Zoology, Bio and Pharma Research
Content Available at www.saapjournals.org
(An International Online Peer-Reviewed Journal) ISSN (O): 3139-3233

Review Article
OPEN ACCESS

TRANSDERMAL DRUG DELIVERY SYSTEM: A COMPREHENSIVE OVERVIEW OF RECENT PROGRESS AND ENHANCEMENT STRATEGIES

KOMPALA KIRAN KUMAR*, K. INDRA CHENNAREDDY B. GAYATRI, CHANDU BABU RAO

Priyadarshini Institute of Pharmaceutical Education and Research, 5th Mile, Pulladigunta, Guntur-522017, Andhra Pradesh, India.

Article History: Received: 26 Mar 2026, Revised: 09 Apr 2026, Accepted: 19 May 2026

***Corresponding Author**
Kompala Kiran Kumar

Abstract
Transdermal drug delivery systems have emerged as a research issue of interest in the pharmaceutical technology field, as well as one of the most commonly procured pharmaceutical products in the global market. The associated disadvantages of other delivery routes, including oral and parenteral, can be overcome by the use of these systems. The authors will examine the existing tendencies and the way transdermal technologies will be applied in the future, paying particular attention to the development of detailed insight into transdermal drug delivery systems and improvement strategies. The largest organ in the body is the skin, which is a good location for the administration of several medicines. There are various benefits of transdermal drug delivery systems compared to traditional delivery systems. Also, transdermal drug delivery systems [TDDS] offer extended therapeutic levels, decreased side effects, elevated bioavailability, elevated patient compliance, and simple discontinuation of drug treatment. In the article, I will first discuss each of the transdermal enhancement procedures applied in the creation of first-generation transdermal products.

Keywords: *Tdds; Transdermal Patch; Permeation Enhancer; Partition Coefficients; Iontophoresis, Systemic blood circulation.*

INTRODUCTION

Transdermal drug delivery systems [TDDS], also known as patches, offer another way of administering medications through the skin. The systems are supposed to be good at delivering therapeutic doses of medication into the bloodstream, reaching effective levels of disease prevention and treatment [1]. A transdermal patch is a drug-impregnated bandage that sticks to the skin and releases a specific dosage of medication, which is frequently used in the healing of damaged parts. The approach to the administration of drugs has a number of benefits as compared to the oral, intravascular, subcutaneous, and transmucosal dosage routes [2]. It offers superior care and a lower likelihood of side effects, constant drug concentration, and beating the obstacles of the traditional oral or injectable method. Transdermal drug delivery is especially appropriate in cases when the disease needs long-term and repeated dosage [3].

Even though oral delivery of drugs is effective in the delivery of drugs that have a high epithelial permeability and aqueous solubility, weakly water-soluble drugs may be difficult to deliver orally. These constraints of the oral route (hepatic first pass metabolism resulting in low oral bioavailability, high frequency of dosages, large doses, amongst others) prompted the need to use alternative methods of administration in an attempt to maximize bioavailability and overcome the physiological biases caused by the unique physiological environment, e.g., pH, bile salts, enzymes, intestinal motility, and hydrodynamics.[4]

Advantages

- Due to the continual advancements in innovation, plus the capability to deliver the medication to the site of action without disrupting the skin, transdermal delivery is becoming one of the most acknowledged methods of drug delivery [5].
- Escaping drug exposure to the gastrointestinal tract (GIT), hepatic first-pass metabolism, enzymatic breakdown, and gastrointestinal discomfort.

Disadvantages

- Transdermal drug delivery systems are incapable of conveying ionic medications/drugs.
- Drugs with a size greater than 500 Daltons are not appropriate for transdermal delivery. Transdermal administration allows for prolonged drug delivery, but it can be costly due to complex formulations [6].

1. Skin And Drug Permeation

In order to comprehend the concept of Transdermal Drug Delivery Systems [TDDS], it is important to discuss the structural and biochemical features of

human skin to gain an understanding of the barriers it forms and how the rate of access to the body via the skin is influenced by drugs. One of the body's largest organs is the skin, which occupies about 2 square meters of the body of an average adult. It gets approximately a third of the total blood flow of the body. Its outermost layer of skin is termed [7].

1 Permeation Process

A transdermal drug may be administered through three routes into the circulation through the skin.
Trans-appendageal route:
This can also be called the SHUNT route. It is permeated across the hair follicles via the sebaceous glands and the sweat glands. The availability of these appendages offers a definite course over the SC. The volume, the follicular number, and the width of the opening are all important parameters in the transportation of drugs through appendages.
Transcellular route:
Even though this is believed to be the fastest route, there are great barriers to the drug molecules as they have to surpass both the hydrophilic and the hydrophobic structures. The candidate to cross through this route needs to fragment and permeate through the corneocytes.[16] Partitioning of hydrophilic molecules is restricted in the cell membrane, but molecule types can enter through this pathway in case they are small in size and/or they are transported by receptor-mediated
transporters.
Intercellular route:
This pathway is also referred to as the paracells pathway. The hydrophilic drugs can be diffused by this route, but it is desirable to have smaller particles used in this route. This restricts the diffusion of drugs due to the presence of tight junctions [8].

TRANSDERMAL DRUG DELIVERY SYSTEM

Innovation in drug delivery systems is a key strategy employed to improve the bioavailability of active pharmaceutical ingredients (APIs). To date, oral delivery systems remain the most. Supreme means of administering API based on the advantages it presents, including the availability of dosage administration, pain-free ease of administration, convenience, ability to self-administer, high safety, and compliance by the patient [9]. Although there are these benefits, there are limitations of oral delivery systems, which include poor stability of the drugs in the gastrointestinal tract and exposure to first-pass metabolism. An example of this is that the drug can be degraded due to an enzyme reaction or being subjected to the acid in the stomach These disadvantages are habitually witnessed during the demand for peptide or protein-based medication [10]. Consequently, intravenous (IV) injection is considered one of the most promising drug delivery systems since it is able to reach as high as 100 bioavailability rates, precise dosing, and evading hepatic metabolism. It is not surprising, though, that there are certain possible drawbacks of the IV administration route, such as it is an invasive mode of delivery.

2. Basic Components Of Tdd's

. Liner
- Drug
- Polymer matrix
- Permeation enhancers
- Adhesives
- Backing membrane
- Other Components

1. Liner
Transdermal drug delivery Systems utilize the skin as the site of drug administration. The drug administered enters the body through blood vessels in the skin and circulates within the body.
2. Drug
To enable drug absorption through the skin, drugs must exhibit specific physicochemical traits. These include effectiveness, non-irritating properties, low molecular weights [up to 1000 Daltons], low melting points, short half-lives, and affinities for both lipophilic and hydrophilic compounds.
3. Polymer Matrix:
The polymer controls the release of the drug from the device. The following criteria should be
3.4 Permeation enhancers
These substances have the ability to reversibly alter the structure of the stratum corneum, thereby increasing the permeation of drugs from the skin into the bloodstream. They achieve this by disrupting the highly organized intercellular lipid layers of the stratum corneum, either by inserting amphiphilic molecules or by extracting lipids.

4.TYPES OF TRANSDERMAL PATCHES

4 A single layer of drug:
The drug is found in the adhesive layer in this type. The adhesive layer is also needed to fix the different layers together as well as to release the drug to the skin. The adhesive is enclosed in a temporary liner as well as a backing [11].

1. multi-layer drug in adhesive

This also is like the single layer with one difference that it has an immediate drug release layer and the second layer will be a controlled release layer besides the adhesive layer. The drug release is done by the layer of adhesive. This patch is also lined temporarily, and lined permanently.
2. Reservoir system
In such a system, the drug reservoir is formed between a backing layer that has no holes and a rate-controlling membrane. Only the rate-controlling membrane is accessible to the release of the drug, be it micro-porous or non-porous. The drug can take the form of a solution, suspension, gel or be dispersed in a solid polymer matrix in the drug reservoir compartment. Hypoallergenic adhesive polymer may be applied to the

outer surface polymeric membrane that is compatible with the drug.

3. Matrix system:

3.1 Drug-in-adhesive system:

In this form, the drug reservoir is created by dispersing the drug in an adhesive polymer and then solvent cast or melting (in the instance of hot-melt adhesives) the medicated adhesive polymer on an impervious underlay. Unmediated adhesive polymer layers are then applied on the top of the reservoir as protection [12].

TECHNIQUES OF THE PREPARATIONS OF TDDS:

The membrane procedure is asymmetric through the use of TPX membrane:

This can be made as a prototype patch, where a heat-sealable polyester film (type 1009, 3m) with a concave of 1cm diameter will be used as the backing membrane. The sample of the drug is deposited on the concave membrane that is covered with the asymmetric membrane made of TPX

(poly(4-methyl-1-pentene)) and closed by an adhesive [13].

[(Asymmetric TPX membrane preparation):

These are prepared with the help of dry/wet inversion procedure. At 60degc a solution of TPX is prepared by dissolving it in a solvent (cyclohexane) and nonsolvent additives. The solution containing the polymer is incubated at 40deg C over a period of 24 hours and poured on the glass plate to a desired thickness using a Gardner knife. [14]

TRANSDERMAL DRUG DELIVERY SYSTEM MECHANISM

1. Trans epidermal Absorption:

The transdermal drug delivery system has a mechanism that is the diffusion of the drug molecules within the drug reservoir in the transdermal patch through the skin epidermal layers. The skin is a barrier and the stratum corneum provides the major obstructions that are regarded as the rate limiting membrane of transdermal drug delivery system [15].

2. Absorption through the Trans follicular:

The follicular glands have follicular pores (openings on the skin where the hair shaft is present) which are relatively larger than the lipophilic and eccrine sweat glands. These are the pores which are most effective in percutaneous absorption of drugs [16,17].

The kinetics of transdermal permeation are as follows:

The process of transdermal permeation of a drug follows the following steps:

I. Stratum corneum sorption.

ii. Drug penetration through viable epidermis. iii. Absorption of the drug into the network of capillary in the dermal papillary layer.

The penetration of the drug is only possible in the event that it has some physicochemical characteristics.

The rate of skin permeation (dq/dt) is expressed as;

(dq/dt) = Ps (Cd-Cr) ------- (1)

Where;

(dq/dt) = rate of drug permeation

P s = Coefficient of penetration of skin tissue by penetrates (drug molecule)

Cd = Concentration of drug in the donor compartment (on the surface of stratum corneum) Cr =

Concentration of drug in receptor compartment (amount of drug in systemic circulation) The permeability co-efficient is obtained as: - ps=ksxsddsxhss/hs ------- (2)

Where;

Ks = Interfacial partition Coefficient of an interfacial partitioning of a penetrant molecule of a transdermal therapeutic system onto the stratum corneum.

DSS =apparent diffusivity of an apparent state diffusion through study of penetrate molecule of skin tissue.

Where;

Hs = thickness of skin tissue. Since; the values of Ks, DSS and Hs do not change under the conditions given, then the permeability coefficient (Ps) of a skin penetrant can be assumed to be constant. By looking at equation (1), it is evident that only when Cd >>Cr, a constant rate of drug permeation may be attained.

Then equation (1) becomes.

(dq/dt) = P s. Cd ---------(3)

To maintain Cd constant, the rate (Rr) at which the drug was applied off the transdermal device should be constant or higher (compared to the rate of skin uptake R a). i.e.

Rr >>Ra

Because, Rr, exceeding Ra, Cd (drug concentration of skin) is sustained at a concentration equal or superior to the (Cs) equilibrium solubility of the drug in stratum corneum. i.e.

Cd >>C Hence an equilibrium points of skin permeation

(dq/dt) max is achieved by equation (dq /dt) max = Ps.C.

EVALUATION PARAMETERS:

1. Interaction studies:

Excipients are integral components of almost all pharmaceutical dosage forms. The stability of a formulation, amongst other factors, depends on the compatibility of the drug with the excipients. The drug and the excipients must be compatible with one another to produce a product that is stable, it is mandatory to detect any possible physical or chemical interaction, as it can affect the bioavailability and stability of the drug. [18]

2. Thickness of the patch:

The thickness of the drug-loaded patch is measured at different points by using a digital micrometer, and the average thickness and standard deviation are determined for the same to

ensure the thickness of the prepared patch.[19]

USES OF TRANSDERMAL DRUG DELIVERY SYSTEM

8.1. Pain Management

- The provision of analgesics like fentanyl and buprenorphine.
- Offers chronic pain patients stable plasma drug levels.
- Less gastrointestinal side effects than oral opioids.

8.2. Cardiovascular Disorders

- Angina pectoris patches of nitroglycerin. Clonidine patches Clonidine patches are used to treat hypertension.
- Its delivery is continuous and not episodic, which means that there are no peaks and troughs of drug concentration in the blood.

8.3 PRESENT TRENDS AND STRATEGIES OF TDDS.

8.1 New Generation Formulations:

Polymeric nanoparticles such as PLGA or chitosan are used to enhance solubility and prolonged delivery. Lipid-based carriers (liposomes and solid lipid nanoparticles, nano emulsion have been shown to improve bioavailability and permeation. Special nanostructures e.g., nanotubes and targeted delivery nanocarriers using metallic nanostructures [20].

8.2 Physical Enhancing Technologies:

- Makes channels that are micron-sized using the stratum corneum and causes no great pain.
- Types Solid, hollow, dissolvable and coated MNs each according to various delivery requirements.
- Facilitated the delivery of more macromolecules (peptides, vaccines, biologics) and real time imaging in case of sensors [21].

FUTURE ISSUES IN TRANSDERMAL DRUG DELIVERY SYSTEM

Skin Barrier Limitations Stratum corneum is the largest obstacle. Only drugs that are low in molecular weight, lipophilic and high-potency can penetrate ctively.

- Changeability of Skin Properties.
- Age
- Gender
- Skin thickness
- Dose Limitation & Drug loading.
- TDDS can only be used with low-dose drugs.
- High-dose drugs require:
- Huge patch size (low patient compliance)

RECENT INNOVATION OF TRANSDERMAL DRUG DELIVERY SYSTEM

1. Iontophoresis:

Iontophoresis is a technique that employs physiologically acceptable electrical currents, which are usually between 0.1 to 1.0 mA/cm 2. This electric current is used to assist the movement of charged permeants to the skin by using electrostatic forces [19]. It operates by forming an electrical potential difference that is used to propel ionic drugs across the skin and to the body. The difference between iontophoresis and other transdermal enhancement techniques is in the fact that iontophoresis follows the concentration gradient [based on the drug concentration] and the electrical potential gradient as the forces. This not only allows charged species but also unchanged molecules, which can be transported by the process called electro-osmosis [22,23].

LIMITATIONS OF TRANSDERMAL DRUG DELIVERY SYSTEM

Skin Barrier Restriction

- The stratum corneum (outermost skin layer) is highly resistant to penetration.
- Only drugs with low molecular weight (lipophilic properties) and potent activity can effectively cross [24-26].
- Hydrophilic or large biomolecules (like peptides, proteins, and vaccines) are poorly absorbed [27].

CONCLUSION

It has tremendous benefits over the conventional drug delivery systems, including high bioavailability rate, bypassing of first-pass metabolism, stable plasma drug concentrations, lack of invasiveness, extended therapeutic response, decreased adverse responses, and enhanced patient compliance. These systems are especially useful in case of drugs that need long-term and frequent administration, and they offer convenient, cost-effective, and self-delivery method to patients. The skin anatomy and physiology is essential in the understanding of the mechanism of action of TDDS.

AUTHOR CONTRIBUTIONS

All authors are contributed equally.

FINANCIAL SUPPORT

None

DECLARATION COMPETING INTEREST

The authors have no conflicts of interest to declare.

ACKNOWLEDGEMENTS

None

REFERENCES

1. Introduction to Basics of Pharmacology and Toxicology: Volume 1: General and Molecular Pharmacology: Principles of Drug Action Raj GM, Raveendran R, editors. Introduction to Basics of Pharmacology and Toxicology: Volume 1: General and Molecular Pharmacology: Principles of Drug Action. Singapore: Springer Nature; 2019. doi:10.1007/978-981-32-9779-1.
2. Patel A, Cholkar K, Mitra AK. Recent developments in protein and peptide parenteral delivery approaches. Ther Deliv. 2014;5(3):337–365. doi:10.4155/tde.14.5.

3. Lang X, Wang T, Sun M, Chen X, Liu Y. Advances and applications of chitosan-based nanomaterials as oral delivery carriers: a review. Int J Biol Macromol. 2020;154:433–445. doi:10.1016/j.ijbiomac.2020.03.148.
4. Ramadon D, McCrudden MT, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: current trends and applications. Drug Deliv Transl Res. 2022;12(4):758–791. doi:10.1007/s13346-021-00909-6.
5. Subedi RK, Oh SY, Chun MK, Choi HK. Recent advances in transdermal drug delivery. Arch Pharm Res. 2010;33(3):339–351. doi:10.1007/s12272-010-0301-7.
6. Chen Y, Yang Y, Xian Y, Singh P, Feng J, Cui S, et al. Multifunctional graphene oxide-reinforced dissolvable polymeric microneedles for transdermal drug delivery. ACS Appl Mater Interfaces. 2020;12(1):352–360. doi:10.1021/acsami.9b19518.
7. Rani CHU, Sumalatha G, Rao CB, Varalakshmi TN. Alzheimer's disease: pharmacotherapeutic interventions. Int J Pharm Chem Sci. 2013;2(2):1010–1018.
8. Ye R, Yang J, Li Y, Zheng Y, Yang J, Li Y, et al. Fabrication of tip-hollow and tip-dissolvable microneedle arrays for transdermal drug delivery. ACS Biomater Sci Eng. 2020;6(4):2487–2494. doi:10.1021/acsbiomaterials.0c00120.
9. Prasanthi G, Chandu BR, Pradeep Kumar Y, Swarnalatha D, Gopinath C. Chemical pharmacology of khat leaves. J Glob Trends Pharm Sci. 2014;5(4):2024–2029.
10. Rastogi V, Yadav P. Transdermal drug delivery system: an overview. Asian J Pharm. 2012;6(3):161–170. doi:10.22377/ajp.v6i3.51.
11. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: a review. Biomater Res. 2021;25(1):24. doi:10.1186/s40824-021-00226-6.
12. Lal B, Gadewar M. Transdermal drug delivery system: a novel alternative for drug delivery. J Pharm Res Int. 2022;34(10):1–10. doi:10.9734/JPRI/2022/v34i7A35448.
13. 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(1):47–56.
14. Sreekanth N, Awen BZ, Rao CB. Development and validation of new analytical methods for the estimation of capecitabine in pharmaceutical dosage form. Res J Pharm Biol Chem Sci. 2010;1(2):39–46.
15. Ghadge RS. Transdermal drug delivery system. J Res Agric Anim Sci. 2022;9(6):31–48.
16. Nama S, Chandu BR, Awen BZ, Khagga M. Development and validation of a new RP-HPLC method for the determination of aprepitant in solid dosage forms. Trop J Pharm Res. 2011;10(4):487–494.
17. Wokovich AM, Strasinger C, Kessler J, Cai B, Westenberger B, Rhee MJ, et al. Cold flow measurement of transdermal drug delivery systems (TDDS). Int J Adhes Adhes. 2015;59:71–76. doi:10.1016/j.ijadhadh.2015.02.002.
18. Zaid Alkilani A, McCrudden MT, Donnelly RF. Transdermal drug delivery: innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. Pharmaceutics. 2015;7(4):438–470. doi:10.3390/pharmaceutics7040438.
19. Raj GM, Raveendran R, editors. Introduction to Basics of Pharmacology and Toxicology: Volume 1: General and Molecular Pharmacology: Principles of Drug Action. Singapore: Springer Nature; 2019. Chapter 1. doi:10.1007/978-981-32-9779-1_1.
20. Ravilla S, Chandu BR, Nama S. Erythrocytes as carrier for drugs, enzymes and peptides. J Appl Pharm Sci. 2012;2(4):166–176.
21. Gindi S, Methra T, Chandu BR, Boyina R, Dasari V. Antiurolithiatic and in vitro antioxidant activity of leaves of *Ageratum conyzoides* in rats. World J Pharm Pharm Sci. 2013;2(2):636–649.
22. Patel A, Cholkar K, Mitra AK. Recent developments in protein and peptide parenteral delivery approaches. Ther Deliv. 2014;5(3):337–365. doi:10.4155/tde.14.5. *(Duplicate of Ref. 2)*
23. Wen NX, Venkatraman S. Protein delivery options: how well have we succeeded? Ther Deliv. 2015;6(5):537–539. doi:10.4155/tde.15.11.
24. Hwisa NT, Gindi S, Rao CB, Katakam P. Evaluation of antiulcer activity of *Picrasma quassioides* Bennett aqueous extract in rodents. Vedic Res Int Phytomedicine. 2013;1:27–33.
25. Singh I, Morris AP. Performance of transdermal therapeutic systems: effects of biological factors. Int J Pharm Investig. 2011;1(1):4–9. doi:10.4103/2230-973X.76721.
26. Awen BZ, Rao CB, Ramalingam P, Katakam P. Antibacterial and antifungal activity of some new 7-amino-dibenzo(b,e)azepinones. Inventi Impact Med Chem. 2010.
27. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2008;26(11):1261–1268. doi:10.1038/nbt.1504.