

**AN OVERVIEW OF TRANSDERMAL DELIVERY SYSTEM****RESHMI JAYAPRAKASH, JAHNARA HAMEED, ANUPRIYA\***

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**ABSTRACT**

Recently, most widely using conventional dosage form such as tablet, capsules, and injections but due to some case we are preferable to choose transdermal drug delivery system (TDDS) because conventional oral dosage form undergo first pass metabolism. In TDDS, skin is the effective medium for the penetration of drug into systemic circulation. This system required very low dose for the effective result or action. One of the major disadvantages of TDDS is penetration rate is very low through the stratum corneum. Nowadays, different types of skin penetration enhancement techniques are used for increasing the penetration. These types of techniques can be also increase the bioavailability. The patients have more preferable to choose this type of drug delivery system because it has more advantages than conventional dosage form. This article is discusses about the anatomy and physiology of skin and its drug penetration capacity, polymers used in transdermal drug delivery and different types of TDDS.

**Keywords:** Transdermal drug delivery, Skin, Polymers, Enhancement techniques.© 2017 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2017.v10i10.19909>**INTRODUCTION**

Transdermal drug delivery system (TDDS) means TDDS. It is also known as patches. The first transdermal patches were approved by food and drug administration in 1981. Now-a-days this route is more popular and easy method for the application of drug to patient and also increases the therapeutic benefits to patient. This is the more successful delivery method for releasing of drug into the body. The system also more popular in pharmaceutical industry. It is very effective and produces sustained release to the body [1]. At present, different transdermal drugs are used for various disease such as hyoscin for motion sickness, nitroglycerine, and clonidine used for cardiovascular disease and fentanyl used for chronic pain. This system having several advantages and disadvantages are given below in Table 1.

**ANATOMY AND PHYSIOLOGY OF SKIN [5-7]**

Transdermal delivery mainly depends on the skin nature. Skin is the main route of administration of drug to body. Skin is the largest organ in the body. It provides microbial protection and produces sense. Mainly human body consists of three different types of skin layers (Fig. 1); these layers are responsible for the drug delivery to body.

1. Epidermis (20-89  $\mu\text{m}$ )
2. Dermis (0.3-3 mm)
3. Hypodermis.

**Epidermis**

The striated, vascular, and cellular epidermis are a multiple layered. This layer is occupying in different regions of the body with different thickness (Table 2). It consists of two types of epidermal layer.

- Stratum corneum: It is the outermost layer of the skin. This layer is also known as honey layer. In this region having 10-25 layers of keratinized dead cells, they called as corneocytes. This layer is the principle barrier for the penetration of drug, and also lipids are aligned in multiple bilayers. It prevents the excess loss of water from body and also permits lipid soluble topical agents.
- Viable epidermis: This layer is located on the beneath of the stratum corneum. It comprises of different layers in this region such as stratum granulosum, stratum lucidum, stratum spinosum, and stratum basal (Fig. 2).

**Dermis**

This layer is made up of a matrix of connective tissues such as lymph, nerves, and blood vessels. This layer provides oxygen to skin and also eliminate the waste product and toxins. Sweat glands and hair follicles are present in this region.

**Hypodermis**

It comprises subcutaneous fat tissue; it supports the dermis and epidermis. It is the deeper layer. This layer helps to provide mechanical protection support the nutrients and also it regulates the temperature.

**PENETRATION OF DRUG THROUGH SKIN**

In skin drug molecules are penetrate directly to the stratum corneum, this is achieved by mainly through three pathways such as hair follicles, sweat duct, and sebaceous gland (Fig. 3). In stratum corneum having lot of water it act as plasticizers; they are avoid the cracking of stratum corneum. The drug contains any hydrophilic chemicals it diffuses or passes through the aqueous membrane similarly lipophilic chemicals it diffuse through lipid membrane [8]. This type of molecular transport of drug through barrier is determined by fluxes. At a given period of time no. of molecules pass through specific area of cross section is known as flux. Flux is determined by using an equation 1.

$$J = m/At \quad (1)$$

J=Flux,  
m=Mass of compound,  
A=Area of cross section,  
t=Time.

The molecules are migrating through the barrier; this migration is happen because of external force applied on individual solute molecule [9]. Penetration of drug through outer membrane of stratum corneum obeys Fick's first law. Fick's first law is state that flux is directly proportional to concentration gradient. Fick's first law determined using an equation 2 [10,11].

$$dm/dt = -DS (dC/dx) \quad (2)$$

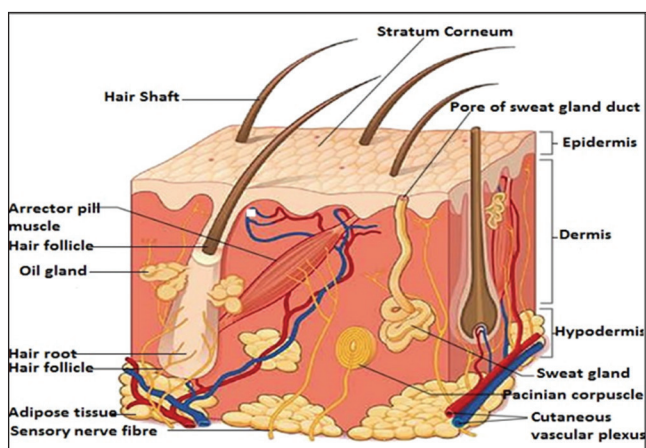
**Table 1: Advantages and disadvantages of TDDS**

Advantages of TDDS [2,3]	Disadvantages of TDDS [4]
Reduce the peak plasma levels of drug this leading to decrease side effect	Drugs having very low or high partition coefficient fail to reach systemic circulation
Reduce the fluctuation in plasma levels of drugs	Patients having higher molecular weight fail to penetrate the stratum corneum
Avoid 1 <sup>st</sup> pass metabolism of drug	High melting of drug due to low solubility of both water and fat
It is a painless treatment	
Enhancement of patient compliance	
Reduction of dosing frequency	
Easy elimination of drug delivery in case of toxicity	

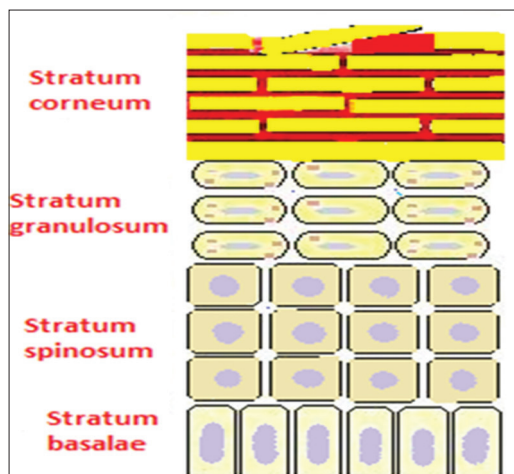
TDDS: Transdermal drug delivery system

**Table 2: Thickness of different skin region**

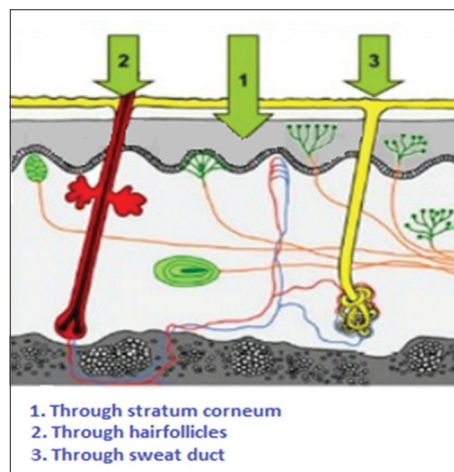
Skin region	Thickness (µm)
Palm	400
Forehead	13
Back	10
Abdomen	15
Forearm	16
Scrotum	05



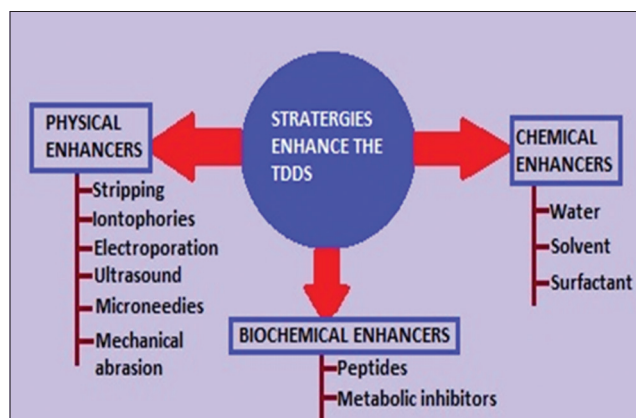
**Fig. 1: Normal skin structure**



**Fig. 2: Different layers of epidermis**



**Fig. 3: Drug penetration pathway**



**Fig. 4: Enhancement strategies of TDDS**

Three strategies are used for enhance TDDS (Fig. 4). They are chemical, physical, and biochemical enhancement. When a compound is bind or interact with stratum corneum contain lipoidal membrane there by increase the permeability is known as chemical enhancement [12,13]. Biochemical enhancement directly increases the permeability of stratum corneum lipid membrane and also indirectly affects the skin permeability through change in the lipid metabolism [14]. Physical enhancement increases the drug delivery using some devices such as stripping, iontophoresis, electroporation, ultrasound, microneedles, and mechanical abrasion [15,16].

**TYPES OF TDDS [2,17]**

TDDS classified into three types

1. Reservoir system
2. Matrix system
3. Microreseviour system.

dm=Change in mass of material, g  
 dt=Change in time, sec  
 D=Diffusion coefficient, cm<sup>2</sup>/sec,  
 S=Barrier surface area, cm<sup>2</sup>,  
 dC=Change in concentration of material, g/cm<sup>3</sup>.

### Reservoir system

In this system, drug reservoir can be aligned between backing layer and rate controlling membrane. Drug may be in the form of suspension, gel or solution. These drugs are dispersed on the solid polymeric matrix (Fig. 5).

### Matrix system

The matrix system is classified into two types of systems (Fig. 6):

- Drug adhesive system: The drug reservoir is formed by the dispersion of drug to an adhesive polymer; then, it is spread on the medicated adhesive polymer or melt on backing layer.
- Matrix dispersion system: The drugs are homogeneously dispersed in the lipophilic or hydrophilic polymer matrix. The drug having polymer is fitted on a particular base plate. From a drug impermeable backing layer, it self spreads to form a strip of adhesive rim instead of applying the adhesive or phase of drug reservoir.

### Microreservoir system

This system is the combination of matrix dispersion and reservoir. First drug is dissolved in an aqueous solution of water-soluble polymer, then it is dispersed in lipophilic polymers to form microscopic spheres of drug reservoir (Fig. 7).

### COMPONENTS OF TDDS

- Release liner: This liner should be chemically inert. This liner provides intimate contact to skin. A protective line is covering the patch during the storage condition. It is removed before the application of patch to the skin.
- Backing layer: This layer is protecting the patch from the external environment. It should be a penetration enhancer and it is made up of different types of polymers such as polyethylene, polyolefin, and polyester film [18].
- Membrane: This layer is cover or seals the backing to forming a pocket. Drug matrix occupies in this pocket.
- Enhancers and excipients: Different types of enhancers and excipients are increasing the skin permeability, e.g., Propylene glycol, isopropyl myristate, and n-methyl-pyrrolidone [19-21].
- Pressure sensitive adhesive: This binds to the skin due to the intermolecular and intratomic force and it achieves good contact [22].

### POLYMERS

Polymers are the backbone of TDDS. Polymers play a key role in human body. Polymers are classified into three types: Natural, semisynthetic, and synthetic (Fig. 8). Selection of polymer is very important for the development of product. And also polymers having several ideal properties, these properties are playing a major role in this system. Ideal properties such as [23,24]:

- It should be chemically inert.
- It should be nontoxic.
- It doesn't decompose during storage.
- Diffusion of drug is dependent on the chemical, physical character of polymer and also depends on molecular weight of polymer.

Main uses of natural polymer are it is biodegradable, good cytocompatibility. Synthetic polymers are mainly used for different purposes such as film (polyethylene), rope and automotive (polypropylene), insulation and packaging (polystyrene), cable wire insulator (polyvinyl chloride), and aqueous soluble thickening agent (polyvinyl alcohol) [25,26]. Different types of polymers are used based on the type of actions. The polymers and drugs are arranged like a "sandwich" model in the TDDS. Polymers are preventing the leakage of drugs and provide a sustained release into the body. The polymers are selected depend on the pH of particular region of body. The polymers swell and release the drug at only that region of pH. In TDDS using different polymers given below in Table 3 [27,28].

### ROLE OF ADHESION IN DRUG DELIVERY

In TDDS, main principle is it selectively adheres to the skin and provides drug release. Drug delivery is varied in age and gender function.

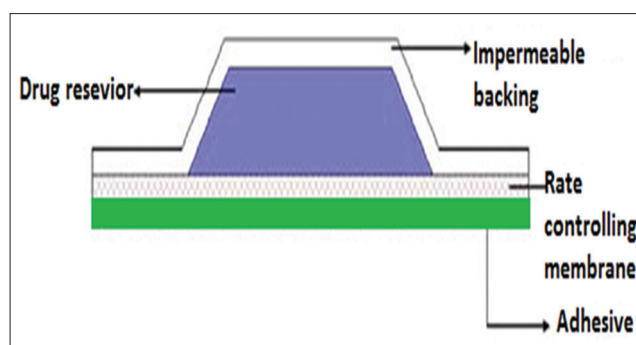


Fig. 5: Reservoir system

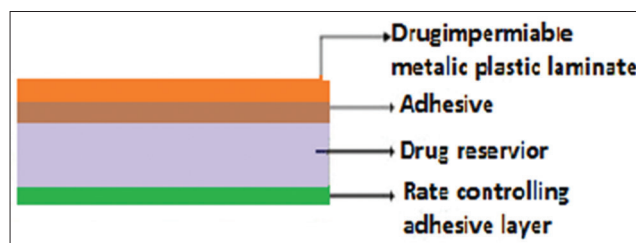


Fig. 6: Matrix system

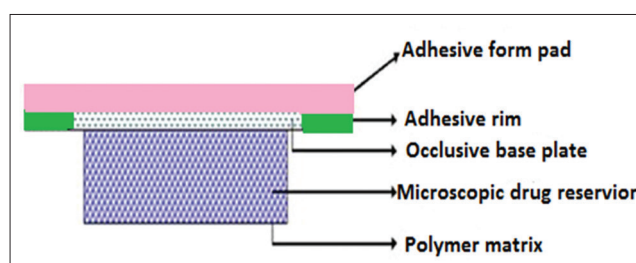


Fig. 7: Microreservoir system

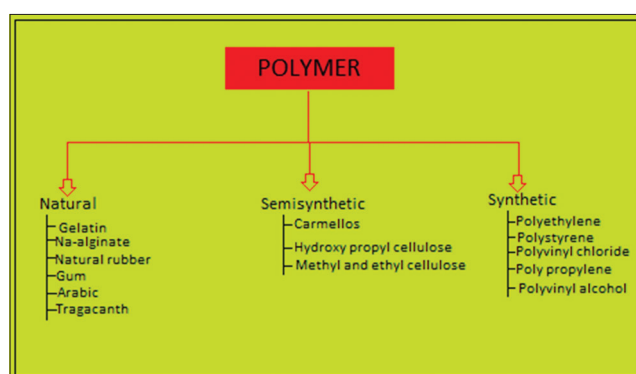


Fig. 8: Classification of polymer

Because in this system drug release is through the skin and also younger and older patients having different skin natures. Younger skin is greater dehydrated while aged skin has less moisture content so younger skin has more elasticity than aged skin so we carefully select the adhering material for the drug release. This type of condition role of adhesion is very important [29]. Here, drug absorption based on the drug partition between TDDS and skin. Good permeation and action is depending on the proper adhesion of patch. After the application of patch the adhesion covers the particular effective area, that area only provides greater action [30]. And also so many factors are affecting the drug absorption such as thickness of skin, skin temperature, blood flow, no. of hair follicles, skin cleansing, sweat gland function, pH of skin

Table 3: Types of polymers used in TDDS

Types	Polymers
Matrix formers	Poly ethylene glycol Ethyl cellulose and polyvinylpyrrolidone Hydroxy methyl cellulose Organo gels
Rate controlling	Silicon rubber Polyurethane
Pressure sensitive adhesives	Silicon Polyisobutylene Polyacrylates
Thermoplastic hot melt pressure sensitive adhesives	Compounded Ethylene vinyl acetate co-polymer Paraffin wax Low density polypropylene Styrene-butadiene co-polymer Ethylene-ethacrylate co-polymer Uncompounded Polyesters Polyamides Polyurethanes
Backing layer	Polyurethane PVC PE EVA

PVC: Polyvinylchloride, PE: Polyethylene, EVA: Ethylenevinyl acetate

surface, and body temperature [31-33]. After the application of patch, it warms the skin temperature that lead to increase the flow of drug to skin. During the gradually increasing of skin temperature swells the polymer and sustained release of drug to stratum corneum [34].

#### FACTORS AFFECTING DRUG PENETRATION

Two types of factors affect the drug penetration such as biological and physiochemical factors these factors are listed below [35-38]:

- Biological factors
  - Skin age
  - Skin condition
  - Species difference
  - Blood supply
  - Skin metabolism
  - Regional skin site.
- Physiochemical factors
  - Temperature and pH
  - Skin hydration
  - Diffusion coefficient
  - Drug content
  - Molecular size and shape
  - Partition coefficient.

#### CONCLUSION

TDDS more convenient method for the delivery of drug to human body. This type of drug delivery patients can easy to handle. It provides a sustained release through the skin. Skin and patch adhesion is the important factor for the delivery of drug. Drug should have definite molecular weight about <500 Dalton (low molecular weight) and also lipophilicity and water solubility should be medium level. Otherwise, drug penetration and its therapeutic effect cannot reach the target site. During the delivery of drug, it provides a constant blood flow and also predetermined rate of drug release. The enhancement techniques such as iontophoresis using small voltage and electrophoresis using high voltage to passing the lipid barrier and push the drug molecule into systemic circulation.

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