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A Detailed Review of Transdermal Drug Delivery System

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ABSTRACT:

Transdermal drug delivery systems (TDDS), sometimes known as "patches," are dosage forms designed to disperse a therapeutically active dose of medication across a patient's epidermis in order to cause systemic effects. Drug delivery can easily be applied to the surface of the human skin. The skin on an adult average has a surface area of around 2 m^2 and receives approximately 1/3 of the blood that circulates throughout the body. In the last few years, the pharmaceutical industry has placed a greater emphasis on establishing controlled medication delivery. On average, there are between 10 and 70 hair follicles and 200 to 250 sweat ducts per square centimeter on the surface of the human body. Currently , 74% of medications are taken orally, and their effectiveness is shown to be subpar. The development of transdermal drug delivery systems aimed to enhance such characters. Researchers have been drawn to the transdermal route of medication delivery because of its various biological benefits. Still, The biggest obstacle to properly delivering medication molecules to the systemic circulation via this route is the superb impermeable quality of skin. Human societies have been applying substances to their skin for cosmetic and medical purposes for thousands of years.

However, the utilization of the skin as a medicine delivery system did not begin until the 20th century. Merriam Webster indicates that the term "transdermal" was first used in 1944, indicating that it is a relatively new 1944, emphasizing how new this idea is to the fields of medicine and pharmacy. Transdermal medications come in separate, self-contained dose forms. Although it has significantly improved medical practice, transdermal drug delivery has not yet reached its full potential as a substitute for oral medication administration and hypodermic injections. Drugs can be delivered continuously and under control through the skin to the systemic circulation with transdermal treatment systems. A transdermal drug delivery system is a controlled medication application that is applied to the skin with the purpose of delivering a specific dosage of medication via the skin and into the bloodstream. It is also noteworthy because to its intriguing advantages, which include reduced absorption, more consistent plasma levels, enhanced bioavailability, fewer adverse effects, and higher product quality.

INTRODUCTION

A key component of innovative drug delivery systems is the transdermal drug delivery system, which dates back to the tenth century and uses the skin as an administration site for prolonged drug delivery.[1]

The concentration of a drug at the site of action determines its pharmacological reaction, which in turn depends on the dose form and the degree of absorption of the drug there. This includes both the desired therapeutic impact and the undesired adverse effect.[2]

Since ancient times, transdermal medication application has been widely recognized. Older cultures employed plasters, pastes, ointments, and intricate infusions to cure a range of ailments and symptoms. Since ancient times, transdermal medication application has been widely recognized. Salvationist ancient cultures treated a wide range of symptoms and illnesses with ointments, pastes, plasters, and intricate infusions.[3]

Transdermal therapeutic systems are defined as self contained discrete dosage form which, when applied to the intact skin ,deliver the drug, through the skin ,at control rate to the systemic circulation.[4]

The most common form of drug delivery is the oral route .In this route of administration has notable advantage and also has significant drawbacks such as first pass metabolism ,drug degradation in gastro

intestional tract due to enzymes and pH.to overcome these difficulties a novel drug delivery system was developed.[5]

These dosage forms have the ability to deliver drugs to the skin's dermal tissue and reasonable epidermis for localized therapeutic impact.[6]

TDDS is a device that offers an alternate method of providing medication and can have either an active or passive design. These devices make it possible to administer medications via the skin's barrier.[7]

The first transdermal system, Transderm SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with travel. Most transdermal patches are designed to release the active ingredient at a zero order rate for a period of several hours to days following application to the skin. This is especially advantageous for prophylactic therapy in chronic conditions. .[8]

ADVANTAGES

- Benefits keeps enzymatic breakdown and first-pass metabolism at bay by git.
- Self-administration of a transdermal medicine is feasible.
- The bloodstream releases medications from topical patches over an extended period of time.
- Patches cause less pain than alternative distribution methods.
- Transdermal patches have less side effects than oral treatments.
- Incompatibilities with Git are prevented.
- The dosage and expected treatment outcomes are known in advance.
- The duration of this treatment is longer.[9]

DISADVANTAGES

- Only small lipophilic drugs can be delivered currently through the skin.
- Drug molecule must be potent because patch size limits the amount that can be delivered not suitable for high drug doses.
- Adhesion may vary with patch type and environmental conditions.
- Skin irritation and hypersensitivity reactions may occur .
- The barrier functions of the skin change from one site to another on the same person ,from person to person and with age .[10]

ANATOMY AND PHYSIOLOGY OF SKIN: .[11]

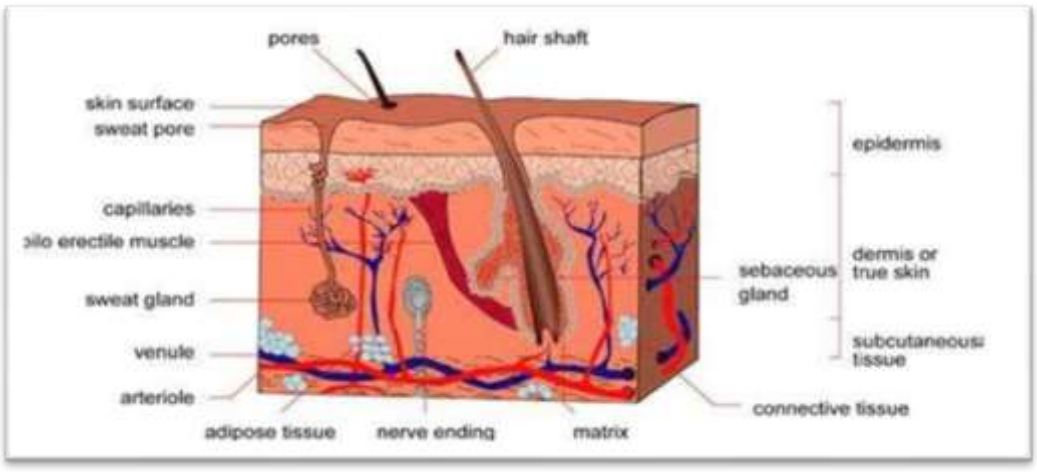

Fig 1 :-structure of skin

To improvise the current potential of TDDS it is necessary to understand the very basic of skin anatomy. Skin is multi-layered organ composed of many histological layers. The major divisions of the skin, from top to bottom, are the, epidermis, the dermis and the hypodermi .

Epidermis: .[12] Stratified, squamous, keratinizing epithelium. Keratinocytes comprise the major cellular component (> 90%) and are responsible for the evolution of barrier function. Keratinocytes change their shape, size and physical properties when migrating to the skin surface The dermis is where systemic absorption occurs.

Dermis the site of system absorption:[13]The dermis is composed of an amorphous colloidal ground substance imbedded in a fibrous protein matrix mostly composed of collagen, elastin, and reticulum. It has a thickness of 0.2–0.3 cm. It is separated into two distinct zones: the deeper coarse reticular layer (the primary structural layer of skin) and the superficial finely structured thin papillary layer next to the epidermis.

Hypodermis: The innermost layer of the skin is called the hypodermis, or subcutaneous tissue. Internal organs are shielded from harm by the insulating and shock-absorbing properties of subcutaneous tissue. Blood veins, nerves, lymph vessels, and hair follicles pass through the layers that contain fat. The skin's outermost layer, the stratum corneum, acts as a strong barrier to prevent medication penetration. : [14]

Absorption Through the Skin: [15]

The drug can be absorbed by various pathways through the skin depending on the physicochemical properties of the drug. Both lipophilic and hydrophilic drugs are absorbed from different routes. The upper stratum corneum of the skin opposes the absorption of drug but presence of various absorption routes facilitates the entry of drug and transport of drug to the systemic circulation. Various drug absorption routes are as follows:

a) Transfollicular route

Transfollicular route is the shortest pathway that drug has to follow to reach the systemic circulation that provides a large area for diffusion of drugs. Skin has various sweat glands, oil glands, hair follicles and pores opening to the outer surface of the skin via their ducts. These ducts offer a continuous channel across the stratum corneum for drug transport but various factors like secretion from glands, content and amount of secretion etc., affect the transport of drugs through this route.

b) Transcellular route

Drug delivering through this route passes from corneocytes which has highly hydrated keratin creating hydrophilic pathway. Corneocytes are surrounded by lipids connecting these cells. So a drug requires a number of partitioning and diffusion steps. It is the most widely used route by various types of drugs. In transcellular route drug passes through the matrix of the cells. This route is suitable for hydrophilic drugs. The drug passes through the corneocytes of stratum corneum

c) Intercellular route

As name indicates in intercellular pathway the drug diffuses through the continuous lipid matrix present between the cells. The barrier property of this route is due tortuous structure formed by corneocytes and thedrug has to pass through the alternating lipid and aqueous domain by partitioning into the lipid bilayer and diffusing to the inner side.

- **PATHWAYS OF DRUG ABSORPTION THROUGH THE SKIN :** [16]

Drug molecules may penetrate the skin along the hair follicles are sweet ducts and then be absorbed through the pellicular epithelium and sebaceous glands during the initial transient diffusion stage of percutaneous permission. They may also diffuse through shunts, especially those provided by the relative Lee widely distributed hair follicles and eccrine glands. Factors affecting transdermal permeation

1) PHYSICOCHEMICAL PROPERTIES OF THE PENETRANT MOLECULE

A. Coefficient of partition[17]

]For optimal transdermal permeability, a lipid/water partition coefficient of 1 or higher is usually needed. Chemical alteration can change it without compromising the drug's pharmacological action.

B. The pH levels

Applying solutions with extremely high or low pH values can harm the medication.

C. Skin hydration: [18]

The skin swells, softens, wrinkles, and has a noticeable increase in permeability when it is saturated with water. In actuality, hydration of the stratum corneum plays a significant role in speeding up the pace at which most things penetrate the skin.

D. Temperature: As a result of the diffusion coefficient decreasing with decreasing temperature, a material's rate of penetration through human skin might vary tenfold for considerable temperature variations

E. Diffusion coefficient: [19]

Penetration of drug depends on diffusion coefficient of drug. At a constant temperature the diffusion coefficient of drug depends on properties of drug, diffusion medium and interaction between them.

f) Drug concentration: The concentration gradient across the barrier determines the flow, and a higher concentration gradient indicates a higher drug concentration across the barrier**.**

2) BIOLOGICAL FACTORS: : [20]

A. Skin Age:

Younger and adult skin are more porous than those of elderly people. The child's skin exhibits a hazardous effect because of a larger surface area relative to body weight, the study claims. Certain compounds have significant side effects, such as hexachlorophene, strong steroids, and boric acid.

B. Variations among species:

The keratinization, thickness, and density of skin appendages change among species, which can affect how well a TDDS patch penetrates the skin.

C. Skin condition: [21]

Many solvents, like methanol and chloroform, harm skin cells and encourage penetration. Skin conditions are altered when a patient is ill. Although the best barrier is an unbroken skin layer, penetration might be impacted by the factors outlined above.

D. Blood flow: Transdermal absorption may be impacted by modifications in peripheral circulation. localized areas of skin Site-specific differences include skin thickness, stratum corneum type, and appendage density. These elements have a big impact on penetration. Skin metabolism Skin metabolism controls the effectiveness of pharmaceuticals absorbed through the skin since it breaks down steroids, hormones, chemical carcinogens, and some medications.

- **ENVIROMENTAL FACTOR:**

A. Air Pollution:

When an air pollution layer forms on the skin's surface, the release of drugs is slowed down. The presence of different chemicals in the air can react with the drug and lessen its efficiency, and germs in the air can easily interfere with skin health.

B. Cold season:

Dry and itchy skin is a result of the cold weather. Since the water level of the skin is so low at that point, moisturizing agents can both promote the drug's penetration into the skin and improve its drying impact..

COMPONENTS OF A TRANSDERMAL DELIVERY SYSTEM :[23]

The main components of a transdermal drug delivery system are:

- release -which shields the patch from storage and is taken off before use;
- the medication,-which is the drug solution in direct contact with the release liner;
- the adhesive-which joins the patch's parts and binds it to the skin.

❖ **Enhancers of penetration** [24]:

Generally speaking, substances that facilitate the entry of medications given topically are called penetration enhancers, accelerants, or absorption promoters. Penetration enhancers are added to a formulation to improve the solubility and diffusivity of medications through the skin, which would reversibly lower the skin's barrier resistance.

❖ **PERMEATION ENHANCERS** [25]

Accelerants, sorption promoters, and penetration enhancers are other names for permeability enhancers. They are the substances that increase skin permeability by changing the skin's ability to act as a barrier against intended penetration. Since the lipid part of the intracellular channel is the primary route of drug absorption, it is viable in the initial step of absorption.

The ideal permeation enhancer features are:

- a reversible and controlled action.
- should not result in electrolyte or bodily fluid loss.
- The polymer ought to be stable.

➢ Polymers ought to be safe. Polymer production ought to be simple.

FACTORS AFFECTING TRANSDERMAL BIOAVAILABILITY: [26]

Two major factors affect the bioavailability of the drug through transdermal routes:

(1)Physiological factors (2) Formulation factors

Physiological factors include:

1. The skin's stratum corneum layer;
2. ii) the anatomic location of application on the body;
3. iii) skin ailments and disorders Skin metabolism
4. (iv) Sensitization and irritation of the skin Among the formulation factors are:

(i) The use of penetration enhancers;

(ii)the usage of vehicles and membrane

TRANSDERMAL PATCH TESTING AND EVALUTION DRUG EXCIPIENT INTERACTION STUDIES:[27]

1)Thickness of patches 2)Weight variation 3)Drug content 4)Content uniformity 5)Moisture content

6)Water vapor transmission studies 7)In-vitro drug release studies

8)In- vitro skin permeation study

Patch thickness

A digital micrometer is used to measure the thickness of medication patches, and the average thickness and standard deviation are calculated to guarantee the thickness of the prepared patch at various points. Screw gauges and dial gauges for traveling microscopes are used to measure the thickness of films.

2. Variation in weight

A particular patch section needs to be divided into several sections and weighed using a digital balance. From the individual weights, the average weight and standard deviation value must be determined. Before testing, the prepared patches were allowed to dry for four hours at 600°C.

3. Content of drugs: [28]A particular patch area dissolves in a given volume of an appropriate solvent. Following that, a filter media is used to filter the solution, revealing the drug content.s

test for uniformity of dose unit:

To perform the test, weigh a portion of the patch precisely and cut it into small pieces. These fragments are moved to a volumetric flask of a certain capacity. They are subsequently dissolved in an appropriate solvent and sonicated to extract the drug entirely from the patch and to the desired level. After letting the resultant solution settle for about an hour, the supernatant is appropriately diluted with the right solvent to achieve the required concentration.

5. Percentage moisture uptake[29]

The prepared patches are to be weighed individually and to be kept in a desiccator containing saturated solution of

potassium chloride in order to maintain 84% RH. After 24 hrs the films are to be reweighed and determine the percentage moisture uptake by below formula S

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

6. **Water vapour permeability (WVP) evaluation :**

Water vapour permeability can be determined by a natural air circulation oven. The WVP can be determined by the following formula

WVP=W/A

Where, WVP is expressed in gm/m2 per 24 hrs,

W is the amount of vapour permeated through the patch expressed in gm/24 hrs .

7. **In vitro release studies:** [30]ccc Paddle over disc apparatus Cylinder apparatus

The reciprocating disc

8. **In vitro permeation studies**: [30]

Diffusion cells can be used for in vitro permeation studies. Completely developed abdomen skin in male Westar rats weighing 200–250 grams. The dermal side of the skin is cleaned thoroughly with distilled water to remove any adhering tissues or blood vessels, and is then placed on a magnetic stirrer with a small magnetic needle for uniform diffusant distribution. Before beginning the experiment, the abdominal region's hair must be carefully removed using an electric clipper. Through the use of a thermostatically regulated heater, the temperature of the cell is kept at 32 ± 0.5°C.

Challenge and future prospect:

TDD is a non-invasive delivery method that avoids some bioavailability issues that come with oral drug delivery because of poor absorbability and metabolism issues. It is generally thought to be easy to administer, even in more vulnerable age groups, such as pediatric and geriatric patients. The skin provides an easy and patient-friendly target for medication delivery due to its large surface area and accessibility. Transdermal administration has several major advantages, including the elimination of first-pass metabolism, steady distribution, enhanced patient compliance, decreased systemic medication interactions, sustained drug release, and typically higher therapeutic efficacy..

CONCLUSION:

Research scientists working on transdermal drug delivery systems might find useful information on the systems' evolution process in the transdermal drug delivery system review articles.Many factors must be taken into account for transdermal medicine application to be successful.Given that the skin's primary roles are containment and protection, targeting the skin for drug administration would appear extremely challenging.

However, an increasing number of novel pharmaceutical items are being created for transdermal distribution as a result of our growing understanding of the composition and function of the skin as well as how to modify these characteristics.

References:

1. Purushotham, K. and Vijetha, K.A., 2023. A review on transdermal drug delivery system. GSC Biological and Pharmaceutical Sciences, 22(2), pp.245-255.
2. Sharma, N., Agarwal, G., Rana, A.C., Bhat, Z.A. and Kumar, D., 2011. A review: transdermal drug delivery system: a tool for novel drug delivery system. Int J drug dev Res, 3(3), pp.70-84.
3. Ramteke, K.H., Dhole, S.N. and Patil, S.V., 2012. Transdermal drug delivery system: a review. Journal of Advanced Scientific Research,
4. Prabhakar, D., Sreekanth, J. and Jayaveera, K.N., 2013. Transdermal drug delivery patches: A review. Journal of Drug Delivery and Therapeutics,
5. Mishra, B. and Bonde, G.V., 2020. Transdermal drug delivery. In Controlled drug
6. Choudhary, N., Singh, A.P. and Singh, A.P., 2021. Transdermal drug delivery system: A review. JPP, 8, pp.5-9
7. .Yadav.,2012. Transdertmal drug delivery system. Internal journal of pharmaceutical8. Tanwar, H. and Sachdeva, R., 2016. Transdermal drug delivery system: A review.
8. International journal of pharmaceutical sciences and research, 7(6), p.2274.
9. Soni, A., Dua, J.S. and Prasad, D.N., 2022. Article reviewing transdermal drug delivery system. Journal of Drug Delivery and Therapeutics, 12(1), pp.176-180.
10. Rastogi, V. and Yadav, P., 2012. Transdermal drug delivery system: An overview. Asian Journal of Pharmaceutics (AJP), 6(3).
11. Lal, B. and Gadewar, M., 2021. A Concise Review on Transdermal Drug Delivery System. Annals of the Romanian Society for Cell Biology,
12. Bala, P., Jathar, S., Kale, S. and Pal, K., 2014. Transdermal drug delivery system (TDDS)a multifaceted approach for drug delivery. J Pharm Res, 8(12), pp.1805-1835.
13. Reddy, Y.K., Reddy, D.M. and Kumar, M.A., 2014. Transdermal drug delivery system: a review. Indian Journal of Research in Pharmacy and Biotechnology, 2(2), p.1094.
14. Supe, S. and Takudage, P., 2021. Methods for evaluating penetration of drug into the skin: A review. Skin research and technology, 27(3), pp.299-308.
15. Jhawat, V.C., Saini, V., Kamboj, S. and Maggon, N., 2013. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. Int J Pharm Sci Rev Res, 20(1), pp.47-56
16. Dhawale, T.A., Pande, S.D., Sonawane, M.K., Jambhale, A.R. and Giri, R.R., SelfEmulsifying Drug Delivery System a Tool for Enhancement of Solubility: A Critical Review.
17. Kakar, S., Singh, R. and Rani, P., 2016. A review on transdermal drug delivery. Innoriginal Int J Sci, 3(4), pp.1-5.
18. Shashidhar, P., Afshan, I., Sunitha, M. and Ramakrishna, D., 2017. FORMULATION, CHARACTERIZATION AND IN-VITRO EVALUATION OF DULOXETINE HYDROCHLORIDE TRANSDERMAL PATCHES.
19. Bose, P., Jana, A., Mandal, S. and Chandra, S., 2021. Transdermal drug delivery system: Review and future. Annals of the Romanian Society for Cell Biology, pp.3420-3436.
20. Palanisamy, P., Jaykar, B., Venkateswarlu, B.S. and Chandira, R.M., 2020. Suriyan. D. A Review on Transdermal Drug Delivery System. Indian Journal of Natural Sciences, 10(61), pp.27035-27056.
21. Bose, P., Jana, A., Mandal, S. and Chandra, S., 2021. Transdermal drug delivery system: Review and future. Annals of the Romanian Society for Cell Biology, pp.3420-3436.
22. , J.G. and Lambert, D.G., 2011. Anaesthesia, critical care, and pain in the 21st century: the first decade. British journal of anaesthesia, 107(1), pp.1-2.

23. Fathima, S.A., Begum, S. and Fatima, S.S., 2017. Transdermal drug delivery system. International journal of pharmaceutical and clinical research, 9(1), pp.35-43.

24. Deulkar, D.A., Kubde, J.A., Hatwar, P.R. and Bakal, R.L., 2024. A review on transdermal drug delivery system. GSC Advanced Research and Reviews, 18(2), pp.347-361.

25. Sarika, V. and Moulika, G., Transdermal Drug Delivery Systems: An Overview.

26. SYSTEM", International Journal of Emerging Technologies and Innovative Research (www.jetir.org), ISSN:2349-5162, Vol.7, Issue 7, page no.703-719,

27. Kulkarni, M.P. and Vandana, P.B., 2018. Transdermal drug delivery: A novel approach for intended drug action. International Journal for Advance Research and Development, 3(3), pp.127-136.

28. Patel, D. and Kavitha, K., 2011. Formulation and evaluation aspects of transdermal drug delivery system. International journal of pharmaceutical sciences review and research, 6, pp.1-12.

29. Ghume, V.K., Golhar, A.R., Merekar, A.N., Dokhe, M.D. and Parjane, S.K., 2020. Transdermal drug delivery system: A review. Am. J. PharmTech Res, 10, pp.34-47.

30. Alkilani, A.Z., Nasereddin, J., Hamed, R., Nimrawi, S., Hussein, G., Abo-Zour, H. and Donnelly, R.F., 2022. Beneath the skin: a review of current trends and future prospects of transdermal drug delivery systems. Pharmaceutics, 14(6), p.1152