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FILM FORMING SYSTEM: A REVIEW

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ABSTRACT

Topical film forming system is a novel approach for treatment of skin diseases give both topical and transdermal treatment. Rate and extent of drug absorbed through skin depends on the physiology of skin and properties of drug. FFS is defined as non-solid doses form which produces film in situ i.e., on the evaporation of vehicle, excipients in the formulations form film on skin. These are mainly drug and film forming polymers. Film forming system formulations consist of spray, solution, gel, and emulsion. Formed film acts as a matrix for sustained release of drug and it also improves the patient compliance. It can provide some desirable performance over conventional pharmaceutical dosage formulation such as easily applied, improve drug delivery, reduce dose frequency, omitted first pass effect, and enhance drug delivery. Various hydrophilic and hydrophobic polymers are used to give desired film properties, used either single or in combination with two or more polymers.

Keywords *–Polymeric film forming, Plasticizers, Epidermis, Drug*

INTRODUCTION

Drug product administered *via* topically through skin fall into two general categories-1) For local action, to stratum corneum and 2) For systemic effect to epidermis and dermis of skin. Drug release and absorption mainly depends on skin physiology and drug properties. First barrier for the drug absorption through skin is Stratum corneum. Only small amount of drug reaches at the target site. Conventional topical formulations includes gels, cream, ointment, patches, lotions, etc. have several limitations. Film Forming System (FFS) is alternative to these systems and acts as a novel approach of drug delivery through skin.

FFS is defined as non-solid doses form which produces film on the evaporation of vehicle, excipients in the formulations form film on skin. This is the drug and film forming polymer system, formed film acts as a matrix for sustained release of drug[1].

FFS is created by using physical process in which polymer particle coalescence and then solvent evaporation causes particle deformation. Plasticizers are added for the softening of film. Release profile of drugs from film depends on the rate of solvent evaporation[2]. Film formation facilitates the prolonged administration to the skin and drying of film improves its skin retention ability, it improves the treatment of skin infection. It also improves the patient compliance[3].

FFs have great application in topical therapy as it is easily applied to skin and also overcome the troubles with the other topical and oral doses form[4].

SKIN

The Skin is a function as the main physical barrier which protects us from external environment. It is generally described in terms of three tissue layers as depicted in Figure 1.

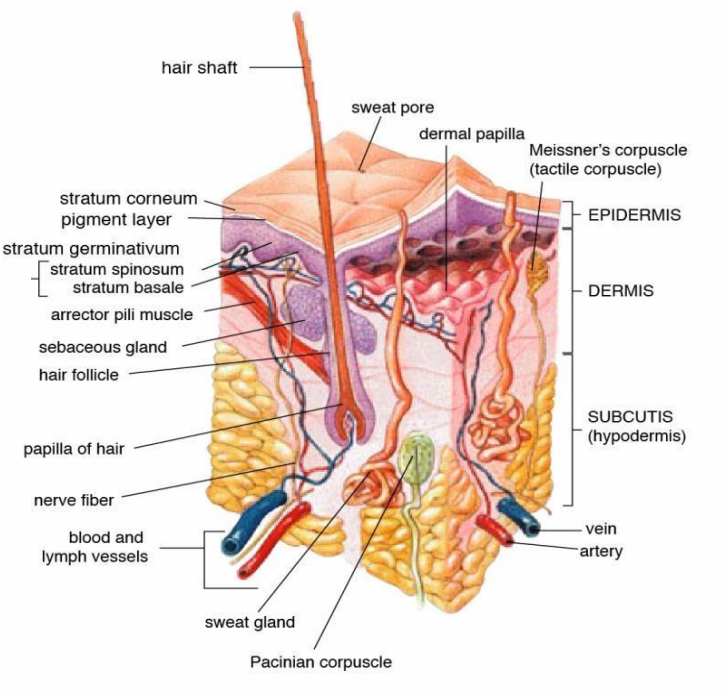

Fig. 1: Structure of skin

One of the best biological barrier and it is largest organ of human body and contributes to 16%-18% to normal body weight and total area about 2 $m^{2,5}$.

Skin composed of 3 main layers:

- Epidermis
- Dermis
- Subcutaneous

Epidermis

It is the squamous, stratified, keratinized epithelial layer (20-200 μm thick). It can produce yellow and brown black pigment melanin which contributes color and absorb UV light. Microscopic sections of the epidermis show two main parts: the Stratum Corneum (SC) and the stratum germinativum. The stratum corneum is the outer most Horney, very thin layer and consists of compacted flattened, dehydrated, keratinized cells in stratified layer. It can resist over 80% of skin permeability. It also consists of nearly non-permeable cornified cells called corneocytes. Keratinized layer of skin is responsible for keeping water in the body and other harmful chemicals out which making skin natural barrier for infection[6] (Figure 2).

- Stratum Lucidum is the additional thin layer of keratinized cells which are located beneath the stratum corneum. Mainly present on the palm of hand and on feet soles.
- Stratum Granulosum is a layer where keratinization begins. In this layer, lamellar granules appear and merge with the cell membrane, and these cells release glycophospholipids into intercellular space that forms the main constitute of the water permeability barrier.
- Stratum Spinosum the spinous cell layer of the skin composed of keratinocytes with a characteristic 'prickly' appearance due to the presence of desmosomes, important structural filament called cytokeratin.
- Stratum Basaleis a continuous single layer consists of columnar epithelial cells also called basal layer or stratum germinativum. It consist of Melanocytes, Langerhan and Merked cells.

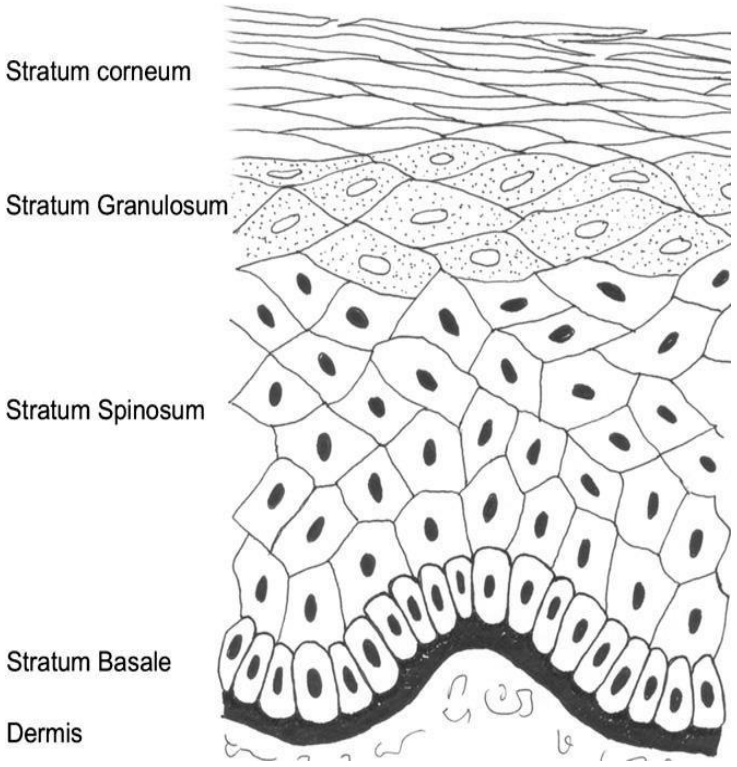

Fig. 2: Section of epidermis showing main layers

Dermis

It is composed of connective tissues connected tightly to epidermis by a basement membrane. It consists of hair follicles, sweat glands, sebaceous gland, lymphatic vessels, and blood vessels. The blood vessel in dermis provides nourishment and waste removal from its own cells. It is responsible for biochemical and biological degradation of material transported across skin. Beneath the dermis, the fibrous tissue opens out and merges with the fat-containing subcutaneous tissue.

Subcutaneous

Subcutaneous fat layer serves as a cushion for the dermis and epidermis. It also provides a thermal barrier. It consists of loose connective tissue, adipose tissue and elastin. It serves as a fat storage area; regulate temperature, nutritional support and mechanical protection. It carries main blood vessels and nerves to skin and may contain sensory organs[1].

FILM FORMING SYSTEM

Mechanism of film formation and permeation

Film forming system is applied directly to the skin and it forms a thin, transparent film *in situ* upon solvent evaporation as shown in Figure 3[7].

After application of the formulation to the skin, the composition of the film forming system changes significantly due to the loss of the volatile components of the vehicle which results in formation of residual film on the skin surface. In this process the concentration of drug increases, reaching saturation level and with the possibility of reaching super saturation level on the skin surface. Super saturation results in the enhanced drug flux through the skin by increasing the thermodynamic activity of the formulation without affecting the skin's barrier, thereby reducing the side effects or irritation.

The concept of super saturation can be explained by the modified form of Fick's law of diffusion. The Fick's law of diffusion given by

Eq.,

$$J = \frac{DKCv}{h}$$

Where
J=Rate of drug permeation per unit area of skin per unit time (flux)
D=Diffusion coefficient of drug
Cv=Concentration of drug
h=Thickness of barrier to diffusion

From this equation, it is clear that the rate of drug permeation across the skin is proportional to the concentration of the drug. However this is true when the entire drug is dissolved in the vehicle.

Equation describes the modified form of Fick's law of diffusion:

$$J=\alpha\ D/\gamma h$$

Where, a=thermodynamic activity of drug within formulation
γ=thermodynamic activity of drug within membrane

According to this equation, the flux of the drug is directly proportional to the thermodynamic activity of the system, which is related to saturation. However increasing the super saturation increases thermodynamic instability[5].

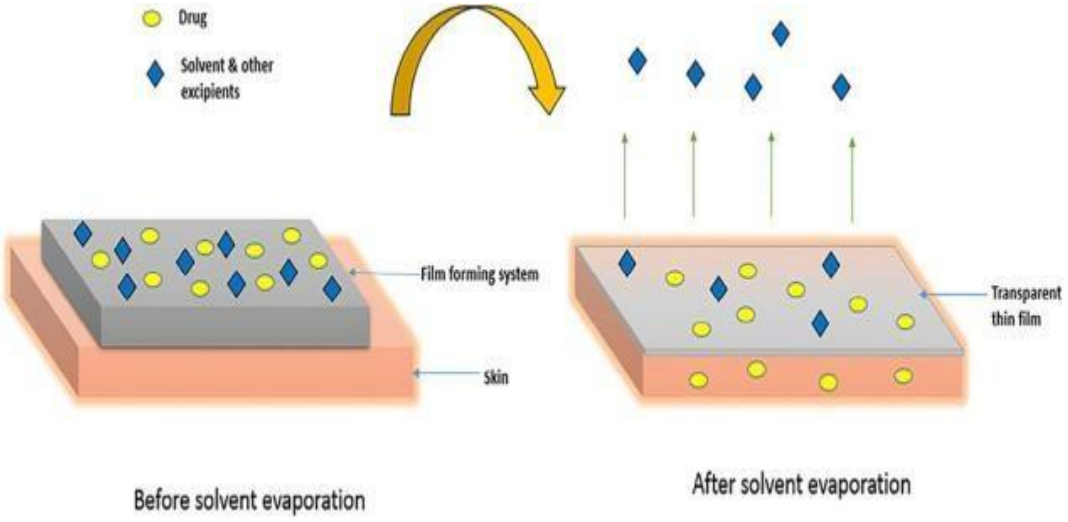

Fig. 3: Mechanism of film formation

Film forming application

Film forming systems offer a number of advantages over more conventional formulation.

- They can provide a unit dose and reduced dose frequency.
- Improved drug delivery.
- Easily applied to large application areas and the rapidly drying/absorbing nature can help to minimize losses of product onto cloths or other people.
- Fast dissolving and also we can make from it sustained drug delivery.
- Good patient compliance, reduced dose frequency.
- Hepatic first pass effect is omitted and GIT is avoided.
- Used in the wound care, as a tissue glues for closing of operative wound.

- In the application active ingredient through beauty product, e.g. Silicone film forming technology used as peel off mask for skin hydration treatment, acne problems etc.
- As a barrier membrane to protect workers in industry from strong acids, bases, IR rays, UV rays, hazardous chemicals etc. e.g.: UV protective creams, hydrophilic and hydrophobic ointments and creams[7,8].

PROPERTIES OF FILM

Almost all desirable properties of a coating film strongly depend upon the quality and integrity of the coating film which in turn depends upon the polymer chemistry, formulation variables, and the glass transition temperature of the dry film and the surface characteristics of the substrate among other factors.

Film Formation depends upon the Chemical and Physical Property, Molecular weight, Cross-linking, Density, Glass Transition Temperature, Viscosity of polymeric solution.

Formulation variables

- At the early stages of drying, the rate of solvent evaporation is essentially independent of the presence of polymer.
- The rate of evaporation depends upon-
  - The vapor pressure
  - The ratio of surface area to volume of the film
  - The rate of air flow[9].

The film forming preparation can be applied to the site regardless of shape and area, and can be retained for a long time as compared to conventional semi-solid preparations. Fig A)[7] shows that FFS forms an almost completely transparent fast drying film on application. Fig B)[7] shows that after drying, a non-tacky, flexible and easily peelable film is formed (Figure 4). There is an excellent adhesion of the formed film to the skin, hence wipe off resistance. Therefore the risk of transfer of active other people or clothes is reduced[9]

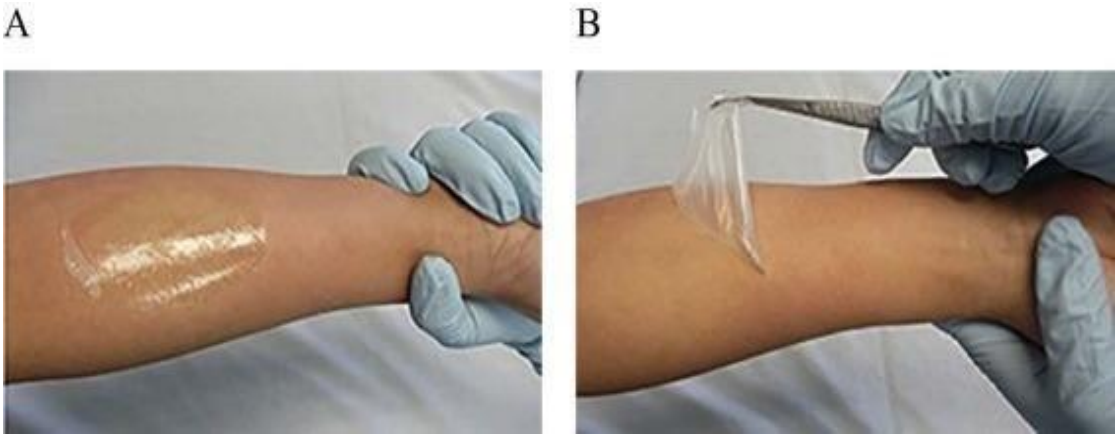

Fig. 4: (A) Before drying (B) After drying

1.1 Disadvantages of other topical preparations

Following are the disadvantages of other topical preparations which are overcome by film forming system:

- They are greasy and sticky preparations that can adhere to cloths, others skin and difficult to remove from skin, cloths and hair hence low patient compliance.
- Uncomfortable in hot climate.
- Wool fat and wool alcohol may cause sensitization in some people.
- Feasible for a less number of drugs.
- Slow onset of action, there is no rapid, bolus type drug administered by this route.
- Drugs incorporated into semisolids show penetrate into skin layers to reach the site of action but systemic delivery of drugs is limited due to various factors.
- These preparations can easily wipe off and hence repeated administration is required in chronic disease (Table 1).

Table 1: Comparison of topical drug delivery system

Features	Patches	Film forming system
Visual appearance	Highly visible	Almost invisible
Skin feel	Non-sticky, non-greasy	Non-sticky, non-greasy
Administer	Convenient	Convenient
Dose adjustment	Low	High
Dosing frequency	1-7 day	1-2 day
Sustained release	Yes	Yes
Occlusive properties	Yes	No
Wipe off resistance	Yes	Yes
Residual remaining	Possible	No

COMPONENTS OF FFS

Drug

For transdermal application of film forming system, the drugs required 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, which cause no skin irritation and which are relatively stable to enzymes present in the epidermis. Choice of the drug incorporated within the preparation depends on its solubility, lipophilicity and molecular weight. Stratum corneum is as a barrier for drug permeability across the skin, skin permeability increases with increasing lipophilicity, an octanol-water partition coefficient (log P=1-3), drugs oil and water solubility are ideal characteristics for good skin penetration. Nature of the polymer used in the FFS also has impact on the release and absorption of active components. Due to formation of skin reservoir, for rapid penetration through skin barriers drug would be more lipophilic, which will more suitable for achieving the sustained delivery profile (Table 2).

Table 2: Ideal properties of drug for transdermal and topical delivery

Parameters	Properties
Dose	<10 mg/day
Half life	10 hr. or less
Mol weight	<500 Dalton's
Log p	Between 1-3
Skin reaction	Non irritating
Oral bioavailability	Low

Polymer

Polymers are used in FFS provide excellent elasticity and flexibility, superior adhesion power when formed on the skin (Placeholder1)and form non-sticky film. Polymer is required to be soluble in highly volatile solvent and form clear, flexible film at skin surface temperature (28-32 °C).To achieve desired film properties, polymers are used either single or in combination with of two or more polymers. Polymers are mainly incorporated to give wide range of release and some polymers serves as an anti-nucleation and inhibits crystallization of drug (desirable feature of FFS polymer), which maintain the super saturation and improve of sustained delivery of drug. A polymer immobilizes the drug in a matrix on skin and also has impact on enhancing or retarding drug penetration. These are the effects due to the interaction of polymer with drug (Table 3).

Table 3: Properties of polymers used in FFS

Polymers	Properties
Hydroxy propyl methyl cellulose (HPMC)	White powder, odorless, tasteless. Soluble in water, but insoluble in diethyl ether, acetone and anhydrous alcohol. In cold water it will swells, acts as film forming agent, thickener, emulsifier, stabilizer and adhesion.
Hydroxyl propyl cellulose (HPC)	White to slightly yellow colored powder, odorless and tasteless. Soluble in water below 40 °C and soluble in polar organic solvents. It forms flexible film in combination with other polymers.
Poly vinyl pyrrolidine (PVP)	Soluble in water and other solvents. Adhesion and binding property.
Poly vinyl alcohol (PVA)	White odorless, soluble in water. Excellent film forming and adhesive properties.
Chitosan	Excellent film forming ability. Enhance release and permeation profiles. Control drug release.
Eudragit	Elastic, transparent, self-adhesion. Good adhesion to skin.
Ethyl cellulose	Non-toxic, non-irritating, non-allergic material. Good film forming properties that form tough film

Solvents

The solvents are very important components of FFS. It is acts as a solubilizing component for drug as well as polymer. Solvent is not a actual part of film former on skin because it evaporates quickly. Only solvents which have wide range of solubility for drug and polymer are used. In FFS solvents should be highly volatile at skin surface temperature, leaving behind drug and polymer (form film) and provides short drying time. Solvent also has direct impact on drug flux and permeation enhancing properties which can promote drug transport across skin although there is a short contact with skin[3]. Solvent should well spread on skin to form the smooth film with uniform thickness. These requirements of solvent are not fulfilled by water, so volatile organic solvents which have a short drying time and better patient compliance such as ethanol, ethyl acetate, isopropanol etc.

Plasticizers

In FFS main use of plasticizers are to facilitate the flexibility of film and improve adhesion of film to the skin. Plasticizers are mixed with polymers to produce clear, flexible film with low visible on skin. Efficacy of plasticizers depends on the polymer so no other rules can be applied to determine the concentration of plasticizers to be used in FFS. Proper amount of plasticizers will used. If low amount of plasticizers used it causes brittleness of film with low adhesion to skin and if excessive amount used it produce smooth but sticky film. Plasticizers improve the tensile strength of film, having low skin permeability to prevent leaking from the film. A leaking may raise the deterioration of the film properties. They are compatible with the polymers used in the formulation[3].

FORMULATIONS

Sprays/solutions

In Film forming system polymer is a main component. Film forming solution or spray is applied as a solution or spread on the surface of the skin and on evaporation of the solvent transparent film formed on skin. Film forming solution/spray is the advanced systems in the transdermal system. It composes four main components such as; drug, polymer, volatile, non-volatile solvent system and penetration enhancers[9].

A polymeric film forming topical spray formulation consist of hydrophilic film forming polymer present in amount about 2-50%, volatile solvent (20-99%). When formulation spreaded on human skin, it provides bio adhesive, micro porous, stable film by

evaporation of solvent. Nonvolatile components are added to prevent the drug precipitation when the volatile solvent gets evaporated. These components are chosen that itself rapidly partition into stratum corneum with drug which increases drug diffusivity. Polymer and solvent are mixed together and stirring of solution overnight to make clear solution of polymer. Film forming solutions can be applied using an applicator to the skin and allowed to dry[10].

Gel

Pharmaceutical film forming gel forms the thin, transparent film that facilitates the prolonged contact of drug with skin and its drying improves skin retention ability. Gel was characterized for their pH, viscosity, drug content, and mechanical properties of film. In gel preparation with polymer gelling agents are also added (Table 4).

Table 4: Properties of gelling agents used in FFS

Gelling agent	Properties
Hydroxy propyl methyl cellulose (HPMC)	Produces a smooth, clear gel. Effective in concentration of 2-6% as gelling agent.
Poloxamer	Liquid at cool temperature (0-10 ℃) and gel at room temperature. Concentration 20-30%.
Carbopol 940	Very great clarity in water. Forms clear gels with HCL.
Carbopol 941	Produces low viscosity gel. Very clear gel.
Gallangum	Thermo reversible highly transparent gel formed on cooling. Concentration 0.5-1.5% w/w.
Alginate	Thermo irreversible gel, do not melt on heating, 1-2 % w/w

Emulsions

Emulsions are semisolid or liquid preparations having the ability to solubilize both lipophilic and hydrophilic drugs. Pharmaceutical emulsions consist of mixtures of aqueous phase and oily phases which are stabilized by suitable emulsifying agents. These can be oil-in-water (O/W) emulsions (oil phase is dispersed in the water phase) or water-in-oil (W/O) emulsions (water phase dispersed in an oily continuous phase).Film forming emulsions containing film forming polymers, oil phase and aqueous phase. It extends contact time with affected area and can treat larger area of skin and allows sustained drug delivery depends on the characteristics of API and the type of emulsion[9].

EVALUATION PARAMETERS

Film formation

The films are formed in a Petri dish or on an excised pig ear skin. Film-formation is evaluated and rated as complete and uniform, incomplete or non-uniform, with or without precipitation of the film-forming polymer. The cosmetic aspects of the film are given in terms of transparency or opaque, sticky or dry, peelable or non-peelable[3].

Film flexibility

Film flexibility is evaluated on the basis of cracking and skin fixation and this is determined by stretching the skin in 2–3 directions. The film is rated flexible if there is no cracking or skin fixation and non-flexible if there is cracking and skin fixation[11].

Drying time

For the evaluation of the drying time the formulation is applied to the inner sides of the forearm of a volunteer. After a fixed time period a glass slide is placed on the film without pressure. If no liquid is visible on the glass slide after removal, the film is considered dry. If remains of the liquid are visible on the glass slide the experiment is repeated with an increase in drying time. A good FFS should have a minimum drying time to avoid long waiting time for the patient[11].

Stickiness

The stickiness of the film formed is determined by pressing cotton wool on the dry film with low pressure. Depending on the quantity of cotton fibers that are retained by the film, the stickiness is rated high if there is dense accumulation of fibers on the film, medium if there is a thin fiber layer on the film and low if there is an occasional or no adherence of fibers. This evaluation parameter is essential, as the formulation should be non-sticky to avoid adherence to the patient's clothes[8].

Mechanical properties

The polymeric films are produced by solvent evaporation on a Teflon plate. The dry films are cut with the help of a scalpel. Film thickness is measured with a digital micrometer. The mechanical properties of the films are determined with a tensile tester.

The tensile strength (σ) is calculated as:

$$\Sigma=F_{max}/A\ (N/m^2)$$

Where F_{max} (N) is the maximum force and A (m^2) is the cross-sectional area[12].

Determination of the water vapor permeability

The water vapor permeability is defined as the quantity of water transmitted through a unit area of film in unit time. These water vapor permeation data are important in determining the permeation characteristics of the film as they have influence on skin properties like hydration of stratum corneum, blood flow, and skin temperature[10]. Films are produced with a solvent evaporation technique on a Teflon plate and dried for 72 h at room temperature. Circular samples are cut from the dry film sheets. For the sample preparation glass vials with an opening are filled with distilled water, covered with the circular film samples and a silicone ring, and sealed tightly with an aluminum vial cap. The weight of the vial is determined and then placed into a desiccator creating an atmosphere of 58% relative humidity or low relative humidity (approximately 0%). They are kept at a determined temperature for 72 h and weighed after predetermined intervals. From the weight loss of the vials W (g) the water vapor permeability is calculated as the amount of water that permeates through the film in relation to the surface area A (cm^2) and the time t (h)[12]:

$$WVP=W/At$$

Swab studies

Swab test can be performed to evaluate the residence time of film forming system. For adhesion testing, glass was used as a polar, hydrophilic substrate. Glass was chosen as test surface because films adhering strongly to it would also show strong adherence to skin because both materials display a polar surface structure[13].

Dry swab test: This test indicates the behavior of FFS on the skin in dry condition. Dry swab test can be carried out on a glass plate. The glass plate is marked with 6 squares of 1 × 1 cm^2. Developed formulation is applied in this area. Dry cotton swabs of the same volume are taken. Swabbing on the applied film is carried out at 0 min, 30 min, 2 h, 4 h, 6 h and 8 h and checked for drug content after extraction of drug from the swab.

Wet swab test: This test depicts the behavior of FFS when it comes in contact with water or sweat. The procedure for the wet swab test is the same as dry swab test except the swab taken is soaked in water before and then the formulations are swabbed with this wet swab.

Film topography

Atomic Force Microscopy (AFM) provides information about the topographic and mechanical properties of the polymeric films and helps to match the mechanical properties of the formed films to those of skin. It generates a Nanoscale image of the film's homogeneity and roughness and requires no special treatment prior to the measurement[14].

Film homogeneity

Raman spectroscopy provides information about the chemical composition of the polymeric films. The chemical maps obtained from Raman spectra provide a measure of chemical homogeneity of films. Techniques based on Raman scattering can also be used to track the permeation of topically applied compounds through the skin[14].

In vitro diffusion study

The *in vitro* diffusion studies are used to predict the permeation characteristics of drug *in vivo*. Franz diffusion cell is used to determine the release profile of the drug from the film forming system. The cell is made up of two compartments, the donor and the receiver compartment between which the diffusion membrane is attached (egg membrane or cellophane). The donor compartment is exposed to the atmosphere and the receptor compartment contains the diffusion medium. The sampling arm in the receptor compartment allows for sampling. Predetermined quantity of the drug containing film forming formulation is placed on the donor compartment. Samples are collected and analyzed by suitable spectroscopic method for drug release[8].

Ex vivo permeation study

The *ex vivo* permeation studies are performed to study the effects of skin barrier on the developed film forming system. Franz diffusion cell/Keshary–Chien diffusion cell can be used for permeation study. Rat's skin is mounted between the two compartments, stratum corneum facing the donor compartment and dermis facing the receptor compartment. The formulation is applied to the skin surface which forms a film after drying. The receptor compartment contains phosphate buffered saline (pH 7.4) maintained at 37 ± 0.5°C. Aliquots are collected at specific time intervals and analyzed by suitable spectroscopic method[10].

Skin penetration studies

The formulation is applied evenly on the skin using a pipette or a spatula. After fixed time intervals (e.g. 15 min, 1 h, 3 h, 6 h, 8 h, etc.) post application, the remaining formulation is removed. The film is wiped off with the help of cotton pads and the amount of drug present in the cotton pads is calculated, which is equivalent to the amount of drug remaining in the film. Therefore the amount of drug penetrated can be calculated by subtracting the remaining amount from the total amount of drug present in the formulation[15].

CONCLUSION

The film forming system is a better alternative to the both topical and transdermal conventional formulations. These film forming systems are simple and offer advantages of transparency, non-greasy, lower skin irritation, wipe off resistance, longer retention, greater increased dosage flexibility, and improved patient compliance. It remains adhere to the affected part for longer time period, provide sustained release of drug.

REFERENCES

1. Kathe K, Kathpalia H. Film forming systems for topical and transdermal drug delivery. Asian Journal of Pharmaceutical Sciences. 2017; 12 (6) :487-497.
2. Frederiksen K, Guy RH, Petersson K. The potential of polymeric film-forming systems as sustained delivery platforms for topical drugs. Expert Opinion on Drug Delivery. 2016; 13 (3) :349-360.
3. Frederiksen K, Guy RH, Petersson K. Formulation considerations in the design of topical, polymeric film-forming systems for sustained drug delivery to the skin. European Journal of Pharmaceutics and Biopharmaceutics. 2015; 91 :9-15.
4. Mohamed MS, Eid AMM, Elgadir MA, Mahdy ma. Preparation and release charcteristics of itraconazole polymeric films for topical application. 2013; 5(3) :167-170.
5. Bornare SS, Aher SS, Saudagar RB. A review: Film forming gel novel drug delivery system. International Journal of Current Pharmaceutical Research. 2018; 10 (2) :25-8.
6. Bharkatiya M, Nema RK. Skin penetration enhancement techniques. Journal of Young Pharmacists. 2009; 1(2):110-115.
7. Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian Journal of Pharmaceutical Sciences. 2016; 11(5) :559-74.
8. Vij NN, Saudagar RB. Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of terbinafine hydrochloride. International Journal of Pharmaceutical Science Research. 2014; 5(9) :537-554.
9. Schroder IZ. Film forming polymeric solution as drug delivery system for the skin. 2007; 168(1-2) : 1-153.
10. Bharkatiya M, Nema RK, Bhatnagar M. Development and characterization of transdermal patches of metoprolol tartrate. Asian Journal of Pharmaceutical and Clinical Research. 2010; 3(2): 130-134.
11. Šveikauskaitė I, Briedis V. Effect of film-forming polymers on release of naftifine hydrochloride from nail lacquers. International Journal of Polymer Science. 2017; 1-7.
12. Schroeder IZ, Franke P, Schaefer UF, Lehr CM. Development and characterization of film forming polymeric solutions for skin drug delivery. European Journal of Pharmaceutics and Biopharmaceutics. 2007; 65(1) :111-121.
13. Lunter DJ, Daniels R. New film forming emulsions containing Eudragit® NE and/or RS 30D for sustained dermal delivery of nonivamide. European Journal of Pharmaceutics and Biopharmaceutics. 2012; 82(2) :291-298.
14. Garvie-Cook H, Frederiksen K, Petersson K, Guy RH, Gordeev S. Characterization of topical film-forming systems using atomic force microscopy and Raman microspectroscopy. Molecular Pharmaceutics. 2015; 12(3) :751-757.
15. Garvie-Cook H, Frederiksen K, Petersson K, Guy RH, Gordeev SN. Biophysical elucidation of the mechanism of enhanced drug release and topical delivery from polymeric film-forming systems. Journal of Controlled Release. 2015; 212:103-112.