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AN OVERVIEW ON TRANSDERMAL DRUG DELIVERY SYSTEM

Aftab, Aparna Joshi, Vaishali Rajput, Kapil Kumar*, Ikram and Priyanshi Chauhan

Department of Pharmaceutics, Global Institute of Pharmaceutical Education and Research, Kashipur- 244713, Uttarakhand, India.

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***Corresponding Author**
Prof. Kapil Kumar
Department of Pharmaceutics, Global Institute of Pharmaceutical Education and Research, Kashipur- 244713, Uttarakhand, India.

ABSTRACT

Human civilizations have used chemicals as cosmetic and therapeutic agents on the skin for thousands of years. The use of the skin as a medicine delivery method did not begin until the 20th century, though. A transdermal patch is an adhesive patch applied to the skin that contains medication that is intended to be transdermally absorbed into the bloodstream. This frequently encourages the healing of a body part that has been hurt. Transdermal drug delivery has an advantage over other drug delivery methods, such as oral, topical, intravenous, intramuscular, etc. Therapeutic agent application topically has several benefits over traditional oral and invasive medication delivery strategies. Further offering a prolonged period of regulated medication release. The preparation procedures for various transdermal patch types, including membrane matrix, drug-in-adhesive, and micro reservoir patches, are covered in this review article. The various transdermal dosage form evaluation techniques have also been studied.

KEYWORDS: Transdermal Patch, Matrix Patches, Reservoir Type, Membrane Matrix, Drug-In-Adhesive Patches, Micro Reservoir Patches.

INTRODUCTION

To administer a specific amount of medication through the skin and into the bloodstream, a transdermal patch is employed. The FDA initially approved transdermal patch products in 1981. Drugs given in standard dosage forms frequently cause wide changes in plasma drug concentrations, which might result in unfavourable toxicity or ineffectiveness. Compared to conventional injection and oral procedures, TDDS has many benefits.[1] It lessens the burden that taking medication orally frequently places on the liver and digestive system. The idea of a regulated drug delivery system or therapeutic system was developed as a result of these factors, as well as additional factors including recurrent dosing and unexpected absorption. It is practical, particularly for patches that only need to be applied once each week. Such a simple dosing regimen aids in patient adherence to drug therapy.[2]

Advantages: There are many advantages associated with Transdermal drug delivery systems[3]

- Bypassing hepatic and pre-systemic metabolism, the medicines' bioavailability is increased.
- IV therapy's risks and drawbacks are avoided. Less frequent doses and actions that last longer and with more predictability**.**
- It is quite helpful for people who are queasy or unconscious.
- Because this distribution route avoids direct effects on the stomach and intestine, medications that induce gastrointestinal disturbance may be suitable candidates.
- Transdermal drug administration is ideal for medications that need relatively constant plasma levels.[2]

Disadvantages[4,5]

- Local irritation at the application location is a possibility.
- The medication, the adhesive, or other excipients in the formulation of the patch can all result in erythema, irritation, and local edoema.
- Could result in allergic reactions.
- A molecular weight of 500 Da or less is required.
- A log P (octanol/water) between 1 and 3 is necessary for permeate to cross SC and the underlying aqueous layers due to the sufficient aqueous and lipid solubility.[2]

PHYSIOLOGY OF THE SKIN

A typical adult's skin has a surface area of around 2 m2, and it gets about one-third of the blood that circulates through the body. The uppermost layer of skin, the epidermis, has four morphologically distinct regions: the basal layer, the spiny layer, the stratum granulosum, and the uppermost stratum corneum. The epidermis is made up of highly cornified (dead) cells that are continuously encased in a matrix of lipid membranous sheets. Ceramides, cholesterol, and free fatty acids make up the special composition of these extracellular membranes. Every square centimetre of human skin is known to have

between 200 and 250 sweat ducts and 10 to 70 hair follicles on average. It is one of the human body's organs that is easiest to access.[6,7]

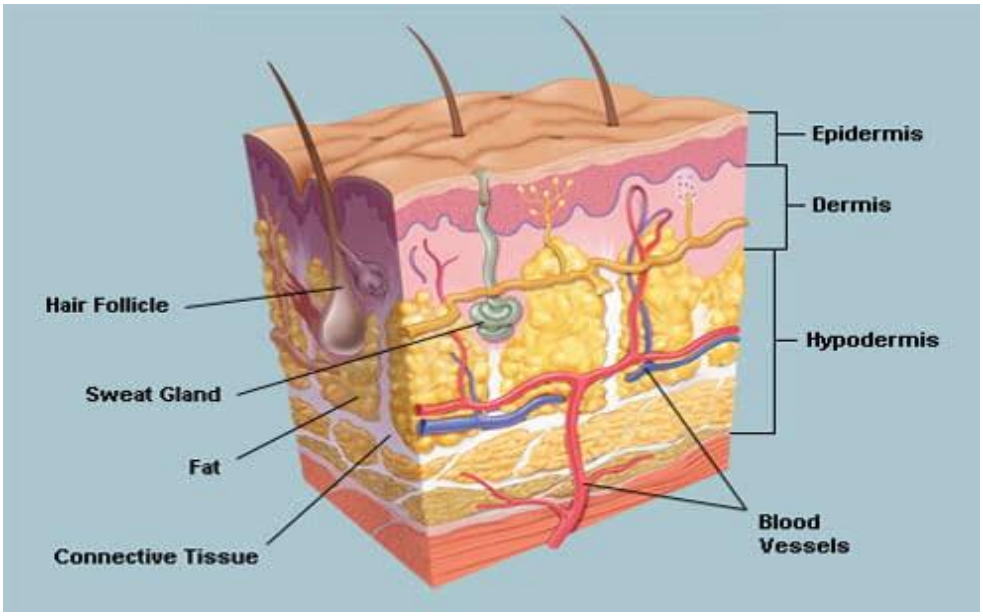

Figure 1: Structure of skin.

SKIN PATHWAYS FOR TRANSDERMAL DRUG DELIVERY SYSTEMS

Drugs can penetrate and pass through the skin in a number of ways when administered to the skin's surface. Drugs can enter the body either transepidermally (through the stratum corneum) or transappendageally (via the appendages). There are two distinct ways to penetrate the stratum corneum: (1) through the corneocytes and lipid lamellae alternately (transcellular route); and (2) over the tortuous track between the lipid lamellae (intercellular route).[8]

It is generally acknowledged that the intercellular pathway is the most common way to penetrate the stratum corneum. The heavily cross-linked cornified membrane covering the keratinocytes is mostly to blame for this. Water and other tiny hydrophilic molecules cannot, however, totally be eliminated from transcellular transport.[9]

The eccrine sweat gland duct or the follicular duct are both included in the appendage route or shunt route. While the follicular duct contains mostly lipophilic material, the eccrine sweat glands are predominantly hydrophilic. Sebum that is excreted into the follicular duct entrance is mostly to blame for this. It is widely acknowledged that intact stratum corneum serves as the primary conduit for passive skin permeation because of its enormous surface area.[10]

DESIGN OF TRANSDERMAL DELIVERY SYSTEM.[11,12]

1. **Matrix or Monolithic:** The drug is bound to the inert polymer matrix, which also regulates the drug's release from the apparatus.
2. **Reservoir or Membrane:** The release of drugs is not regulated by the polymer matrix. The rate-limiting barrier for drug release from the device is instead provided by a rate-controlling membrane that is present between the drug matrix and the sticky layer.[9]
3. The main components to a transdermal patch are.
4. **Polymer matrix**– backbone of TDDS, which regulates the drug's release. Polymers should not degrade while stored, should not be hazardous, and should not be expensive. They should also not be chemically reactive. A polymer must meet the following requirements in order to be employed in a transdermal system. the following polymers may be suitable for transdermal devices.
5. **Natural Polymers:** Cellulose derivatives, Zein, Gelatin, Waxes, Proteins, Gums, Natural rubber, Starch.
6. **Synthetic Elastomers:** Polybutadiene, Hydrin rubber, polysiloxane, silicone rubber, Nitrile, Acrylonitrile, Butylrubber, Styrenebutadiene, Neoprene etc. **Synthetic Polymers**: Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyvinylpyrrolidone, Polymethyl methacrylate, Epoxy, Polyurea, etc.
7. **Drug**- The transdermal route is an extremely attractive option for the drugs with appropriate pharmacology and physical chemistry. The following are some of the desirable properties of a drug for Transdermal delivery. Transdermal patches offer much to drugs which undergo extensive first pass metabolism, drugs with narrow therapeutic window, or drugs with short half life.eg fenatyl, nitroglyceriene etc.[13]

8. **Permeation enhancers**- Drug penetration enhancers interact with the proteins or lipids that make up the structural elements of the stratum corneum to increase its permeability, allowing for higher therapeutic levels of drug absorption.
9. The partial leaching of the epidermal lipids by the chemical enhancers, which improves the skin conditions for wetting and for transepidermal and transfollicular penetration, is thought to be the cause of the improvement in oil-soluble medication absorption.
10. The improved transdermal permeability of water-soluble medicines may be caused by the miscibility and solution characteristics of the enhancers utilised.
11. Pharmaceutical researchers have worked very hard on transdermal permeation experiments employing various drug moieties as enhancers.[14]

PREPARATION OF TRANSDERMAL PATCHES- Several processes can be used to prepare transdermal medication delivery patches.

1. **Mercury Substrate Method:** In this procedure, plasticizer and the necessary amount of medication are dissolved in a predefined amount of polymer solution. The aforementioned solution should be agitated for a while to create a uniform dispersion. It should then be set aside until all air bubbles have been eliminated before being poured into a glass ring that will be placed over the mercury surface in a glass petri dish. An inverted funnel is positioned above the petri dish to control the solvent's rate of evaporation. The films that have dried out must be kept in a desiccator.[15-18]
2. **Circular Teflon Mould Method:** Solutions with different ratios of polymers are utilised in an organic solvent. Half as much of the same organic solvent is used to dissolve the calculated amount of medication. Addition of plasticizer to the drug polymer solution. Stirring the entire mixture before pouring it into a teflon mould is required. Furthermore, the rate of solvent vaporisation was controlled by setting an upside-down glass funnel on a teflon mould. For 24 hours, the solvent is allowed to evaporate. The films that have dried up must be kept in a desiccators.[19-21]
3. **Glass Substrate Method:** After allowing the polymeric solutions to expand, the necessary amount of plasticizer and drug solution is added, and 10 minutes are spent stirring. It is then poured into a clean, dry anumbra petriplate after being set aside for a while to release any trapped air. By inverting a glass funnel over the petriplate, the rate of solvent evaporation can be adjusted. The dry films are removed from over night and kept in a desiccator.[22]
4. **By Using IPM Membranes Method:** This method involves dispersing the medicine over a period of 12 hours in a magnetic stirrer in a solution of water and propylene glycol containing carbomer 940 polymers. Triethanolamine is to be added in order to neutralise the dispersion and make it viscous. If the drug's solubility in aqueous solution is very low, buffer pH 7.4 can be employed to create solution gel. The IPM membrane will integrate the produced gel.[23-26]
5. **By Using EVAC Membranes Method:** 1% carbopol reservoir gel, polyethylene (PE), and ethylene vinyl acetate copolymer (EVAC) membranes can be employed as rate control membranes to prepare the target transdermal treatment system. Propylene glycol is used to make gel when the medication is not soluble in water. Propylene glycol is used to dissolve the drug; carbopol resin will then be added to the solution and neutralised using a 5% w/w sodium hydroxide solution. A sheet of backing layer covering the designated area is placed on top of the medicine (in gel form). To create a leak-proof device, a rate-regulating membrane will be applied over the gel, and the edges will be heated to seal them.[27-28]

Table no-:1 Marketed preparation for TDDS.[29,30]

Brand Name	Drug Name	Manufacturer	Indications
Nicotine II^{R}	Nicotine	Novartis	P'cological Smoking cessation
Matrifen^{R}	Fentanyl	Nycomed	Pain Relief patch
NuPatch 100	Diclofennac diethylamine	Zydus Cadila	Anti-inflammatory
Alora	Estradiol	TheraTech, Proctol	Postmenstrual syndrome
Nuvelle TS	Estrogen, Progestrone	Ethical holdings	Hormone Replacement
Nittrodisc	Nitroglycerin	Roberts p'ceuticals	Angina Pectoris
Estraderm	Estradiol	Alza/Norvatis	Postmenstrual syndrome

CONCLUSION

The prediction shows that TDDS has the potential to be both hydrophobic and hydrophobic.

The delivery system to optimize this drug is the mechanism of more social biological interaction of the various and essential polymers. Drugs showing metabolic and unstable status in the first state are suitable candidates for transdermal drug delivery systems. Many new researches are going on at the present time to incorporate new drugs through this system.

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REFERENCES

1. Gaur PK, Mishra S, Purohit S, Dave K. Transdermal drug delivery system- A review. Asian Journal of Pharmaceutical and Clinical Research, 2009; 2: 14-20.

2. Chioma ED. Formulation and evaluation of etodolac niosomes by modified ether injection technique. Universal Journal of Pharmaceutical Research, 2016; 1(1): 1-4.
3. Heather AE. Transdermal Drug Delivery: Penetration Enhancement Techniques. Current Drug Delivery. 2005; 2:23-33.
4. Yie W, Chien, Novel Drug Delivery Systems, 2nd ed, M. Dekker, 2005; 50: 301-380.
5. Eseldin Keleb, Rakesh Kumar Sharma, Transdermal Drug Delivery System-Design and Evaluation, International Journal of Advances in Pharmaceutical Sciences, 2010; 1(3): 201-211.
6. Nwobodo NN, Adamude FA, Dingwoke EJ, Ubhenin A. Formulation and evaluation of elastic liposomes of decitabine prepared by rotary evaporation method. Universal Journal of Pharmaceutical Research, 2019; 4(3): 1-5.
7. Ankush I, Shembale, Useful Permeation Enhancers for Transdermal Drug Delivery A Review, IJPRD, 2010; 5: 1-6.
8. Gurpınar SS, Devrim B, Eryılmaz M. *In-vitro* antibacterial activity of *lactobacilli* metabolites loaded hydrogel formulations against *pseudomonas aeruginosa*. Universal Journal of Pharm Research, 2019; 4(4): 9-11.
9. Hadgraft J.W, and Somers G.F, Review Article Percutaneous absorption, International Journal of Pharmaceutics, 2005; 305: 2-12.
10. Fatima AA, Chukwuka UK. Development and *in-vitro* evaluation of matrix-type transdermal patches of losartan potassium. Universal Journal of Pharmaceutical Research, 2017; 2(2): 16-20.
11. Gilbert S, Banker, Christopher T, Rhodes, Modern Pharmaceutics, 2nd Ed, Revised and Expanded, 40: 263-298.
12. Ugochukwu AE, Nnedimkpa OJ, Rita NO. Preparation and characterization of Tolterodine tartrate proniosomes, Universal Journal of Pharmaceutical Research, 2017; 2(2): 1-3.
13. Lyn Margetts, and Richard Sawyer, Transdermal Drug Delivery: Principles And opioid Therapy, Continuing Education in Anaesthesia, Critical Care & Pain, 2007; 7(5): 171-176.
14. Mohamed Aqil, Yasmin Sultana and Asgar Ali, Matrix Type Transdermal Drug Delivery Systems of Metoprolol Tartrate, In- vitro Characterization, Acta Pharm, 2003; 53: 119-125.
15. Elsaied EH, Dawaba HM, Ibrahim EA, Afouna MI. Investigation of proniosomes gel as a promising carrier for transdermal delivery of Glimepiride. Universal Journal of Pharmaceutical Research, 2016; 1(2): 1-10.
16. Basubramanian V, Iyer and Ravindra C, Vasavada, Evaluation of Lanolin alcohol flims and Kinetics of Triamcinolone Acetonide Release, Journal of Pharmaceutical Sciences, 1979; 68(6): 119-125.
17. Chauhan N, Kumar K, Pant NC. An updated review on transfersomes: a novel vesicular system for transdermal drug delivery. Universal Journal of Pharmaceutical Research, 2017; 2(4): 42-45.
18. Chowdary K.PR and Naidu R.A.S, Preparation and Evaluation of Cellulose Acetate Films as Rate Controlling Membranes for Transdermal use, Indian Drugs, 1991; 29(7): 312-315.
19. Obanewa OA, Oyeniran OT. Development and estimation of anti-inflammatory activity of topical etoricoxib emulgel by carrageenan induced paw oedema method. Universal Journal of Pharmaceutical Research, 2019; 4(3): 22-26.
20. Mamatha T, Venkateswara Rao J, Mukkanti K, Development of Matrix Type Transdermal Patches of Lercanidipine Hydrochloride, Physicochemical and in-vitro Characterization, DARU, 2010; 18(1): 9-16.
21. Francis DJE. Development and evaluation of matrix type transdermal patches of pioglitazone hydrochloride. Universal Journal of Pharmaceutical Research, 2016; 1(1): 17-20.
22. Sridevi S, Chary M.G, Krishna D.R, Prakash V, Diwan, Pharmacodynamic Evaluation of Transdermal Drug Delivery System of Glibenclamide in Rats, Indian Journal of Pharmacology, 2000; 32: 309-312.
23. Umar S, Onyekachi MK. Development and evaluation of transdermal gel of Lornoxicam. Universal Journal of Pharmaceutical Research, 2017; 2(1): 15-18.
24. Sharma Teja, Rawal Gaurav, Transdermal Therapeutic Systems, An overview, International Journal of Pharmaceutical & Biological Archives, 2011; 2(6): 1581-1587.
25. Wiechers J, Use of Chemical Penetration Enhancers in Transdermal Drug Delivery-Possibilities and Difficulties, Acta Pharm, 1992; 4: 123.
26. Okorochukwu Nnamdi, Ihuaku Emmanuel C. Development and characterization of mucoadhesive patches for buccal delivery of pregabalin. Universal Journal of Pharmaceutical Research, 2017; 2(3): 6-9.
27. Manvi F.V, Dandagi P.M, Gadad A.P, Mastiholimat V.S and Jagdeesh T, Formulation of Transdermal Drug Delivery System of Ketotifen Fumarate, IJPS, 2003; 65(3): 239-243.
28. Kanikkannan N, Jayaswal S.B and Singh J, Transdermal Delivery of Indomethacin: Release Profile of Drug from Polymeric Patches, Indian Drugs, 30(9): 441-445.
29. Sankar V, Velrajan G, Palaniappan R and Rajasekar S, Design and Evaluation of Nifedipine Transdermal Patches, IJPS, 2003; 65(5): 510-515.
30. Ryan F, Donnelly, Paul A, McCarron, Design and Physicochemical Characterization of a Bioadhesive Patch for Dose-Controlled Topical Delivery of Imiquimod, International Journal of Pharmaceutics, 2006; 307: 318-325.