AN OVERVIEW OF TRANSDERMAL DELIVERY SYSTEM

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Received: 13 May 2017, Revised and Accepted: 01 July 2017

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.

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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 µm)
2. Dermis (0.3-3 mm)
3. Hypodermis.

Epidermis

The strated, vascular, and cellular epidermis is 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 basale (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.

\[ J = \frac{m}{At} \]  

\[ J = \text{Flux,} \]
\[ m = \text{Mass of compound,} \]
\[ A = \text{Area of cross section,} \]
\[ t = \text{Time.} \]

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].

\[ \frac{dm}{dt} = -DS \left( \frac{dC}{dx} \right) \]
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]. Physical 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. Microreservoir system.
Reservoir system
In this system, drug reservoir can 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 classified into two types of systems (Fig. 6):
- Drug adhesive system: The drug reservoir formed by the dispersion of drug to an adhesive polymer; then, it 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 drugs having polymer is fitted on a particular base plate. From a drug impermeable backing layer, it self it spread 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 enhancers and it is made up of different type’s polymers such as polyethylene, polyolefin, and polyester film [18].
- Membrane: This layer is cover or seals the backing to forming a pocket. Drug matrix is occupy 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 is bind to the skin due to the intemolecular and intratatomic 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 depended on the chemical, physical character of polymer and also depend 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 “sand witch” model in the TDDS. Polymers are preventing the leakage of drugs and provide a sustained release into the body. The polymers are select depend on the pH of particular region of body. The polymers are 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 adhere the skin and provide drug release. Drug delivery is varied in age and gender function.
Polymers used in TDDS

| 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, Polyeurethane |
| Pressure sensitive adhesives | Silicon, Polyisobutylene, Polycrylates |
| Thermoplastic hot melt pressure sensitive adhesives | Ethylene vinyl acetate co-polymer, Paraffin wax, Low density polypropylene, Stereone-butadiene co-polymer, Ethylene-ethylacrylate co-polymer, Uncompounded Polymers, Polymides, Polyurethanes |
| Backing layer | Polyethylene, PVC, PE, EVA |

PVC: Polyvinylchloride, PE: Polyethelene, 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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