Review Article

RFP Journal of Dermatology
Volume 7 Number 1, January - June 2022

Conventional Vs Transdermal Drug Delivery System

Sandhiya V[1], Praveen Kumar M[2], Prasanth Raj C N[3], Nirmal P[4], Mano A[5], Suhaib I[6]

How to cite this article:
Sandhiya V, Praveen Kumar M, Prasanth Raj C N, et al. Conventional Vs Transdermal Drug Delivery System. RFP Journal of Dermatology 2022;7(1):17-23.

ABSTRACT

Many medications are now administered orally; however they are not as effective as they should be. Beyond the local application site, transdermal delivery technology is being explored to treat a wide range of diseases. Because of reduced first pass metabolism, avoidance of an adverse gastrointestinal environment, and the potential to provide extended and regulated drug delivery, transdermal drug administration offers substantial benefits over oral treatment. Transdermal drug delivery systems (TDDS) are topically applied patches that release medications for systemic effects at a predetermined and regulated rate. It works by putting a medication inside a patch and wearing it for a long time on the skin. As a result, a steady concentration of medication remains in the bloodstream for an extended period of time. TDDS products include Scopolamine, Nicotine, Testosterone, Fentanyl, and Clonidine. Numerous active compounds with variable molecular size and structure cannot be maintained in transdermal form, despite their many benefits.

Keywords: Transdermal patch, Skin, Permeation pathways, Matrix.

Author Afliation:

[1]Assistant Professor, [2-6]B. Pharmacy Student, Department of Pharmaceutics, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Tamil Nadu 600097, India.

Corresponding Author:

Sandhiya V, Assistant Professor, Department of Pharmaceutics, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Tamil Nadu 600097, India.

Email: Sandhiyavaithi@gmail.com

Received Date: 02.03.2022
Accepted Date: 28.05.2022

INTRODUCTION

Transdermal Drug Delivery System

Drug delivery system (DDS) is a generic term for a series of physicochemical technologies that can control delivery and release of pharmacologically active substances into cells, tissues and organs, such that these active substances could exert optimal effects.[1,2] In other words, DDS covers the routes of administration and drug formulations that efficiently deliver the drug to maximize therapeutic efficacy while minimizing any side effect[3-5] Depending on the delivery route, there are many types of administration modalities, such as oral administration, transdermal administration, lung inhalation, mucosal administration, and intravenous injection.[6]

At present, the most common form of delivery of drugs is the oral route administration. This route has notable advantages like easy administration, pain free, cheap but unfortunately it has some flaws namely poor bioavailability due to hepatic metabolism and the tendency to produce rapid blood level spikes, leading to a need for high and/or frequent dosing, which can be both cost prohibitive and inconvenient.[7]

To overcome this weakness, transdermal drug delivery system (TDDS) was developed, which has improvement in therapeutic efficacy and safety of drugs by more precise (targeted site), spatial and temporal placement within the body thereby reducing the size, number of doses and fewer side effects.

A transdermal drug delivery system (TDDS) represents the most attractive method among other conventional forms. TDDS is commonly used instead of oral medications or topical creams. Furthermore, TDDS is more capable of surpassing hepatic first pass metabolism, the degradation of the drug substance when it reaches the liver, which reduces the effect of the drug sustaining

© Red Flower Publication Pvt. Ltd.

steady blood levels for a longer time frame, and reduced gastrointestinal discomfort. Thus, TDDS offers competitive advantages over traditional methods that improve bioavailability and patient compliance.

To acquire the principle of the transdermal drug delivery system, one must first understand the morphological, biophysical and physicochemical properties of the skin, as well as the qualities that contribute to the barrier function and rate of drug entry into the body via skin.

Skin

The skin is the largest organ of the body, with a total area of about 20 square feet. The skin is made up of three layers: Epidermis (outermost layer), dermis (inner layer), and subcutaneous tissues (deepest layer).

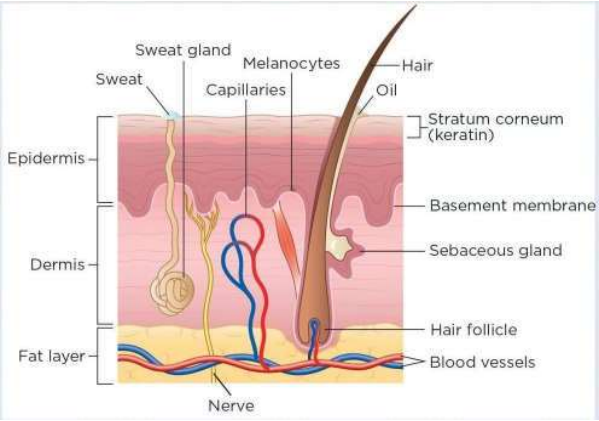

Fig. 1: Anatomy of skin.[16]

Epidermis

The epidermis is composed of two layers: Stratum corneum (nonviable epidermis) and viable epidermis.[8] The epidermis contains no blood vessels, and cells in the deepest layers are nourished almost exclusively by diffused oxygen from the surrounding air[9] and to a far lesser degree by blood capillaries extending to the outer layers of the dermis. The main types of cells that make up the epidermis are Merkel cells, keratinocytes, with melanocytes and Langerhans cells also present. The epidermis can be further subdivided into the following strata (beginning with the outermost layer): corneum, lucidum (only in the palms of hands and bottoms of feet), granulosum, spinosum, and basale. Cells are formed through mitosis at the basale layer. The daughter cells (see cell division) move up the strata, changing shape and composition as they die due to isolation from their blood source. The cytoplasm is released and the protein keratin is inserted.

They eventually reach the corneum and slough off (desquamation). This process is called "keratinization". This keratinized layer of skin is responsible for keeping water in the body and keeping other harmful chemicals and pathogens out, making skin a natural barrier to infection.

Dermis

The dermis is the layer of skin beneath the epidermis that consists of connective tissue and cushions the body from stress and strain. The dermis is tightly connected to the epidermis by a basement membrane. It also harbours many nerve endings that provide the sense of touch and heat. It contains the hair follicles, sweat glands, sebaceous glands, apocrine glands, lymphatic vessels and blood vessels. The blood vessels in the dermis provide nourishment and waste removal from its own cells as well as from the stratum basale of the epidermis.[10]

The dermis is structurally divided into two areas: a superficial area adjacent to the epidermis, called the papillary region, and a deep thicker area known as the reticular region.[10]

Hypodermis

The hypodermis is also known as subcutaneous tissue, is not part of the skin, but lies below the dermis of the cutis. Its purpose is to attach the skin to underlying bone and muscle as well as supplying it with blood vessels and nerves. It consists of loose connective tissue, adipose tissue and elastin. The main cell types are fibroblasts, macrophages and adipocytes (subcutaneous tissue contains 50% of body fat). Fat serves as padding and insulation for the body.[10]

The sweat glands (2-5 million) produce sweat (pH 4.0-6.8) and may also secrete protein or antibodies. Their main function is to aid heat control; approximately 400 glands per square centimeter are particularly concentrated in the palms and soles. Sebaceous glands are most numerous and largest on the face, forehead, ear, on the midline of the back and anogenital surfaces, but it is not present on palms and soles. The glands vary in size from 200-2000 um in diameter. The nose contains a maximum amount of sebaceous glands because it secretes sebum an oily material

from cell disintegration. The primary components are free fatty acids, glycerides, cholesterol, esters of cholesterol, and squalene. It acts as a source of the stratum corneum plasticizing lipid & skin lubricant and maintains an acidic condition on the skins outer surface.[11]

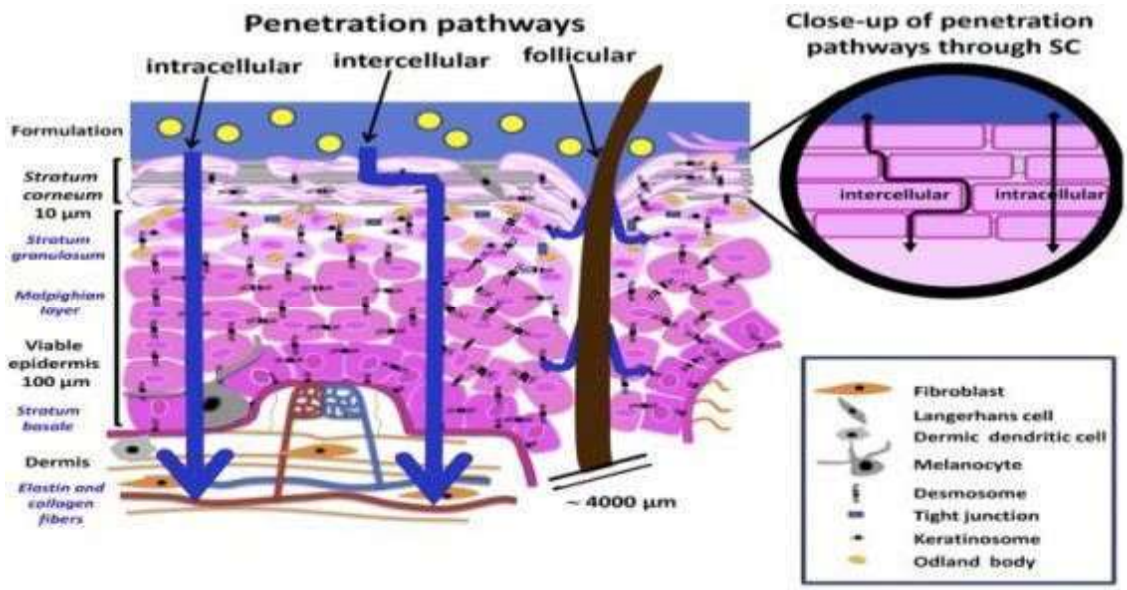

Fig. 2: Drug penetration pathway.[8]

Drug permeation

The transepidermal and transappendegeal channels are the two probable routes for medication entry via intact skin. The transepidermal pathway involves molecules passing through the stratum corneum, a multi-layered, multi-cellular barrier with a complex architectural design. Intra-or inter-cellular transepidermal penetration are two different types of transepidermal penetration. Hydrophilic or polar solutes can be transported intracellularly through corneocytes, terminally developed keratinocytes. Diffusion of lipophilic or non-polar solutes through the continuous lipid matrix is enabled through transport via intercellular gaps. Molecules move through sweat glands and past hair follicles on their way to the scalp via the transappendegeal route.

TRANSDERMAL PATCHES

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. This patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive.[7]

Scopolamine patches was first transdermal drug delivery for systemic delivery which was approved by U.S. FDA in 1979, which was used to treat motion sickness. After a decade in 1991 nicotine patches were introduced and became huge success. Later on many drugs were introduced in TDDS form.

Components of TDDS

- Liner: Protects the patch while it is being stored. The liner is removed before use.
- Drug: Active ingredient is present with direct contact to the liner.
- Adhesive: Its purpose is to adhere the patch's components together as well as to adhere the patch to the skin. It should be easily removed from the smooth surface without leaving any residue.
- Backing: The backing materials must be flexible while also having a high tensile strength.
- Permeation Enhancer: These compounds are useful for increasing stratum corneum permeability by interacting with structural stratum corneum components such as proteins or lipids in order to achieve higher therapeutic levels of the drug. They change the protein and lipid packaging of the stratum corneum, chemically altering the barrier functions and

increasing permeability.

- Polymer Matrix: Polymers are the main component of TDDS, controlling drug release from the device. Polymer matrices can be made by dispersing the drug in a liquid or solid state synthetic polymer base.

Criteria for TDDS

- Drug must be high lipophilic (ideal log PO/W ≈ 2).
- Drug must have low molecular weight, below 500 Dalton.
- Must also have low melting point, below 150 °C.
- Sufficient solubility in water at pH 6 to 7.4 (e.g., ≈ 0.05 to 1mg/ml if target delivery rate is in the mg range per day).
- Formulation ingredients must not close drug specific pathways. For example, it has been shown that shunt diffusion plays a major role in caffeine absorption, provided that pores are not closed by ingredients like waxes before drug application.[12]
- The formulation of passive systems must enhance drug partitioning into and transport across the skin layers, maintain a nearly constant drug activity gradient throughout the skin over the specified application duration, and ensure a high drug depletion rate of the patch from a physicochemical standpoint.
- Selecting and designing a polymer is a difficult undertaking that necessitates a full understanding of the surface and bulk properties of the polymer that can provide the appropriate chemical, interfacial, mechanical, and biological functions.
- All device ingredients must be well tolerated by the skin and support continuous medication penetration through the skin at a repeatable rate for the duration of the application.
- While considering the TDDS route, one must take a notice on immune and inflammatory cells of the dermis which react on any mechanically or chemically induced irritation.
- The transcellular pathway requires repeated drug partition and diffusion across structured bilayers, and seems to be usually less important.

Types of transdermal patches

There are different types of transdermal patches:

- Matrix
- Reservoir
- Drug in adhesive
- Multilaminate

Matrix

The matrix system, also known as a monolithic device, has a drug layer made of a semisolid matrix that contains a drug solution or suspension. This patch's sticky layer partially covers the drug layer and surrounds it.

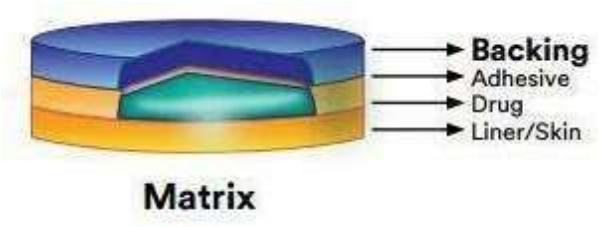

Fig. 3: Matrix patch.[15]

Reservoir

Unlike the single layer and multi-layer drug-in-adhesive systems, the reservoir transdermal system has a separate drug layer. The drug layer is a liquid compartment containing a drug solution or suspension that is separated by the adhesive layer. The drug reservoir is completely encapsulated in a shallow compartment molded from a drug-impermeable metallic-plastic laminate, with a rate-controlling membrane made of a polymer (like vinyl acetate) on one surface.[13,14] This patch is also backed by the backing layer.

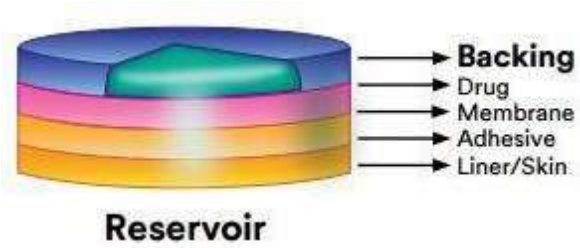

Fig. 4: Reservoir patch.[15]

Drug in adhesive

The adhesive layer of this sort of patch is responsible for adhering the multiple layers together, as well as the overall system to the skin, containing the

medicine, and releasing the drug. A temporary liner and a backing surround the adhesive layer.

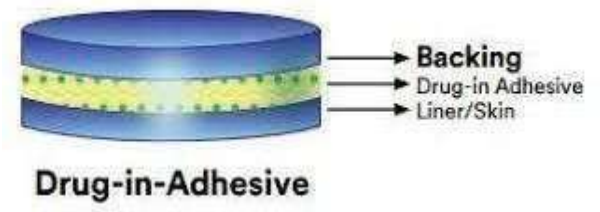

Fig. 5: Drug in adhesive.[15]

Multilaminate

The multi-layer drug-in-adhesive patch is similar to the single-layer system but it differs in that it adds another layer of drug-in-adhesive, usually separated by a membrane. One layer is for immediate release of the drug and the other is for control release of drug from the reservoir[13] This patch also has a temporary liner-layer and a permanent backing. The drug release from this depends on membrane permeability and diffusion of drug molecules.

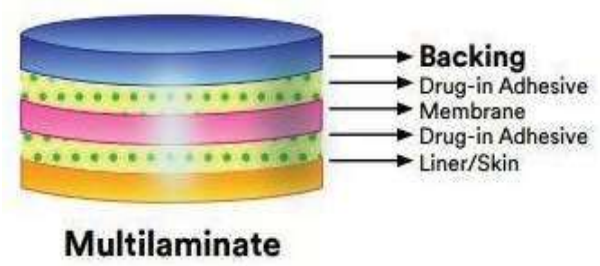

Fig. 6: Multilaminate patch.[15]

Vapor patches

In a vapor patch, the adhesive layer not only serves to adhere the various layers together but also to release vapor. Vapor patches release essential oils for up to 6 hours and are mainly used for decongestion. Other vapor patches on the market improve quality of sleep or aid in smoking cessation.[13]

Advantages of transdermal patches:

- Dosing frequency is being reduced.
- More consistent plasma levels.
- Useful for potent medicines.
- Bioavailability has been improved.
- Reduction of negative effects.
- The ability to discontinue drug administration simply by removing the transdermal delivery system from the skin (patch).
- It provides a continuous infusion of the medicine over a long period of time.
- Probably more difficult to abuse than any other preparation.
- Patient compliance is enhanced, and inter- and intra-patient variability is reduced because of the simpler treatment regimen.

Disadvantages of transdermal patches:

- There's a chance that the application site will irritate you.
- Drugs or excipients cause skin irritation or contact dermatitis.
- Because of the skin's low permeability, the number of medications that can be given this way is limited.
- Physicians must be educated and patients/ parents must be directed.
- For penetration into the stratum corneum, the medication must have the desired physicochemical qualities.
- The skin's barrier function varies from one area to the next on the same individual, from person to person.
- The patch will not stay to the skin for long period due to heat, cold, sweating (perspiring), and showering.
- Bathing or swimming causes patches to peel off completely; patches can also fall off when walking.

Why TDDS is used in alternative for conventional delivery system?

TDDS is an ongoing research topic. It has been offered as an alternative to needle based immunizations since the medication is given directly to immunogenic Langerhans cells on the skin. Transdermal medication delivery allows for targeted drug release into the patient's bloodstream, resulting in fewer systemic side effects and, in certain cases, increased efficacy over other dosage forms. Because of its ease of use, it is often used as a substitute for intravenous anesthetics and oral opioids. This alternative route for medicine delivery offers a less expensive and more convenient option to address diseases.

Topical medications are medications which are applied on the skin that rely on passive diffusion into the skin itself, creating a local effect. Whereas transdermal medications refer to medications that are applied to the skin but involve skin penetration enhancing compounds or technology that increase the amount of drug that can cross the skin barrier, often to the point that the drug can enter the systemic circulation and exert effects in areas other than the site of application.[15] Transdermal products use a variety of techniques to improve penetration through the Stratum Corneum, the skin's principal barrier, allowing enough medication to reach systemic circulation or deeper underlying tissues.

Transdermal Market

Transdermal medication delivery devices are being utilized to treat a variety of illnesses, including chronic pain, central nervous system problems, and cardiovascular disease. The global market for transdermal medicines is being driven by the growing incidence of targeted illnesses and greater use of contraceptives.

As said the market for transdermal products has been steadily increasing, and this trend is expected to continue in the near future. TDD products are continuing to provide actual therapeutic value to patients all across the world. According to P&S market research, TDDS market is forecasted to cross over USD 7.5 billion around 2023. In the United States, more than 35 TDD products have been approved for sale, and roughly 16 active components have been approved for usage in TDD products around the world. North America is a significant revenue generator in the transdermal drug delivery systems market.

The TDDS market is experiencing the fastest growth in demand due to advances in healthcare and spending in India and China.

Table 1: Showing FDA approved drugs for TDDS.

Year	Generic Names	Indication
1979	Scopolamine	Motion sickness
1984	Clonidine	Hypertension
1990	Fentanyl	Chronic pain
1991	Nicotine	Smoking cessation
2007	Rotigotine	Parkinson's disease

CONCLUSION

Transdermal medication delivery systems have been proven to be a safe and effective method of drug delivery. Scientists with a high rate of achievement are exploiting their potential role in controlled release all over the world. Transdermal delivery is a surprising successful mode of administration if a medication has the proper balance of physical chemistry and pharmacology. Transdermal medication administration allows for site - specific treatment, reducing or eliminating diseases, adverse medication reactions, drug/drug interactions, and side effects that can lead to GI, hepatic, renal, or other difficulties. It has the potential to remove the use of needles for the administration of a wide range of pharmaceuticals in the future. TDDS has a lot of potential because it can be used to turn both hydrophobic and hydrophilic active substances into promising medications. Greater understanding of the diverse mechanisms of biological interactions as well as polymers is essential to optimise this drug delivery method. Because of the TDDS's numerous benefits, several new studies are now being conducted to include newer medicines into the system. Transdermal medication administration is becoming the most generally recognized method of drug administration because to recent technological developments and the integration of the drug to the site of action without rupturing the outer membrane. This article provides valuable information on how transdermal medicines are better than conventional drugs. At the moment, global sales of TDDS are lower than those of conventional forms, but we hope that the TDDS will make a name for itself.

Conflicts of interest: None

Authors' contributions: All authors made contributions to the article.

Availability of data and materials: Not applicable.

Financial support and sponsorship: None.

Consent for publication: Not applicable

REFERENCES

1. Vega-Vásquez P, Mosier NS, Irudayaraj J. Nanoscale drug delivery systems: from

medicine to agriculture. Front Bioeng Biotechnol. 2020;8:79.

2. Vargason AM, Anselmo AC, Mitragotri S. The evolution of commercial drug delivery technologies. Nat Biomed Eng. 2021.
3. Mali AD, Bathe R, Patil M. An updated review on transdermal drug delivery systems. Int J Adv Sci Res. 2015;1(6):244–54.
4. Li C, Wang J, Wang Y, Gao H, Wei G, Huang Y, et al. Recent progress in drug delivery. Acta Pharm Sin B. 2019;9(6):1145–62.
5. Kumar JA, Pullakandam N, Prabu SL, Gopal V. Transdermal drug delivery system: An overview. Int J Pharm Sci Rev Res. 2010;3(2):49–54.
6. Jeong, W.Y., Kwon, M., Choi, H.E. et al. Recent advances in transdermal drug delivery systems: a review. Biomater Res 25, 24 (2021).
7. Jain, N. K., Controlled and Novel Drug Delivery, CBS Publishers, and Distributors, 2002, 107.
8. Reddy et al. "Transdermal Drug Delivery System: A Review." Research Journal of Pharmaceutical Dosage Forms and Technology, vol. 5, no. 4, 2013, pp. 202-212.
9. Stücker M, Struk A, Altmeyer P, Herde M, Baumgärtl H, Lübbers DW (February 2002). "The cutaneous uptake of atmospheric oxygen contributes significantly to the oxygen supply of human dermis and epidermis". The Journal of Physiology. 538 (Pt 3): 985–94.
10. https://en.wikipedia.org/wiki/Human_skin#cite_note-St%C3%BCcker2002-13.
11. Dr. B.Arul and Dr. R. Kothai, Noval Drug Delivery System, edition 2020, S.vikas and Company (Medical Publisers).
12. Otberg, N.; Patzelt, A.; Rasulev, U.; Hagemeister, T.; Linscheid, M.; Sinkgraven, R.; Sterry, W.; and Lademann, J. The role of hair follicles in the percutaneous absorption of caffeine. Br. J. Clin. Phamacol. 2007; 65: 488-492.
13. "Transdermal patch," Wikipedia, 06-Apr-2017. [Online].Available: https://en.wikipedia.org/wiki/Transdermal_patch. [Accessed: 03-Apr-2017].
14. Lewis et al. "Design and Evlauation of Matrix Type and Membrane Controlled Transdermal Delivery Systems of Nicotine Suitable for use in Smoking Cessation." Indian Journal of Pharmaceutical Sciences, 2006, pp. 179-184.
15. Marjukka Suhonen TA, Bouwstra J. Chemical enhancement of percutaneous absorption in relation to stratum corneum structural alterations. J Control Release 1999:59:149-161.
16. https://www.nursingtimes.net/clinical-archive/dermatology/skin-1-the-structure-and-functions-of-the-skin-25-11-2019/
17. https://biotextiles2017blog.wordpress.com/transdermal-patch/