Indian Journal of Pharmacy and Pharmacology 2021;8(1):5–9

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pharmacy and Pharmacology

Journal homepage: https://www.ijpp.org.in/

Review Article

Transdermal drug delivery system: A review

Neha Choudhary[1,*], Ajeet Pal Singh[1], Amar Pal Singh[1]

[1] *St. Soldier Institute of Pharmacy, Lidhran Campus, Jalandhar, Punjab, India*

ARTICLE INFO

Article history:
Received 15-03-2021
Accepted 17-03-2021
Available online 19-04-2021

Keywords:
Advantages/Disadvantages
Skin types
Factors affecting permeation
Components
Evaluations

ABSTRACT

Transdermal Drug Delivery System is controlled medicated that is set on the skin to deliver a particular portion of medicine through the skin and into the circulatory system. It is likewise significant because of its interesting benefit such as less absorption, more uniform plasma levels, improved bioavailability, decrease side effect, efficacy and quality of the product. Transdermal dose structures may give clinicians a chance to offer more therapeutic alternatives to their patients to upgrade their consideration.

1. Introduction

Now a day many drugs are administered orally, but they are observed not more effective as desired so to upgrade such character TDDS was created. Drug delivery administered by the skin and attain a systemic effect of drug is called as transdermal drug delivery system.[1] These are kind of dosage form which includes drug transport to reasonable epidermis and potentially dermal tissue of the skin locally therapeutic effect.[2] While an exceptionally significant division of the drug is transported in systemic blood circulation. A transdermal dermal patch is characterized as a medicated adhesive patch which is set over the skin to deliver a particular dose of medication by the skin with a foreordained rate of release to reach into the circulation system.[3]

1.1. Advantages of transdermal drug delivery system[4,5]

1. Self-medication is possible
2. Side effect gets reduced
3. Plasma drug concentration becomes maintained
4. Drug duration of action are extendable
5. GIT incompatibilities get avoided
6. Number of dosage frequency reduced
7. Easier to remember and used
8. Large area of application in comparison with nasal and buccal cavity

1.2. Disadvantages of transdermal drug delivery System[6,7]

1. Chances to allergic reaction
2. High molecular drug level cannot to attain therapeutic level
3. It is deliver to ionic drug
4. It requires significant lag time

1.3. Anatomy and physiology of skin

Human skin consist of three distinct which are discuss follow as

1.4. Epidermis

The epidermis is a stratified, squamous, keratinizing epithelium. The complex layer of epidermis varies in

* *Corresponding author.*
E-mail address: ajaykumar.rana97@gmail.com (N. Choudhary).

https://doi.org/10.18231/j.ijpp.2021.002

contingent upon cell size, thickness and number of cell layers of epidermis which are going from 0.8 mm on palms and soles down to 0.06 mm on the eyelids. About 90% epidermal cells are keratinocytes or chest rated in five layers and creates keratin protein and 8% melanocytes are available. They create melanina yellow or dark colored dark shade that adds to skin shading and ingests harming UV light. A Langerhans cell emerges from red bone marrow and moves to epidermis, where they constitute little portion of epidermis cells. Markel cells are slightest several of epidermal cells.[8]

1.5. Dermis

Dermis is 3 to 5 mm thick layer and is made out of a lattice of connective tissue, which contains veins, lymph vessels and nerves. The cutaneous blood supply has basic capacity in direction of body temperature. It additionally gives supplements and oxygen to the skin while removing toxins and squander items. Vessels reach to inside 0.2 mm of skin surface and give sink conditions to most atoms entering the skin hindrance. The blood supply in this manner keeps the dermal centralization of a saturate low and the subsequent fixation contrast over the epidermis gives fundamental focus inclination to transdermal penetration.[9]

1.6. Hypodermis

The hypodermis or subcutaneous fat tissue underpins the dermis and epidermis. It fills in as a fat storage area. This layer controls temperature, gives wholesome help and mechanically security. It conveys chief veins and nerves to skin and may contain tangible weight organs. For transdermal medication conveyance, sedate needs to infiltrate through all these three layers and venture into foundational flow while if there should be an occurrence of topical medication conveyance just entrance through stratum corneum is fundamental and after that maintenance of medication in skin layers is desired.[10]

1.7. Mechanism of transdermal permeation[11,12]

Transdermal permeation of a drug delivery system based on the

1. Permeation of drug by feasible epidermis
2. Sorption through stratum corneum
3. take up of the drug moiety through the capillary system in the dermal papillary layer

The rate of transdermal drug permeation, dQ/dt, through several layers of skin tissues which can be expressed as

$dQ/dt = Ps(Cd - Cr)$ ..... (1)

Where

dQ/dt = Rate of skin permeation

Cd and Cr = the concentrations of skin penetrate in the donor phase (stratum corneum) and the receptor phase (systemic circulation)

Ps = overall permeability coefficient of the skin

P_s is defined as by L john

$P_S = K_S D_{SS}/H_S$ .....(2)

Where,

K_s = Partition coefficient of the penetrant

D_{ss} = Apparent diffusivity of penetrant

H_s = Thickness of skin

At constant rate of drug permeation is achieved when $C_d > C_r$ Then equation (1) becomes

$dQ/dt = PS.CD$ .....(3)

(dQ/dt) becomes as constant when C_d value remains genuinely constant done the span of skin permeation. To retain the C_d at a constant value, it is simple to make the drug to be released at a rate (R_r) which is regularly more prominent than the rate of skin take-up (R_a) therefore $R_r >> R_a$.

Thusly, the drug concentration on the skin surface (C_d) is kept up at a level which is constantly more prominent than the equilibrium (or saturation) solubility of the drug in the stratum corneum (C^e_S), i.e., $Cd >> C^e_S$; and a most extreme rate of skin permeation (dQ/dt)m, as written by equation.

$(dQ/dt)m = PSC^e_S$

Where (dQ/dt)m=Magnitude of Rate of skin permeation

P_S = the skin permeability coefficient of drug

C^e_S- equilibrium solubility in the stratum corneum

1.8. Basic components of transdermal system[17]

1.9. Polymer matrix / Drug reservoir[18]

Polymers are the essential parameter of TDDS, which control the release of the drug from the gadget. Polymer matrix can be set up by dispersion of drug in solid or liquid state synthetic polymer base.

The following criteria should be satisfied for a polymer to be used in transdermal system.

1. Drug should be non-reactive and stable
2. Polymer easily available, manufactured in desired formulation
3. It should be constant release of drug through the life of system
4. Mechanical properties should not be change uncertainty big amount of drug include.

1.10. Drug

For developing a TDDS, the drug is very important part of chosen with great care. The some of the desire properties of TDDS are

1.10.1. Physiochemical properties

1. A molecular weight of drug should be less than nearly 1000 Dalton

Table 1: Factors affecting permeation

Physicochemical properties of permeation [13,14]	
Partition coefficient	Lipid and Water Soluble containing drugs are positively absorbed through the skin. Intercellular route which are capable for drugs with moderate partition coefficient (logK 1 to 3) and having high lipophilicity. The transcellular route presumably prevails for more hydrophilic atoms (logK < 1).
Molecular size	Molecular size of drugs are very effective for designated as candidates for transdermal delivery which have tend to fall inside thin range of molecular weight of 100 to 500 Dalton.
Solubility/melting point-	Lipophilic molecules have a tendency to permeate through the skin quicker than more hydrophilic molecules. Drugs with high melting points have moderately low aqueous solubility at ordinary and Pressure and temperature.
Ionization	According to pH-partition theory only the unionized form of the drug can permeate by the lipid barrier in important quantities.
Physiological & pathological conditions of skin [15,16]	
Reservoir effect of horny layer	This is present in deeper layer because of irreversible binding of a part that have applied drug with the skin.
Lipid film	The lipid film on the skin surface goes about as a defensive layer to keep the expulsion of moisture from the skin and aides in keeping up the barrier function of stratum corneum.
Skin hydration	Skin hydration can be accomplished essentially by covering the skin with plastic sheeting, prompting amassing of sweat and improve the infiltration by opening the densed, closely packed cells of the skin and rises its porosity
Skin temperature	Rises in skin temperature rises the rate of skin penetration this is expected to accessibility of energy required for diffusivity.
Regional variation	Contrasts in nature and thickness of the barrier of skin cause variety in the permeability
Pathological injuries to the skin	Wounds that disturb the coherence of the stratum corneum, expands penetrability because of expanded vasodilatation caused by removal of the barrier layer
Self-metabolism	Catabolic catalysts present in the epidermis which may reduce the drug inactive over digestion or this method the topical bioavailability of the drug.
Skin barrier properties in the neonate and young infant	The pH of skin surface of new borns is higher than those in adult skin. The skin surface of the infant is marginally hydrophobic and moderately dry and harsh when looked at to that of older infants. Stratum corneum hydration stabilizesby the age of 3 months.
Skin barrier properties in aged skin	There are changes in the physiology of matured skin (>65 a long time). The corneocytes are appeared to rises in surface area which may have suggestions for stratum corneum function because of the subsequent diminished volume of intercorneocyte space per unit volume of stratum corneum.
Body site	Skin structure are differs at various places in body. Genital tissue typically gives the most permeable site to transdermal drud delivery system. The skin of the head and neck is moreover moderately porous contrasted with different locales of the body for example, the arms and legs.
Penetration enhancers	Low permeability of drugs over the skin can be enhanced by the advancement of penetration enhancers.(Patel et al,2012)

Table 2: The polymers used in transdermal system

Polymers	**Example**
Natural Polymers:	Zein, gelatin cellulose derivatives, gums, natural rubber, shellac, waxes and chitosan etc.
Synthetic Elastomers	Hydrin rubber, Polyisobutylene, polybutadiene, silicon rubber, nitrile, Neoprene, Butyl rubber, Acrylonitrile etc.
Synthetic Polymers	Polyvinylchloride, polyethylene, polyvinyl alcohol, polypropylene, polyamide, Polyacrylate, polyuria, Polyvinylpyrrolidone, Polymethylmethacrylate etc.

2. It should have low melting Point.
3. It should have affinity for both hydrophilic and lipophilic phases.

1.10.2. Biological properties

1. Half-life of drug should be short.
2. Drug must not encourage a cutaneous allergic and irritant. response.
3. Daily dose of the order of a few mg/day.
4. Drugs should be administered for a long period of time.

1.10.3. Permeation enhancers

By the rises the permeability of stratum corneum in order to achieve greater therapeutic levels of the drug penetration enhancer associate with basic part of stratum corneum i.e Lipids and proteins. It is two types' chemical and physical Permeation enhancers. [19]

1. Physical Permeation enhancers
   The sonophoresis or phonophoresis methods are examples of physical technique of improvement have been utilized for enhancing percutaneous penetration

of different therapeutic agents.

2. Chemical Permeation enhancers
   Chemicals enhancers promote the penetration of topically applied drugs are generally discussed absorption promoters and accelerants.

Table 3: Classification of chemical enhancers

Chemical enhancers	Example
Terpenes	Carvone, menthol
Fatty acids	Lauric acid
Alcohols	Ethanol
Pyrollidones	Azone

1.11. Physical enhancers

Techniques are instances of actual methods for improvement that have been utilized for upgrading percutaneous entrance (and absorption) of different remedial specialists.[20]

1.12. Backing laminate

Backing laminate layer are following points must be considerable-

1. It should be chemical resistance
2. It must be flexible
3. It is having good tensile strength
4. It should be non-irritant

Examples of backings laminate are polyester film and polyethylene film, polyolefin film

1.13. Release liner

It is the essential packaging material which can be secure the patch that will remove amid use of patch to the skin. It is comprised of base layer which might be non-occlusive (example paper fabric) or occlusive such as polyethylene, polyvinylchloride.

1.14. Evaluation of transdermal patches[21,22]

1. Thickness
2. Weight uniformity
3. Content uniformity test
4. Moisture content
5. Tensile Strength
6. Drug content
7. Shear adhesion test
8. Peel adhesion test:
9. Thumb tack test:
10. Rolling ball test:
11. Probe tack test:
12. In vitro release studies
13. In vivo Studies

2. Disclosure Statement

There are no conflicts of interest.

3. Conclusion

TDDS used for the used for drug therapy for a less absorption, more uniform plasma levels, improved bioavailability, decrease side effect, efficacy and quality of the product. A patch has some simple components, which perform a vital role in the release of drug through the skin. Future prospective of TDDS would be focused on the controlled therapeutic use.

4. Source of Funding

None.

5. Conflict of Interest

None.

Acknowledgment

The authors acknowledge the chairman of Mr. Anil Chopra, Vice Chairperson Ms. Sangeeta Chopra & Pro-Chairman Mr. Prince Chopra, St. Soldier Group of Educational Society, Jalandhar for providing the necessary facilities to complete this review work.

References

1. Kandavilli S, Nair V, Panchagnula R. Polymers in transdermal drug delivery systems. *Pharm Technol*. 2002;26(5):62–81.
2. Divya A, Rao MK, Gnanprakash K, Sowjanya A, Vidyasagar N, Gobinath M. A review on current scenario of transdermal drug delivery system. *Int J Res Pharm Sci*. 2012;3(4):494–502.
3. Bhowmik D, Chiranjib, Chandira M, Jayakar B, Sampath KP. Recent advances in transdermal drug delivery system. *Int J Pharm Tech Res*. 2010;2(1):68–77.
4. Chein YW. Transdermal Controlled Systemic Medication. New York and Basel: Marcel Dekker Inc; 1987.
5. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: a review. *Pharm Innov*. 2012;1:66–75.
6. Sharma RK, Keleb E, Mosa EB, Aljahwi AAZ. Transdermal drug delivery system- design and evaluation. *Int J Adv Pharm Sci*. 2010;1:201–11.
7. Dhiman S, Thakur GS, Rehni AK. Transdermal patches: a recent approach to new drug delivery system. *Int J Pharm Pharm Sci*. 2011;3(5):26–34.
8. Robinson JR, Lee VH. Controlled drug delivery fundamentals and applications. 2nd ed. New York; 2005.
9. Wilson R, Waugh A, Grant A. Anatomy and physiology in health and illness. 9th ed.; 2001.
10. Kumar D, Sharma N, Rana AC, Agarwal G, Bhat ZA. A review: transdermal drug delivery system: tools for novel drug delivery system. *Int J Drug Dev Res*. 2011;3(3):70–84.
11. Yadav V. Transdermal drug delivery system: review. *Int J Pharm Sci Res*. 2012;3(2):376–82.
12. Mathur V, Satrawala Y, Rajput MS. Physical and chemical penetration enhancers in transdermal drug delivery system. *Asian J Pharm*. 2010;4(3):173. doi:10.4103/0973-8398.72115.

13. Wiechers J. Use of chemical penetration enhancers in Transdermal drug delivery-possibilities and difficulties. *Acta pharm*. 1992;4:123.
14. Govil SK. Drug Delivery Devices. Tyle P, editor. New York: Marcel Dekker; 1988.
15. Jayaswal SB, Sood R. Transdermal drug delivery system- A Review. *Eastern Pharm*. 1987;30(357):47–50.
16. Kavadya Y, Behera B, Mohanty P, Routray D, Ghosh S, Das L. Study of physiological and pathological skin changes in neonates: An east indian perspective. *Indian J Paediatr Dermatol*. 2018;19(1):40. doi:10.4103/ijpd.ijpd_21_17.
17. Jain NK, Jain SK. Controlled and Novel Drug Delivery. New Delhi: CBS Publishers and Distributors; 2002.
18. Chien YW. Novel drug delivery systems, Drugs and the Pharmaceutical Sciences. New York: Marcel Dekker; 1992.
19. Parivesh S, Sumeet D, Abhishek D. Design, Evaluation, Parameters and Marketed Products of transdermal patches: A Review. *J Pharm Res*. 2010;3(2):235–40.
20. Mitragotri S, Blankschtein D, Langer R. Transdermal drug delivery using low-frequency sonophoresis. *Pharm Res*. 1996;13(3):411–20.
21. Sharma S, Khurana G, Gupta R. A Review on Pharmaceutical Validation and Its Implications. *Indian J Pharm Biol Res*. 2013;1(03):100–10. doi:10.30750/ijpbr.1.3.14.
22. John L. Review on Transdermal Drug Delivery System. *Int J Pharma Res Health Sci*. 2014;2(4):261–72.

Author biography

Neha Choudhary, Research Scholar

Ajeet Pal Singh, Academic Dean

Amar Pal Singh, Principal

Cite this article: Choudhary N, Singh AP, Singh AP. Transdermal drug delivery system: A review. *Indian J Pharm Pharmacol* 2021;8(1):5-9.