Appearance** | Highly Visible | Almost Invisible | Visible |
| **Skin Feel** | Non-Sticky, Non-Greasy | Non-Sticky, Non-Greasy | Sometimes Sticky, Greasy |
| **Administration** | Convenient | Convenient | Sometimes Messy |
| **Dose Adjustment** | Low | High | High |
| **Dosing Frequency** | 1-7d | 1-2d | 1d or less |
| **Sustained Release** | Yes | Yes | No |
| **Occlusive Properties** | Yes | No | No |
| **Wipe Off Resistance** | Yes | Yes | No |
| **Residual Remains** | Possible | No | No |

## EVALUATION

### 1. Film formation

The films are formed in a Petri dish or on a removed pig ear skin. Film-formation is examined and rated as full and uniform, incomplete or non-uniform, with or without

precipitation of the film-forming polymer. The cosmetic characteristics of the film are mentioned in terms of transparent or opaque, sticky, or dry, and peelable, or non-peelable.[30]

**2. Film flexibility**

Film flexibility is measured based on cracking and skin fixation, and this is done by stretching the skin in 2-3 directions. The film is categorized as flexible if there is no cracking or skin fixation and non-flexible if there is cracking and skin fixation.

**3. Drying time**

For the evaluation of the drying time, the formulation is applied to the inside of the forearm of a volunteer. After a specific period, a glass slide is put on the film without pressure. If no fluids are visible on the glass slide after removal, the film is considered dry. If residues of the liquid are visible on the glass slide, the experiment will be repeated with an increase in drying time. A proper FFS should have a minimum drying time to prevent an extended waiting time for the patient.

**4. Stickiness**

The stickiness of the film formed is tested by pressing cotton wool on the dried film with low pressure. Depending on the number of cotton Fibers that are held by the film, the stickiness is graded as high if there is a dense accumulation of Fibers on the film, medium if there is a thin Fiber layer on the film, and low if there is infrequent or no adhesion of Fibers. This evaluation characteristic is vital since the formulation should be non-sticky to avoid adhesion to the patients' clothes.[24]

**5. Determination of water vapour permeability**

The water vapor permeability is defined as the quantity of water transmitted through a unit area of film in a given time. These water vapor permeation statistics are significant in establishing the penetration characteristics of the film as they have an effect on skin parameters such as hydration of the stratum corneum, blood flow, and skin temperature.

Films are developed using a solvent evaporation process on a Teflon plate and dried for 72 hours at room temperature. Circular samples are cut from the dry films. For the sample

preparation, glass vials with an opening are filled with distilled water, coated with the circular film samples and a silicone ring, and sealed firmly with an aluminum vial lid. The weight of the vial is calculated and then placed into a desiccator, providing an environment of 58% relative humidity or low relative humidity (about 0%). They are stored at a specified temperature for 72 hours and weighed after certain intervals. From the weight loss of the vials W (g), the water vapor permeability is estimated as the amount of water that penetrates through the film in proportion to the surface area A (cm2) and the time t (h).[16]

**6. Swab study**

A swab test may be done to evaluate the residence time of the film-forming system. For adhesion tests, glass is employed as a polar, hydrophilic substrate. Glass is chosen as the test surface because films sticking firmly to it would likewise demonstrate strong adherence to skin because both materials possess a polar surface structure.[31]

Dry swab test: This test evaluates the behavior of FFS on the skin in a dry state. A dry swab test can be performed on a glass plate. The glass plate is marked with six squares of 1 × 1 cm2. The developed formulation is applied in this area. Dry cotton swabs of the same volume are collected. Swabbing on the applied film is performed at 0 min, 30 min, 2 h, 4 h, 6 h, and 8 h and is checked for drug content following the extraction of drug from the swab.

Wet swab test: This test demonstrates the response of FFS when it comes in contact with water or perspiration. The technique for the wet swab test is the same as for the dry swab test; only the swab taken is soaked in water prior, and then the formulations are swabbed with this wet swab.[32]

**7. *In-vitro* diffusion study**

*In-vitro* diffusion experiments are used to predict the permeation characteristics of drugs *in-vivo*. The Franz diffusion cell is utilized to determine the release profile of the medication from the film-forming mechanism. The unit is made up of two compartments, the donor compartment, and the receiver compartment, between which the diffusion membrane is attached (egg membrane or cellophane). The donor compartment is exposed to the atmosphere, while the receptor compartment contains the diffusion medium. The sample arm in the receptor compartment permits sampling. A predetermined quantity of the drugs

containing the film-forming formulation is applied to the donor compartment. Samples are collected and examined by appropriate spectroscopic techniques for drug release.[24]

**8. *Ex-vivo* permeation study**

The *Ex-vivo* permeation investigations are done to examine the effects of the skin barrier on the developed film-forming system. Franz diffusion cell or Keshary-Chien diffusion cell may be used for permeation investigation. The rat's skin is positioned between the two compartments: the stratum corneum towards the donor compartment and the dermis toward the receptor compartment. The formulation is applied to the skin surface, which creates a film after drying. The receptor compartment contains phosphate-buffered saline (pH 7.4) kept at 37 ± 0.5 °C. Samples are collected at specific time interval and analysed by suitable spectroscopic method.[33]

**9. Skin penetration studies**

The formulation is spread evenly on the skin using a pipette or a spatula. After predetermined time intervals (e.g., 15 min, 1 h, 3 h, 6 h, 8 h, etc.) post-application, the residual formulation is removed. The film is wiped off with the use of cotton pads, and the amount of drug contained in the cotton pads is estimated, which is proportional to the amount of drug left in the film. Therefore, the quantity of drug penetrated may be determined by subtracting the remaining amount from the overall amount of drug contained in the formulation.[34]

**COMMERCIALIZED FILM FORMING PRODUCTS [12]**

Several industries have tried to create film-forming systems as a drug delivery platform and have marketed their products successfully. The firms with their supplies based on film forming technique are listed in Table 2.

**Table-2. Commercialized film forming system.**

| Product | Drug | Company | Formulation type |
|---|---|---|---|
| Lamisil Once® | Terbinafine hydrochloride | Novartis Consumer Health, Australasia, Pty Ltd | Film forming Solution. |
| Axiron® | Testosterone | Lilly USA, LLC | Film forming spray. |
| Medspray® the Patch-in-a-Can® | Terbinafine hydrochloride | MedPharm Ltd, UK | Film forming spray. |
| Liqui-Patch technology | Testosterone hydrocortisone | Epinamics GmbH, Germany | Film forming spray. |
| Durapeel Technology | Ropivacane | Crescita Therapeutics, Inc | Film forming gel |
| PharmaDur®Technology | Hydroquinone | Polytherapeutics, Inc | Film forming emulsion-gel |

**APPLICATION DEVICES**

An important issue in the continued advancement of film-forming solutions as an application device. Primarily, it is possible to apply the substance using either a pipette or a brush. However, the most effective method for applying the film-forming liquid would be through spraying. This would guarantee a controlled administration, specifically delivering an exact quantity onto a specified area of the skin with minimum patient participation. Utilizing a spraying apparatus would also greatly facilitate patient care [34], which is an essential condition for ensuring satisfactory patient compliance.

Suggestions for acceptable spraying devices are accessible in the literature. Morgan et al. for example created a metered dose topical aerosol for the application of ethanolic solutions of steroidal hormones [35]. The device comprised of a pressurized aerosol container with a metered valve, a nozzle with a specified spray angle, and a nozzle shroud to assure a perpendicular position of the nozzle to the skin. Leichtnam et al. have suggested similar devices, pressurized and mechanical, for the delivery of an ethanolic testosterone spray. Mechanical spraying systems are typically used for liquids with low viscosities and have the benefit that the filling can be accomplished without specific equipment. Pressurized devices on the other hand are more expensive to construct but can also deliver liquids with higher

viscosities. They usually offer a finer droplet size and consequently a more uniform distribution of the formulation over the sprayed surface than the mechanical devices. [36]

Metered-dose spraying devices have been utilized earlier with appropriate precision for the delivery of steroidal hormones.[37][38] For the application of the film-forming system, a spraying device is required, which is not necessary for the other dosage forms.

## APPLICATIONS

- Initially film forming techniques were mainly used in the field of surgery or wound care. Film-forming solutions or gels have been utilized as tissue glue for the closing of operative wounds.

- These wound care preparations can be without medications or with antibacterial agents to prevent infections in the wound.[38]

- It can also be utilized for non-medical reasons, such as the delivery of active ingredients contained in beauty items like silicone film-forming technologies used to produce cosmetic creams and ointments.[39]

- It can also be utilized as a transparent peel-off mask technology for skin hydration treatment, pimple problems, etc. [40]

- The film-forming process also has potential application as a substrate for various barrier membranes utilized in the industry. Barrier membranes are commonly used to protect workers from detergents, acids, bases and other dangerous chemicals, infra-red heat, UV exposure etc., e.g. hydrophilic, and hydrophobic creams and ointments, UV protective creams.[41]

- Film-forming polymers are sprayed on the soil which generates a membrane film thereby increasing the integrity of the soil and elevating the soil temperature, which is effective in crop protection.[42]

## CONCLUSION

In the upcoming years, topical drug delivery will be popularly used to improve patient compliance. The film-forming formulations give a novel platform to deliver drugs to the skin, both topical and transdermal. These film-forming techniques are simple and offer the benefits

of transparency, non-greasiness, decreased skin irritation, wipe-off resistance, enhanced dosing flexibility, and improved patient compliance. Also, it remains adhered to the affected part for a prolonged period without getting rubbed off. It provides sustained action and better relief than the conventional gels, therefore frequent reapplication is not necessary.

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