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**FILM FORMING SYSTEMS: AN EMERGING PLATFORM FOR DRUG DELIVERY**

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**ABSTRACT**

The objective of this review is to assess the potential of polymeric film forming systems as sustained delivery platform for topical drug delivery. The advantageous and superior cosmetic attributes of FFS (compared to conventional semi-solid formulations) that offer significantly improved patient compliance are also addressed. The conventional dosage forms require multiple daily applications frequently which results in poor patient compliance, especially in the treatment of chronic skin diseases. Consequently, development of sustained delivery systems for topical drugs permitting less frequent dosing is of continuing interest for dermatological therapy. In the current discussion, the film forming systems are described as a promising choice for topical and transdermal drug delivery.

**Keywords: Film forming systems, transdermal drug delivery, sustained release**

**INTRODUCTION**

The skin is the most easily reachable organ of the body and acts as a barrier against the molecules of the environment due to its low permeability to macromolecules. Percutaneous absorption of drug through skin mainly occurs via stratum corneum. This in turn is

made up of dead, keratinized epidermal cells and act as a barrier for penetration of drugs [1]. Therefore permeation of drug molecules across the skin is difficult. The aim of drug administration through skin is to treat skin diseases and absorption of drug via topical

and transdermal route. The present dosage forms i.e. patches, ointments; creams etc. are having certain limitations. Skin irritation is caused by patches, due to their occlusive properties causing obstruction of sweat ducts, which in turn prevents loss of water vapour from skin surface, difficulty in applying on the curved surface, pain while peeling off and poor aesthetic appeal [2]. Whereas, creams and ointments overcome some of these drawbacks but have other issues like they do not have persistent contact with the skin surface and can be easily wiped off by patient's clothes [3]. Therefore, repeated application is required in case of chronic disease. These semisolid dosage forms leave a sticky and greasy feel after application leading to poor patient compliance. Therefore, there is a need for development of a dosage form which permits less frequent dosing by maintaining a close contact with the skin for prolonged time period thereby improving the patient compliance [4].

But how these can be achieved? Two ways are envisaged involving formation of drug reservoirs on and in the skin. These require formation of a residual film of formulation, in which drug maintains same solubility and is resistance to washing and wear. Furthermore, it depends on manipulation of the formulation's transformation after

application to rapidly transfer drug into the outer layers of the SC, the slow diffusion from which can subsequently control delivery of the drug [5].

Therefore the aim of sustained dermal delivery will depend on: [6-9]

- Residual surface film
- Volatile excipients, evaporation of solvent which results in supersaturation
- Physiochemical properties of drug that governs the affinity for, and ability to diffuse through the SC

Film forming preparations are defined as non solid dosage forms that produce a substantial film in situ after application on the skin or any other body surface. Such compositions can either be liquids or semisolids with a film forming polymer as basic material for the matrix. The formed film is sufficiently substantial to provide a sustained drug release to the skin [10].

#### **Advantages of FFS:**

##### **Wearing comfort [12]**

The film formed on the skin by the polymeric solution is colorless, transparent and therefore almost invisible. When compared to patches that are highly visible this is an advantage of FFS. Moreover, this will have a positive impact on patient compliance

especially in female patients who prefer a discreet medication.

The films have flexibility and are thin. Therefore, the formed films are more comfortable to wear than the patches which are rigid and thick.

Semisolids formulations are also discreet forms as they do not persist visually on skin. But they leave a sticky or greasy feel after application. This can be avoided by film forming compositions.

### Application

For film forming system a spraying device is required that is not required for the other dosage form. By using spraying device the dosing of film forming solution can be performed with a higher accuracy than in case of semisolid formulations [13].

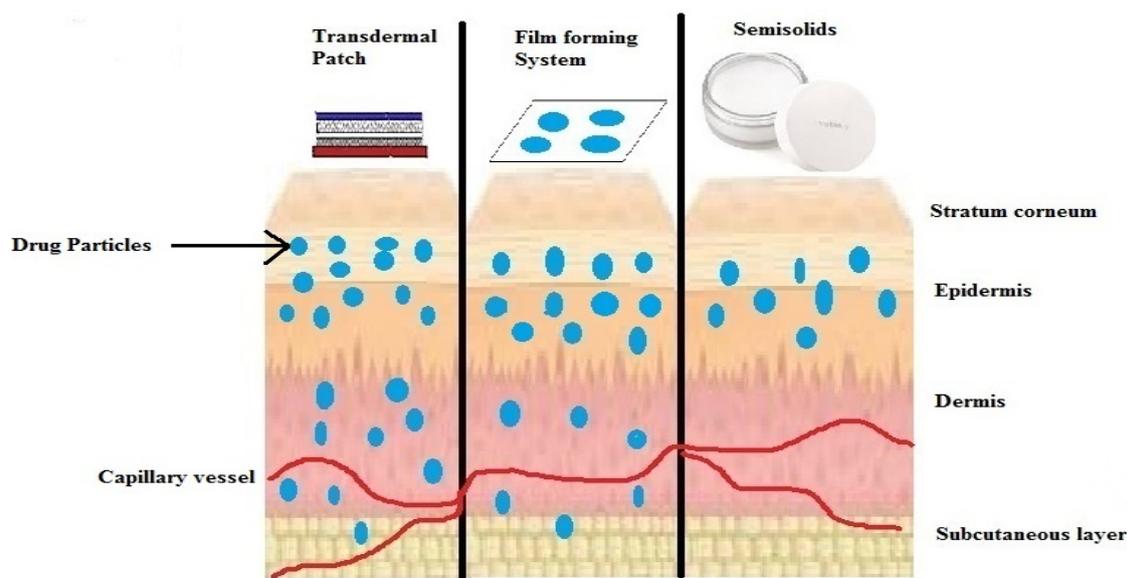
### Drug delivery

Film forming formulations provide a sustained drug release due to drug reservoir on the skin. The polymer matrix serves as fixation for the drug which is also an advantage because the drug cannot be wiped off contrary to the situation with semisolids. However transdermal patches provide more sustained delivery as depicted by **Table 1**.

### Cost

With regard to the manufacturing cost the manufacturing process of film forming solutions is quite simple. Contrary to the development of transdermal patches expensive equipment is not required.

An application device is needed for film forming systems which would generate additional cost in comparison to other dosage form.



Release profile of topical & transdermal Drug delivery systems.

Figure 1: Release profile of topical and transdermal drug delivery systems

### Comparison of topical drug delivery system

FFS forms an intermediate between the transdermal patches and semisolid dosage forms. Thus exhibiting the advantages of both the systems. **Table 1** summarizes the superiority of film forming systems over patches and ointments. In case of transdermal patches the drug is stored in a reservoir from which drug is released slowly and absorbed into capillaries from where it is transported to systemic circulation or it is formulated as a topical patch so as to penetrate into skin layers to reach the site of action but systemic delivery of drugs is limited due to various factors. Drugs incorporated into semisolids show their activity on the skin surface or penetrate into skin layers to reach the site of action but systemic delivery of drugs is limited due to various factors as shown in **Figure 1**. Film forming systems can function as both semisolids and patches and can provide topical as well as transdermal delivery as desired [14].

FFS are either dispersions or solutions of film forming polymer, depending on the solubility's of the polymer in the selected solvent, this will influence the film formation mechanism. Films formed by emulsions are cloudy and are less cosmetically acceptable as compared to transparent films of solutions.

In solution, the polymer chain comes in closer contact as the solvent evaporates, eventually forming a film. From polymer dispersion, the film is created via the physical process of polymer particle coalescence, the particle deforming as capillary forces increases with solvent evaporation as shown in **Figure 2**. Addition of plasticizer is required to lower the minimum film forming temperature thereby softening the polymer particles and facilitating their coalescence. The rate of film formation depends on evaporation of solvent evaporation that can, in turn give rise to differences in drug release profiles [15-16].

### Components of film forming systems

Drug for transdermal application of film forming systems the drugs need to have suitable properties which are independent of the dosage form. Generally the drugs which are applicable to these systems are highly potent which permeate the skin rapidly as revealed in **Table 2**, which causes no skin irritation and which are relatively stable to the enzymes present in the epidermis. Other properties of the drug suitable for transdermal drug delivery are listed below [17].

### Polymers

Polymers are the foundation of the FFS and a variety of polymers are available for the

preparation of these systems. In order to achieve the desired film properties, these polymers can be used alone or in combination with other film forming polymers. These polymers should form a clear flexible film at skin temperature. The list of polymers along with their properties are mentioned in **Table 3 [11 &17]**.

### Solvents

Solvents play a major role in film formation. They help in solubilizing the drug as well as affects permeation of drug through skin, Which in turn affects the flux. Depending upon the nature of the solvent and its permeation enhancing properties it can promote the drug transport to different extent in spite of its short contact time with the skin. This should be kept in mind for formulation development.

In addition to its solubilizing properties a suitable solvent for a film forming solution is required to be highly volatile to provide short drying times and thus good patient compliance. Solvents used are listed below in **Table 4 [11 &18]**.

### Plasticizer

Plasticizer is used to facilitate film forming and to increase the flexibility of the resulting film. Additionally, the formulation experiments have shown that the skin adhesion of the films can be modulated with the help of plasticizer. It has to be miscible with the polymer to produce clear films with low visibility on the skin.

It should have preferably low skin permeability to prevent leaking from the formed film. A substantial leaking would not only raise safety concerns but would also lead to a deterioration of the film properties. Commonly used plasticizers are glycerine, polyethylene glycol, sorbitol, dibutyl phthalate, propylene glycol and triethyl citrate [19].

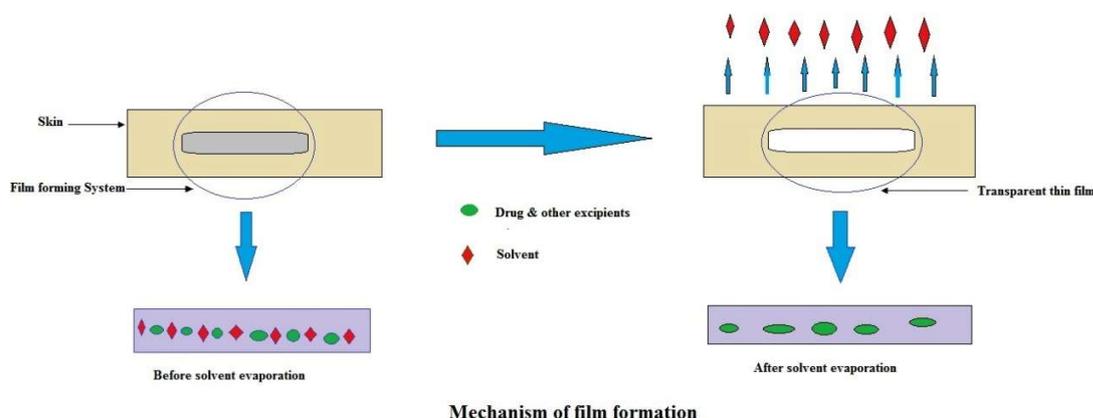
### Commercialized film forming products [20-25]

A number of film forming systems are developed and marketed by the company successfully. The companies with their products based on film forming technology are listed below in **Table 5**.

**Table 1: Comparison of topical drug delivery systems [11]**

	Patches	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

**Film formation mechanism**



**Figure 2: Mechanism of film formation**

**Table: 2 Ideal properties of drug for transdermal drug delivery**

Parameter	Properties
Dose	<10mg/day
Half life	10h or less
Molecular weight	<500 dalton
Partition coefficient log P	Between 1 and 3
Skin reaction	Non irritating non sensitizing
Oral bioavailability	Low

**Table 3: Polymer with their properties**

Polymer	Properties
HPMC	Produce a light, non greasy uniform film with good texture
Ethyl cellulose	Surface active agent, therefore adsorbs water providing easy dispersion, lubricity and comfort feel in occlusive state on application to skin Non toxic, nonirritating material
Hydroxyl propyl cellulose	Good film forming properties that form tougher films
PVP	Non ionic, pH insensitive polymer , water soluble
Chitosan	Excellent film forming properties
Eudragit	Excellent film forming ability Increases permeability and penetration of drug Self adhesive, good adhesion to skin

**Table 4 : Solvent and their categories**

Category	Solvents
Glycols	Propylene glycols, polyethylene glycols
Alcohols	Ethanol, butanol, isopropanol, benzyl alcohol
Other solvents	Ethyl acetate, oleic acid, isopropyl myristate

**Table 5: Commercialized film forming products**

Product	Drug	Formulation type
Lamisil once	Terbinafine hydrochloride	Film forming solution
Axiron	Testosterone	Film forming spray
Medspray the patch in a can	Terbinafine hydrochloride	Film forming spray
Liqui-patch technology	Testosterone hydrochloride	Film forming spray
Durapeel technology	Ropivacaine	Film forming gel
PharmaDur technology	Hydroquinone	Film forming emulsion –gel

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## Applications

### Arthritis

Gels are most commonly used topical preparations for the treatment of various diseases. Gels proved to be a good replacement for those formulations which seems to be uncomfortable when applied by another route such as oral route, as it may lead to peptic ulcers (in excessive usage of NSAIDS). Transdermal patches or films may be used as an alternative for the oral route for using NSAIDS. In the case of Rheumatoid arthritis, the treatment is carried out by regular usage of NSAIDS. Application of gels is easily wiped off due to clothes on joints and films may provide dryness and irritation after prolonged usage due to adhesive in it. Thus, there is a need to develop novel drug delivery systems for the treatment of rheumatoid arthritis, which are available in gel form but when applied on skin surface transform into film. These film forming gels (FIFOGE) are a novel approach helpful in providing sustained release of drug indomethacin [26].

### Wound care

In the past film forming preparations have been known predominantly from the field of surgery or wound care. Film forming solutions or gels has been used for example as tissue glues for the sealing of operative

wounds. The film formers mainly used in this area are fibrin as natural material and cyanoacrylates (octyl- and butylcyanoacrylate) as synthetic polymers [27]. Cyanoacrylates or recently acrylate polymers have also been used for the closure of superficial wounds as liquid bandages [28]. While most film formers are incorporated into the formulations as already polymerised material the cyanoacrylates are often applied as monomers. The polymerisation of the monomers takes place in situ and is catalysed for example by the presence of water on the skin. The velocity of the polymerisation process has to be controlled thoroughly to avoid inconveniences for the patient as the process is exothermic. Wound care preparations can either be drug free or combined with antimicrobial drugs to reduce the risk of infections in the wounds [29-30].

### Ostomy care

Apart from the wound care film forming preparations are also administered in ostomy care to protect the skin surrounding the ostomy wound from the aggressive bodily fluids [31].

### Mucoitis

Mucoitis induced by anti-neoplastic drugs is an important, dose-limiting and costly side effect of cancer therapy. The ulcerative

lesions produced by mucotoxic chemotherapy are painful, restrict oral intake and, importantly, act as sites of secondary infection of oral flora. Pretreatment assessment of oral cavity hygiene and mouthwashes seem to be effective in preventing the onset of oral mucositis. Some therapeutic agents, such as benzydamine, imidazole antibiotic and povidone iodine have shown some clinical evidence of their efficacy in reducing oral mucositis. Bioadhesive polymers appear to be particularly attractive for the development of drug delivery systems to improve intraoral administration and reduce the frequency of application and the amount of drug administered. Gels and films may be most suitable for this type of application and they are able to cover a wide area of mucosa for both drug delivery and physical protection [32].

Film forming gel formulations were prepared using mucoadhesive polymer to produce a physical barrier around the ulcers and form a medicated film for delivery of either diclofenac sodium or ofloxacin to treat the formed ulcer.

### **FUTURE PROSPECTS**

Polymeric film-forming systems (FFS) created in situ are promising sustained delivery platforms for topical drugs. With an

appropriate vehicle composition, FFS can facilitate an initial 'burst' release of drug, establishing a reservoir on and/or in the stratum corneum, from which a sustained, slower delivery to target sites in the lower skin layers can subsequently occur.

In conclusion, it appears that polymeric film-forming systems do have a positive role to play in the next generation of topical formulations designed to offer sustained drug delivery to and into the skin. The superior cosmetic attributes of FFS, compared to conventional semi-solid topical products, coupled with the potential for less frequent dosing regimens, are attractive features in terms of patient compliance and therapeutic outcome, especially for the treatment of chronic skin diseases.

Further research concerning the delivery kinetics and the suitability of this dosage form for a broader range of drugs is necessary for a better evaluation of the opportunities and the limitations of these delivery systems. Once this knowledge has been gained the film forming polymeric solutions might indeed present a viable alternative to the conventional dosage forms for the skin in the future.

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