



STICK TO IT: A COMPREHENSIVE REVIEW OF TRANSDERMAL PATCH TECHNOLOGY

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ABSTRACT

An innovative way to medication distribution, transdermal patches provide a regulated, non-invasive, and patient-friendly substitute for conventional techniques. Transdermal patch technology is thoroughly reviewed in this article, which also examines its fundamental ideas, essential elements, and many medical treatment uses. Advances in adhesive and matrix technologies, the mechanics of medication absorption via the skin, and methods for overcoming obstacles such as skin irritation and restricted permeability are among the topics discussed. Recent advancements including smart patches with real-time monitoring features and patches augmented by microneedles are also highlighted in the review. The potential of transdermal patches to transform healthcare delivery and open the door to more effective and individualized treatment solutions is highlighted in this article by discussing both the advantages and disadvantages of this technology.

KEYWORDS: *Transdermal patches, TDDS, Enhancer for Permeation, Folding endurance, permeability.*

1. INTRODUCTION

Through the use of a special membrane, a patch of transdermal —also called to as a patch of skin—it controls the rate at which the medication in the liquid form in the reservoir inside the transdermal patch can pass through the skin and into the blood stream. For few medications to be utilised in a skin patch, they must be mixed with substances that improve their penetration of the skin, including alcohol. Medications that are applied as skin patches include nitro-glycerin (for angina), nicotine (for quitting smoking), oestrogen (for menopause and to prevent osteoporosis after menopause), lidocaine (for shingles pain; herpes zoster) and scopolamine (for motion sickness). However, some chemicals, like molecules of insulin, are very big to fit by way of the epidermis. Applying transdermal patches to the skin removes the need for pumps or syringes to gain vascular entry. In the 1970s, these patches were created, and the FDA authorised the first one in 1979 to cure motion sickness. [1, 2]. Delivering a amount of therapeutically effective medication through the skin of patient is the aim of TDDS (transdermal drug delivery systems) [3–4].

Traditional drug regimens that call for many doses have a lot of issues and side effects; include less bioavailability because of first pass metabolism of hepatic. TDDS takes this away. For these medications, the aim of dosage design is to optimise the flow of medication into the systemic circulation through the skin while reducing metabolism in the skin and drug retention [5]. Self-contained, discrete dose forms known as TDDS (transdermal drug delivery systems) can be used to healthy skin to allow the drug or drugs to enter the bloodstream at a regulated pace. Transdermal administration is acknowledged as a viable method for both local and systemic medication delivery [6]. TDDS not only allows for the drug of continuous injection with short biological half lives but TDDS also avoids pulsed entry into the bloodstream, which often leads to undesirable side effects. It also provides consistent, controlled drug administration. Novel medication delivery approaches have emerged, including transdermal drug administration methods, controlled release system and transmucosal drug delivery systems [7].

1.1 Definition

A transdermal patch or skin patch also called as medicated adhesive patch is applied to the skin for the purpose of deliver a specific medication amount into the bloodstream through the skin. [8]

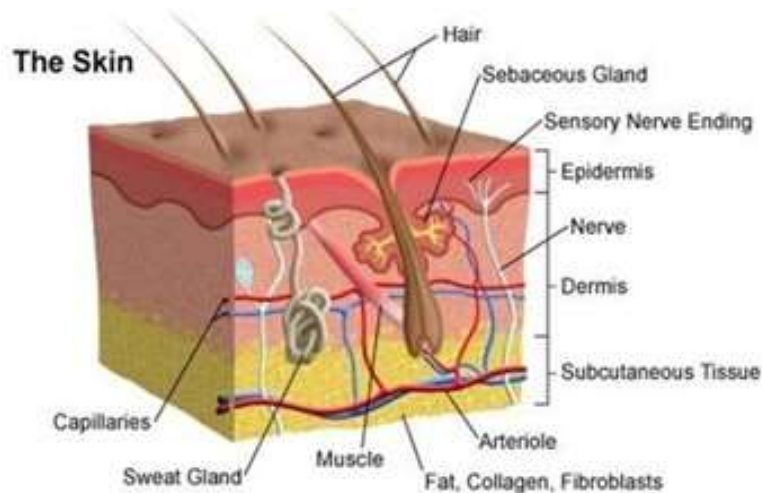


Figure 1. Structure of skin for transdermal drug delivery systems

2. TRANSDERMAL DRUG DELIVERY ADVANTAGES [9-14]

1. TDDS is a system of drug delivery that applies a gadget, which is called a patch, to the surface of skin enters into the systemic circulation at a predetermined concentration for therapeutic advantage. This prevents other restrictions brought on by another dosage forms.
2. TDDS provides consistent drug penetration through the skin, resulting in a steady serum drug level, which is the therapeutic objective.
3. For patients who have trouble taking medications orally, It can be used in place of the oral drug administration method.
4. Patients who are unconscious or feel queasy can use it as an alternative.
5. Since there won't be any direct drug delivery, patients with gastrointestinal issues can receive medication through TDDS.

3. DISADVANTAGES

1. Because of one or more than one system components, some of the patients develop contact dermatitis at the site of application, necessitating treatment discontinuation.
2. Because the skin's imperability naturally limits drug entrance, these patches are only appropriate for drugs which are powerful.
3. Few medications are painful, such as the transdermal patch of scopolamine, which is applied behind the ear.
4. Adhering for a long time is challenging. [15, 16]

4. TRANSDERMAL PATCH: [17-20]

To deliver the specific medication quantity into the bloodstream through the skin at a predetermined rate of release, a adhesive medicinal patch (transdermal patch) which is put to the skin above the epidermis. The most popular transdermal technology available today is mostly based on patches, which are semi-permeable membranes. A TDDS (transdermal drug delivery system), often known as "transdermal patches" and "skin patches," is therapeutically effective dose form that is meant to be injected into a patient's bloodstream through their skin.



Figure 2. Structure of Transdermal Patch



5. APPLICATIONS OF TRANSDERMAL PATCHES [37-39]

- The patch of nicotin, which helps people quit smoking tobacco by releasing nicotine in controlled dosages, so it is the most famous transdermal patch in the US.
- Two opioid drugs, buprenorphine (marketed as BuTrans) and fentanyl (marketed as Duragesic), are frequently administered in patch form to treat extreme pain 24/7.
- Menopausal symptoms and postmenopausal osteoporosis are occasionally treated with oestrogen patches. The patch of contraceptive (also known as Ortho Evra or Evra) is another transdermal patch for hormone delivery.

6. TRANSDERMAL PATCHES' CONSTITUENT PARTS

1. Matrix of Polymers: The polymer regulates the release of drug from the device. To be used in the transdermal patches, a polymer must meet the following requirements.

Types of polymers include:

- Natural polymers:** which include starch, gum, shellac, proteins, gelatin, cellulose derivatives, and waxes.
- Artificial Elastomers:** Neoprene, Nitrile, Acrylonitrile, Hydrin Rubber, and Silicone Rubber.
- Synthetic polymers:** include epoxy, polyvinyl chloride, polyvinyl alcohol, polypropylene, polyethylene, polyamide, and polyurea.

2. Drug: -The solution of drug in close proximity to the release liner.

Physicochemical Characteristics

- The medication's molecular weight should be under 1000 Daltons.
- Both lipophilic and hydrophilic phases should be favoured by the medication.
- The drug's melting point should be low.

3. Enhancer for Permeation: The flow of the drug J. can be inscribed through the skin. Given that

$$J = D \frac{dc}{dx},$$

J represents the flux.

D is an acronym for diffusion coefficient.

C represents the concentration of the diffusing spectrum.

X is a coordinate in space.

4. Extra excipients: (a) Adhesives: The device's face or back can be covered with the pressure-sensitive adhesive.

- It must not cause irritation.
- It must be removed simply.
- It shouldn't leave behind any residue that is impossible to wash off.
- It must have superior skin contact.
- Compatibility with the drug both chemically and physically.
- Drug penetration shouldn't be impacted.

5. Linear: - Protect the patch during the time of storage. The linear is removed before to usage.

6. Backing: - Shield the transdermal patch from the weather. [21–30]

7. Elements that influence transdermal bioavailability [31–36]

The drug's transdermal bioavailability is influenced by two main factors:

1. Physicochemical Elements

(a) Hydration of the skin: When the skin and water comes in touch, its permeability increases crucial element boosting skin penetration is hydration. Thus, transdermal delivery is the method used to apply humectant.

(b) pH and temperature: Changes in pH cause a tenfold increase in medication penetration. When the temperature decreases, the diffusion coefficient also decreases. How weak bases and weak acids separate is determined by the pKa or pKb and pH values. The unionised drug's percentage in the skin indicates the concentration of drug. Therefore, two crucial variables influencing medication penetration are pH and temperature.

2. Aspects of Biology

(a) Skin condition: Many solvents, including methanol and chloroform, as well as acids and alkalis, harm skin cells and encourage penetration. Skin conditions change when a patient is ill. Although healthy skin provides a better barrier, penetration is impacted by the aforementioned factors.

(b) Skin age: Younger skin has a higher permeability than older skin. Children are especially susceptible to pollutants absorbing via their skin. Therefore, skin age a main parameters that affect penetration of medication in transdermal drug delivery system.



8. EVALUATION METHODS: [40–51]

1. Patch thickness: Using a digital micrometre, the thickness of the drug-loaded patch is measured at various spots. The average thickness and standard deviation are then calculated to guarantee the thickness of the created patch.

2. Weight uniformity: Before testing, the produced patches must be dried for four hours at 60°C. A predetermined patch area must be sliced into several sections and weighed using a digital balance. From the individual weights, the average weight and standard deviation values must be computed.

3. Folding endurance: a strip of a particular material has to be cut uniformly and folded repeatedly until it breaks. The folding endurance was determined by counting the number of times the film could be folded in the same spot without breaking.

4. The percentage Content of moisture: Each manufactured film must be weighed separately and stored in a desiccator keeping fused calcium chloride for a whole day at room temperature. The films must be reweighed after a day in order to calculate the moisture content as a percentage using the formula below.

Percentage moisture content = [Initial weight- Final weight/ Final weight] ×100.

5. Moisture uptake percentage: To maintain 84% relative humidity, the weighted films must be stored at room temperature for 24 hours in a desiccator filled with a saturated potassium chloride solution. Following a 24-hour period, the films must be reweighed in order to calculate the percentage moisture uptake using the formula below.

Percentage moisture uptake = [Final weight- Initial weight/ initial weight] ×100.

6. Drug content: A predetermined patch area needs to dissolve in a predetermined volume of an appropriate solvent. After passing the solution through a filter medium, the drug content must be examined using the appropriate technology (either the UV or HPLC method). The average of three separate samples is shown by each value.

9. REFERENCES

1. Shaila L, Pandey S and Udupa N. Design and Evaluation of Matrix Type Membrane Controlled Transdermal Drug Delivery System of Nicotin Suitable for Use in Smoking Cessation. *Indian Journ. Pharm. Sci.* 2006;68: 179-184
2. Aarti N, Louk A.R.M.P, Russel.O.P and Richard H.G. Mechanism of Oleic Acid Induced Skin Permeation Enhancement in Vivo in Humans. *Jour. Control. Release.* 1995; 37: 299-306.
3. Kumar JA, Pullakandam N, Prabu SL, Gopal V. Transdermal drug delivery System: An overview. *Int J Pharma Sci Rev Res* 2010; 3(2):49-53.
4. Jain NK. *Advances in controlled and novel drug delivery.* 1st Ed. CBS Publishers and distributors, New Delhi, 2001, 108-110.
5. Shivaraj A, Selvam RP, Mani TT, Sivakumar T. Design and evaluation of transdermal drug delivery of ketotifen fumarate. *Int J Pharm Biomed Res* 2010; 1(2):42-47.
6. Selvam RP, Singh AK, Sivakumar T. Transdermal drug delivery systems for antihypertensive drugs - A review. *Int J Pharm Biomed Res* 2010; 1(1):1-8.
7. Hadgraft J, Guy R, In: *Transdermal Drug Delivery*, Vol. 35, Marcel Dekker, Inc: New York and Basel, 296.
8. Wiechers J. Use of Chemical Penetration Enhancers in Transdermal Drug Delivery-Possibilities and Difficulties. *Acta Pharm.* 1992: 4: 123.
9. Latheeshjhal L, Phanitejaswini P, Soujanya Y, Swapna U, Sarika V, Mouluka G, *Transdermal Drug Delivery Systems: An Overview*, *Int J Pharm Tech Res* 2011; 3(4):2140-2148.
10. Chien YW, *Novel drug delivery systems, drugs and the Pharmaceutical sciences*, Vol.50, Marcel Dekkar, New York, 1992, 797.
11. Banker GS, Rhodes CT. *Modern pharmaceuticals*, third edition, New York, Marcel Dekkar Inc, 1990.
12. Guy RH. Current status and future prospects of transdermal drug delivery. *Pharm Res* 1996; 13:1765-1769.
13. Benson HAE. *Transdermal Drug Delivery: Penetration Enhancement Techniques*, *Current Drug Delivery* 2005; 2:23-33.
14. Guy RH, Hadgraft J, Bucks DA, *Transdermal drug delivery and cutaneous metabolism*, *Xonobiotica* 1987; 7:325-343.
15. Shaila L, Pandey S, Udupa N. Design and Evaluation of Matrix Type Membrane Controlled Transdermal Drug Delivery System of Nicotin Suitable for Use in Smoking Cessation. *Indian Journal of Pharmaceutical Sciences.* 2006; 68:179-184.
16. Aarti N, Louk Armp, Russel Op. Richard Hg. Mechanism of Oleic Acid Induced Skin Permeation Enhancement in Vivo in Humans. *Jour. Control. Release.* 1995; 37:299-306.
17. GuptaV, YadavSK, Dwivedi AK, GuptaN. *Transdermal Drug Delivery: Post, Present, Future Trends.* *Int J Pharm Life Sci* 2011; 12:1096-1106.
18. RaviS, Sharma PK, Bansal M. A Review: Transdermal Drug Delivery of Nicotine. *Int J Drug Dev Res* 2011; 3:01-08.
19. PatelD, PatelN, Parmar M, KaurN. Transdermal Drug Delivery System: Review. *Int J Bio Pharm Toxicol Res* 2011; 1:61-80.
20. Sachan R, Bajpai M. Transdermal Drug Delivery System: A Review. *Int J Res Dev Pharm Life Sci* 2013; 3:748-765.
21. Rajesh N, Siddaramaiah, Gowda Dv, Somashekar Cn. Formulation and Evaluation of Biopolymer Based Transdermal Drug Delivery. *Int J Pharm Pharm Sci.* 2010; 2(2):142-147.
22. Hanumanaik M, Patil U, Kumar G, Patel S K, Singh I, Jadatkar K., *Design, Evaluation and Recent Trends in Transdermal Drug Delivery System: A Review.* *IJPSR.* 2012; 3(8): 2393-2406.
23. Chandrashekhhar N S, Shobha Rani R H. Physicochemical and Pharmacokinetic Parameters in Drug Selection and Loading of Transdermal Drug Delivery. *Indian Journal of Pharmaceutical Sciences.* 2008; 70(1): 94-96.
24. Scheindlin S. *Transdermal Drug Delivery: Past, Present, Future.* *Molecular Interventions.* 2004; 4(6): 308-312.
25. Aungst Bj *Structure/Effect Studies of Fatty Acid Isomers as Skin Penetration Enhancers and Skin Irritants.* *Pharm Res.* 1989; 6: 244-7.
26. Ongpipattanakul B, Burnette Rr, Potts Ro, Francoeur Ml Evidence That Oleic Acid Exists in A Separate Phase Within Stratum Corneum Lipids. *Pharm Res.* 1991; 8: 350-4.



27. Sinha Vr, Kaur Pm Permeation Enhancers for Transdermal Drug Delivery. *Drug Dev Ind Pharm.* 2000; 26: 1131–40.
28. Barry Bw, Williams Ac Terpenes As Skin Penetration Enhancers. *Marcel Dekker.* 1993; 9: 95–111.
29. Williams Ac, Barry Bw, Terpenes and the Lipid-Protein-Partitioning Theory of Skin Penetration Enhancement. *Pharm Res.* 1991; 8: 17–24.
30. Vaddi Hk, Ho Pc, Chan Sy, Terpenes in Propylene Glycol as Skin-Penetration Enhancers: Permeation and Partition of Haloperidol, Fourier Transform Infrared Spectroscopy and Differential Scanning Calorimetry. *J Pharm Sci.* 2002; 91: 1639–51.
31. Asbill Cs, El-Kattan Af, Michniak B, Enhancement of Transdermal Drug Delivery: Chemical And Physical Approaches. *Crit Rev Ther Drug Carrier Syst.* 2000; 17: 621–58.
32. Krishnaiah Ys, Satyanarayana V, Bhaskar P, Influence of Menthol and Pressure-Sensitive Adhesives on the in vivo Performance of Membrane-Moderated Transdermal Therapeutic System of Nicardipine Hydrochloride in Human Volunteers. *Eur J Pharm Biopharm.* 2002; 55: 329–37.
33. Okabe H, Obata Y, Takayama K, Nagai T., Percutaneous Absorption Enhancing Effect and Skin Irritation of Monocyclic Monoterpenes. *Drug Des Deliv.* 1990; 6: 229–38.
34. Jain NK. *Controlled and Novel Drug Delivery.* CBS Publishers and Distributors, New Delhi, 2002, 107.
35. Chien YW. *Novel drug delivery systems: Drugs and the Pharmaceutical Sciences.* Vol.50, Marcel Dekker, New York, 1992:797.
36. Jain NK. *Controlled and novel drug delivery, 1st edition,* CBS publishers and distributors, New Delhi, 1997.
37. Loyd V. Allen Jr, Nicholas G. Popovich, Howard C. Ansel. *Pharmaceutical dosage forms and drug delivery systems, 8th Edition.,* Wolter Kluwer Publishers, New Delhi, 2005 pp. 298–299.
38. Kumar P, Sankar C, Mishra B. Delivery of macromolecules through skin. *The Indian Pharmacist* 2004,5(3): 7-17.
39. Kumar R, Philip A. Modified Transdermal Technologies: Breaking the Barriers of Drug Permeation via the Skin. *Trop J Pharm Res.* 2007, 6(1):633–644.
40. Rizwan M, Aqil M, Talegoankar S, Azeem A, Sultana Y, AliA. Enhanced transdermal drug delivery techniques: an extensive review on patents. *Recent Pat Drug Deliv&formul.* 2009, 3(2):105-24.
41. Cheston M. Berlin. *Clinical report- Alternative Routes of Drug Administration- Advantages & Disadvantages (subject review).* Pediatrics 1997.
42. Rizwan M, Aqil M, Talegoankar S, Azeem A, Sultana Y, AliA. Enhanced transdermal drug delivery techniques: an extensive review on patents. *Recent Pat Drug Deliv&formul.* 2009, 3(2):105-24.
43. Weiner E, Victor A, Johansson ED. Plasma levels of d-Norgestel after oral administration. *Contraception* 1976, 14: 563-570.
44. Keith AD, Polymer matrix consideration for Transdermal Devices. *Drug Dev Ind Pharm.* 1983, 9: 605-625.
45. Karim A. Transdermal absorption: a unique opportunity for constant delivery of nitroglycerin. *Drug Dev Ind Pharm.* 1983, 9: 671.
46. Helier J, Trescony PV. Controlled drug release by polymer dissolution II, Enzyme mediated delivery device. *J. Pharm.Sci.* 1979, 68: 919.
47. <http://www.pharmainfo.net/reviews/transdermal-drug-delivery-technology-revisited-recent-advances>
48. <http://www.pharmainfo.net/jasmine-jose/transdermal-patches-innovative-technology>
49. Hopp SM. Developing Custom Adhesive Systems for Transdermal Drug Delivery Products. *Pharmaceutical Technology* 2002, 30-36.
50. <http://ezinearticles.com/?Transdermal-Drug-Delivery,-Transdermal-Patches&id=155961>
51. Hopp SM. Developing Custom Adhesive Systems for Transdermal Drug Delivery Products. *Pharmaceutical Technology* 2002, 30-36.