IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
October 2021 Vol.:22, Issue:3

Review on Transdermal Drug Delivery System

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Dinesh.P. Patil[1*], Vivek Chaudhary[2], S.R.Tambe[3], Jayesh.V.Musale[4], Mehfoozur Rahman[5], Pratiskaha Nahar[6], Renuka Joshi[7]

[1,2] Shri Jagdishprasad Jhabarmal Tibrewala University, Rajasthan-333001, India.

[3] MGV'S Samajshri Prashant Dada Hiray, College of Pharmacy, Malegaon, Nashik, India.

[4, 5, 6, 7] MGV's Institute of Pharmacy (D. Pharmacy), Malegaon, Nashik, India.

Submitted: 23 September 2021
Accepted: 29 September 2021
Published: 30 October 2021

Keywords: Transdermal drug delivery, patches, skin, therapeutics efficacy

ABSTRACT

Transdermal drug delivery system also called as 'Patches'. TDDS plays vital role in medical field but not yet this system achieved a potential like oral delivery or hypodermic injection. It is more accepted than another system because of remarkable benefit like less absorption, improved bioavailability, decrease side effects, more uniform plasma levels. It is system in which delivery of active pharmaceutical ingredient occurs via skin. This system can effectively improve the therapeutic efficacy and safety of the drugs because drug penetration occurs at a predetermined and controlled rate. Skin is very effective intermediate from which drug absorption take place and come into the circulatory system. This review article mainly focused on outline of transdermal delivery system, layers of skin, factors of system, as well as components, advantages and disadvantages of the transdermal drug delivery system.

HUMAN JOURNALS
www.ijppr.humanjournals.com

INTRODUCTION:

The uncovering of Transdermal Drug Delivery System (TDDS) is a development in the sector of controlled drug delivery system [1]. It becomes a great field of interest. Another name of Transdermal drug delivery system (TDDS) is Patches [2, 3]. It is defined as self controlled, discrete dosage forms. When these patches are applied to the skin, drugs penetrate through the skin into the systemic circulation [4]. Transdermal systems plays vital role for disease that required chronic treatment [5]. Transdermal SCOP was first transdermal system, approved by FDA (1979). It was used for the prevention of nausea and vomiting. The main aim of TDDS is to deliver drugs into systemic circulation via skin at fixed rate with minimum patient variation.[6].

To facilitate delivery of drugs through human skin complete physicochemical, morphological and biophysical characteristics of skin to be considered.[7] TDDS is effective alternative to injectables and oral routes, as well as it increases patience compliance and prevent first-pass metabolism respectively[8].

The achievement of this system is that currently there are 35 TDD preparations accepted in the USA. It is used to treat hypertension, angina, female menopause, local pain control and more.[9]As well as this system is also helps in the treatment of neuropathic pain, hair loss, genital herpes, headache, migraine and sexual dysfunction [10].

Merits of Transdermal delivery system over Conventional route [11, 12]

1. TDDS is best route for pediatric patients.
2. It is suitable route for an unconscious patient.
3. Low chances of overdose and easy detection of drug
4. It provides stable plasma levels.
5. It is easy to use and non-invasive.
6. Transdermal delivery avoids the stomach environment where the drug can be degraded.
7. Drug release can be stopped at any point after removal of patch from the site of action.

Anatomy of Skin

It is a largest organ of human body, with 20 sq. feet total area, situated on the outmost layer which protects human body, from outside environment like temperature, some kind of chemicals, various shocks, UV radiation. Its primary function is to maintain body hydration. (13)

Skin has three layers, starting from outside.

1. The outer epidermis
2. The Inner dermis
3. Subcutaneous tissue deep in the inner skin.

1. Epidermis(14)

The outermost layer of skin provides a waterproof barrier. Epidermis creates our skin tone. It is stratified, squamous, keratinizing epithelium. Epidermis is composed of four layers: Stratum corneum (outermost layer), Stratum granulosum, Stratum spinosum and Stratum Basal.The attachment like nail, hair, sweat glands and sebaceous gland are derived from epidermis. The multi-layered epidermis varies in thickness which mainly depends upon cell thickness and layers of epidermis. This layer is also called as horny layer. It is approximately 10mm thick It contains 10 to 25 layers of dead, keratinized cells called corneocytes. It is flexible but relatively impermeable. The stratum corneum is the principal barrier for the penetration of drug.

2. Dermis(15)

Dermis also referred as corium. It is very sensitive and highly vascular part of skin just beneath the stratum basal of epidermis, having 3-5mm thickness. This second layer of skin contains blood vessels, lymph vessels and nerves. Network of arteriole of the dermis nourishes the dermal tissue and stratum basal epidermis also it provides nutrients and oxygen to the skin, whole removing toxins and waste products.

3. Subcutaneous Tissue layer(16)

It is the last layer of skin also known as hypodermis. It is fat tissue layer that supports the dermis and epidermis. The majority of fat stored in the subcutaneous layer. It helps in regulation of temperature a swell as offers nutritional and mechanical support. Thickness of

this fatty layer is different in every part of body. This layer carries main blood vessels and nerves to skin and may contain sensory pressure organs. For transdermal drug delivery, drug has to go through all these three layers and reach into systemic circulation while in case of topical drug delivery only penetration through the stratum corneum is vital and then retention of drug in skin layer.

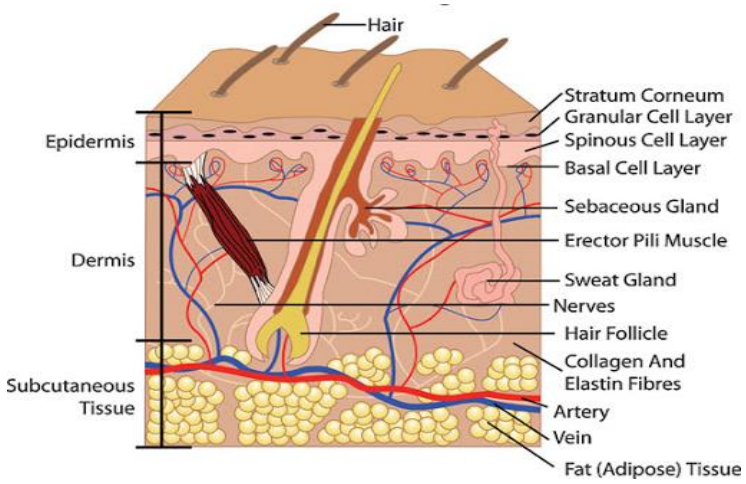

Fig. No. 1 Human Skin Diagram

Transdermal Patches [17]

Transdermal patch is a medicated adhesive patch. This patch is placed on skin surface to deliver specific amount of medication through the skin and plainly into systemic circulation. Often this patch provides healing to an affected area of the body. The benefit of this route over another route like topical, oral etc is that it gives a controlled release of the drug into the patient. A broad variety of pharmaceuticals can be delivered by the "patches".

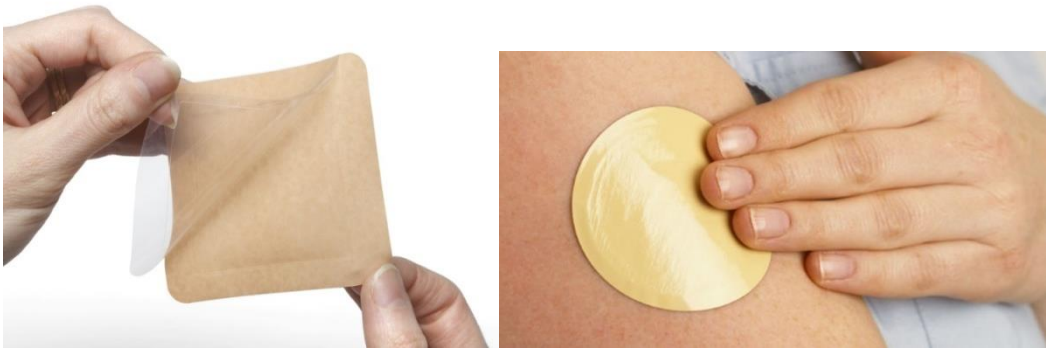

Fig. No. 2 Transdermal Patches

Principal of Transdermal drug delivery system[18]

Previously skin was only considered as impermeable protective barrier, afterward exploration were carried out which provide some evidence related to use of skin as a route for systemic administration. Skin is most accessible organ as well as it is most intensive organ of the body. There are various steps involved in transportation of drug (patch to systemic circulation), this process include,

1. Diffusion of drug from drug reservoir to the rate controlling membrane.
2. Diffusion of drug from rate limiting membrane to stratum corneum.
3. Sorption by stratum corneum and penetration through viable epidermis.
4. Uptake of drug by capillary network in the dermal papillary later.
5. Effecton target organ

Types of transdermal patches[19,20]

1. Single-layer drug in adhesive

In this type layer of adhesive contains the drug entity. This layer serves to join the various layers together and also responsible for delivering drug to the skin. The adhesive layer enclosed by a temporary liner and a backing laminate.

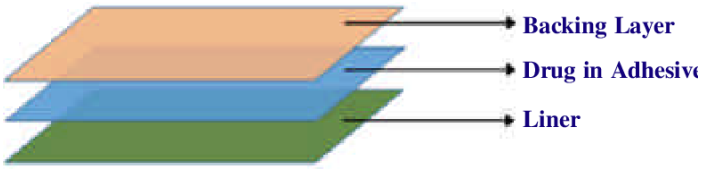

Fig. No. 3: Single layer drug in adhesive

2. Multi-layer drug in adhesive

Multi-layer is alike to the single layer, the only difference is that it contain immediate drug release layer, which will be controlled release with layer of adhesive. In multi layer the adhesive layer is in charge for the releasing of the drug.Multi layer type also enclosed between temporary liner layer and a permanent backing layer.

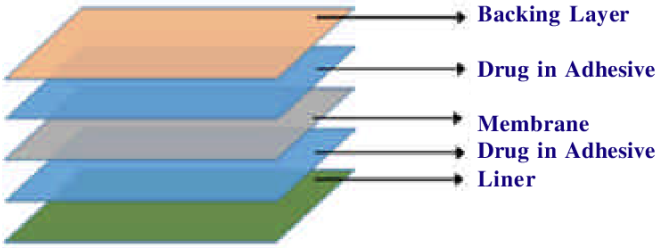

Fig. No. 4 Multi layer drug in adhesive

3. Vapor patch

In vapor patch, the adhesive layer not only sticks to various layers together but also release vapor. This vapor patch releases essentials oils for up to 6 hours and are utilize in decongestion. Some other marketed vapor patches used to improve quality of sleep and also used for cigarette cessation.

4. Reservoir system

In reservoir system the drug reservoir is enclosed between the two layers, in that one is impervious backing layer and second one is a rate-controlling membrane. The specific amount of drug only releases through the rate-controlling membrane. In the compartment of drug reservoir, drug may in the form of a solution, suspension; gel in a solid polymer matrix Hypoallergenic adhesive can be compatible with drug so that it can be applied as outer surface polymeric membrane.

Factors that influence transdermal drug delivery [20]

Physiological factor

1. Skin hydration
2. Temperature and pH
3. Diffusion coefficient
4. Drug concentration
5. Partition coefficient
6. Molecular size and shape

Biological factors

1. Skin condition
2. Skin age
3. Blood flow
4. Regional skin sites
5. Skin metabolism
6. Species differences

Precautions should be taken while applying transdermal patch: [21]

1. Before the application of patch, the part of skin should be cleaned.
2. Do not cut the patch into two parts, otherwise drug may release.
3. Removed old patch, before applying new one.
4. Site of administration of patch should be accurate.
5. Care should be taken while applying or removing the patch because anyone handling the patch can absorb the drug from the patch.

Basics component of TDDS

1. Basics component of TTDS includes:
2. Drug
3. Membrane
4. Polymer matrix
5. Permeation enhancers
6. Backing laminates
7. Release liner
8. Other excipients

1. Drug [22,23]

The drug used in TDDS should be chosen effectively. TDDS system possesses many advantages to drugs that undergo first pass metabolism, drug having narrow therapeutic window or drugs with short half-life.

Properties of a drug

1.The drug should have ample of solubility in oil and water.

2. Molecular weight of the drug should be <1000daltons.

3. The drug should have low melting point.

4. The half-life of drug should be short.

5. The drug must not provoke allergic response.

6. Drugs that shows extensive first-pass metabolism are suitable for TDDS Examples of drugs that are appropriate for TDDS include, Atenolol, Metoprolol tartrate, Verapamil hydrochloride, carvedilol.

2. Polymer matrix:[24,25]

Polymer is the core of TDD system. These polymers control the release of the drug from the device. This matrix can be prepared by dispersion of drug into liquid or solid synthetic polymer base.

Properties of Polymer matrix:

1.It should have good stability as well as compatibility with respective drug and other materials of the system.

2.They should provide efficient release of a drug via the device.

3. Chemical functionality and, the molecular weight of polymer should be such that specific drug diffuses properly and gets released through it.

4. It should be stable, non-reactive with the drug.

5. It should be easily manufactured.

6. It should be non-toxic and non-antagonistic to the host molecule. Natural polymers: Gelatin shellac, gums, starch, waxes, etc.

Synthetic polymers: Polyamide, polyvinyl alcohol, polypropylene, polyethylene, polyurea, etc.

Synthetic elastomers: Silicon rubber, Acrylonitrile, Polybutadiene, Polyisobutylenenitrile, etc.

3. Permeation enhancers: [26,27]

Permeation enhancer is defined as the substance that temporarily diminishes the impermeability of the skin. It is also called as penetration enhancer or sorption promoters or accelerants. These substances include water, fatty acids and alcohols, pyrrolidones, terpenes and derivative, essential oil, dimethylsulfoxide, urea and surfactants.

4. Adhesive [28,29]

PSA i.e. Pressure-Sensitive Adhesive, it is the most vital component used in A TDD system.It is the material that maintains an intimate contact between transdermal system and the skin surface. Adhesion of patch to skin is the main function of PSA, but mainly it acts as a matrix for drug as well as excipients. Adhesion is directly related to drug delivery and therapeutic effect.

Ex: Silicones, Polyisobutylene.

Properties of Adhesive

1. It must be compatible to skin.

2. Irritation or sensitization must be minimal.

3. Removal of patch should be without physical trauma.

4. They must be capable of dissolving drug and excipients in sufficient amount for the preferred pharmacological effect without losing their properties.

5. Backing layer: [30, 31]

Backing layer also called as backing laminate it guards patch from outer environment.

Properties of backing layer

1.It must be flexible.

2.It should have good tensile strength.

3.Backing material should have low water vapor transmission to promotes skin hydration.

4.It must be heat sealable.

Ex: Cellulose derivatives, Polypropylene silicon rubber, polyolefin's, polyesters, Polyester-polypropylene films, Polypropylene resin Aluminized plastic laminate.

6. Release Liner:[32]

The primary packaging material of TDDS is release liner. For the period of storage, patch is cover by a protective liner called a release liner. This released liner removes and discharged immediately prior to application of the patch to the skin. Typically, it consists of base layer which may be occlusive (polyethylene) or non-occlusive (paper fabric).

7. Other Excipients[33]

Solvents like methanol, chloroform, acetone isopropanol are used to prepare drug reservoirs and as well plasticizers like triethyl citrate, polyethylene glycol, propylene glycol are used to give plasticity to the transdermal patch.

Evaluation Parameter [34]

1. pH
2. Drug content
3. Viscosity
4. Spreadability
5. Extrudability study
6. Skin irritation studies
7. In vitro release
8. In vivo study

9. Stability

10. Consistency

Ideal Properties of Transdermal Drug Delivery System [35]

Parameter	Properties
Particle size	:<40cm^2
Molecular weight	:<400
Half life	:10or less
Dose frequency	:Should be low(<20mg/day)
Skin reaction	:Non-irritating and non sensitizing
Therapeutic index	:Low
Oral Bioavilibility	:Low

Advantages of TDD System [36, 37]

1. Alternative to parenteral routes, thus overcome the issues like needle phobia.

2. A large surface area of skin allows more absorption of drugs.

3. In addition, it minimizes the risk of toxic side effects, as pharmacokinetics of drugs are more uniform with fewer peaks.

4. It can increase patient compliance, and it is also useful for the patient who suffers from vomiting and unconsciousness.

5. TDDS avoids specific problems (low absorption, gastro-intestinal irritation) related to drug by increasing their therapeutic value.

6. They are noninvasive.

7. The drug applied over skin can be terminated at any time by removing a transdermal patch.

Disadvantages [38]

1. Chances to allergic reaction

2. High molecular drug level cannot to attain a therapeutic level.

3. Only potent drug are appropriate candidates for transdermal delivery.

4. It is not suitable for drug which needs high blood levels.

5. TDDS is quite uneconomic.

6. It is not used for acute conditions, only used for chronic conditions (e.g. hypertension, diabetes, and anginaetc).

REFERENCES:

1. Vilegave K., Chandankar P., Gadiya M., Patil A., Kharjul M.TransdermalDelivery: A Recent Trend in Treatment of chronic diseases .JPR:BioMedRx. 2013; 1(5): 473-479.
2. Wokovich A.M., ProdduturiS., DoubW.H., Hussain A.S.,Buhse L.F. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute.Eur. J. Pharm. Biopharm. 2006; 64: 1–8.
3. Patil P.M., Dr.Chaudhari P. D.Patel J.K., Kedar K. A., Katolkar P. P. Recent trends in challenges and opportunities of Transdermal drug delivery system. Int. J. Drug Dev. Res. 2012; 4(1):39-50.
4. Rasheed S.H., HariBabu R., Md. Mohiddin K., Vineela J.,RavitejaA., Pathuri R. Gajavalli S., Vasantha Naidu L. Transdermal Drug Delivery Syst.em - Simplified Medication Regimen - A Review. Res. J. Pharm. Biol. Chem. Sci. 2011; 2(4): 233-238.
5. Sowmya C, Suryaprakash Reddy C, Amrutha V, Anilkumar D, Lohitha M. Transdermal Therapeutic Systems-An overview.International Journal of Pharmacy and Industraial Research.2012;2:197-211.
6. Tanwar H., Sachdeva R. Transdermal drug delivery system: a review. Int. J. Pharm. Sci. Res. 2016; 7(6):2274-2290.
7. Mali A.D., Bathe R., Patil M. An updated review on transdermal drug delivery systems.Int. J. Adv. Sci. Res.2015; 1(6):244-254.
8. Hafeez A., Dr. Jain U., Singh J., Maurya A., Rana L. Recent Advances in Transdermal Drug Delivery System (TDDS): An Overview. Journal of Scientific and Innovative Research 2013; 2 (3): 733-744.
9. Srivastava S., Maurya A., Gupta P. A review article on transdermal drug delivery system.WJPPS.5 (12): 1702-1725.
10. Marwah H., Garg T., Goyal A.K., Rath G. Permeation enhancer strategies in transdermal drug delivery.Drug Deliv.2014:1-15.
11. Singh K, Arora N, Garg T. (2012a). RFID: a trustable security tool in pharmaceutical industry. Am J Pharm Tech Res.2012; 2:113–27.
12. Singh K, Arora N, Garg T. Superbug: antimicrobial resistance due to NDM-1. Int J Inst Pharm Life Sci. 2012; 2:58–66.
13. Sajid A., Maryam S., Nabeel S.The Structure of Skin and Transdermal Drug Delivery System- A Review. Research J. Pharm. and Tech. 2015; 8 (2):103-109.
14. Abdo J.M., Nikolai A. Sopko,. Milner SMM. The applied anatomy of human skin: A model for regeneration. Wound Medicine.2020; 28:100179.
15. Choudhary N., Singh A., Singh A. Transdermal drug delivery system: A review. Indian Journal of Pharmacy and Pharmacology 2021; 8(1):5–9.
16. Sharma N., Agarwal G., Rana C., Bhat Z.A., Kumar D. Review: Transdermal drug delivery system: a tool for novel drug delivery system. International journal of drug development & research.2011; 3(3):70-84.
17. Kesarwani A., Yadav A.K., Singh S. Gautam H., Singh H. Theoretical aspects of transdermal drug delivery system.Bulletin of Pharmaceutical Research.2013;3(2)78-89
18. Tiwari R., Jaimini M., MohanS.,Sharma S. Transdermal drug delivery system: a Review. Int J. of Ther Appl. 2013; 14:22-28.
19. Hemanth Kumar G. Transdermal drug delivery system: An overview. IJPSR.2012; 3(3):451-457.
20. SachanR.Bajapi M. Transdermal Drug delivery System: A review. IJRDPL.. 2013;3(1),PP:773-790

21. Latheeshjlal.L, P. Phanitejaswini, Y.Soujanya, U.Swapna, V.Sarika, G.Moulika. Transdermal Drug Delivery Systems: An Overview. Int. J. Pharmtech Res 2011; 3(4):2140-2148.
22. Chung SJ. Future drug delivery research in south korea. J. Controlled. Release. 1999; 62: 73-9. 24.
23. Izumoto T, Aioi A, Uenoyana S, Kariyama K, Azuma M. Relationship between the transference of drug from a transdermal patch and physicochemical properties. Chem. Pharm. Bull. 1992; 40: 456-458.
24. Patel D.M., Kavitha K. Formulation and evaluation aspects of transdermal drug delivery system.Int. J. Pharm. Sci. Rev Res.2011;6(2): 83-90.
25. Karande P., Mitragotri S. Enhancement of transdermal drug delivery via synergistic action of chemicals. Biochimica et BiophysicaActa..2009: 2362–2373
26. Maryam S., Sajid A., Nabeel S., Khurram R., Umair A. Moosa R. Formulation considerations and factors affecting transdermal drug delivery system- a review. International Journal of Pharmacy and Integrated Life Sciences.2014; 2(9):20-35.
27. Wokovich A.M., Prodduturi S.,Doub W.H., Hussain A.S., Buhse L.F. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. Eur. J.of Pharm. and Biopharm.2006; 64:1–8.
28. Minghetti P.,Cilurzo F., Tosi L., Casiraghi A., Montanari L. Design of a New Water-Soluble Pressure-Sensitive Adhesive for Patch Preparation. AAPS PharmSciTech 2003; 4 (1):1-9
29. Sharma N. A Brief Review on Transdermal Patches.Organic and Medicinal Chemistry.2018; 7(2):1-5.
30. Waghulde S,Naik P.P., Gorde N., Juvatkar P., Shirodkar P.Y., Kale M.K. Development, Recent Inventions and Evaluation Techniques of Transdermal Drug Delivery System - A Review. Int. J. of Pharm. and Phytopharm. Res. 2013; 3 (2): 152-160.
31. Ezhumalai K., Ilavarasan P., Mugundhan R.M., Sathiyaraj U., RajalakshmiA.N.. Transdermal patches in novel drug delivery system. Int. J. Pharm. Technol.2011;3(2)2402-2419.
32. VermaN.K., Panda P., MishraJ,N., Vishwakarma D.K., Singh A.P., Alam G.. Advances and development in transdermal drug delivery system-A Review. Int J.Adv. Pharm. 2017; 06(02): 49-62
33. Chauhan A., Dr. Kumar K. A comprehensive review on matrix type transdermal patches. World journal of advance healthcare research.2020;4(2):240-245.
34. Chandrashekhar N.S., Shobha Rani R.H. Physicochemical and Pharmacokinetic Parameters in Drug Selection and Loading for Transdermal Drug Delivery IJPS. 2008; 70(1): 94–96.
35. KakarS.,Singh R., Semwal A. Transdermal drug delivery as a boon.Asian Pac. J. Health Sci.2014; 1(1): 13-25.
36. Bozorg B. D.,Banga A.K. Effect of Different Pressure-Sensitive Adhesives on Performance Parameters of Matrix-Type Transdermal Delivery Systems. Pharmaceutics 2020; 12: 209.
37. Reddy Y.K., Reddy D.M.,Kumar M.A. Transdermal Drug Delivery System: A Review.IJRPB..2014;2(2)1:094-1103
38. Deshwal and Verma, Optimization Techniques in Transdermal Drug Delivery system, IJPSR, 2012: 3(8); 2362-2370.