ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 5, 2025

Online - 2455-3891
Print - 0974-2441

Review Article

APPLICATION OF FILM SPRAY TECHNOLOGY FOR THE ENHANCEMENT OF TRANSDERMAL DRUG DELIVERY SYSTEM- A REVIEW

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Received: 19 February 2025, Revised and Accepted: 14 April 2025

ABSTRACT

Conventional topical formulations are more beneficial for drug delivery systems and treatments, yet they hold a few drawbacks, including irritability, lower bioavailability of actives in sites, and poor local and systemic effects. In this present topical research, Film-Forming Sprays, falling under sprayed solutions, which would form a thin film coming into a contact with wound or open skin, acting as reservoirs for extended release of the active ingredient, like patches, but would ensure skin contours is the step to exceed the limitations of the conventional topical preparations. On contrast with conventional preparations, film-forming sprays have a prolonged release nature with uniform distribution of drugs and dosages, enhanced activities system availability, better penetrability, and ease of administration. This review describes the development of film-forming sprays in topical formulations containing several polymers and excipients that enhance the preparation properties and the stability of the active ingredients. This overview also summarizes the principal parameters in the preparation of film-forming sprays such as spray-ability, spread-ability, and film properties, in addition to the various types of polymeric concentrations, excipients, types of sprayers, and evaluations.

Keywords: Film-forming spray, Topical drug delivery, Polymer-based films, Wound healing, Controlled drug release, Mucoadhesion.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i5.54003. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Topically applied drugs cause both local and systemic effects [1]. Topical efficacy of an administered medication depends upon the physicochemical properties of both the drug and excipients. Excipients support the formulations that allow them to stick to the skin layers for permeation and absorption by crossing the skin barriers and exhibiting therapeutic activity [2]. Skin exhibits low permeability to environmental compounds, its comparatively minimal surface area of 2 square meters, which allows it to receive around half of the blood flow throughout the body, makes it one of the most accessible organs in the human body. It acts as a defense against harmful toxins [3,4].

The external route or topical route provides high surface area with the additional advantage of convenient self-administration by potentially replacing hypodermic injection and oral medication delivery [2]. The stratum corneum is the outermost skin layer and the primary site of skin's percutaneous absorption, comprises sudoriferous or sweat glands, follicles, and hydrophilic and lipophilic domains. It is located in the level of keratin between the horny cells and has a 20% water content. The percentage of cross-linked keratin in the level of keratin between the horny cells is 20% [1,4].

The conventionally used topical dosage forms such as creams, patches, and ointments have various disadvantages such as hypersensitivity, irritation, scaling up in the production, uneven distribution, high dosing frequency, and poor application. A novel approach that can replace the conventional topical and transdermal formulations is the film- forming system (FFS) [4]. Is defined as a non-solid dosage form that when applied topically, forms a film on the skin. The formed film can be either a solid polymeric entity that serves as a matrix for the prolonged release of the drug into the skin or a residual liquid film that is quickly absorbed in the stratum [5-10].

Definition and mechanism of action of film-forming spray (FFS)

A film is formed in contact at the therapeutic location mediated by a sprayed solution drug delivery technique called an FFS [11,13,14]. The drug released at a controlled rate from the polymer matrix, almost in the same manner that a patch releases its contents after forming a film [1]. FFS is compared with the other topical applications; however, to create films in the regular structure of the skin or wound since the tiny droplets of the film-forming solution may reach deeply entrenched places. In this, the drugs will access the target tissue more readily. The dosages for the film-forming sprays can also be varied depending on the volume of solution in each spray to create localized or systemic effects. An FFS disperses uniformly and its user-friendliness can improve patient compliance [11,13-19]. Water spreads the thin film quickly [11,16]. This thin, smooth, non-sticky film improves the harsh, sticky texture of patches, ointments, gels, and other comparable items, in addition to being more pleasant for patients to move around on [17,18].

In addition, the thin film facilitates easier penetration to the wound moisture site or equilibrium maintenance. Just as patch preparations may cause discomfort or infection with poor patch preparation, poor wound humidity can do the same [19-21]. A special sprayer type is used to spray the solution forming droplets to create the film. Even all of these sprays have a unique set of specifications and applications; they are all unquestionably capacity of being used in medical field [21].

VARIOUS TYPES OF FORMULATIONS FOR FILM FORMATION

Sprays and solutions that form films are elegant and new concepts in the transdermal sustained-release drug delivery systems. The skin had smeared with a liquid or solution of the polymeric drug solution, which dries up to leave an almost transparent thin coating [9]. The four main ingredients in film-forming sprays and solutions are drugs, solvent systems, polymers, and penetration enhancers. The non-volatile component should prevent the drug from precipitating in solution when the volatile solvent component of the solvent system evaporates. The non-volatile ingredient is selected to disrupt the order of intercellular lipids and quickly separate into the stratum corneum, improving the diffusivity and skin penetration of the medication [7,8]. It also permeates the medication (drugs) distribution across the stratum corneum.

Table 1: Various types of film-forming sprayers (FFS) [22-26]

Spray specification	Features	References
Ordinary spray	• Usage of plastic or aluminum containers with a specification of 0.3 mm aperture and 1.2 mm diameter dip tube. • No other specific or advanced technology is involved. • It sprays 0.11–0.35 g/mL of film-forming solution at an angle of 78.69–87.39°. • And leakage rate: 0.01–0.03%. • Can be used in vertical or horizontal orientation. • Horizontal spray nozzle maintains sterility during application and storage. • - Spray force depends on polymer type and concentration.	[22-26]
Metered dosage spray	• Used for novel delivery like transdermal or transmucosal drug delivery. • The amount of solution sprayed is crucial for drug dosage determination. • Some factors affect the volume of spray: bottle capacity, container position, and homogeneity of particle dispersion. • Normal spray duration is about 90–10 s. • Spray angle is 83.51°. • Leakage rate is about 0.01–0.02%.	[22-26]
Electrostatic spray	• It is generally applied in agricultural sector primarily as an insecticide treatment. • It also enhances spray efficiency, droplet formation rate, and coverage uniformity while reducing drift loss. • Efficiency of spray depends upon the viscosity, surface tension, and electrical resistivity. • Required conductivity is about 10^8 to 10^5 S/m. • Droplet diameter is about 6.3–26 µm.	[22-26]
Ultrasonic spray	• It produces nanoscale droplets with thin-film properties. • It produces a uniform droplet<10 µm in diameter. • Also operates in high and low pressure. • Droplet diameter is about 1–10 µm. • Nozzle diameter is about 0.5 mm. • Uses a working electrode with a resonance frequency of 10 MHz. • It is also used in medical applications such as layer-by-layer coating films. • Also appropriate for utilizing a various source of polymers from natural and synthetic.	[22-26]

There are three forms of film-forming formulas, they are,

- Film-forming spray/solutions
- Film-forming gel
- Film-forming emulsion.

Table 2: Various types of formulations used for film-forming

Category	Description	References
Film-forming spray/ solutions	Sprays and solutions that form films are a novel approach in transdermal sustained-release drug delivery. A polymeric drug solution was applied to the skin, and upon drying, it dispersed into a thin transparent film.	[9]
	Application: It dries to form a film, which is peel-able after treatment; it can used for bed return patients	[7-9]
	Example: Ketorolac film-forming polymeric solution using Eudragit in ethanol and PVP.	[9,10,27,28]
Film-forming gel	Gels are semi-solid systems containing liquid immobilized within a three-dimensional solid network, which can be hydrophobic or hydrophilic.	[29,57]
	Hydrogels: Hydrophilic polymers have been used as aqueous gels with water as the internal phase.	[30]
	Types: Two types of film-forming gels are available, they are Hydrophilic (hydrogels) and hydrophobic gels.	
	Application: It can be used in thighs, stomach or arms, and shoulders, once it dries gel form a bioadhesive gel layer.	[31]
Film-forming Emulsion	Semi-solid or liquid form of film-forming emulsion that solubilizes both lipophilic and hydrophilic drugs. It is a mixture of oily and aqueous phases stabilized by emulsifying agents.	[33]
	Types of emulsions: Oil-in-water (O/W) and water-in-oil (W/O), depending upon the hydrophilic-lipophilic balance (HLB) of the emulsifier.	[33]
	Emulsifying agents: Polymers, surfactants, proteins (e.g., gelatine), finely divided solid particles (e.g., bentonite).	[34]
	Advantages: It covers a skin area with extended contact, making it suitable for chronic dermal therapy.	[35]

Mechanism involved in the film-forming spray

A thin, transparent film has left behind on the skin after the solvent evaporates from the Film-forming spray system. Because vehicle components are volatile and evaporate after being applied on the skin surface, thus the formula is greatly changed into a higher-strength film residue left on the skin surface. The drug concentration is increased in this stage, as it approaches supersaturation and it enhances the drug flux by increasing the skin's thermodynamic activity but without compromising its defense barrier. This formulation can thus, it can be used without any skin irritation or adverse effect [36,37].

The following explained modified version of Fick's law of diffusion discusses about the supersaturation. The following formula is describing about the Fick's law of diffusion barrier:

$$J = DKCv/h \quad (1)$$

Where,

J - Indicates drug permeation rate (flux)

D - Indicates drug diffusion coefficient

Cv - Indicates drug concentration

h - Represents the thickness of the barrier to diffusion.

Table 3: Components involved in film-forming spray

Components	Characteristics	References
Drug	Film-forming sprays are utilized to administer the hydrophobic and hydrophilic drugs. Drugs with the high strengths, are easily absorbed drugs can be administered via the skin are fairly painless.	[37,40,41]
Polymer	Polymers can be used alone or in combination with other film-forming polymers to deliver the desired film properties. These polymers should combine at skin temperature to form a transparent, flexible film. Polyvinyl pyrrolidine, hydroxypropyl methylcellulose, chitosan, silicones, and polydimethylsiloxane are some examples of polymers.	[42-46]
Solvents	Other categories of solvents were utilized while the film-forming spray, solvents play a critical part in dissolution as well as penetration of the drug. The safety of such solvents is questionable in the long term due to their repeated utilization. For example, benzyl alcohol, butanol, propylene glycol, ethanol, isopropanol, as well as ethyl acetate.	[47-51]
Plasticizer	The plasticizer is mainly used in film-forming systems to provide them with more tensile strength and flexibility. Such plasticizers must not diffuse quickly into the skin and should be compatible with the used polymers. Examples such as propylene glycol, glycerine, polysorbate 80, polyethylene glycol, sorbitol, triethyl citrate, triacetin, and dibutyl phthalate were used as a plasticizer.	[52-54]
Permeation enhancer	Permeation enhancers are the compounds which are added in transdermal drug delivery systems (TDDS) that serves to enhance the quantity of material (drug) which can pass through the skin. Examples of permeation enhancers include alcohols such as ethanol, propylene glycol, and isopropyl alcohol.	[54]

The equation shows the drug concentration is directly proportional to the rate of penetration of the drugs to the skin. This, however, is the case when the drug has been dissolved completely in the vehicle. There is a clear and direct relationship between drug flux and the system's thermodynamic activity to saturation as shown in this equation [11]. The higher saturation, however, the higher the thermodynamic instability. FFS avoids this instability problem by creating a supersaturated system instantaneously after its application on the skin. Therefore, compared to other transdermal administration forms, it enhances the uptake of drugs through the skin [17,38].

This equation represents that the concentration of the drug and the rate at which it permeates the skin is directly proportionate. That is correct, though, if the medication has completely dissolved within the vehicle.

Equation 2 is the modified form of Fick's law of diffusion:

$$J = \alpha D/\gamma h \quad (2)$$

Where

α - Indicates the thermodynamic activity of the drug within the formulation

γ - Indicates the thermodynamic activity of the drug within the membrane.

Therefore, according to this equation, the flow of drug relies directly on the saturation-related thermodynamic activity of the system. In contrast, thermodynamic instability increases with supersaturation [39].

EVALUATION PARAMETERS INVOLVED IN FFS [13,55,56]

Organoleptic parameters

Testing and observation ranged from color, odor, appearance, and many other physical attributes that described the FFS.

pH

The pH of the solution was measured using a digital pH meter. Before measuring the pH of several data sets, the pH meter had calibrated using phosphate support pH values of 4.0, 7.0, and 10. It was measured by immersing the pH meter's cathode into 20 mL of shower solution for a short period. The pH for each detailing was calculated a few times, and average attributes were considered.

Viscosity

The viscosity of the spray solution was determined using a Brookfield viscometer.

Surface tension and spray angle

The surface tension and spray angle of the formulation can be measured using a technique called Drop Count Method, where stalagmometer is used for same. The mathematical formulae to calculate were mentioned below.

$$\text{Surface tension}(\sigma) = \sigma 1 \times \rho 2\ n1/\rho 1\ n2 \quad (3)$$

Where,

σ and $\sigma 1$-denotes the Surface tension of the test liquid and the reference liquid usually, water, respectively

$\rho 1$ and $\rho 2$ denote the density of reference liquids 1 and 2, respectively

n1 denotes the number of drops of reference fluid falling from point A to B

n2 denotes the number of drops of topical film-forming spray (test) solution falling from point A to B.

$$\text{Spray angle } (\theta) = \tan\text{-}1\ (l/r) \quad (4)$$

Where,

θ denotes the angle,

l denotes the distance between the sprayer and the paper,

r denotes the radius a sprayed circle.

Evaporation time/film formation time

The time it took for the film to completely dry, or evaporation time, was noted. How many solutions would have been sprayed onto the glass surface and how much time it would take for the film to become thoroughly dried.

Stickiness of film

The film adhesion was tested using fabric fibers, which were pressed against the film with minimal force and found to be gripped by the film. The degree of stickiness was rated as high, medium, and low.

Stability studies

Stability analyses of five sprays were formulated and preserved for 3 months. The formulations were filled in close-lid APF containers resting of ICH recommendations for the below conditions: 30°C±2°C/75±5% RH. For initial data, samples from all sprays were collected at 0 and 3 months for assessment on the characteristics of appearance, pH, and viscosity.

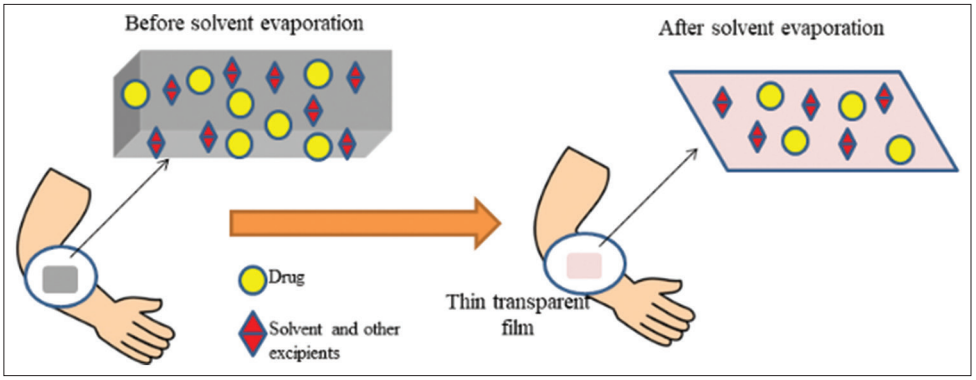

Fig. 1: Mechanism of film-forming system

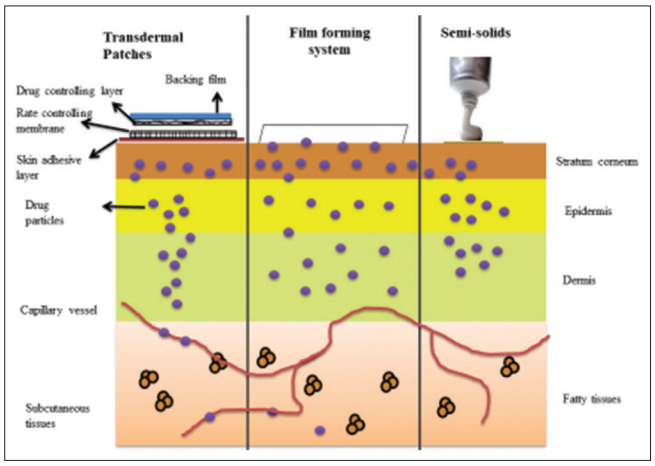

Fig. 2: Release profile of drug through topical and transdermal drug delivery system

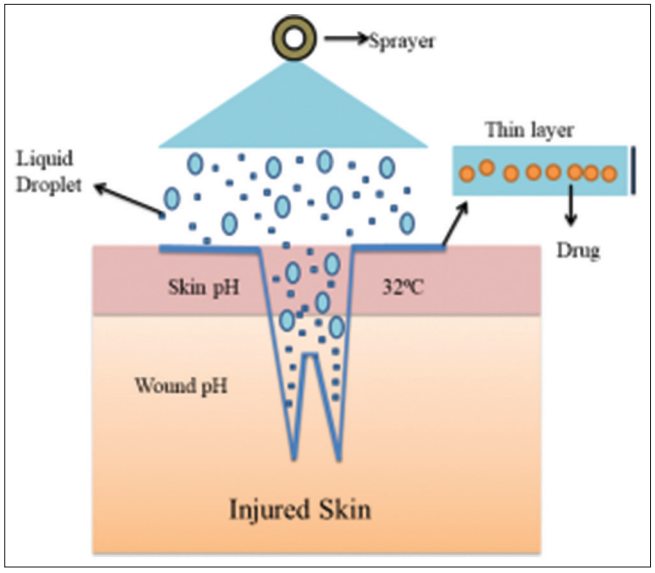

Fig. 3: Penetration of topical drug through skin

CONCLUSION

Therefore, it concludes that film-forming spray drug delivery system is a potentially helpful method of medication administration. Spray film-forming systems have been one of the modern drug delivery methods for local, topical, and transdermal administration. It is a unique and helpful technique offering a sustained-release drug delivery system with increased resistance time, minimized skin irritation and dosing frequency, improved skin adhesion properties, increased drug release, and improved patient compliance. Polymers and excipients in film-forming sprays increase the stability of the active ingredients and the properties of the preparations. Films with different properties will result from different combinations between polymer and excipient. Therefore, all types of polymers and excipients would thus be incorporated into the composition of the film-forming spray, and the parameters by which they would be evaluated, and also thoroughly examined regarding the formulation properties.

AUTHORS' CONTRIBUTIONS

Mr. Jana Arun: Writing – review and editing, designed the review. Dr. GNK. Ganesh: Writing – review and editing, designed the review. Ms. Disha Bhattacharya: collected documents and literatures and Mr. Jagan Subramanian: Editing, designed the review.

COMPETING INTERESTS

The authors declare no conflicts of interest, financial or otherwise.

FUNDING

No funding.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not required for this study.

REFERENCES

1. Kathe K, Kathpalia H. Film forming systems for topical and transdermal drug delivery. Asian J Pharm Sci. 2017;12:487-97. doi: 10.1016/j.ajps.2017.07.004
2. Saravanan J, Elango K, Daisy Chellakumari S, Arulkumar K. Formulaton and evaluation of film forming gel of diclofenac diethylamine. World J Pharm Pharm Sci. 2018;6:1106-17. doi: 10.20959/wjpps20186-11757
3. Singh V, Singh MF, Kukreti G, Agarwal A, Bajaj H. Rheumatoid arthritis: Treatment by film forming gel. J Analg. 2015;3:9-14. doi:10.14205/2311-0317.2015.03.01.2
4. Bornare SS, Aher SS, Saudagar RB. A review: Film forming gel novel drug delivery system. Int J Curr Pharm Res. 2018;10(2):25-8. doi: 10.22159/ijcpr.2018v10i2.25886
5. Bajaj H, Kumar T, Singh V. Film forming gels: A review. Res J Pharm Biol Chem Sci. 2016;7(4):2085-91.
6. Rechard GJ, Wilkis ES, Metanomski WV, Kahovec J, Hees M, Stepto R, *et al*., editors. Compendium of Polymer Terminology and Nomenclature. United Kingdom: Royal Society of Chemistry; 2018.
7. Algin-Yapar E, Inal Ö. Transdermal spray in hormone delivery. Trop J Pharm Res. 2014;13(3):469-74. doi: 10.4314/tjpr.v13i3.23
8. Lu W, Luo H, Wu Y, Zhu Z, Wang H. Preparation and characterization of a metered dose transdermal spray for testosterone. Acta Pharm Sin B. 2013;3(6):392-9. doi: 10.1016/j.apsb.2013.10.003
9. Lulla A, Malhotra G, Raut P. Topical Spray Compositions. Patent US6962691; 2000.
10. Misra A, Pal R, Majumdar SS, Talwar GP, Singh O. Biphasic

testosterone delivery profile observed with two different transdermal formulations. Pharm Res. 1997;14(9):1264-8.
11. Ranade S, Bajaj A, Londhe V, Babul N, Kao D. Fabrication of topical metered dose Film forming sprays for pain management. Eur J Pharm Sci. 2017;100:132-41. doi: 10.1016/j.ejps.2017.01.004
12. Zhuang C, Zhong Y, Zhao Y. Effect of deacetylation degree on properties of Chitosan films using electrostatic spraying technique. Food Control. 2019;97:25-31. doi: 10.1016/j.foodcont.2018.10.014
13. Bakshi A, Bajaj A, Malhotra G, Madan M, Amrutiya N. A novel metered dose transdermal spray formulation for oxybutynin. Indian J Pharm Sci. 2008;70(6):733-9. doi: 10.4103/0250-474X.49094
14. Geh KJ, Stelzl A, Gröne A, Wagner L, Förster B, Winter G. Development of a sprayable hydrogel formulation for the skin application of therapeutic antibodies. Eur J Pharm Biopharm. 2019;142:123-32. doi: 10.1016/j.ejpb.2019.06.015
15. Lu W, Luo H, Zhu Z, Wu Y, Luo J, Wang H. Preparation and the biopharmaceutical evaluation for the metered dose transdermal spray of dexketoprofen. J Drug Deliv. 2014;2014:697434. doi: 10.1155/2014/697434
16. Paradkar M, Thakkar V, Soni T, Gandhi T, Gohel M. Formulation and evaluation of clotrimazole transdermal spray. Drug Dev Ind Pharm. 2015;41(10):1718-25. doi: 10.3109/03639045.2014.1002408
17. Tan X, Feldman SR, Chang J, Balkrishnan R. Topical drug delivery systems in dermatology: A review of patient adherence issues. Expert Opin Drug Deliv. 2012;9(10):1263-71. doi: 10.1517/17425247.2012.711756
18. Devaux S, Castela A, Archier E, Gallini A, Joly P, Misery L, *et al*. Adherence to topical treatment in psoriasis: A systematic literature review. J Eur Acad Dermatol Venereol. 2012 May;26:61-7. doi: 10.1111/j.1468-3083.2012.04525.x
19. Dhiman S, Singh TG, Rehni AK. Transdermal patches: A recent approch to new drug delivery system. Int J Pharm Pharm Sci. 2011;3(Suppl 5):26-34.
20. Okan D, Woo K, Ayello EA, Sibbald G. The role of moisture balance in wound healing. Adv Skin Wound Care. 2007;20(1):39-53. doi: 10.1097/00129334-200701000-00013
21. Bishop SM, Walker M, Rogers AA, Chen WY. Importance of moisture balance at the wound-dressing interface. J Wound Care. 2003;12(4):125-8. doi: 10.12968/jowc.2003.12.4.26484
22. Ruela AL, Perissinato AG. Evaluation of skin absorption of drugs from topical and transdermal formulations. Braz J Pharm Sci. 2016;52(3):527-44. doi: 10.1590/s1984-82502016000300018
23. Garg T, Rath G, Goyal AK. Comprehensive review on additives of topical dosage forms for drug delivery. Drug Deliv. 2015;22(8):969-87. doi: 10.3109/10717544.2013.879355
24. Chang RK, Raw A, Lionberger R, Yu L. Generic development of topical dermatologic products: Formulation development, process development, and testing of topical dermatologic products. AAPS J. 2013;15(1):41-52. doi: 10.1208/s12248-012-9411-0
25. Radhakrishnan A, Kuppusamy G, Karri VV. Spray bandage strategy in topical drug delivery. J Drug Deliv Sci Technol. 2018;43:113-21. doi: 10.1016/j.jddst.2017.09.018
26. Ibrahim SA. Spray-on transdermal drug delivery systems. Expert Opin Drug Deliv. 2015;12(2):195-205. doi: 10.1517/17425247.2015.961419
27. Gohel MC, Nagori SA. Fabrication of modified transport fluconazole transdermal spray containing ethyl cellulose and Eudragit RS100 as film Formers. AAPS PharmSciTech. 2009;10(2):684-91. doi: 10.1208/s12249-009-9256-8
28. Yu Z, Liang Y, Liang W. Development and *in vitro* evaluation of estradiol transdermal film-forming spray. Acta Pharm Sin. 2013;48(5):746-51.
29. Rehman K, Zulfakar MH. Recent advances in gel technologies for topical and transdermal drug delivery. Drug Dev Ind Pharm 2013;40(4):433-40. doi: 10.3109/03639045.2013.828219
30. Nerkar TS, Gujarathi NA, Rane BR, Bakliwal SR, Pawar SP. *In-situ* gel: Novel approach in sustained and controlled drug delivery system. Int J Pharm Sci. 2013;4(4):1-18.
31. Vij NN, Saudagar RB. Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of terbinafine hydrochloride. Int J Pharm Sci Res. 2014;5(9):537-54.
32. Kim DW, Kim KS, Seo YG, Lee BJ, Park YJ, Youn YS, *et al.* Novel sodium fusidate-loaded film-forming hydrogel with easy application and excellent wound healing. Int J Pharm. 2015;495(1):67-74. doi: 10.1016/j.ijpharm.2015.08.082
33. Otto A, du Plessis J, Wiechers JW. Formulation effects of topical emulsions on transdermal and dermal delivery. Int J Cosmet Sci. 2009;31(1):1-19.
34. Nielloud F, Marti-Mestres G. Pharmaceutical Emulsions and Suspensions. New York: Marcel Dekker, Inc.; 2000. doi: 10.1201/9780429344688
35. Lunter D, Daniels R. *In vitro* skin permeation and penetration of nonivamide from novel film-forming emulsions. Skin Pharmacol Physiol. 2013;26(3):139-46. doi: 10.1159/000348464
36. Frederiksen K, Guy RH, Petersson K. The potential of polymeric film-forming systems as sustained delivery platforms for topical drugs. Expert Opin Drug Deliv. 2016;13(3):349-60. doi: 10.1517/17425247.2016.1124412
37. De Oliveira FF, de Menezes LR, Tavares MI. Film-forming systems in topically administered pharmaceutical formulations. Mater Sci Appl. 2020 Aug 14;11(8):576-90.
38. Devaux S, Castela A, Archier E, Gallini A, Joly P, Misery L, *et al*. Adherence to topical treatment in psoriasis: A systematic literature review. J Eur Acad Dermatol Venereol. 2012 May;26:61-7. doi: 10.1111/j.1468-3083.2012.04525.x
39. Brown MB, Jones SA, Limited M. Topical Film Forming Monophasic Formulations. Patent CA2622624C; 2006.
40. Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. Thin films as an emerging platform for drug delivery. Asian J Pharm Sci. 2016;11(5):559-74. doi: 10.1016/j.ajps.2016.05.004
41. Alberti I, Grenier A, Kraus H, Carrara DN. Pharmaceutical development and clinical effectiveness of a novel gel technology for transdermal drug delivery. Expert Opin Drug Deliv. 2005;2(5):935-50. doi: 10.1517/17425247.2.5.935
42. Williams AC, Walters KA. Chemical penetration enhancement: Possibilities and problems. In: Walters KA, Roberts MS, editors. Dermatologic, Cosmeceutic, and Cosmetic Development: Therapeutic and Novel Approaches. New York: Informa Healthcare; 2007. p. 502.
43. Felton LA. Film coating of oral solid dosage forms. Encyclopedia Pharm Technol. 2007;3:1729-47. doi: 10.1081/E-EPT4
44. Nandi S, Mondal S. Fabrication and evaluation of matrix type novel transdermal patch loaded with tramadol hydrochloride. Turk J Pharm Sci. 2022;19(5):572-82. doi: 10.4274/tjps.galenos.2021.43678
45. Patel DP, Setty CM, Mistry GN, Patel SL, Patel TJ, Mistry PC, *et al*. Development and evaluation of ethyl cellulose-based transdermal films of furosemide for improved *in vitro* skin permeation. AAPS PharmSciTech. 2009;10:437-42. doi: 10.1208/s12249-009-9224-3
46. Platon VM, Dragoi B, Marin L. Erythromycin formulations-a journey to advanced drug delivery. Pharmaceutics. 2022;14(10):2180. doi: 10.3390/pharmaceutics14102180
47. Bodmeier R, Paeratakul O. Dry and wet strengths of polymeric films prepared from an aqueous colloidal polymer dispersion, Eudragit RS30D. Int J Pharm. 1993 Jul 31;96(1-3):129-38.
48. Maitra J, Shukla VK. Cross-linking in hydrogels-a review. Am J Polym Sci. 2014 Jan;4(2):25-31. doi: 10.5923/j.ajps.20140402.01
49. Raghavan SL, Trividic A, Davis AF, Hadgraft J. Crystallization of hydrocortisone acetate: Influence of polymers. Int J Pharm. 2001 Jan 16;212(2):213-21.
50. Padula C, Nicoli S, Santi P. Innovative formulations for the delivery of levothyroxine to the skin. Int J Pharm. 2009;37:12-6. doi: 10.1016/j.ijpharm.2008.12.028
51. Gennari CG, Selmin F, Franzè S, Musazzi UM, Quaroni GM, Casiraghi A, *et al*. A glimpse in critical attributes to design cutaneous Film-forming systems based on ammonium methacrylate. J Drug Deliv Sci Technol. 2017;41:157-63. doi: 10.1016/j.jddst.2017.07.009
52. Gungor S, Erdal MS, Özsoy Y. Plasticizers in transdermal drug delivery systems. In: Recent Advances in Plasticizers. Vol. 5. Rijeka: IntechOpen; 2012. p. 91-112.
53. Bornare SS, Aher SS, Saudagar RB. A review: Film forming gel novel drug delivery system. Int J Curr Pharm Res. 2018;10(2):25-8. doi: 10.22159/ijcpr.2018v10i2.25886
54. Polymers BASF. Available from: https://www.basf_ps_pharma_product-overview.pdf [Last accessed on 2021 Apr 16].
55. Lambers H, Piessens S, Bloem A, Pronk H, Finkel P. Natural skin surface pH is on average below 5, which is beneficial for its resident flora. Int J Cosmet Sci. 2006;28:359-70. doi: 10.1111/j.1467-2494.2006.00344.x
56. Nesseem DI, Eid SF, El-Houseny SS. Development of novel transdermal self-adhesive films for tenoxicam, an anti-inflammatory drug. Life Sci. 2011;89(13-14):430-8. doi: 10.1016/j.lfs.2011.06.026
57. Mustaffa MF, Ramasamy K, Jaafar N, Hazizul Hasan M, Ramli NA, Suratman S, *et al*. *In-situ* film-forming solution for topical application of terbinafine HCl: Biopharmaceutical evaluation and *in vivo* antifungal performance using animal model. Int J Appl Pharm. 2021;13:98-105. doi: 10.22159/ijap.2021v13i6.42589