



## TRANSDERMAL DRUG DELIVERY SYSTEM

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### ABSTRACT

Today about 74% of capsules are taken orally and are observed no longer to be as effective as two desired. To enhance such characters transdermal drug transport device was once emerged. Drug delivery thru the skin to reap a systemic effect of a drug is regularly known as transdermal drug delivery and differs from normal topical drug delivery. Transdermal medication shipping structures(TDDS) are measurements assortments incorporates sedate transport to reachable epidermal as well as dermal tissues of the pores and skin for adjacent restorative effect while a noteworthy division of medication is transported into the foundational blood course. The adhesive of the transdermal drug shipping gadget is critical to the safety, efficacy and exceptional of the product.

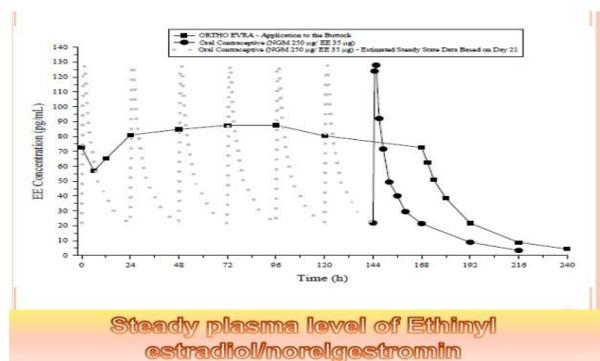
**KEYWORDS:** Transdermal Drug Delivery System, Systemic Blood Circulation, Topical Drug Delivery.

### 1.0 INTRODUCTION

The most frequent structure of drug delivery is the oral route. In this route of administration has gorgeous blessings and additionally have signification downside like first ignore metabolism, drug degradation in gastrointestinal tract due to enzymes, pH etc. To overcome these two difficulties a Novel Drug shipping system was once developed.<sup>[1]</sup> The TDS are defined as self contained, self discrete dosage forms, which when applied to the intact skin deliver the drug at a controlled rate to the systemic circulation. A simple patch that you stick onto your skin like an adhesive bandage, which utilize passive diffusion of drug across the skin as the delivery mechanism.<sup>[3]</sup> In recent years it has been shown that skin is a useful; route for drug delivery to the systemic circulation. Transdermal drug shipping systems (TDDS), additionally recognized as “patches,” are dosage varieties designed to deliver a therapeutically high-quality amount of drug two across a patient’s skin. Transdermal drug transport device has been in existence for a long time.<sup>[2]</sup> Transdermal drug transport machine includes all topically administered drug two formulations meant to deliver the active ingredients into the circulation. They provide controlled non-stop delivery of tablets thru the pores and skin to the systemic circulation. The drug is by and large delivered thru the skin with the resource of transdermal patch. A Transdermal patch is a medicament adhesive patch that is placed on the skin to delivery a specific dose of medication. A drug is applied in a tremendously high dose to the internal of a patch, which is worn on the skin for an prolonged length of time.<sup>[3]</sup>

### 1.1 Advantages<sup>[4-6]</sup>

1. Steady permeation of drug across the skin, allowing consistent serum drug level, often a goal therapy.
2. It delivers a steady infusion of the drug over an extended period of time. Adverse effects and the therapeutic failure can be avoided.
3. Transdermal drug delivery can be used as an alternative delivery system for patients who cannot tolerate oral dosage forms.
4. Self administration is possible with this system.
5. It increases the therapeutic value of many drugs by avoiding specific problems associated with the drug.
6. The drug input can be terminated at any point of time by removing transdermal patch.
7. Allows effective use of drugs with short biological half life.
8. Drug input can be promptly interrupted when toxicity occurs.
9. Provides steady plasma levels of highly potent drugs.



**Steady plasma level of Ethinyl estradiol/norelgestromin**

**Figure. 1: Steady plasma level.**

## 1.2 Disadvantages<sup>[1,5,7]</sup>

1. Skin structure poses a barrier on the mw of the drug (<500Da).
2. Adhesive may not adhere well to all types of skin.
3. Drug or drug formulation may cause skin irritation or sensitization.
4. It may be uncomfortable to wear.
5. TDDS are more costly than the conventional dosage forms.
6. Many drugs especially drugs with hydrophilic structures permeate the skin too slowly may not achieve therapeutic level.
7. The barrier function of the skin changes from one site to another on the same person, from person to person and also with age.

## 2.0 History<sup>[8]</sup>

The first transdermal patch was approved in 1981 to prevent the nausea and vomiting associated with motion sickness. The FDA has approved, till 2003, more than 35 transdermal patch products, spanning 13 molecules (In USA). The US transdermal market approached \$ 1.2 billion in 2001. It was based on 11 drug molecules, fentanyl, nitroglycerin, estradiol, ethinylestradiol, norethindroneacetate, testosterone, clonidine, nicotine, lidocaine, prilocaine, and scopolamine. Two new, recently approved transdermal patch products (a contraceptive patch containing ethinylestradiol and norelgestromin, and a patch to treat overactive bladder, containing oxybutynin).

## 3.0 SKIN<sup>[1,9-11]</sup>

### SKIN - PROTECTION & TOUCH

Structure of skin

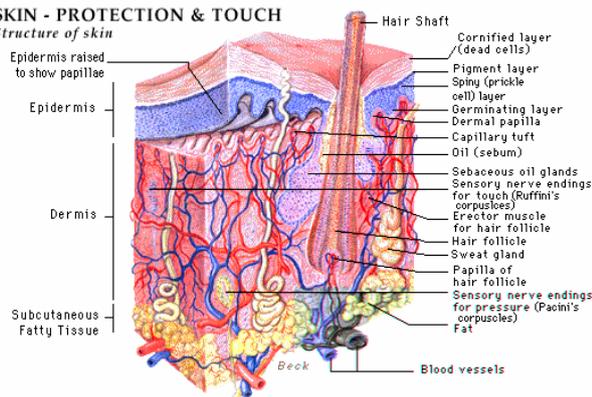


Figure. 2: Structure of Skin.

The skin is the biggest organ of the body, with an all out region of around 20 square feet. The skin shields us from microorganisms and the components, manages body temperature, and licenses the impressions of touch, warmth, and cold.<sup>[12]</sup> The skin of a normal individual human covers a surface territory of almost 2m<sup>2</sup> and gets around 33% of the blood flowing by means of the body. Infinitesimally skin is made out of three most imperative histological layers: epidermis, dermis and subcutaneous tissues. The epidermis is what's more partitioned into two sections the nonviable epidermis (stratum corneum) and the practical epidermis. The conceivable epidermis is isolated into four layers, viz., stratum lucidum, stratum

granulosum, and stratum spinosum and stratum germinativum.<sup>[13]</sup>

## 3.1 Skin has three layer<sup>[12-13]</sup>

- The epidermis, the uttermost layer of skin, offers a water-verification limit and makes our pores and skin-tone.
- The dermis, underneath the epidermis, contains serious connective tissue, hair follicles, and sweat organs.
- The progressively significant subcutaneous tissue (hypodermis) is made of fat and connective tissue.

**3.1.1 Epidermis:** The epidermis of the skin is an always recharging stratified squamous epithelium. It comprises for the most part of keratinocytes, yet in addition of Langerhans cells, melanocytes, and Merkel cells laying on a supporting dermis that contains the nerve and vascular systems, which feed the epidermis. The dermis is additionally the area of epidermal members, fibroblasts, pole cells, macrophages, and lymphocytes. Epidermal undifferentiated cells are in charge of the capacity of the epidermis to supplant itself, both in typical conditions and in horrendous skin misfortune, for example, from consumes and skin ulceration.<sup>[14]</sup> The epidermis is isolated into following parts. The stratum corneum and stratum germinativum. The stratum corneum frames the external most layer of the epidermis and comprises numerous layers of compacted, straightened, got dried out keratinized cells in the stratified layer. Water substance of stratum corneum is around 20%. The dampness required for stratum corneum is around 10% (w/w) to keep up adaptability and delicate quality. The stratum corneum is in charge of the obstruction capacity of the skin and carries on as an essential hindrance to percutaneous ingestion. It is comprised of three layers in thicker parts-stratum granulosum, stratum lucidum, stratum spinosum. Evacuation of these layers results in expanded penetrability and water misfortune.

**3.1.2 Dermis<sup>[12-16]</sup>:** The dermis is a connective tissue layer that gives the skin the greater part of its substance and structure. The dermoepithelial intersection contains various interdigitations that assistance grapple the dermis to the overlying epidermal layer. The papillary layer has free connective tissue, pole cells, leukocytes, and macrophages. The reticular dermis has denser connective tissue and less cells than does the papillary layer. The dermis has a rich layer of blood and lymphatic vessels, including the arteriovenous anastomoses vital in thermoregulation. The dermis additionally contains various nerve endings, including a wide assortment of the cutaneous tangible nerve receptors.<sup>[12]</sup> The dermis is comprised of standard system of hearty collagen filaments of genuinely uniform thickness with routinely set cross striations. This organize or the gel structure is in charge of the flexible properties of the skin. Below the dermis there is a fat containing subcutaneous tissue. Upper segment of the dermis is framed into edges containing lymphatics and nerve endings.<sup>[13]</sup>

### 3.1.3 Subcutaneous<sup>[9,10-16]</sup>

Padding the epidermis and dermis is the subcutaneous tissue or fat layer where fat is made and put away. It goes about as a warmth encasing and a safeguard. It basically has no impact on the percutaneous retention of medications since it lies beneath the vascular framework. This is a sheet of the fat containing areolar tissue known as the shallow sash. appending the dermis to the basic structures.<sup>[16]</sup>

### 4.0 Transdermal Permeation<sup>[2,5,17,18]</sup>

Prior skin was considered as an impermeable protective boundary, but afterward examinations were carried out which demonstrated the utility of skin as a course for systemic organization. Skin is the foremost seriously and really available organ of the body as it were a fraction of millimeter of tissue isolates its surface from the underlying capillary organize.

**The different advances engaged with transport of medication from fix to fundamental dissemination are as follows<sup>[17,18]</sup>**

1. Diffusion of medication from medication repository to the rate.
2. Diffusion of medication from rate constraining film to stratum corneum.
3. Sorption by stratum corneum and entrance through suitable epidermis.
4. Uptake of medication by narrow system in the dermal papillary later.
5. Effect on target organ.

### 5.0 Care taken while applying Transdermal patch<sup>[11,19]</sup>

1. The piece of the skin where the fix is to connected ought to be appropriately cleaned.
2. Fix ought not be cut since cutting the fix decimates the medication conveyance framework.
3. Before applying another fix it ought to make certain that the old fix is expelled from the site.
4. Care ought to be taken while applying or expelling the fix since anybody dealing with the fix can assimilate the medication from the fix.
5. The fix ought to be connected precise to the site of organization.

### 6.0 Properties that influence Transdermal delivery of the drug<sup>[6,14,21]</sup>

- a. Arrival of the medicament from the vehicle.
- b. Entrance through the skin obstruction.
  - Skin structure and its properties.
  - The entering atom and its physical-synthetic relationship to skin and the conveyance stage.
  - The stage or conveyance framework conveying the penetrant.
  - The blend of skin, penetrant, and conveyance framework.
- c. Actuation of the pharmacological reaction.

### 7.0 Factors That Influence Transdermal Drug Delivery<sup>[14,22-24]</sup>

#### **Biological factors include**

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

#### **Physiological factors include**

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

### 7.1 Basic Components of Tdds<sup>[10,11,27,28]</sup>

- I. The drug
- II. Polymer matrix
- III. Permeation enhancers
- IV. Adhesive
- V. Backing layer.

#### **I. DRUG: I.**

The tranquilize is in direct contact with discharge liner.  
Ex: Nicotine, Methotrexate, and Estrogen.

#### **A portion of the alluring properties of a medication for transdermal conveyance**

1. The medication atom ought to have a satisfactory dissolvability in oil and water
2. The medication ought to have a sub-atomic weight not exactly roughly 1000 daltons.
3. The medication ought to have low softening point.
4. The medication particle would require a reasonable segment coefficient to infiltrate the stratum corneum.

**II. Polymer Matrix:** These polymers control the arrival of the medication from the medication repository.

Regular polymers: shellac, gelatin, waxes, gums, starch and so on  
Manufactured polymers: polyvinyl liquor, polyamide, polyethylene, polypropylene, Polyurea polymethyl methacrylate and so on.

**III. Permeation Enhancers:** Substances exist which incidentally lessen the impermeability of the skin are known as accelarants or sorption advertisers or infiltration enhancers. These incorporate water, pyrolidones, unsaturated fats and alcohols, azone and its subsidiaries, alcohols and glycols, basic oils, terpenes and subordinates, sulfoxides like dimethyl sulfoximide and their subordinates, urea and surfactants.

#### **IV. Adhesive**

Serves to adhere the patch to the skin for systemic delivery of drug.  
Ex: Silicones, Polyisobutylene.

## V. Backing Layer

Backing layer protects patch from outer environment.  
Ex: Cellulose derivatives, Polypropylene silicon rubber.

## 8.0 Types of Transdermal Patches<sup>[18,31-33]</sup>

### a) Single layer drug in adhesive

In this sort the cement layer contains the medication. The cement layer not just serves to follow the different layers together and furthermore in charge of discharging the medication to the skin. The glue layer is encompassed by a transitory liner and a sponsorship.

### b) Multi-layer drug in adhesive

This sort is additionally like the single layer however it contains a quick medication discharge layer and other layer will be a controlled discharge alongside the glue layer. The cement layer is in charge of discharging of the medication. This fix likewise has an impermanent liner-layer and a lasting support.

**c) Vapour fix:** In this sort of fix the job of glue layer not just serves to follow the different layers together yet in addition fills in as discharge vapor. The vapor patches are new to the market, normally utilized for discharging of basic oils in decongestion Various different kinds of vapor patches are additionally accessible in the market which are utilized to improve the nature of rest and diminishes the cigarette smoking conditions.

**d) Reservoir framework:** In this framework the medication store is installed between an impenetrable sponsorship layer and a rate controlling film. The medication discharges just through the rate controlling film, which can be permeable or nonporous.

## 9.0 Factors Affecting Transdermal bioavailability<sup>[26,28,29]</sup>

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

(1) Physiological factors (2) Formulation factors

### Physiological factors include

- i. Stratum corneum layer of the skin
- ii. Anatomic site of application on the body
- iii. Skin condition and disease
- iv. Skin metabolism
- v. Skin irritation and sensitization

### Formulation factors include

- (i) Penetration enhancers used.
- (ii) Vehicles and membrane used.
- (iii) Physical chemistry of transport.
- (iv) Method of application.
- (v) Device used.

## 10.0 Types of Transdermal Drug Delivery System

### There are main four types of TDDS

- Membrane moderated system.
- Adhesive diffusion controlled system.
- Matrix dispersion system.

- Micro reservoir system.

11.0 Ideal properties of drugs for TDDS <sup>[30-32]</sup>	
Parameters	Properties
Dose	Should be low (low than 20 mg/day)
Half-life	10 or less (h)
Molecular weight	<400 Da
Partition	Log P (octanol-water) between 1.0 and
Coefficient	4.0
Skin permeability	>0.5 x 10 <sup>-3</sup> cm/h
Coefficient	
Liophilicity	10 < Ko/w < 1000
Oral bioavailability	Low
Therapeutic index	Low
Melting point	<2000C
pH	Between 5.0 and -9.0

## 12.0 Mechanism of Action of Transdermal Patch

The use of the transdermal fix and the progression of the dynamic medication constituent from the fix to the circulatory framework by means of skin happen through different techniques.

## 13.0 Popular uses

➤ The most astounding selling transdermal fix in the United States is the nicotine fix, which discharges nicotine in controlled dosages to help with discontinuance of tobacco smoking. The main economically accessible vapor fix to lessen smoking was affirmed in Europe in 2007.

➤ Two narcotic meds used to give nonstop help to extreme agony are frequently endorsed in fix structure: Fentanyl (promoted as Duragesic) and Buprenorphine (showcased as BuTrans).

➤ Estrogen patches are at times recommended to regard menopausal side effects just as post-menopausal osteoporosis. Other transdermal patches for hormone conveyance incorporate the preventative fix (advertised as Ortho Evra or Evra).

➤ Nitroglycerin patches are now and then recommended for the treatment of angina in lieu of sublingual pills.

➤ The hostile to hypertensive medication Clonidine is accessible in transdermal fix structure under the brand name Catapres-TTS.

➤ Emsam, a transdermal type of the MAOI selegiline, turned into the main transdermal conveyance operator for an energizer endorsed for use in the U.S. in March 200.

## 14.0 CONCLUSION

The transdermal drug delivery gadget has gain importance in current year as the transdermal route is an extremely attractive alternative for the drug with appropriate Pharmacology and bodily chemistry. The transdermal drug shipping has capable advantage of avoiding hepatic first ignore metabolism, improve to bioavailability, decrees gastro intestinal infection due to nearby contact with gastric mucosa, keeping steady blood degree for a longer period of time ensuing in

decreases of dosing frequency and improved patient compliance. In recent years it has proved that benefits of intravenous drug infusion can be closely duplicated except unsafe outcomes through using pores and skin as part of drug administration to grant continuous transdermal drug infusion thru intact pores and skin.

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