1

ISSN: 2348-6295

Journal of Pharma Creations (JPC)

JPC |Vol.12 | Issue 1 | Jan - Mar -2025

www.pharmacreations.com

DOI : https://doi.org/10.61096/jpc.v12.iss1.2025.19-26

Review

A Review on Transdermal Drug Delivery System

Dr. M. Swetha[1*], Munavarunnisa[2], Nagulapalli Rishitha[2], Nandipati Amali[2], Nannuri Lohitha Lakshmi[2]

[1]Associate Professor, Department of Regulatory affairs, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya (Affiliated to Osmania University),
[2]Scholar, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya.

*Author for Correspondence: Dr. M.Swetha
Email: swethasnvpm@gmail.com

Published on: 10 Dec 2024

Published by:
DrSriram Publications

2024| All rights reserved.

Creative Commons Attribution 4.0 International License.

Abstract

As an alternative to traditional needle injections, a number of non-invasive administrations have recently surfaced. Among these, a transdermal drug delivery system (TDDS) is the most appealing due to its low rejection rate, exceptional ease of administration, and exceptional patient convenience and persistence. In addition to the pharmaceutical industry, TDDS may find use in the skin care sector, which includes cosmetics. This approach can avoid local drug concentration accumulation and nonspecific drug delivery to tissues that are not the drug's target because it primarily uses local administration. Nevertheless, the physicochemical characteristics of the skin result in a number of barriers and limitations in transdermal delivery, and a great deal of research has been done to address these issues. We outline the various TDDS method types that are currently available in this review, as well as critically discuss each method's unique benefits and drawbacks, characterization techniques, and potential. Advances in the study of these substitute techniques have demonstrated the high efficiency that TDDS possesses, which is anticipated to find use in a variety of domains.

Keywords: Transdermal drug delivery system, Low rejection rate, Non specific drug delivery, Characterization techniques, Local administration, Domain.

INTRODUCTION

Fundamentally, the stratum corneum (SC), the skin's tough and lipid-rich outer layer, has limited transdermal drug delivery (TDD) by making the skin impermeable to the majority of biopharmaceuticals and small molecules. Figure 1a depicts the skin's anatomical structure Creams, gels, ointments, and non-invasive transdermal patches are the only formulations available for percutaneous delivery due to the hydrophobic nature of the skin's outer layer. The pharmacokinetic characteristics of substances applied topically vary greatly because the skin is a biological barrier that is both versatile and effective, with a complex physiology and heterogeneous anatomy. Several systemic physiologically based models are available for evaluating xenobiotic

transdermal delivery and cutaneous absorption from the pharmacokinetic and toxic kinetic perspectives. The SC lends itself as the rate-limiting step in the course of cutaneous penetration or transdermal absorption three pathways allow molecules to move through the SC: transcellular, intercellular, or appendageal. The majority of products use passive diffusion phenomena associated with intercellular absorption to reach the viable epidermis.[1]

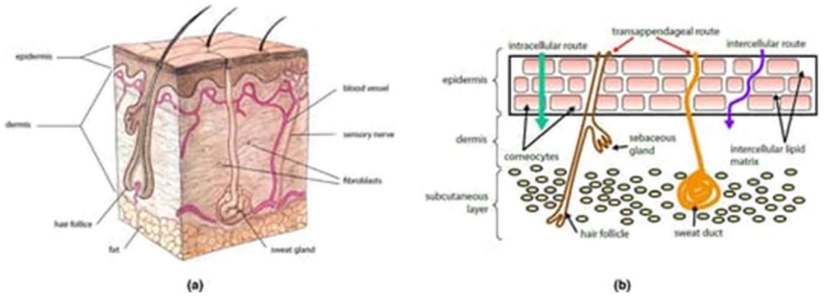

Fig1: Anatomy of skin and entry route of drug

TDDS are regarded as patient-friendly because they are non-invasive, do not require professional administration, reduce gastrointestinal (GI) side effects, and improve patient adherence. Furthermore, bioavailability, efficacy, and translocation are enhanced because they avoid the metabolic processes that oral administration exhibits. Additionally, it does away with the need for medically trained professionals to administer the intrusive, irritating needles that produce medical waste and present a risk of infection. Transdermal drug delivery has several drawbacks, such as the possibility of skin sensitization or irritation, discomfort from adhesives, poor skin adhesion, expense, and selectivity for particular physicochemical drug properties. In addition to the transdermal patch itself, the body site of application, blood flow in the skin caused by additives, and body temperature must all be taken into account in order to achieve the desired systemicity with a drug.A qualified medical professional should always decide on the dosage size and frequency because the active surface of the patch that comes into contact with the skin controls the dosage through the patch surface area. [2]

Advantages[3]

• Benefits for medications with low therapeutic indices and short half-lives: TDDS offers constant, regulated release, improving drug bioavailability.
• Bypasses the liver and gastrointestinal system: Prevents first-pass metabolism, enhancing drug absorption and effectiveness.
• Reduces dosing frequency and daily intake: Continuous drug release leads to fewer doses and a lower total daily intake, potentially improving patient compliance.
• Minimizes side effects: Helps maintain stable plasma drug concentrations, reducing fluctuations and the risk of side effects associated with peak drug levels.
• Non-invasive and easy to use: TDDS is an ideal alternative for patients who cannot take oral medications, such as those with swallowing difficulties.

Disadvantages [3]

• Drugs that induce skin irritation or sensitization should not be administered transdermally.
• Because the skin's inherent impermeability restricts drug absorption, only medications with comparatively high potencies are appropriate for transdermal delivery.
• Ensuring that the systems adhere well to diverse skin types and under varying climatic circumstances can provide technical problems.
• It can be difficult to maintain a steady concentration gradient for drug administration.

Basic components [3-5]

1. Polymer matrix
2. The drug
3. Permeation enhancer
4. Other excepients

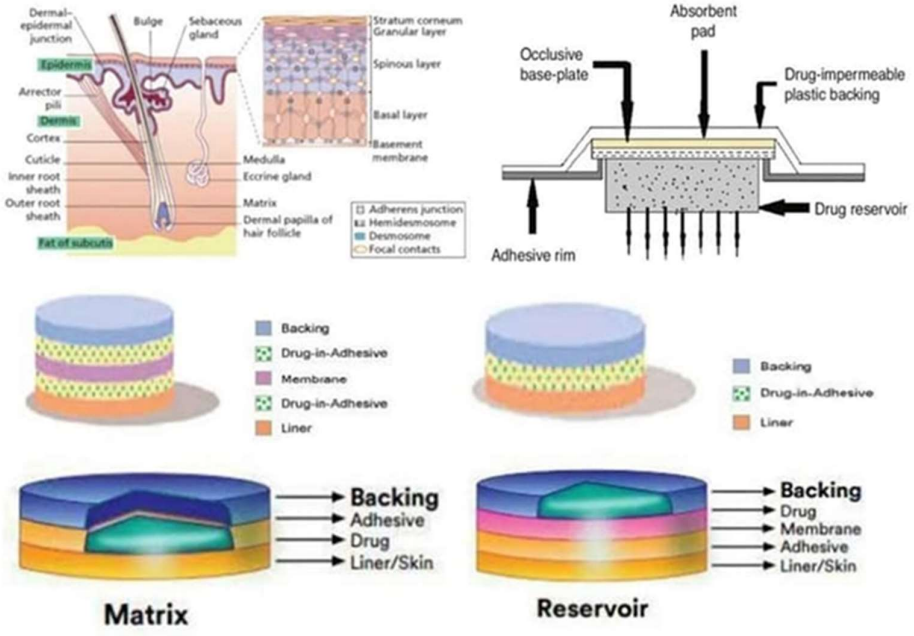

Fig 2: Basic components of transdermal patch

Polymer Matrix

In a transdermal system, the polymer regulates the drug's regulated release. A polymer needs to fulfill the following requirements in order to be used in such a system

- The medication should be able to diffuse and be released through the polymer if its molecular weight, glass transition temperature, and chemical functionality are compatible with the polymer.
- The polymer should be inexpensive, stable, non-reactive with the medication, and simple to make and shape into the required shape.
- The polymer and the byproducts of its breakdown must be non-toxic and not result in any negative physiological effects.
- Even when significant amounts of the active ingredient are added, the mechanical characteristics of the polymer should continue to be adequately stable.

Polymers used as matrix are Possible useful polymers for transdermal devices are:
Natural Polymers:
Cellulose derivatives, Zein, Gelatin
Synthetic Elastomers: Polybutadiene, Hydrin rubber etc.
Synthetic Polymers : Polyvinyl alcohol, Polyvinyl chloride

The Drug

A transdermal drug delivery system developed successfully depends on the medicine being carefully chosen. According to Guy et al. (1987) and Flynn & Stewart (1988), the following are essential desirable characteristics for a medication meant for transdermal delivery:

Characteristics of Physicochemistry

- A molecular weight of less than roughly 1000 daltons is required for the medication.
- The medication needs to be able to bind to both hydrophilic and lipophilic phases since excessive partitioning can make it difficult for the drug to penetrate the skin effectively.
- The drug's melting point should be low.

The properties of biology

- The medication should be strong, and a few milligrams each day should be the usual dosage.
- A short half-life (t1/2) is desirable for the medication.

- The medication must not irritate the skin or trigger allergic reactions.

Permeation enhancers

These are substances that alter the skin's barrier function to increase skin permeability and facilitate more effective drug penetration. The following formula provides the rate of drug flow (J) over the skin:

J=D× dx dc

Here, D stands for the diffusion coefficient, which is influenced by the resistance of the membrane as well as the molecule's size, shape, and flexibility. The geographic coordinate is x, and the drug concentration is denoted by C.

Although it can be difficult to solve for flux under different circumstances, this equation captures the essential ideas of flux enhancement. The drug's molecular characteristics and the energy needed to open a pore in the epidermal membrane affect the diffusion coefficient, but the concentration gradient is thermodynamic. As a result, improving flux throughout the skin requires taking into account:

Lattice energies and distribution coefficients that affect drug partitioning are examples of thermodynamics.

Molecular Size and Shape: The drug's physical attributes.

Cutting Down on Energy for Hole Formation: Cutting down on the energy required to open a pore in the epidermis.

Studies of protein and lipid kinetics are part of the mostly empirical process of altering the skin's barrier.

These may conveniently be classified under the following main headings:

Solvents

Pyrrolidones-

Pyrrolidone,

N-methyl

Surfactants

Commonly used surfactants include sodium lauryl sulfate, decoded dimethyl sulfoxide, dioctyl sulphosuccinate, and anionic surfactants.

Surfactants Without Ionics

Pluronic F68, F127, and so forth.

Sodium taurocholate, sodium deoxycholate, and sodium are examples of Bile Salts.

Other chemicals

These consist of calcium thioglycolate, N,N-dimethyl-m-toluamide, urea, a moisturizing and keratolytic agent, and anticholinergic substances.

Other excipents

Pressure-sensitive adhesives, which can be applied to the front or back of the device and extend peripherally, are commonly used to secure transdermal devices to the skin. The following requirements must be fulfilled by these adhesives. [6]

- Non-irritating: During application, the adhesive shouldn't cause skin irritation, sensitization, or disturbance of the skin's natural flora.
- Strong Adhesion: During the dosage period, it should stick to the skin firmly and not be impacted by activities like exercise or washing.
- Simple Removal: It should be possible to remove the adhesive without damaging the skin.
- No Residue: After removal, there shouldn't be any unwashable residue left on the skin.
- Good Skin Contact: Both macroscopically and microscopically, the adhesive must guarantee outstanding skin contact.

Backing membrane[7]

Flexible materials called backing membranes offer a solid connection to the drug reservoir, stop the drug from leaking through the top, and enable printing. When the product is applied to the skin, these impermeable materials shield it. Metallic plastic laminates, plastic backing with occlusive base plates (like aluminum foil) and absorbent pads, and adhesive foam pads (like flexible polyurethane) with occlusive base plates (like aluminum foil discs) are a few examples of backing membranes.

The face adhesive system should also fulfil the following criteria:

- The drug, excipients, and permeation enhancers utilized in the device should all be chemically and physically compatible with the backing membrane.

- The backing membrane should not interfere with the drug's ability to penetrate.
- The backing membrane shouldn't obstruct the delivery of blended or simple permeation enhancers.

Adhesives[8]

Pressure-sensitive adhesives have traditionally been used to attach all transdermal devices to the skin. These adhesives can be applied to the device's face or back, covering the entire perimeter. The following requirements must be fulfilled by both kinds of adhesive systems.

- They shouldn't disturb the natural skin flora during contact, nor should they cause irritation or sensitization.
- They ought to stay firmly attached to the skin during the dosage period, holding their place even when exercising or taking a bath.
- They ought to be simple to take off.
- They shouldn't leave the skin with an unwashable residue.
- Both at the macroscopic and microscopic levels, they should offer superior (intimate) skin contact.

Various approaches to transdermal devices [9]

1. Membrane permeation controlled TDDS
2. Adhesive dispersion type TDDS
3. Polymer matrix diffusion controlled TDDS
4. Micro reservoir type TDDS

Membrane permeation controlled TDDS

The drug reservoir is situated between a rate-controlling membrane and a drug-impermeable backing membrane in this kind of transdermal drug delivery system (TDDS). The rate-controlling membrane, which may be microporous or non-porous, is the only way the drug is delivered. The medication in the reservoir could be a gel, dispersion, suspension, or solution in a polymer matrix. By altering the permeability coefficient, the thickness of the rate-controlling membrane, or the composition of the polymers, the release rate can be regulated. To guarantee a steady drug release rate, a small coating of sticky polymer is also placed to the exterior.

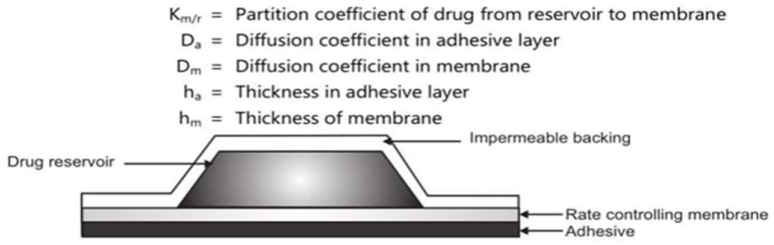

Fig 3: Polymer membrane permeation controlled TDDS

Adhesive dispersion type TDDS

- In this method, the medication is directly dispersed in an adhesive polymer to create the drug reservoir.
- After that, a flat sheet of drug-impermeable backing membrane is covered with this medicated sticky polymer.
- To create an adhesive diffusion regulating DDS, a non-medicated rate controlling polymer of constant thickness is then applied over the drug reservoir layer.

The rate of drug release is given as:

dQ Ka/r Da dt = ha CR

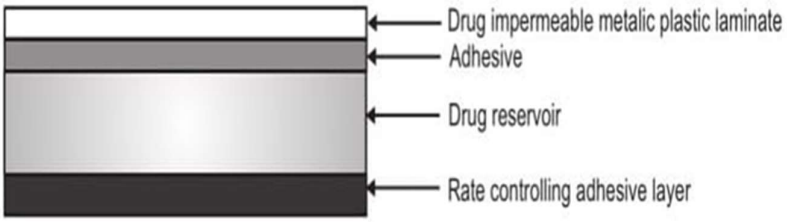

Fig 4: Adhesive dispersion type TDDS

Polymer Matrix Diffusion Controlled TDDS[9]

- The drug is uniformly distributed throughout a hydrophilic and lipophilic polymer matrix to create a drug reservoir.
- Next, the resulting medicated polymer is molded onto a medicated disc with a specified thickness and surface area.
- Another method for creating a drug reservoir is to dissolve the drug and polymer in a common solvent, followed by the solvent's evaporation at a high temperature.
- A base plate with a drug-impermeable backing membrane is subsequently covered with this polymer-disc drug reservoir.

The following provides the medication release rate:

$$\frac{dQ}{dt} = \left[\frac{AC_p D_p}{2t}\right]^{1/2}$$

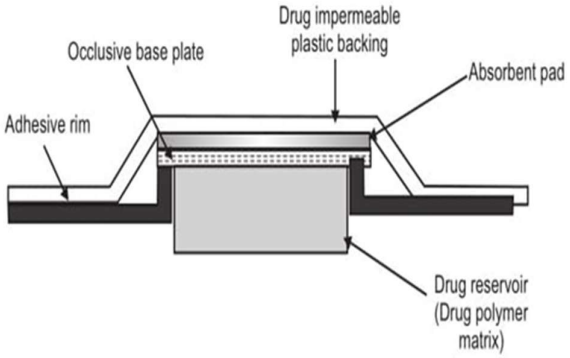

Fig 5: Cross sectional view of matrix diffusion controlled TDDS

Micro Reservoir Type TDDS[9]

To enhance the medication release, a coating of biocompatible polymer can be applied on top. A combination of reservoir and matrix diffusion type drug delivery system.

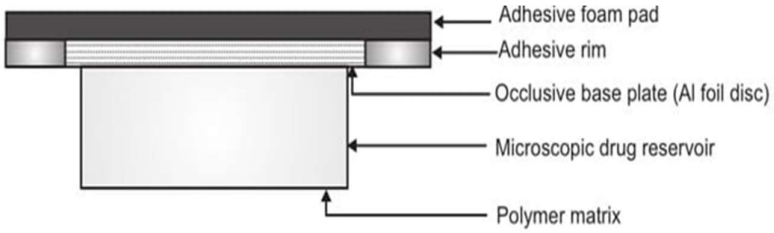

Fig 6: Micro reservior dissolution controlled TDDS

- A drug reservoir is formed by first suspending an aqueous solution of water soluble polymer. This drug suspension is homogenously dispersed in a lipophilic polymer by high energy dispersion technique.
- This forms the microscopic spores of drug reservoir which are supported over an occlusive pad and are

thermodynamically unstable.

- Stabilization by cross linking the polymer chain insitu using cross linking agent.
- It can be further coated with a layer of biocompatible polymer to improve the drug release.

Marketed products of transdermal patches

Table 1: Marketed products of transdermal patches

Brand Name	Drug	Manufacturer	Indications
Nicotinell®	Nicotine	Novartis	Pharmacological smoking cessation
Matrifen®	Fentanyl	Nycomed	Pain relief patch
Ortho Evra™	Norelgostromin/ Ethinyl Estradiol	ORTHO-McNEIL	Postmenstrual syndrome
NuPatch 100	Diclofenac diethylamine	Zydus Cadila	Anti Inflammatory
Neupro®	Rigotine	UCB and Schwarz Pharma	early-stage idiopathic Parkinson's disease
Alora	Estradiol	TheraTech/Proctol and Gamble	Postmenstrual syndrome
Nicoderm®	Nicotine	Alza/GlaxoSmithKline	Smoking cessation
Estraderm	Estradiol	Alza/Norvatis	Postmenstrual syndrome
Climara	Estradiol	3M Pharmaceuticals/Berlex Labs	Postmenstrual syndrome
Androderm	Testosterone	TheraTech/GlaxoSmithKline	Hypogonadism in males
Nitrodisc	Nitroglycerin	Roberts Pharmaceuticals	Angina pectoris
Transderm-Scop®	Scopolamine	Alza/Norvatis	Motion sickness
Nuvelle TS	Estrogen/Progesterone	Ethical Holdings/Schering	Hormone replacement therapy

CONCLUSION

To sum up, transdermal drug delivery systems (TDDS) offer a very creative and efficient way to administer drugs, with a number of benefits over traditional oral or injectable techniques. TDDS can reduce adverse effects, improve patient compliance, and produce consistent, dependable therapeutic results by permitting the controlled release of therapeutic agents through the skin. For patients who struggle with injections or who are managing chronic conditions, this non-invasive approach is especially helpful. But issues like skin permeability, drug stability, and the capacity to transport big molecules continue to be major obstacles to this technology's wider use. These problems are being addressed by ongoing developments in formulation design, including the creation of innovative permeation enhancers, microneedles, and systems based on nanotechnology. TDDS has enormous potential for the future with further research focused on enhancing its efficacy, broadening its applications, and resolving the outstanding issues. Drug delivery could undergo a revolution as technology develops, providing a more accurate, effective, and patient-friendly substitute for conventional techniques.

REFERENCES

1. S.P. Vyas and R.K. Khar, Controlled Drug Delivery -concepts and advances,Vallabh Prakashan, New Delhi, First edition 2002.
2. Textbook of Novel drug delivery system (Nirali prakashan) by Dr.K.Jesindha beyatricks and Mrs.Ashwini S .joshi.
3. Erdő, F., Kato, Y., Hashimoto, N., Karvaly, G., and Nakamichi, N. (2016). Methodological positioning and critical assessment of the transdermal microdialysis technology. A review. Controlled Release Society Official Journal, 233, 147-161.
4. Pastore, M. N., Horstmann, M., Roberts, M. S., & Kalia, Y. N. (2015). Examine the pharmacology, development, and history of transdermal patches. 2179–2209 in British Journal of Pharmacology, 172.

5. Economidou, S. N., Lamprou, D. A., & Douroumis, D. (2018). 3D printing applications for transdermal drug delivery. International Journal of Pharmaceutics, 544(2), 424.
6. Di Stefano, A., Marinelli, L., Cerasa, L. S., & Sozio, P. (2012). Alzheimer's disease is treated with transdermal donepezil. Neuropsychiatric Disorder and Therapy, 8, 361–369.
7. Y W. Chien, Novel Drug Delivery Systems, 2nd edition, revised and expanded, Marcel Dekker, Inc., New York, 1992.
8. Robinson, J. R., Lee V. H. L, Controlled Drug Delivery Systems, Marcel Dekker, Inc., New York, 1992.
9. Encyclopedia of Controlled Delivery. Edith Mathiowitz, Published by Wiley Interscience Publication, John Wiley and Sons, Inc, New York. Chichester/Weinheim.
10. N.K. Jain, Controlled and Novel Drug Delivery, CBS Publishers & Distributors, New Delhi, First edition 1997 (reprint in 2001).