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A Review on Film Forming Gel Novel Drug Delivery System

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ABSTRACT

A film-forming gel is an innovative approach that is optional for conventional dosage forms applied to the skin. There are several transdermal formulations such as creams, ointment, gels, or patches, etc. But from these transdermal gel is more preferable than other transdermal formulations. The drug release is achieved by polymer solution which is directly applied on the skin in the form of liquid that forms a transparent invisible film in situ after solvent evaporation. Transdermal drug delivery system (TDDS) and dermal drug delivery system have been provided some desired performances that involve restriction of first metabolic pathways, enhancing drug bioavailability, decreasing dose frequency and stabilizing drug delivery profiles over conventional pharmaceutical dosage formulations. This review aimed to search for an optional dosage form to minimize skin irritation, enhance skin adhesion along with drug release, and improve patient compliances. Because of their irregular rheological behavior, polymeric gels are advantageous in case of ease of preparation, application, adhesion to the application surface, and capability to transport several varieties of drugs.

KEYWORDS: *Film-forming gels, transdermal drug delivery, semi-solids*

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INTRODUCTION

The skin is a major route for both the dermal and transdermal delivery systems.[1,2] The drug release is achieved by polymer solution which directly applied on the skin in the form of liquid that forms a transparent invisible film in situ after solvent evaporation.[3–5] Transdermal drug delivery system (TDDS) and dermal drug delivery system have been provided many desired advantages over conventional pharmaceutical dosage formulations that involve restriction of first metabolic pathways, enhancing drug bioavailability, decreasing dose frequency, and enhancing patient compliances.[6]In the transdermal delivery skin is the main route for the drug absorption. Skin is made by two main layers that involve epidermis and dermis. The outmost layer of the skin is the epidermis, that acts as a physical barrier for the penetration of the drug. The epidermis made up of several kinds of cells such as keratinocytes, melanocytes, and Langerhans cells.[7] The epidermis has been classified into four layers that included stratum corneum (SC), stratum granulosum (SG), stratum spinosum (SS), and stratum basale(SB). The major layer of skin isstratum corneum, which having thickness 15-20 µm, and acts as a rate-limiting barrier throughout transdermal drug diffusion.[8] Another layer of skin is the dermis, which has a thickness between 1,000 µm-2,000μm and made up of papillary dermis, reticular dermis, and hypodermis.[7,9] Structures such as the hair follicles, sweat glands, blood vessels, nerve fibers, and lymphatic vessels are surrounded in the dermis which enhances the TDDS by trapping the drug carriers and forming a reservoir, permitting a prolong release of the drugs and also deliver drugs into the systemic circulation bythe circulatory and lymphatic system.[7,8]The review is being carried out to enhance drug delivery through skin permeation. A film-forming gel is an innovative approach that is an option for conventional dosage forms applied to the skin. There are several transdermal formulations such as creams, ointment, gels, or patches, etc. The main aim of drug release through the skin is for the topical treatment of various skin diseases or transdermal absorption of drugs in the systemic circulation. The topical administration provides a large surface which promotes easy application by self-administration and

also acts as an option for oral dosage formulations of drugs and hypodermic administration.[10]Various semisolid dosage forms applied topically such as ointments and creams but have some limitations like less contact to the skin surface and easily take away by patient's clothes so there is need to a repetitive application at every time in case of long-lasting infections such as ringworm, athlete's foot, and candidiasis and Similarly ointments and creams leave a sticky and lubricious sensation after application which leads to patient non-compliance.[11]The objective of this review was to develop such a dosage form which reduces the dose frequency by keeping close contact with the skin to promote slow drug release that provides a prolonged-time period thus it increases patient compliance. The film-forming gel is a non-solid dosage form that creates a film in situ when the application over the skin or any other body part. Film-forming gel system made up of drugs with film-forming excipients in a suitable solvent.[12] After interaction with the skin it forms a film of solid polymeric material which provides a matrix to get sustained release of drug on skin which rapidly absorbed in the stratum corneum.[11]

Mechanism of film formation and Permeation

A film-forming gel is being used topically over the skin that sticks to the body and forms a thin, transparent film *in situ* via solvent evaporation.[12]Gel serves as an emollient or protective effect on the affected body by infections and for both local action or transdermal diffusion of active ingredients for systemic effect.[11,13] The film-forming system may be a dispersion or mixture of active ingredients and film-forming excipientsin volatile solvents. hence the formation of film over the skin by the mechanism of solvent evaporation as revealed in Fig. 1.Afterward the concentration of drug increases, until the saturation level, and it may the probability of getting super saturation level on the skin surface. Super saturation effects due to more drug flux through the skin by enhancing the thermodynamic activity of the formulation without disturbing the skin barrier, thus minimizing the side effects or irritation.[12]

The phenomenon of super saturation can be described by the modified form of Fick's law of diffusion.

Fick's law of diffusion is given in Equation(2.1) and modified form of Fick's law of diffusion Equation (2.2)

$$J = DKC\ v/h \quad \text{..... (2.1)}$$

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 the above equation(2.1) is explained that the rate of drug permeation throughout theskin is proportional to the concentration of the drug. However, this is true whenall the drug is dissolved in the vehicle.

$$J = \alpha\ D/\gamma\ h \quad \text{.....(2.2)}$$

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

According to equation (2.2), 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 as well as thermodynamic instability.

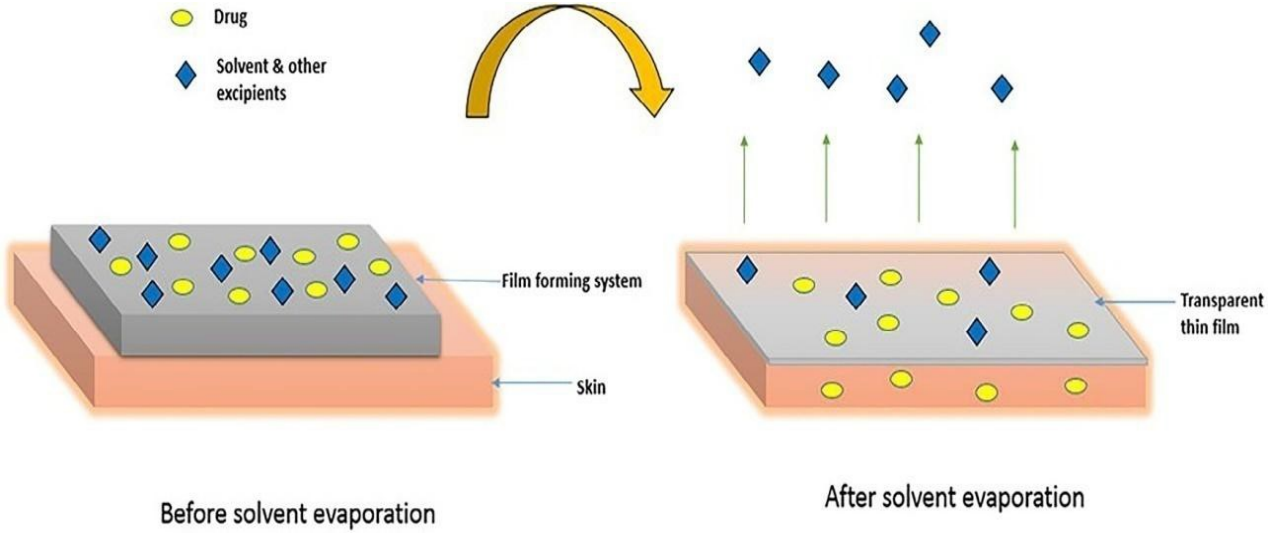


Fig. 1 – Mechanism of film formation

Film Forming System produces supersaturated systems instantly after application tothe skin, that overcomes the problem of instability. Therefore, it increases thedrug permeation through the skin as compared to other transdermal dosageforms.[14]

Properties of the film-forming system:

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.

- FFS creates supersaturated systems immediately after application to the skin, overcoming the problem of instability.
- It improves drug permeation through the skin and compared to othertransdermal dosage forms.
- The delivery efficiency of the film-forming solutions for ethinylestradiol wasinvestigated.[4]

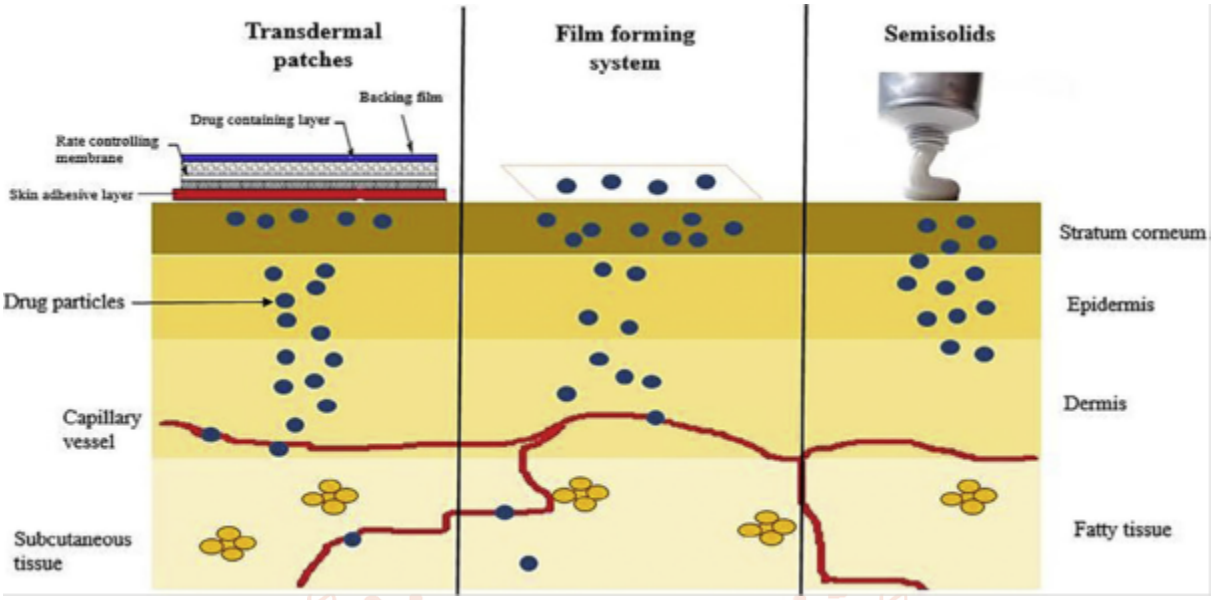
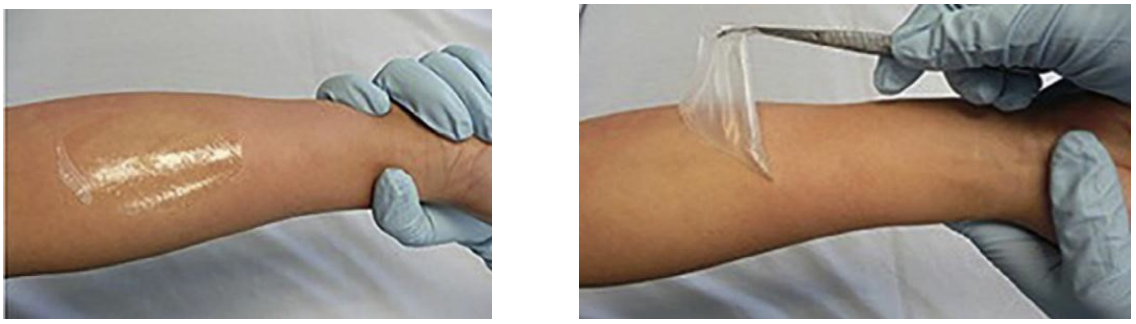


Fig 2 Release profile of the topical and transdermal drug delivery systems

- The permeation of ethinylestradiol from the FF solution prepared with or without enhancer was compared to the permeation from the patch through human skin (epidermis) in vitro e.g commercially available patch (EVRA®).[15]
- The film-forming formulations such as solution, gel showed a higher permeation than the commercial transdermal patch.[16]
- FFS formulation is prepared Without enhancer and transport more than double ethinylestradiol than the marketed patch.
- The formulation is delivered with enhancer about seven times as much ethinylestradiol as that of the marketed patch.
- These systems prove to be useful in enhancing drug permeation.

The film-forming system in that apply a thin layer of the formulation(strata) directly to the affectedarea and allow the gel to dry in 5-6 min to forms film and to maintain in continuous contactwith the skin (24 hrs /day).[17]



A **B**

Fig. 1 – Appearance of the film-forming system: (A) Formation of a transparent film onApplication; (B) Non-tacky, flexible, easily peelable film after drying.

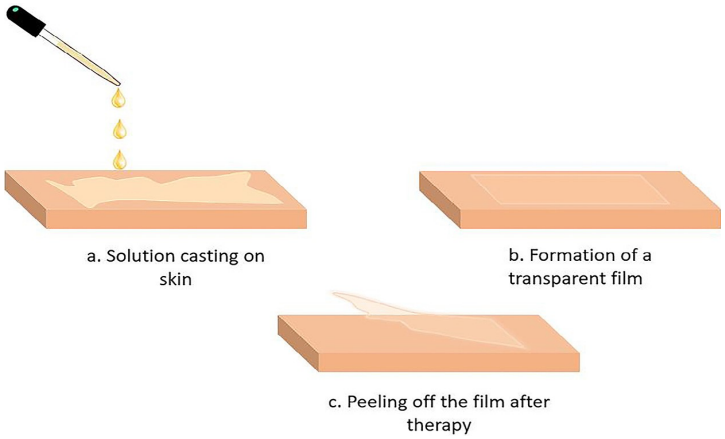


Fig 3 Application of film-forming solution on the skin

Following administration, the film can be peeled off once the desired results are obtained or for the termination of therapy as shown in fig. 3[17]

Composition of film-forming polymeric gels:

Suitable drugs:

The usage of the developed formulations for dermatological indications is theoretically possible as well but cannot be recommended sometimes due to the nature of the solvent in the compositions. Dermatological diseases are often associated with inflamed skin where the administration of ethanolic solutions might be painful for the patient and thus not acceptable.

For a transdermal application, suitable drugs have to fulfill certain requirements that are independent of the dosage form.[18]

- Generally, the drugs which apply to these systems are highly potent which permeation through the skin rapidly, which causes no skin irritation.
- Only potent drugs for a route of application with a daily dose of less than 10 mg.
- The molecular weight of the drug is important in drug permeation as small molecules crossing human skin than large molecules.
- Size of the molecule below 500 Da for sufficient mobility in the skin structure.
- Drug passing through the lipophilic, as well as hydrophilic, are in the skin into the systemic circulation way.[19]
- The drug has to pass lipophilic as well as hydrophilic areas in the skin on its way into the systemic circulation it is advantageous if the drug is neither very hydrophilic nor extremely lipophilic (log P_{oct} between 1 and 3). Therefore molecules with a pH value between 5 and 9 in aqueous solutions are preferred for the transdermal application.[20]

Table 1-The ideal properties of the drug suitable for transdermal drug delivery system:[20]

Parameter	Properties
Dose	10mg or less
Mol. Weight	Less than 500 Da
Melting point	<200°c
Partition coefficient Log p(Octanol/water)	Between 1 and 3
Hydrogen binding group	<2
PH value	Between 5 and 9
Skin reaction	Non-irritating and non-sanitizer

Polymer:

Polymers are the foundation of the FFS and a variety of polymers are available for the preparation of these systems. To achieve the desired film properties, these polymers can be used alone or in combination with other film-forming polymers.[21]

- This Polymer used to control drug release is a modification of the film-formingpolymer as a functional excipient.

Polymers	Properties
Hydroxypropyl Methylcellulose (HPMC) HPMC (E4M, E15, E50M K4M)	➢ Produce a light, non-greasy uniform film with good texture. ➢ Produces a smooth clear spreadable gel ➢ Effective in conc. of 2-6% as a gelling agent. ➢ Do not interact significantly with other ingredients. ➢ Surface active agent, therefore adsorbs water providing easy dispersion, lubricity, and comfortable feel in the occlusive state on application to the skin.[22]
Ethylcellulose (EC)	➢ Nontoxic, nonirritating, non-allergic material ➢ Good film-forming properties that form tougher films[23] ➢ Water insoluble[24]
Hydroxypropyl cellulose	➢ Nonionic, pH insensitive polymer ➢ Water soluble[25]
Polyvinyl pyrrolidine (PVP) (PVP K30, PVP VA64)	➢ Solubility in water and other solvents ➢ Adhesive and binding property ➢ Acts as a bioavailability enhancer[26] ➢ are high hygroscopicity, good biocompatibility [27]
Polyvinyl alcohol (PVA)	➢ Water soluble ➢ Excellent film-forming and adhesive properties ➢ Non-toxic and biocompatible[28] ➢ low hydrophilicity, rigid film generation and insufficient elasticity[29]
Chitosan	➢ Excellent film-forming ability ➢ Opens the tight junctions of the mucosal membrane, thereby enhancing the paracellular permeability and penetration of drug[30] ➢ Controls drug release[31] ➢ good biocompatibility[32]
Eudragit (polymethacrylates copolymer) Eudragit RS 100, RL 100, NE, RS 30D, S 100	➢ Transparent, elastic, self-adhesive ➢ Good adhesion to the skin[33]
Silicones Polydimethylsiloxane (PDMS)	Water vapor permeable film ➢ Adequate substantivity and durableFilm[34]
Acrylates copolymer Avalure® AC 118, AC 120	Tough, breathable, abrasion-resistant Films[35]

- These polymers can be used as another film-forming polymer and in combination or alone.[21]
- These polymers should form a clear, transparent and flexible film at skin temperature (28 °C-32 °C).
- It should have a certain inherent affinity and flexibility to the skin to avoid the usage of excessive amounts of plasticizer.[18]

These polymers should form a clear are mentioned in Table 2.

Solvent

The solvents form an important component in film formation. The solvent used in film-forming systems helps in solubilizing the drugs as well as have an impact on drug permeation through the skin[36]. A suitable solvent is used for the formulation of a FF polymeric composition such as ethanol, ethyl acetate, or isopropanol with a better spreading as well as higher volatility.[37]

Commonly used solvents for topical and transdermal use are listed in Table 3.As these solvents are widely used, the safety of these has been established on long term use.[38]

Table 3 solvents used in the topical system

Category	Example
Glycol	Propylene glycols, polyethylene glycols.
Alcohols	Ethanol, butanol, isopropanol, benzyl alcohol, Lanolin alcohols, fatty alcohols.
Other solvents	Ethyl acetate, oleic acid, isopropyl myristate

Plasticizer: Plasticizers are used in the film-forming systems to impart flexibility to the film and improve the tensile strength of the film. Commonly used plasticizers are triethyl citrate, glycerine, dibutyl phthalate, polyethylene glycol, sorbitol, propylene glycol, etc.[39]The formulation experiments have shown that the skin adhesion of the films can be modulated with the help of plasticizers. The plasticizer has to be thoroughly selected concerning the film former. It has to be miscible with the polymer to produce clear films with low visibility on the skin.[40]

Further excipients

Apart from the basic compounds of a film-forming polymeric solution (polymer, solvent, and plasticizer), it can be appropriate to incorporate further excipients into the preparation. For some polymers such as the acryl ate Eudragit E 100, it is beneficial to add a crosslinker (succinic acid) to the composition to improve the film stability. For some drugs, a solubilizer or co-solvent can be required to increase the drug loading of the formulation and the drug flux. Further examples for supplementary excipients are antioxidants to stabilize oxidation sensitive drugs in the preparation during storage, sunscreens for the protection of photosensitive drugs or dyes to facilitate the localization of the formed film for the patient.[41]

Evaluation Tests for Film Forming Gels

Physicochemical properties

Formulations were subjected to evaluation of physical parameters like appearance, pH, phase transition time,film thickness, weight, viscosity, Spreadability.

Film formation

The time needed by the gel to get converted into the film is the phase transition time. One gram of gel was placed on a petri dish which was spread uniformly on it and kept on a hot plate at 37˚C and time needed until gel converts into the film were measured.[42]

Film weight

1 gram of the gel was placed on a Petri dish that was left for drying. after drying the resultant film was weighed on an electronic balance.[39]

Drying time (min)

For the valuation of the drying time, the gel is applied to the internal sides of the forearm of a volunteer, who participated in the study on an informed consent basis. After some time of period take another glass side was placed on the film without applying pressure. If no liquid is visible on the glass slide after removal, the film is considered dry.[43] If remains of liquid were visual on the glass side the experiment is repeated until the film was found to be fully dry. A good FFS should have a minimum drying time to avoid long waiting time for the patient.

Rheological studies

Viscosity was measured by using Brookfield Viscometer LVDV II+ model. Gels were placed under the viscometer to determine the viscosity of the gel. Gels were placed under the viscometer using by S 64 spindle to determine the viscosity of the gel. The viscosity was determined at different RPMs such as 10, 20, 50, 100 RPM and the corresponding viscosity and torque were noted.[44]

Spread ability (cms)

Minimum quantity of the gel was placed between two glass plate and the glass plate on the top was gently slid on the bottom glass slide to determine the spread ability of the gel.

Spread ability was measured based on drag and slip characteristics of gels. The gel was kept in between this slide and another glass slide having the dimension of a fixed ground slide and provided with the hook. A 1 kg weight was placed on the top of the two slides for 5* minutes to expel the air and to provide a uniform film of the gel between the slides. The excess of the gel was removed from the edges. The top plate was then subjected to a pull of 100gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5cm be noted. A shorter interval indicates better spread ability.

Spread ability was calculated using the following formula:

$S = M \times L/T$

Where,

S = Spreadibility,

M = Weight in the pan (tied to the upper slide),

L = Length moved by the glass slide and
T = Time (in sec.) taken to separate the slide each other.[36]

Application of film-forming gel

- Gels are the most commonly used topical preparations used for the treatment of variousdiseases.
- Stratamed®is the first film-forming silicone gel-based wound dressing approved for theuse on open wounds and compromised skin.
- Stratamed® can be used after dermatological intervention (laser treatment, dermalabrasion, chemical peels, removal tattoos) surgeries, trauma burns, etc.
- A silicone-based gel is effective in promoting accelerated epithelisation, reducing theanti-inflammatory response and prevention of scarring.
- Silicone gel (FFG) is used in the treatment and prevention of abnormal scars because I can be used immediately on open wounds and damaged skin.
- Based on the research article of FFG Formulation of example with their uses and treatment are listed in table.5

Table 5 film-forming gel formulation with uses and treatment

Drug	Used and treatment
Indomethacin	Rheumatoid arthritis[45,46]
Terbinafine hydrochloride	Skin infection[47]
Clobetasol propionate	Skin infection[48]
Diclofenacdiethylamine	Arthritis, traumatic pain[49]
Silver sulfadiazine (film-forming hydrogel)	Burns[50]
Flurbiprofen	Rheumatoid arthritis
Bifonazole	Fungal skin infection[51]
Miconazole nitrate	Fungal infection of skin[52]
Ketoprofen,	NSAIDS[53]
Lornoxicam	NSAIDs, used for osteoarthritis, rheumatoid arthritis, and inflammatory condition.[54]

CONCLUSION

Film-forming gels prove to be an effective dosage form for the transdermal delivery of drugs. Also, it remains adhered to the affected part for a longer period without getting rubbed off. It provides sustained effect and better relief than the conventional gels and frequent reapplication is not required. The concept of film-forming gels can change to the treatment concept of various diseases such as arthritis. A lot of work can be carried out in this field.

REFERENCE:

[1] S. Heuschkel, A. Goebel, R.H.H. Neubert, Microemulsions - Modern colloidal carrier for dermal and transdermal drug delivery, J. Pharm. Sci. 97 (2008) 603–631. https://doi.org/10.1002/jps.20995.

[2] M.J. Choi, H.I. Maibach, Liposomes and niosomes as topical drug delivery systems, Skin Pharmacol. Physiol. 18 (2005) 209–219. https://doi.org/10.1159/000086666.

[3] R.B. Saudagar, P.A. Gangurde, Film Forming Gels: A Review, Int. J. Curr. Pharm. Rev. Res. 8 (2017) 244–248. https://doi.org/10.25258/ijcprr.v8i03.9212.

[4] I. Zurdo Schroeder, P. Franke, U.F. Schaefer, C.M. Lehr, Development and characterization of film forming polymeric solutions for skin drug delivery, Eur. J. Pharm. Biopharm. 65 (2007) 111–121. https://doi.org/10.1016/j.ejpb.2006.07.015.

[5] W. Pichayakorn, J. Suksaeree, P. Boonme, T. Amnuaikit, W. Taweepreda, G.C. Ritthidej, Deproteinized natural rubber film forming polymeric solutions for nicotine transdermal delivery, Pharm. Dev. Technol. 18 (2013) 1111–1121. https://doi.org/10.3109/10837450.2012.705297.

[6] P. Carter, B. Narasimhan, Q. Wang, Biocompatible nanoparticles and vesicular systems in transdermal drug delivery for various skin diseases, Int. J. Pharm. 555 (2019) 49–62. https://doi.org/10.1016/j.ijpharm.2018.11.032.

[7] B. Palmer, L. DeLouise, Nanoparticle-Enabled

Transdermal Drug Delivery Systems for Enhanced Dose Control and Tissue Targeting, Molecules. 21 (2016) 1719. https://doi.org/10.3390/molecules21121719.

[8] S. Barua, S. Mitragotri, Challenges associated with penetration of nanoparticles across cell and tissue barriers: A review of current status and future prospects, Nano Today. 9 (2014) 223–243. https://doi.org/10.1016/j.nantod.2014.04.008.

[9] C.M. Schoellhammer, D. Blankschtein, R. Langer, Skin permeabilization for transdermal drug delivery: Recent advances and future prospects, Expert Opin. Drug Deliv. 11 (2014) 393–407. https://doi.org/10.1517/17425247.2014.875528.

[10] M.R. Prausnitz, R. Langer, Transdermal drug delivery, Nat. Biotechnol. 26 (2008) 1261–1268. https://doi.org/10.1038/nbt.1504.

[11] K. Kathe, H. Kathpalia, Film forming systems for topical and transdermal drug delivery, Asian J. Pharm. Sci. 12 (2017) 487–497. https://doi.org/10.1016/j.ajps.2017.07.004.

[12] K. Frederiksen, R.H. Guy, K. Petersson, The potential of polymeric film-forming systems as sustained delivery platforms for topical drugs, Expert Opin. Drug Deliv. 13 (2016) 349–360. https://doi.org/10.1517/17425247.2016.1124412.

[13] K. Frederiksen, R.H. Guy, K. Petersson, Formulation considerations in the design of topical, polymeric film-forming systems for sustained drug delivery to the skin, Eur. J. Pharm. Biopharm. 91 (2015) 9–15. https://doi.org/10.1016/j.ejpb.2015.01.002.

[14] T.T.D. Tran, P.H.L. Tran, Controlled Release Film Forming Systems in Drug Delivery: The Potential for Efficient Drug Delivery, Pharmaceutics. 11 (2019) 290. https://doi.org/10.3390/pharmaceutics11060290

[15] I.Z. Schroeder, P. Franke, U.F. Schaefer, C.M. Lehr, Delivery of ethinylestradiol from film forming polymeric solutions across human epidermis in vitro and in vivo in pigs, J. Control. Release. 118 (2007) 196–203. https://doi.org/10.1016/j.jconrel.2006.12.013.

[16] WO2007031753A2 - Topical film-forming monophasic formulations - Google Patents, (n.d.). https://patents.google.com/patent/WO2007031753A2/en

[17] A. Misra, R. Pal, S.S. Majumdar, G.P. Talwar, O. Singh, Biphasic testosterone delivery profile observed with two different transdermal formulations, Pharm. Res. 14 (1997) 1264–1268. https://doi.org/10.1023/A:1012179529090.

[18] A. Naik, Y.N. Kalia, R.H. Guy, Transdermal drug delivery: Overcoming the skin's barrier function, Pharm. Sci. Technol. Today. 3 (2000) 318–326. https://doi.org/10.1016/S1461-5347(00)00295-9.

[19] M.R. Prausnitz, S. Mitragotri, R. Langer, Current status and future potential of transdermal drug delivery, Nat. Rev. Drug Discov. 3 (2004) 115–124. https://doi.org/10.1038/nrd1304.

[20] I. Alberti, A. Grenier, H. Kraus, D.N. Carrara, Pharmaceutical development and clinical effectiveness of a novel gel technology for transdermal drug delivery, Expert Opin. Drug Deliv. 2 (2005) 935–950. https://doi.org/10.1517/17425247.2.5.935.

[21] S. Karki, H. Kim, S.J. Na, D. Shin, K. Jo, J. Lee, Thin films as an emerging platform for drug delivery, Asian J. Pharm. Sci. 11 (2016) 559–574. https://doi.org/10.1016/j.ajps.2016.05.004.

[22] R. Vijaya, C. Pratheeba, Study of the hydroxy propyl methyl cellulose (hpmc) combinations in the development of transdermal film for amitriptyline hcl, ijpcbs. 5(3) (2015) 548–556.

[23] D.P. Patel, C.M. Setty, G.N. Mistry, S.L. Patel, T.J. Patel, P.C. Mistry, A.K. Rana, P.K. Patel, R.S. Mishra, Development and evaluation of ethyl cellulose-based transdermal films of furosemide for improved in vitro skin permeation, AAPS PharmSciTech. 10 (2009) 437–442. https://doi.org/10.1208/s12249-009-9224-3.

[24] S.M. Trey, D.A. Wicks, P.K. Mididoddi, M.A. Repka, Delivery of itraconazole from extruded HPC films, Drug Dev. Ind. Pharm. 33 (2007) 727–735. https://doi.org/10.1080/03639040701199225.

[25] M. Marucci, H. Andersson, J. Hjärtstam, G. Stevenson, J. Baderstedt, M. Stading, A. Larsson, C. von Corswant, New insights on how to adjust the release profile from coated pellets by varying the molecular weight of ethyl cellulose in the coating film, Int. J. Pharm. 458 (2013) 218–223. https://doi.org/10.1016/j.ijpharm.2013.09.016.

[26] T.T.D. Tran, P.H.L. Tran, Perspectives on Strategies Using Swellable Polymers in Solid Dispersions for Controlled Drug Release, Curr. Pharm. Des. 23 (2016) 1639–1648. https://doi.org/10.2174/1381612822666161021152932.

[27] A.F. Borges, C. Silva, J.F.J. Coelho, S. Simões, Oral films: Current status and future perspectives: I-Galenical development and quality attributes, J. Control. Release. 206 (2015) 1–19. https://doi.org/10.1016/j.jconrel.2015.03.006.

[28] F.K. Alanazi, A.A.A. Rahman, G.M. Mahrous, I.A. Alsarra, Formulation and physicochemical characterisation of buccoadhesive films containing ketorolac, J. Drug Deliv. Sci. Technol. 17 (2007) 183–192. https://doi.org/10.1016/S1773-2247(07)50034-1.

[29] M. Teodorescu, M. Bercea, S. Morariu, Biomaterials of PVA and PVP in medical and pharmaceutical applications: Perspectives and challenges, Biotechnol. Adv. 37 (2019) 109–131. https://doi.org/10.1016/j.biotechadv.2018.11.008.

[30] N. Hameed, V. Glattauer, J.A.M. Ramshaw, Evaluation of polyvinyl alcohol composite membranes containing collagen and bone particles, J. Mech. Behav. Biomed. Mater. 48 (2015) 38–45. https://doi.org/10.1016/j.jmbbm.2015.04.005.

[31] E.A. Kamoun, X. Chen, M.S. Mohy Eldin, E.R.S. Kenawy, Crosslinked poly(vinyl alcohol) hydrogels for wound dressing applications: A review of remarkably blended polymers, Arab. J. Chem. 8 (2015) 1–14. https://doi.org/10.1016/j.arabjc.2014.07.005.

[32] L. Liu, Q. Gao, X. Lu, H. Zhou, In situ forming hydrogels based on chitosan for drug delivery and tissue regeneration, Asian J. Pharm. Sci. 11 (2016) 673–683. https://doi.org/10.1016/j.ajps.2016.07.001.

[33] A. Kaushik, A. Tiwari, A. Gaur, Role of excipients and polymeric advancements in preparation of floating drug delivery systems, Int. J. Pharm. Investig. 5 (2015) 1. https://doi.org/10.4103/2230-973x.147219.

[34] X.T. Dupont, D. Sas, Silicone Film-Forming Technologies for Health Care Applications, n.d. https://www.researchgate.net/publication/237633841.

[35] H. Bajaj, T. Kumar, V. Singh, Film Forming Gels : A Review , . . Res. J. Pharm. , Biol. Chem. Sci. . 7(4) (2016) 2085–2091.

[36] J.W. Lee, J.H. Park, J.R. Robinson, Bioadhesive-based dosage forms: The next generation, J. Pharm. Sci. 89 (2000) 850–866. https://doi.org/10.1002/1520-6017(200007)89:7<850::AID-JPS2>3.0.CO;2-G.

[37] K. Frederiksen, R.H. Guy, K. Petersson, Formulation considerations in the design of topical, polymeric film-forming systems for sustained drug delivery to the skin, Eur. J. Pharm. Biopharm. 91 (2015) 9–15. https://doi.org/10.1016/j.ejpb.2015.01.002.

[38] A.S. Can, M.S. Erdal, S. Güngör, Y. Özsoy, Optimization and characterization of chitosan films for transdermal delivery of ondansetron, Molecules. 18 (2013) 5455–5471. https://doi.org/10.3390/molecules18055455.

[39] V. Singh, G. Kukreti, M.S.-J.P. Res, 2013, Film formers gels (FIFOGE): a novel approach, Academia.Edu. 1(1) (2013) 22–28. http://www.academia.edu/download/33731475/Film-Formers-Gels.pdf (accessed August 22, 2020).

[40] B.J. Thomas, B.C. Finnin, The transdermal revolution, Drug Discov. Today. 9 (2004) 697–703. https://doi.org/10.1016/S1359-6446(04)03180-0.

[41] D. Jones, D. Woolfson, A.F. Brown, Textural, viscoelastic and mucoadhesive properties of pharmaceutical gels composed of cellulose polymers, Int. J. Pharm. 151 (1997) 223–233. https://pure.qub.ac.uk/en/publications/textural-viscoelastic-and-mucoadhesive-properties-of-pharmaceutic (accessed August 22, 2020).

[42] S.S. Bornare, S.S. Aher, R.B. Saudagar, A Review: Film forming gel novel drug delivery system, Int. J. Curr. Pharm. Res. 10 (2018) 25. https://doi.org/10.22159/ijcpr.2018v10i2.25886

[43] I. Šveikauskaite, V. Briedis, Effect of film-forming polymers on release of naftifine hydrochloride from nail lacquers, Int. J. Polym. Sci. 2017 (2017). https://doi.org/10.1155/2017/1476270.

[44] S. Z. Chemate and Shubhangi N. Albhar, Formulation and development of flurbiprofen containing film forming gel, World J. Pharm. Res. Vol 6, (2017).

[45] M. Elmowafy, A. Samy, A.E. Abdelaziz, K.

Shalaby, A. Salama, M.A. Raslan, M.A. Abdelgawad, Polymeric nanoparticles based topical gel of poorly soluble drug: Formulation, ex-vivo and in vivo evaluation, Beni-Suef Univ. J. Basic Appl. Sci. 6 (2017) 184–191. https://doi.org/10.1016/j.bjbas.2017.03.004.

[46] S. Miyazaki, T. Tobiyama, M. Takada, D. Attwood, Percutaneous Absorption of Indomethacin from Pluronic F127 Gels in Rats, J. Pharm. Pharmacol. 47 (1995) 455–457. https://doi.org/10.1111/j.2042-7158.1995.tb05829.x.

[47] R.B. Saudagar, P.A. Gangurde, Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of miconaole nitrate, Res. J. Top. Cosmet. Sci. 8 (2017) 19. https://doi.org/10.5958/2321-5844.2017.00003.6.

[48] A. Verma, S. Singh, R. Kaur, U.K. Jain, Formulation and evaluation of clobetasol propionate gel, n.d. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.954.9563.

[49] Saudagar RB, Sawant MP, Formulation, development and evaluation of sustained release film-forming gel of clobetasol propionate, International Journal of Institutional Pharmacy And Life Sciences (2015) www.ijipls.com.

[50] C.K. Manoj, Hygeia, Journal for drugs and medicines, Formulation, evaluation and optimization of novel silver sulfadiazine loaded film forming hydrogel for burns, Hygeia.J.D.Med. 8 (2016) 1–10. https://doi.org/10.15254/H.J.D.Med.8.2016.156

[51] B.J.P.A. Narkhede Sachine, Formulation and evaluation of film forming gel of bifonazole for local drug delivery, Int. J. Pharm. Sci. 8 (2017) 173–189.

[52] R.B. Saudagar, P.A. Gangurde, Formulation, development and evaluation of film-forming gel for prolonged dermal delivery of miconaole nitrate, Res. J. Top. Cosmet. Sci. 8 (2017) 19. https://doi.org/10.5958/2321-5844.2017.00003.6.

[53] X. Li, R. Zhang, R. Liang, W. Liu, C. Wang, Z. Su, F. Sun, Y. Li, Preparation and characterization of sustained-release rotigotine film-forming gel, Int. J. Pharm. 460 (2014) 273–279. https://doi.org/10.1016/j.ijpharm.2013.11.015.

[54] M.S. El-Ridy, S.A. Yehia, A.M. Mohsen, S.A. El-Awdan, A.B. Darwish, Formulation of Niosomal Gel for Enhanced Transdermal Lornoxicam Delivery: In-Vitro and In-Vivo Evaluation, Curr. Drug Deliv. 15 (2018). https://doi.org/10.2174/1567201814666170224141548.