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A Recent Review on Film Forming Topical Formulation

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ABSTRACT

Film forming topical formulation is solutions / sprays , gels , emulsion are a novel approach is as an alternative to the conventional dosage formed used on the topically on skin , such as ointment , creams or patches .The polymeric solution is an applied to the skin as a liquid and forms a transparent invisible film by solvent evaporation the aim of this review was to search for alternatives to the conventional dosage forms .it is a novel approach helpful in providing sustained release drug delivery system with increase resistance time ,reduce skin irritation , improve skin adhesion property , increase drug release and increase patient comfortability.

Keywords: film forming formulation , transdermal drug delivery ,evaluation parameter.

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INTRODUCTION :-

Skin is an important route of administration of drugs for both local& systemic effect. (1)Topical therapy effect depends on a physiochemical properties of the drug and excipient and ability adhere to the skin during treatment so as to promote the drug penetration through skin barrier (1). The skin is an most rapidly accessible organ of the body & acts as a barrier against the macro &micromolecules of the environment because of its low permiability to such substances (1-4) & surface area of about 2m recieiving about one third of the total blood circulating throughout the body (2-4).

The topical route offers as a large surface & ease to the application via self administration& provides an alternative to oral drug delivery as well as hypodermic injection.(2) Percutaneous absorption of drug content through skin mainly occurs via stratum corneum. (1) stratumcorneum is a thin , outer layer of skin consisting of both hydrophilic & lipophilic domain , hair follicle and sweat gland , stratum corneum has a water content of 20% which lies in keratin layer between horny cells . keratin is 20% cross linked which lies in keratin layer between horny cells.(4)

The recent dosage forms i.e. patches , ointment , creams , etc are associates with several limitations . film forming system (FFS) it is a novel approach which can be used as an alternative to conventional topical and trasdermal formulation (4).It is defined as non-solid dosage form it produces a film in situ i.e. after application on the skin. The formed film can either be a solid polymeric material that acts matrix for sustained release of drug to the skin or a residual liquid films which is rapidly absorbed in the stratum (4-10)

The need for multiple applications on a day is frequently associated with poor compliance of patients . Thus prolonging the existing time of active substances to the skin & thereby reducing the application frequency is a subject of intensive research (7).The formed film is an sufficiently substantial to provide a sustained drug release to the skin.(2)

Film Forming Solution (FFS) (7) may be

-solution

- gel

- emulsion

1.1 Sprays/solutions

Film forming solutions and sprays it is an attractive and novel approachin transdermal sustained drug delivery system. In this the polymeric drug solution isapplied to the skin as a liquid/solution or sprayed on the skin and form asan almost transparentthin film by solvent evaporation [9].

The film forming sprays/solutions are made up of four maincomponents – drug, solvent systems i.e. volatile and nonvolatilevehicles, polymers and penetration enhancers.The nonvolatilecomponent present in the solvent system prevents thedrug from precipitating in solution when the volatile solventcomponent evaporates. (7,8) The non-volatile component is chosensuch that it itself partitions rapidly into the stratum corneumand also aid in partitioning of the drug into the stratumcorneum, as well as increases drug diffusivity by distracting theordered intercellular lipids and enhance permeation through skin. This typeof delivery system creates an invisible depot of drug in thestratum corneum from which the drug can be slowly absorbedinto the systemic circulation. Thus a sustained and improve permeation of drug across the skin can be achieved by following once a day application (7,8). In formulation preparation involves addition of thepolymer to the vehicle and stirring of the solution overnight to ensure complete dissolution of the polymer. Once a clearpolymeric solution is obtained other optional excipients suchas cross linker or plasticizer are added. After addition of all excipientsthe solution is stirred for 24 h (9). For the physicalstability of the API, the polymers are chosen such that they functionas anti-nucleating agents and crystallization inhibitorswhich prevent crystallization of drug even after solvent evaporation e.g. polyvinyl pyrrolidone, polyethylene glycol, hydroxylpropyl methyl cellulose.Film forming solutions can be applied with an a applicatorto the skin and allowed to dry. Film forming spray is manufacturedas a metered dose pump dispenser to supply or give fixedamount of drug and it is sprayed on the topical site to form a transparent film. These systems form a stable fast drying, non-irritating invisible film from which the drug is available for transdermaltherapy (9). Following administration, the film can bepeeled off once the desired results are obtained or for the terminationof therapy .Misra et al. prepared a liquid film forming solution using a mixture of polyvinyl pyrrolidone and polyvinyl alcohol in isopropanolas film forming polymeric solutions for the biphasicdelivery of testosterone (10). Ammar et al. developed a filmforming polymeric solution of ketorolac using Eudragit and polyvinyl pyrrolidone in ethanol as film forming agents (9). The mechanical property and appearance of the prepared formulations was evaluated.Gohel and Nagori developed a fluconazole spray containingethyl cellulose and Eudragit RS 100 as film formers (11).Yuet al. developed transdermal film-forming spray containing estradioland optimized the formulation using different polymersand plasticizers for efficient penetration of estradiol for longerduration of time as compared to gel and patch (12).

1.2. Gels

Gels it is a semisolid dosage form containing both solidand liquid components. The liquid component may be hydrophobic or hydrophilic in nature, immobilized in a threedimensional network of the interconnected solid components(13). Hydrogels are the aqueous gels containinghydrophilic polymers that form three dimensional network inwater(14).It's is a non fluid colloidal network that is expanded throughout its whole volume by a fluid (6)

The administration of film forming gel involves applying a doseon the arms, shoulders, internal parts of the thighs or abdomento form a thin bioadhesive film on the skin (23)

The drug substance is dissolved in film forming vehicle and is thusincorporated in the film formed on skin. The film can functionas an external reservoir or limit the supply of drug substance to the skin thereby controlling the release ofdrug (15).

Complete skin contact with the entire application is essential;therefore, the formulation requires high flexibility to adjust the movement of the skin, high substantivity, strong adhesion to the skin for stable n contineous delivery and absorption of drug.

Hence, along with gelling agents, film forming agents, plasticizers,preservatives etc. are used in the formulation. Compared with other forms, these systems offer easieruseandapplication,appropriate consistency and adhesiveness, good flexibilityand elasticity and ease of manufacturing (16).

Film forming hydrogels are majorly used in wound healing.The formulation applied to the wounded site provides a filmthat is resistant to physiological stress caused by the movementof skin.

1.3. Emulsions

Emulsions are a semisolid or liquid preparations having the abilityto solubilize both lipophilic and hydrophilic drugs. Pharmaceuticalemulsions consist of mixtures of aqueous phase and oily phase stabilized by suitable emulsifying agents (17).These canbe oil-in-water (O/W) emulsions (oil phase is dispersed in thewater phase) or water-in-oil (W/O) emulsions (water phase dispersedin an oily continuous phase).The type of emulsion formeddepends mainly on the type of emulsifiers, which is characterizedby the hydrophilic–lipophilic balance (HLB). The HLB is ascale from 1 to 20 and the higher the HLB, the more hydrophilicis the surface active agent. An emulsifying agent it is asubstance which stabilizes the emulsion. There are differenttypes of emulsifying agents including surfactants, polymers, proteins(gelatin) and finely divided solid particles (bentonite).Film forming emulsions, in addition to the oil phase and theaqueous phase, contain film forming polymer.The volatile componentspresent in the emulsions evaporate leading to thechanges in the tissue, allowing absorption of the drug (18).Theadvantage of film forming emulsions over semisolid formulationsis that, it allows treatment of larger areas of affected skinwith an extended contact time and adequate substantivity, thusallowing sustained dermal therapy of chronic diseases (19).The delivery of the drug through skin depends on a natureof the API and the type of emulsion. The dermal delivery of the lipophilic sunscreen agent ethylhexylmethoxycinnamatewas higher from the W/O emulsion than from the O/W emulsionmost probably because of the occlusive effect of the oilyvehicle. But other studies have shown a discrepancy. It was observedthat the skin permeation of lipophilic parabens wasenhanced from O/W emulsions compared with the W/O emulsion.This was explained by a higher affinity of the parabensfor the vehicle than for the stratum corneum in the case ofthe w/oemulsion(17).

FFS creates supersaturated systems immediately after applicationto the skin, overcoming the problem of instability.Thusit improves the drug permeation through skin compared toother transdermal dosage forms.shown in fig.1

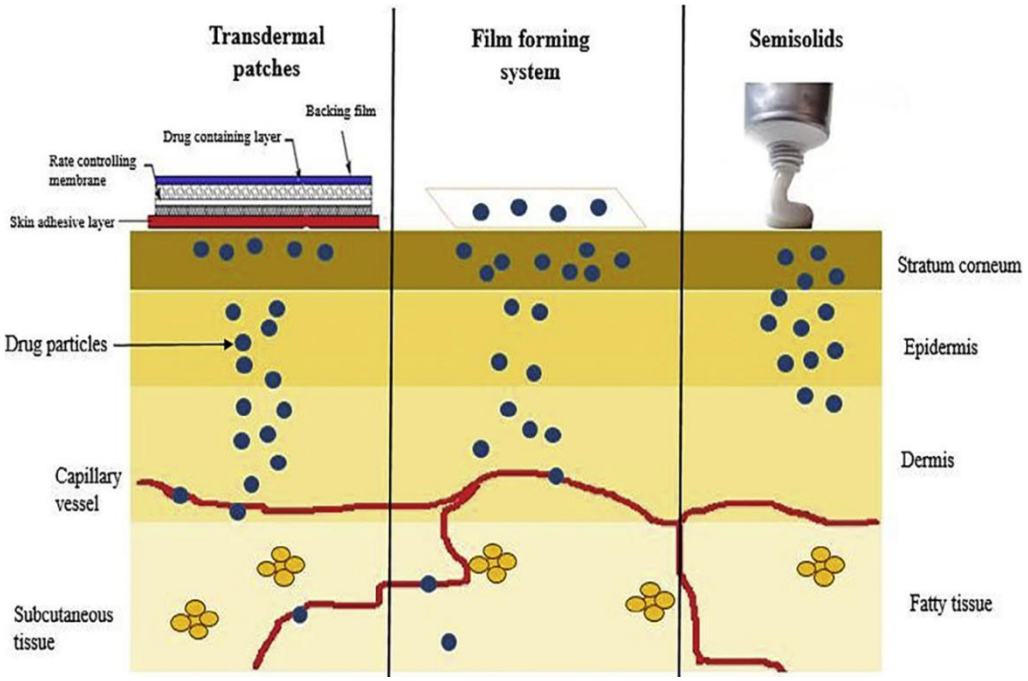

Fig. 1 – Release profile of the topical and transdermal drug delivery system.

2. EVALUATION OF FILM FORMING SYSTEM

2.1. Film formation

The films are formed in a Petri dish or on an excised pig ear skin. Film-formation it is evaluated and rated as absolute or 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(21).

2.2. Film flexibility

Film flexibility is evaluated on the basis of reaction of skin 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.

2.3. Drying time

drying time the formulation is evaluated by 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, thefilm is considered dry (22). 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 minimumdrying time to avoid long waiting time for the patient.

2.4. Stickiness

The stickiness of the film formed is determined by pressingcotton wool on the dry film with low pressure. Depending onthe quantity of cotton fibres that are retained by the film, thestickiness is rated high if there is dense accumulation of fiberson the film, medium if there is a thin fiber layer on the filmand low if there is an occasional or no adherence of fibers. Thisevaluation parameter is essential, as the formulation shouldbe non-sticky to avoid adherence to the patients' clothes (23).

2.5. Mechanical properties

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

2.6. 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 (25). 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 and this sheets use for cover the sample preparation glass vials. For the sample preparation glass vials 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% relativehumidity 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 (cm2) and the time t (h) (24):

2.7. Swab studies

Swab test can be performed to evaluate the residence time offilm forming system. For adhesion testing, glass was used as apolar, hydrophilic substrate. Glass was chosen as test surfacebecause films adhering strongly to it would also show strongadherence to skin because both materials display a polar surfacestructure (26).*Dry swab test:* This test indicate the behavior of FFS on the dry skin condition. Dry swab test can be carried out on a glass plate.The glass plate is marked with 6 squares of 1 × 1 cm2. Developed formulation is applied in this area. Swabbing on the applied film is carried out at 0 min, 30 min, 2 h, 4 h, 6 h and 8 h and checkedfor

drug content after extraction of drug from the swab.*Wet swab test:* This test depicts the activities of FFS when it comes in contact with water or sweat.The procedure for the wet swab test, dry swab test is the same as except the swab taken is soaked in water before and then the formulations areswabbed with this wet swab.

2.8. Film topography

Atomic force microscopy (AFM) provides information about thetopographic and mechanical properties of the polymeric filmsand helps to match the mechanical properties of the formedfilms to those of skin. It generates a nanoscale image of thefilm's homogeneity and roughness and requires no special treatmentprior to the measurement (27).

2.9. Film homogeneity

Raman spectroscopy provides information about the chemicalcomposition of the polymeric films. The chemical mapsobtained from Raman spectra provide a measure of chemicalhomogeneity of films. Techniques based on Raman scatteringcan also be used to track the permeation of topically appliedcompounds through the skin (27).

2.10. In vitro diffusion study

The *in vitro* diffusion studies are used to predict the permeationcharacteristics of drug *in vivo*. Franz diffusion cell is used to determine the release profile of the drug from the filmforming system.The cell is made up of two compartments, thedonor and the receiver compartment between which the diffusionmembrane is attached (egg membrane or cellophane).The donor compartment is exposed to the atmosphere and thereceptor compartment contains the diffusion medium.The samplingarm in the receptor compartment allows for sampling.Predetermined quantity of the drug containing film formingformulation is placed on the donor compartment. Samples arecollected and analyzed by suitable spectroscopic method fordrug release (23).

2.11. Ex vivo permeation study

The *ex vivo* permeation studies are performed to study theeffects of skin barrier on the developed film forming system.Franz diffusion cell/Keshary–Chien diffusion cell can be usedfor permeation study. Rat's skin is mounted between the twocompartments, stratum corneum facing the donor compartmentand dermis facing the receptor compartment. Theformulation is applied to the skin surface which forms a filmafter drying. The receptor compartment contains phosphatebuffered saline (pH 7.4) maintained at 37 □} 0.5 °C. Aliquots arecollected at specific time intervals and analyzed by suitablespectroscopic method (28).

2.12. Skin penetration studies

The formulation is applied evenly on the skin using a pipetteor 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 theamount of drug present in the cotton pads is calculated, whichis equivalent to the amount of drug remaining in the film.Therefore the amount of drug penetrated can be calculated bysubtracting the remainingamount from the total amount ofdrug present in the formulation (29).

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