REVIEW ARTICLE

Transdermal Drug Delivery System: A Recent Review

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Abstract

Transdermal medication delivery is the first and foremost delivery of drugs since the inception of treatment for human beings and diseases. In the olden days all the physician focussed on two methods of administering the drugs the first is the oral delivery next is transdermal delivery. The transdermal delivery has even more advantageous than oral dosage forms in some aspects such as overcoming the drug degradation which happens in the entire length of gastro intestinal tract. The removal of formulation is also easy and its application is easy without any other major ingredients. The present review focuses on its origin, anatomy of skin, and its layers concerning the passage of drugs, advantages, disadvantages, applications, physiological properties, biological properties, and limitations, polymers, and various approaches for patches. The major challenge and success in dosage form is the selection of polymers for formulation and its successful drug delivery. This article narrates the majority of evaluation studies to be carried out for the transdermal patches such as Physicochemical evaluation - Thickness, Uniformity of weight, drug content determination, moisture uptake, flatness, folding endurance, Tack properties, tensile strength, Thumb tack test, rolling ball test, quick stick (peel tack) test, *in vitro* release studies, *in vivo* studies, percentage water vapor permeation test, human model, swellability, polariscopic examination, stability testing and skin irritation study and their procedure and diagram of experimental performance was presented. The prepared patches need to be successfully evaluated for the above tests and suitable bioavailability must be proved for good market product. The content was also made on present available marketed products and its use such as nicotine patch as Nico dermis to help in smoking cessation, nitroglycerin patches for angina pectoris, estradiol patches in combination with levonorgestrel as climara pro for menopausal symptoms, and some other drugs to cure diseases.

Key words: Drug content determination, estradiol patches, moisture uptake, nicotine patch, transdermal medication delivery, uniformity of weight

INTRODUCTION

Ranging the past few decades, passion has been found in the development of novel drug delivery systems for existing drug molecules has been renewed. The development of a novel delivery system for existing drug molecules not only improves the drug's performance in terms of efficacy and safety but also improves patient compliance and overall therapeutic benefit to a significant

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extent. Transdermal drug delivery system (TDDS) are defined as self-contained, discrete dosage forms which are also known as "patches." when patches are applied to the intact skin, deliver the drug through the skin at a controlled rate to the systemic circulation. TDDS are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin.[1-5] The main significance of TDDS is to deliver drugs into systemic circulation into the skin through the skin at predetermined rate with minimal inter and intrapatient variation. At present, transdermal drug delivery is one of the most promising methods for drug application. It mitigates the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliances and minimizes harmful side effects of a drug caused by temporary over dose and is convenience in transdermal delivered drugs that require only once weakly application.

That will improve bioavailability with a more uniform range of plasma levels, a longer duration of action resulting in a particular reduction in dosing frequency with reduced side effects, and improved therapy due to maintenance of plasma levels up to the end of the dosing interval compared to a decline in plasma levels with conventional oral dosage forms. Transdermal delivery not only provides controlled, constant administration of drugs but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into the systemic circulation. The development of TDDS is a multidisciplinary activity that encompasses fundamental feasibility studies starting from the selection of drug molecules to the demonstration of sufficient drug flux in an *ex vivo* and *in vivo* model followed by the fabrication of a drug delivery system that meets all the stringent needs that are specific to the drug molecule (physicochemical and stability factors), the patient (comfort and cosmetic appeal), the manufacturer (scale up and manufacturability), and most important economy. The first transdermal system, transderm SCOP was approved by the Food and Drug Administration in 1979 for the prevention of nausea and vomiting associated with travel. Most transdermal patches are designed to release the active ingredient at a zero order rate for a period of several hours to days following application to the skin. This is especially advantageous for prophylactic therapy in chronic conditions. The evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drug and its metabolites in the urine, and through the clinical response of the patient to the administered drug therapy.[6-10]

ANATOMY OF SKIN

Human skin comprises three distinct but mutually dependent tissues.

a. The stratified, a vascular, cellular epidermis,
b. Underlying dermis of connective tissues, and
c. Hypodermis.

Epidermis

The multilayered envelope of the epidermis varies in thickness, depending on cell size and number of cell layers, ranging from 0.8 mm on palms and soles down to 0.06 mm on the eyelids. Stratum corneum and the remainder of the epidermis so called viable epidermis cover a major area of skin. The epidermis contains no blood vessels and hence nutrients and waste products must diffuse across the dermo-epidermal layer in order to maintain tissue integrity. Likewise, molecules permeating across the epidermis must cross the dermo-epidermal layer in order to be cleared into the systemic circulation. The source of energy for lower portions of epidermis is also glucose, and the end product of metabolism, lactic acid accumulates in skin. The epidermis contains four histologically distinct layers which, from the inside to the outside, are stratum germinativum (growing layer), malpighion layer (pigment layer), stratum spinosum (prickly cell layer), stratum granulosum (granular layer), stratum lucidum and stratum corneum (horny layer).

A representation of the "Brick and Mortar" model of human stratum corneum. Lipid constituents vary with body site (neutral lipids, phingolipids, polar lipids, and cholesterol). Phospholipids are largely absent, a unique feature of mammalian membrane. The architecture of the horney layer may be modeled as a wall-like structure. In this model, the keratinized cells function as a protein "bricks" embedded in lipid "mortar." The lipids are arranged in multiple bi-layers, and it has been suggested that there is sufficient amphiphilic material in the lipid fraction, such as polar-free fatty acids and cholesterol, to maintain a bi-layer form. In the basal layer, mitosis of the cells constantly renews the epidermis and this proliferation compensates the loss of dead Horney cells from the skin surface. As the cells produced by the basal layer move outward, they alter morphologically and histochemically, undergoing keratinization to form the outermost layer of stratum corneum.

Dermis

Dermis is 3–5 mm thick layer and is composed of a matrix of connective tissue, which contains blood vessels, lymph vessels, and nerves. The cutaneous blood supply has an essential function in the regulation of body temperature. It also provides nutrients and oxygen to the skin, while removing toxins and waste products. Capillaries reach to within 0.2 mm of skin surface and provide sink conditions for most molecules penetrating the skin barrier. The blood supply thus keeps the dermal concentration of permeate very low, and the resulting concentration difference across the epidermis provides the essential driving force for transdermal permeation.

Hypodermis (subcutaneous fat layer)

The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area. This

layer helps to regulate temperature and provides nutritional support and mechanic protection. It carries principal blood vessels and nerves to the skin and may contain sensory pressure organs. For transdermal drug delivery drug has to penetrate through all these three layers and reach into systemic circulation while in case of topical drug delivery only penetration through the stratum corneum is essential and then retention of drug in skin layers is desired.[11,12] The structure of the skin was shown in Figure 1.

ROUTES OF DRUG PENETRATION THROUGH SKIN

Drug penetration across the skin can occur through two routes: The transepidermal pathway, which involves penetration through the epidermis, and the transappendegeal pathway, which involves penetration through appendages such as hair follicles and sweat glands.

1. Transepidermal pathway: In this pathway, drugs permeate through the skin's outermost layer, known as the stratum corneum. This layer is a structurally complex, multi-layered, and multi-cellular barrier.[19]
    a. Intra-cellular route: Some drugs can go through specific skin cells called corneocytes, which are specialized skin cells. This route is for substances that dissolve in water (hydrophilic or polar solutes).
    b. Inter-cellular route: Other drugs can move through the spaces between these skin cells. This route is for substances that dissolve in fats (lipophilic or non-polar solutes). They travel through the continuous fatty layer of the skin.
2. Transappendegeal pathway: This pathway involves drugs passing through sweat glands and hair follicles in the skin.
    a. Sweat glands and hair follicles: These are like tiny tunnels or openings in the skin that some Substances can travel through. So, when drugs need to get into our body through the skin, they can either go through the outer layer of skin cells or use these tiny tunnels created by sweat glands and hair follicles. Each pathway has specific characteristics, allowing different types of substances to enter the body.[13,14] The advantages, disadvantages, and applications were given in Table 1.

FORMULATION ASPECTS OF TDDS[30-38]

The basic components to be taken into consideration were

1. Drug
2. Polymer matrix/drug reservoir
3. Permeation enhancers
4. Pressure sensitive adhesives
5. Backing laminates
6. Release liner
7. Other excipients like plasticizers and solvents.

Drug

The selection of drugs for TDDS is based on the physicochemical properties and biological properties of drug molecules. The suitability and the drug requirements are mentioned in Table 2.

Polymer matrix/drug reservoir

The polymers play a major significant role in achieving the controlled drug release from the device. The polymer matrix can be done by dispersion of active ingredients in liquid or solid state in a base. The polymers must offer good compatibility with the drug and the other components of the system and they should provide effective controlled release of drug throughout the formulation with safe nature. The polymers of natural, synthetic, and elastomers were mentioned in Table 4.

Permeation enhancers

The compounds which are used to increase the permeability of stratum corneum by interacting with

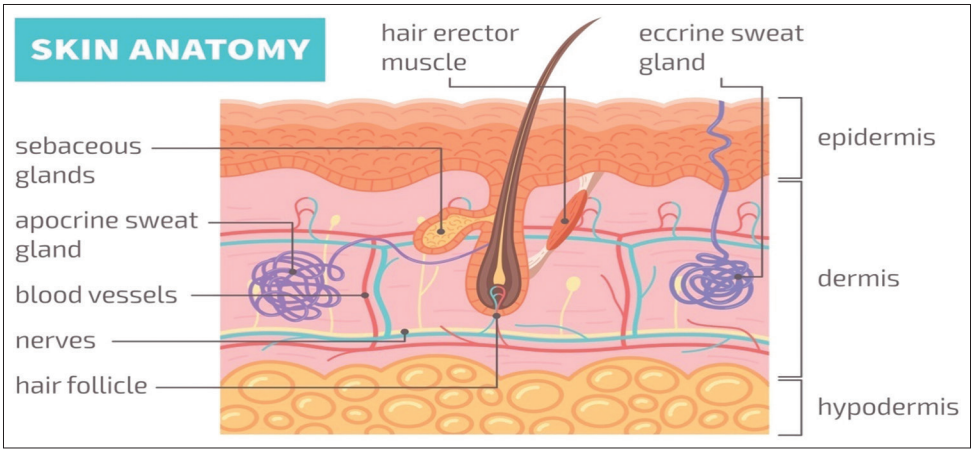


Figure 1: Structure and parts of skin in its inner layers

Table 1: Advantages, disadvantages, and applications[15-29]

S. No.	Advantages	Disadvantages	Applications
1	Capable of delivering medication to the site of action with-out disrupting the skin	Incapable of conveying ionic drugs	Nicotine patch as nico dermis to help in smoking cessation
2	Drug administration is possible in case of unconscious patients	Lesser dose candidates are preferred	Opioid medications fentanyl and buprenorphine for severe pain
3	Easy to discontinue the treatment in case of toxic effects	Not capable of reaching elevated levels of plasma	Estradiol patches as estraderm for treatment of menopausal symptoms
4	Improves drug absorption	Drugs with a greater size than 500 daltons are not suitable	Nitroglycerin patches for angina pectoris
5	Improves patient compliance	Possibility of skin irritation, itching	Clonidine for hypertension
6	Easy to scale up	Long-term adherence cause discomfort to patient	Selegiline for major depressive disorder
7	Reduces GI side effects	Low or high partition coefficients cannot enter into blood stream	Methyl phenidate for attention deficit hyperactivity disorder
8	Decreases dose to be administered	Cannot transit drugs in a pulsatile fashion	Emollient
9	Having a relatively large area of application compared to the buccal or nasal cavity	May be uneconomic	Lubricant in surgical and medical procedures
10	Reduced inter and intrapatient variability	Adhesion may vary with patch type and environmental conditions	Estradiol patches in combination with levonorgestrel as Climara Pro for menopausal symptoms
11	Overcoming hepatic metabolism and enzymatic degradation	Cannot develop if the drug causes irritation to skin	Estradiol patches for postmenopausal osteoporosis
12	Suitable for self-administration	May cause allergic reaction	

Table 2: Physiological properties, biological properties, and limitations[8,17]

S. No.	Physiological properties	Biological properties	Limitations
1	The drug should have molecular weight of <1,000 daltons	Drug should not get extensively metabolized in the skin	Skin permeability of transdermal medication is restricted
2	Drugs have both lipophilic and hydrophilic affinity	Stable in contact with skin	Limited to strong medications and long lag times
3	Drugs should have a low melting point	Should not stimulate immune reaction to the skin	Sensitization may result from a medication composition
4	Drug should be potent	Have short biological half-life	It must be thoroughly considered before deciding to manufacture a transdermal medicine a clinical need
5	Drugs should have short half life	Drugs should be very potent at low concentration	
6	Drug should be non-irritating	Dose is <50 mg/day and ideally <10 mg/day	
7	Formulation should be non-irritant	Drug should not get irreversibly bound to subcutaneous tissue	

structural components of stratum corneum, i.e., lipids or proteins to attain higher therapeutic levels of the drug. They alter the packaging of skin stratum corneum, thus chemically modifying the barrier functions leading to increased permeability. Some examples were caraway oil, cardamom oil, methol, linoleic acid, lemon oil, and

Table 3: Methods to increase drug penetration[30-36]

S. No.	Physical enhancers	S. No.	Chemical enhancers
1	Electrically based techniques such as electroporation, iontophoresis, and ultrasound	1	Sulphoxides- DMSO, DMF
2	Structure-based technique such AS Microneedles	2	Pyrrolidones- N-methyl-2-pyro
3	Velocity based technique such as Jet-propulsion	3	Azones- 1-dodecylazacycloheptan-2-one
Primary types of polymers		4	Glycol- diethylene glycol and tetraethylene glycol
1	Pressure-sensitive acrylic adhesives	5	Essential oils, terpenes, terpenoids, L-Menthol
2	Pressure sensitive silicone adhesives	6	Fatty acids- lauric acid, myristic acid, and capric acid
3	Pressure-sensitive adhesives of the polyisobutylene type.	7	Oxazolidinones- 4-decyloxazolidin-2-one.

Table 4: Polymers used for transdermal drug delivery system[30-36]

S. No.	Synthetic polymers	Synthetic elastomers	Natural polymers
1	Polyvinylalcohol	Hydrin rubber	Proteins
2	Polyvinyl chloride	Polybutadiene	Shellac
3	Polyethylene	Polysiloxane	Starch
4	Acetal copolymer	Chloroprene	Zein
5	Polyamide	Neoprene	Gelatin
6	Polyacrylates	Silicon rubber	Cellulose derivatives
7	Polystyrene	Acrylonitrile	Arabinogalactan
8	Polypropylene	Polyisobutylene	Waxes
9	Polyamide	Nitrile	Gums
10	Poly urea	Butyl rubber	Natural rubber
11	Polyvinyl pyrrolidone		Chitosan
12	Polymethylmethacrylate		

the permeation enhancers of different methods were mentioned in Table 3.

Pressure sensitive adhesives

These ingredients affixes the TDDS firmly to the skin organ.

Backing laminates

These materials must be flexible while processing good tensile strength. Commonly used backing materials are polyesters, polyolefins, and elastomers in clear metallic or pigmented form. In systems containing drug within a liquid orgel, the backing material must be heat-sealable to allow fluid-tight packaging of the drug reservoir using a process known as form-fill-seal. The most comfortable backing will be the one that exhibits lowest modulus or high flexibility, good oxygen transmission, and a high moisture vapor transmission rate. The examples such as vinyl, polyester films, polypropylene resin, polyurethylene, ethylene-vinyl acetate, and aluminized plastic laminate were used.

Release liner

The release liner is in intimate contact with the delivery system, it should comply with specific requirements regarding chemical inertness and permeation to the drug, penetration enhancer, and water. Typically, release liner is composed of a base layer which may be non-occlusive (e.g. paper fabric) or occlusive (e.g. polyethylene and polyvinylchloride) and a release coating layer made up of silicon or teflon.

Other excipients like plasticizers and solvents

Numerous solvents such as acetone, chloroform, isopropanol, methanol, and dichloromethane are used to prepare the reservoir of drug. The plasticizers generally offer plasticity

to patch and the examples were dibutylpthalate, polyethylene glycol, triehtylcitrate, and propylene glycol.

VARIOUS PREPARATION METHODS FOR TDDS

Polymer membrane permeation-controlled TDDS

In this system, the drug reservoir is embedded between an impervious backing layer and a rate-controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or non-porous. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, or gel or dispersed in solid polymer matrix. On the outer surface of the polymeric membrane a thin layer of drug-compatible, hypoallergenic adhesive polymer can be applied. Figure 2 shows the release of polymer membrane permeation-controlled TDDS.

Adhesive diffusion-controlled TDDS

The drug reservoir is formed by dispersing the drug in and adhesive polymer and then spreading the medicated polymer adhesive by solvent casting or by melting the adhesive (in case of hot-melt adhesives) onto an impervious backing layer. The drug reservoir layer is then covered by a non-medicated rate-controlling adhesive polymer of constant thickness to produce an adhesive diffusion-controlling drug delivery system. Figure 3 shows the release of adhesive diffusion-controlled TDDS.

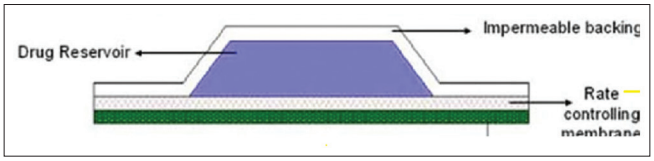


Figure 2: The release of polymer membrane permeation- controlled transdermal drug delivery system

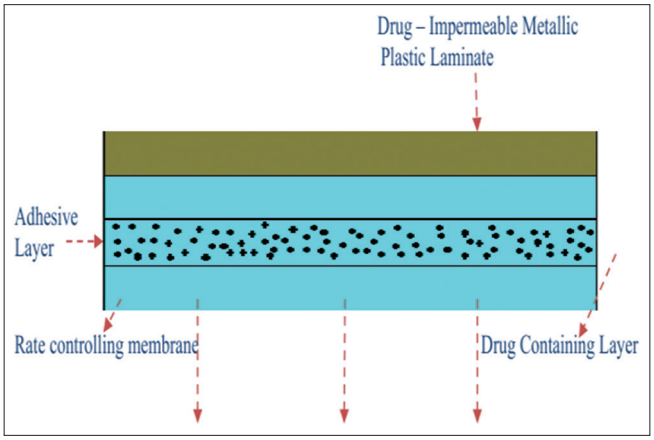


Figure 3: The release of adhesive diffusion-controlled transdermal drug delivery system

Matrix diffusion-controlled TDDS

The active ingredient is dispersed homogeneously in a hydrophilic or lipophilic polymer matrix. This drug-containing polymer disk then is fixed onto an occlusive base plate in a compartment fabricated from a drug-impermeable backing layer. Instead of applying the adhesive on the face of the drug reservoir, it is spread along the circumference to form a strip of adhesive rim. Figure 4 shows the release of drug through matrix diffusion-controlled TDDS.

Microreservoir controlled TDDS

This drug delivery system is a combination of reservoir and matrix-dispersion systems. The drug reservoir is formed by first suspending the drug in an aqueous solution of water-soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unreachable, microscopic spheres of the drug reservoir. Figure 5 shows the release of drugs through micro reservoir-controlled TDDS.

EVALUATION OF TRANSDERMAL DRUG DELIVERY SYSTEM[37-39]

The following evaluation tests were performed for the transdermal dosage forms.

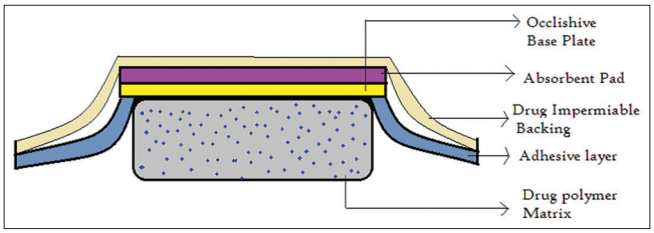


Figure 4: The release of drug through matrix diffusion-controlled transdermal drug delivery system

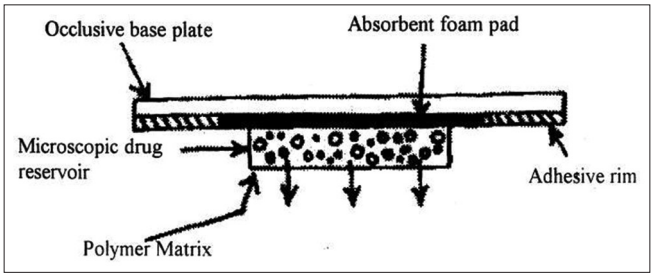
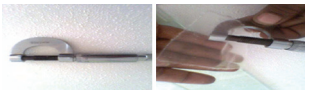
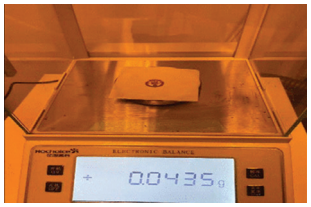
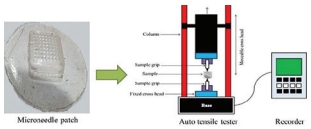
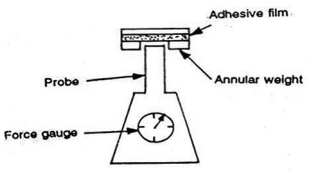
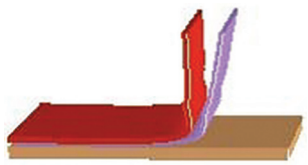
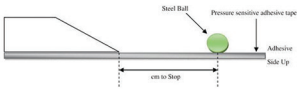
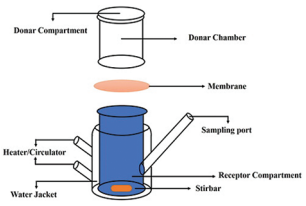
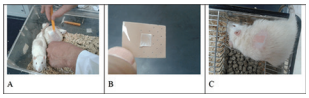
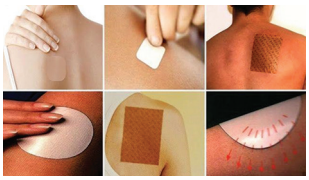
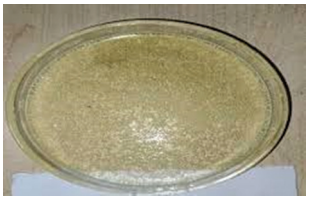
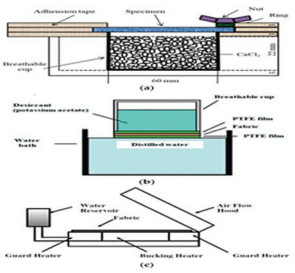
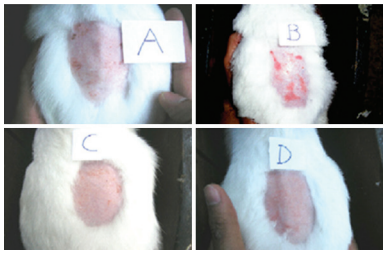


Figure 5: The release of drug through micro reservoir controlled transdermal drug delivery system

S. No.	Name of the evaluation	Procedure	Diagram of device or equipment or performance or observation
1	Physicochemical evaluation-thickness	Determined by traveling microscope, dial gauge, screw gauge or micrometer at different points of the film.	
2	Uniformity of weight	Is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.	
3	Drug content determination	An accurately weighed portion of film (about 100 mg) is dissolved in 100 mL of suitable solvent in which drug is soluble and then the solution is shaken continuously for 24 h in shaker incubator. Then, the whole solution is sonicated. After sonication and subsequent filtration, drug in solution is estimated spectrophotometrically by appropriate dilution	
4	Moisture uptake	Weighed films are kept in a desiccator at room temperature for 24 h. These are then taken out and exposed to 84% relative humidity using saturated solution of potassium chloride in a desiccator until a constant weight is achieved.	
5	Flatness	The length of each strip is measured and variation in length is measured by determining percent constriction. Zero percent constriction is equivalent to 100% flatness.	
6	Folding Endurance	Folding endurance is determined by repeatedly folding the film at the same place until it break. The number of times the films could be folded at the same place without breaking is folding endurance value	
7	Tensile strength	Polymeric films are sandwiched separately by corked linear iron plates. One end of the film is kept fixed with the help of an iron screen and other end is connected to a freely movable thread over a pulley. The weights are added gradually to the pan attached with the hanging end of the thread. A pointer on the thread is used to measure the elongation of the film. The weight just sufficient to break the film is noted.	
8	Tack properties	It is the ability of the polymer to adhere to substrate with little contact pressure. Tack is dependent on molecular weight and composition of polymer as well as on the use of tackifying resins in polymer.	
9	Thumb tack test	The force required to remove thumb from adhesive is a measure of tack.	

S. No.	Name of the evaluation	Procedure	Diagram of device or equipment or performance or observation
10	Rolling ball test	This test involves measurement of the distance that stainless steel ball travels along an upward-facing adhesive. The less tacky the adhesive, the further the ball will travel.	
11	Quick stick (Peel tack) test	The peel force required breaking the bond between an adhesive and substrate is measured by pulling the tape away from the substrate at 90 at the speed of 12 inch/min.	
12	*In vitro* release studies	Transdermal patches can be *in vitro* evaluated in terms of Franz diffusion cell the cell is composed of two compartments: Donor and receptor. The receptor compartment has a volume of 5–12 mL and effective surface area of 1–5 cm^2. The diffusion buffer is continuously stirred at 600 rpm by a magnetic bar. The temperature in the bulk of the solution is maintained by circulating thermostated water through a water jacket that surrounds the receptor compartment. The drug content is analyzed using suitable method, maintenance of sink condition is essential.	
13	In vivo studies	Evaluating transdermal drug delivery system are mouse, hairless rat, hairless dog, hairless rhesus monkey, rabbit, guinea pig etc., Various experiments conducted leads to the conclusion that hairless animals are preferred over hairy animals in both *in vitro* and *in vivo* experiments. Rhesus monkey is one of the most reliable models for *in vivo* evaluation of transdermal drug delivery in man	
14	Human model	Phase I clinical trials are conducted to determine mainly safety in volunteers and phase II clinical trials determine short term safety and mainly effectiveness in patients. Phase III trials indicate the safety and effectiveness in large number of patient population and phase IV trials at post-marketing surveillance	
15	Swellability	The patches of 3.14 cm^2 were weighed and put in a petri dish containing 10 mL of double distilled water and were allowed to imbibe. Increase in weight of the patch was determined at preset time intervals, until a constant weight was observed	
16	Percentage water vapor permeation test	Vials with equal diameters are employed as permeation cells. These vials are cleaned, dried, and then filled with 1 g of fused calcium chloride. A patch with a surface area of 1 cm^2 is measured and affixed to the rim of the vial. The vials are weighed meticulously and then placed in a desiccator containing a saturated solution of potassium chloride to maintain the relative humidity at 63%. After a duration of 72 h, the vials are removed, and their weight is measured once more. This process helps assess the permeation properties of the patch under specific humidity conditions.	

S. No.	Name of the evaluation	Procedure	Diagram of device or equipment or performance or observation
17	Polariscopic examination	This test is performed to identify the physical state of the drug, distinguishing between its crystalline or amorphous form. A segment of the patch is positioned on a slide and examined under a microscope objective to assess the physical characteristics of the drug particles	
18	Stability studies	The stability testing is conducted in accordance with ICH guidelines. The formulated transdermal patches are stored at a temperature of 40°C–0.5°C and a relative humidity of 75–5% or a period of 6 months. Samples are withdrawn at specific intervals, namely 0, 30, 60, 90, and 180 days, and are analyzed appropriately to determine drug content. This testing ensures the stability and quality of the patches over an extended period.	
19	Skin irritation study	The patch is to be removed after 24 h and the skin is to be observed and classified into 5 grades on the basis of the severity of skin injury. Skin irritation and sensitization testing can be performed on healthy rabbits (average weight 1.2–1.5 kg). The dorsal surface (50 cm^2) of the rabbit is to be cleaned and remove the hair from the clean dorsal surface by shaving and clean the surface by using rectified spirit and the representative formulations can be applied over the skin. The patch is to be removed after 24 h and the skin is to be observed and classified into 5 grades on the basis of the severity of skin injury	

CONCLUSION

This review throws a conclusion in the availability of methods to delivery many novel drugs in its suitable patches by using the available polymers such as both the natural and synthetic along with the skin penetrating agents. It also generates advanced thoughts to novel formulators of transdermal drugs delivery products as it describes more on its limitations and also selection of drug and polymer for controlled drug releases and suitable evaluation techniques of both *in vitro* and *in vivo* to be carried for successful product. The coming generations of research would hope so the development of more TDDS in therapy of most of the diseases.

REFERENCES

1. Jalwal P, Jangra A, Dhaiya L, Sangwan Y, Saroha R. A review on transdermal patches. Pharm Res J 2010;3:139-49.
2. Bhowmik D, Chiranjib, Chandira M, Jayakar B, Sampath KP. Recent advances in transdermal drug delivery system. Int J Pharm Tech Res 2010;2:68-77.
3. Kumar JA, Pullankandam N, Prabhu SL, Gopal V. Transdermal drug delivery system: An overview. Int J Pharm Sci Review Res 2010;3:49-54.
4. Divya A, Rao MK, Gnanprakash K, Sowjanya A, Vidyasagar N, Gobinath M. A review on current scenario of transdermal drug delivery system. Int J Res Pharm Sci 2012;3:494-502.
5. Jain NK. Controlled and Novel Drug Delivery. 1st ed. New Delhi: CBS Publisher and Distributors; 2001. p. 100-29.
6. Rani S, Saroha K, Syan N, Mathur P. Transdermal patches a successful tool in transdermal drug delivery system. Plegia Res Lib 2011;2:17-29.
7. Dhawan S, Aggarwal G. Development, fabrication and evaluation of transdermal drug delivery system- a review. Pharm Info Net 2009:1-25.
8. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: A review. Pharm Innov 2012;1:66-75.
9. Mehta R. Topical and Transdermal Drug Delivery: What a Pharmacist Needs to Know. 1st ed. Arizona: NetCE; 2004. p. 1-10.
10. Allen LV Jr., Popovich G, Ansel HC. Pharmaceutical Dosage Forms and Drug Delivery Systems. 8thed. New Delhi: Wolter Kluwer Publishers; 2005. p. 298-9.
11. Tortora G, Derricson B. Principles of Anatomy and Physiology. 11th ed. United States: John Wiley and Sons Inc.; 2009. p. 145-63.
12. Wilson KJ, Waugh A. Ross and Wilson: Anatomy and

Physiology in Health and Illness. 11th ed. United Kingdom: Churchill Livingstone; 2010. p. 353-61.
13. Schoellhammer CM, Blankschtein D, Langer R. Skin permeabilization for transdermal drug delivery: Recent advances and future prospects. Expert Opin Drug Deliv 2014;11:393-407.
14. Shahzad Y, Louw R, Gerber M, Plessis JD. Breaching the skin barrier through temperature modulations. J Control Release 2015;202:1-13.
15. Hafeez A, Jain U, Singh J, Maurya A, Rana L. Recent advances in transdermal drug delivery system (TDDS): An overview. J Sci Innov Res 2013;2:695-709.
16. Rastogi V, Yadav P. Transdermal drug delivery system: An overview. Asian J Pharm 2012;6:161-70.
17. Tanwar H, Sachdeva R. Transdermal drug delivery system: A review. Int J Pharm Sci Res 2016;7:2274-90.
18. Jhawat VC, Saini V, Kamboj S, Maggon N. Transdermal drug delivery systems: Approaches and advancements in drug absorption through skin. Int J Pharm Sci Rev Res 2013;20:47-56.
19. Finnin BC, Morgan TM. Transdermal penetration enhancers: Applications, limitations, and potential. J Pharm Sci 1999;88:955-8.
20. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 8th ed. United States: Lippincott Williams and Wilkins; 2005. p. 298-315.
21. Barry B. Transdermal drug delivery. In: Aulton ME, editor. Pharmaceutics: The Science of Dosage Form Design. United Kingdom: Churchill Livingston; 2002. p. 499-533.
22. Cleary GW. Transdermal controlled release systems. In: Medical Applications of Controlled Release. United States: CRC Press; 1984. p. 203-51.
23. Barry BW. Dermatological Formulations: Percutaneous Absorption Drugs and Pharmaceutical Sciences. Vol. 18. New York City: Marcel Dekker, Inc.; 1983. p. 1-39.
24. Potts RO, Lobo RA. Transdermal drug delivery: Clinical considerations for the obstetrician-gynecologist. Obstet Gynecol 2005;105:953-61.
25. Brown L, Langer R. Transdermal delivery of drugs. Ann Rev Med 1988;39:221-9.
26. Merkle HP. Transdermal delivery systems. Methods Find Exp Clin Pharmacol 1989;11:13553.
27. Samisoe G. Transdermal hormone therapy: Gels and patches. Climacteric 2004;7:347-56.
28. Rajalakshmi P, Mohamed Halith S, Salam SM, Monisha P, Muhilarasi S, Murugan D, *et al*. Review on transdermal drug delivery system. Int J Pharm Sci Rev Res 2023;83:49-57.
29. Ramteke KH, Dhole SN, Patil SV. Transdermal drug delivery system: A review. J Adv Scient Res 2012;3:22-35.
30. Keith AD. Polymer matrix considerations for transdermal devices. Drug Dev Ind Pharm 1983;9:605-25.
31. Bromberg L. Cross linked polyethylene glycol networks as reservoirs for protein delivery. J Apply Poly Sci 1996;59:459-66.
32. Verma PR, Iyer SS. Transdermal delivery of propranolol using mixed grades of eudragit: Design and *in vitro* and *in vivo* evaluation. Drug Dev Ind Pharm 2000;26:471-6.
33. Ubaidulla U, Reddy MV, Ruckmani K, Ahmad FJ, Khar RK. Transdermal therapeutic system of carvedilol: Effect of hydrophilic and hydrophobic matrix on *in vitro* and *in vivo* characteristics. AAPS Pharm Sci Tech 2007;8:E13-20.
34. Gannu R, Vamshi VY, Kishan V, Rao MY. Development of nitrendipine transdermal patches: *In vitro* and *ex vivo* characterization. Curr Drug Deliv 2007;4:69-76.
35. Gale R, Spitze LA. Permeability of camphor in ethylene vinyl acetate copolymers. In: Proceedings: Eighth International Symposium on Controlled Release of Bioactive Materials. Minneapolis, MN: Controlled Release Society; 1981. p. 183.
36. Boretos JW, Detmer DE, Donachy JH. Segmented polyurethane: A polyether polymer, II. Two years-experience. J Biomed Mater Res 1971;5:373-87.
37. Patel DM, Kavitha K. Formulation and evaluation aspects of transdermal drug delivery system. Int J Pharm Sci Rev Res 2011;6:83-90.
38. Shankar PB, Manohar SD, Bhanudas SR. Patches: A novel approach for development of topical drug delivery system. J Adv Pharm Edu Res 2013;3:347-58.
39. Lal B, Gadewar M. Transdermal drug delivery system: A novel alternative for drug delivery. J Pharm Res Int 2022;34:10-24.

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