IJBPAS, January, Special Issue, 2022, 11(1): 169-177

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

A RECENT REVIEW ON TRANSDERMAL DRUG DELIVERY SYSTEM

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Received 10th June 2021; Revised 11th July 2021; Accepted 20th Aug. 2021; Available online 15th Jan. 2022

https://doi.org/10.31032/IJBPAS/2022/11.1.1018

ABSTRACT

An important advancement in the field of medicine has been done by the transdermal drug delivery but yet fully has to gain its capability instead of oral delivery and hypodermic injections. Transdermal drugs have been derived to provide through skin to the systemic circulation for therapeutic benefits. These drugs are being administered in controlled & continuous manner & allows drug with short biological half-lives and elimination of undesirable side-effects (elimination of pulsed entry into systemic circulation). This narrative review article provides information about advantages, disadvantages, factors and recent technology involved in Transdermal drug delivery system.

Keywords: Advancement, Transdermal drug delivery system, recent technology, therapeutic benefits

INTRODUCTION

Different types of skin penetration techniques are widely used to improve the penetration for increasing the bioavailability. Traditional dosage forms such as tablet, capsules and injections are most widely used but now a days transdermal drug delivery system is preferred. This system is delivered drug through topical application (patches or ointment) without any side effects at an adequate quantity.[1]

Merrimu Webster coined the term transdermal in 1944.[2] The transdermal drug delivery system (TDDS) concept was proposed by United States (US) scientists in & around 1980s & 1990s. The Transdermal drug delivery system first came in the United States 20 years ago & was named as transdermal scop for nausea & vomiting which was approved by Food and drug administration in 1979 and FDA also approved Nicotine patches in 1984.[3]

This type of drug delivery system reduces the side effect like presystemic metabolism improves patient reliability & decreases the risk of gastro intestinal problems. The drug administered releases into the patient, permitting a stable blood profile and results in reducing systemic complications.[4]

The exact mechanism of drug kinetics is still unknown as we know transdermal drug delivery system uses passive diffusion for transport drugs across skin. If an excessive drug is delivered and if it is quickly released, then it can lead to drug toxicity. If the drug is coneyed at slow rate, it may lead to loss of effectiveness. Drug dosage, rate of liberated and functioning of cell receptors are the responsible factors for carrying out this system successfully.[5,6,7]

Table 1: Characteristics Of Transdermal Drug Delivery System[8,9,10,11,12]

S. No.	CHARACTERISTICS	COMMENTS
1	Mean Life	Up to 2 years
2	Molecule size	<40cm2
3	Dosage	Once in a day or once in a week
4	Susceptibility	Nonirritant
5	Molecular weight	< 1000 daltons
6	Affinity	Lipophilic & Hydrophilic
7	Melting point	Low

Advantages of Drug:

- Escape GIT Absorption
- Escape First pass hepatic metabolism of drugs
- More enhanced and acceptable patient compliance
- Self-medication is possible
- Reduce frequency of doses
- Controlled release drugs at optimal rate

- Reduces side effects
- Provides appropriateness for self-application.

Disadvantages of Drug:

- Large daily dose should not be given
- Local irritation is the problem
- Drugs with biological long half-life cannot be prepared in TDDS.
- It is not easy to administer.
- It is not economical.[13,14,15,16,17]

Basic Principle Of Transdermal Drug Delivery System

Human Anatomy & Physiology of Skin:

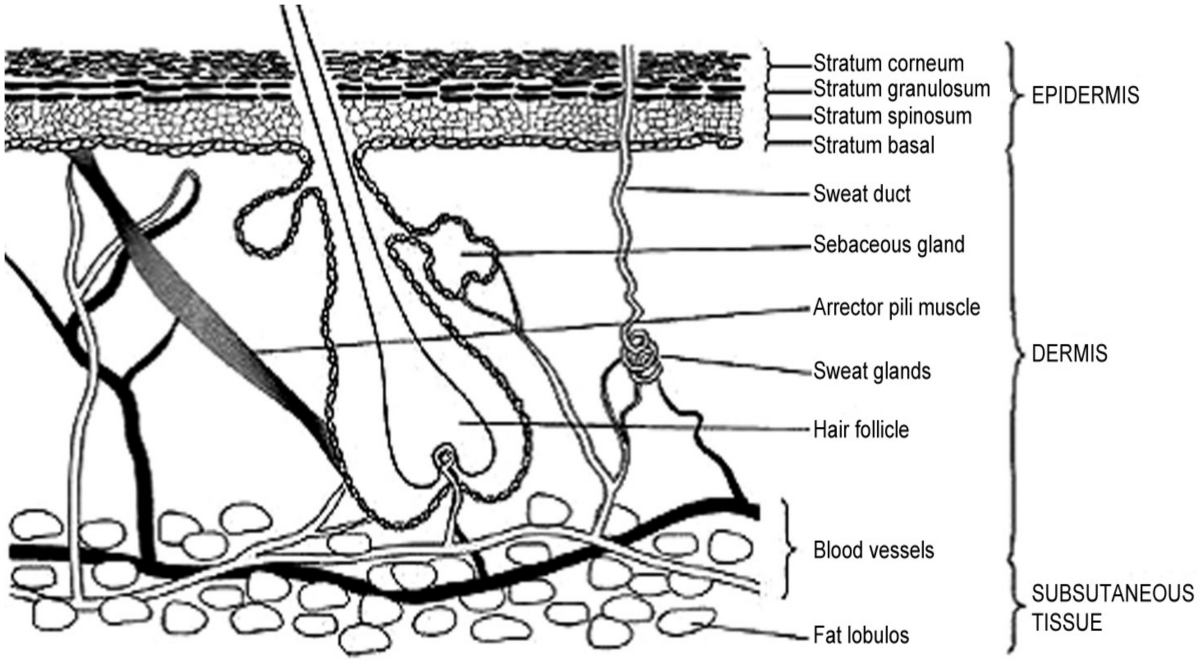

Figure 1.1 Cross-section view of human skin showing different cell layers and appendages[18]

There are three general coating or layers of skin. In order from most superficial to deepest they are the:

- Epidermal layer
- Dermal layer
- Sub-cutaneous fat layer

Epidermis: It is the outermost layer of skin. It consists stratified squamous epithelium & keratinocytes with Langerhans cells, melanocytes, and Merkel cells as a supporting structure consisting the nerve and vascular networks for providing nourishment of the epidermis.

5 layers of epidermis:

➢ Stratum corneum

➢ Stratum lucidum

➢ Stratum granulosum

➢ Stratum spinosum

➢ Stratum basale

Stratum Corneum (Prickle cell layer): Stratum corneum is outermost covering and is made up of keratinocytes. It limits transcutaneous penetration of drug. [19] Stratum corneum consists of lipid & proteins like keratin. It is lipophilic in nature. [20]

Functions:

➢ It provides toughness & flexibility .

➢ Lipids carry water resistant property.

➢ This layer provide protection the deeper layers of skin from microorganisms & lacerations and as it is having dead cells.

➢ It is selective in nature as it allows restricted entry of substances.

Stratum Lucidum (translucent Layer): It is being composed of keratinocytes.

Functions:

➢ This layer helps to keep skin safe from side effects of Ultraviolet radiation exposure.

➢ It lessens the resistance between translucent layer and granular layer.

Stratum Granulosum (Granular Layer): It is a bare mantle layer and consists of keratinocytes. Apoptosis of keratinocytes takes place in stratum granulosum. [21]

Functions:

➢ The Lipid Layer prevents the passage of water from skin

➢ This layer act as protective barrier.

Stratum Spinosum: It is having polygonal keratinocytes**.**[22]

Functions:

➢ This layer helps to strengthen or stiffen and prevent scraping of skin.

Stratum Basale: It is a very broad & deep layer of epidermis consists of keratinocytes & a few stem cells. The tanofilaments are closely associated to desmosomes and hemidesmosomes. 23

Dermal layer: It is the dense & bulky layer of skin. It consists of collagenous fibres & connective tissues such as reticular & elastin fibres to provide mechanical strength & flexibility. It is of two types in respect of organization: Upper papillary layer & Lower reticular layer.

Upper papillary layer: It consists of irregularly arranged connective tissue that consists of collagenous and elastic fibers. Some of fingerlike projections called dermal papillae convey vasa recta that nourishes the outer layer of skin.24

Lower reticular layer: It consists of heavy connective tissue having mesenchymal cells, collagen fibres and coarse elastic fibres. It contains the following:

➢ Neurons

➢ Vascular network

➢ Sebaceous follicles

➢ Glands25

How TDDS works?

Transepidermal Absorption:

The penetration of drug by transepidermal route into the stratum corneum takes place with the help of diffusion process across the tissues as stratum corneum is the main resistance for absorption through this route. Thus, permeation requires partitioning of the drug into stratum corneum & frequent crossings of cell membrane.[26]

Transfollicular Absorption:

It targets drugs to the hair follicles by means of micro- and nano-particles of drug. It comprises hair follicles & sebaceous glands. It follows shortest route by which drug enters into systemic circulation for administering drug molecules on a large area.[27,28]

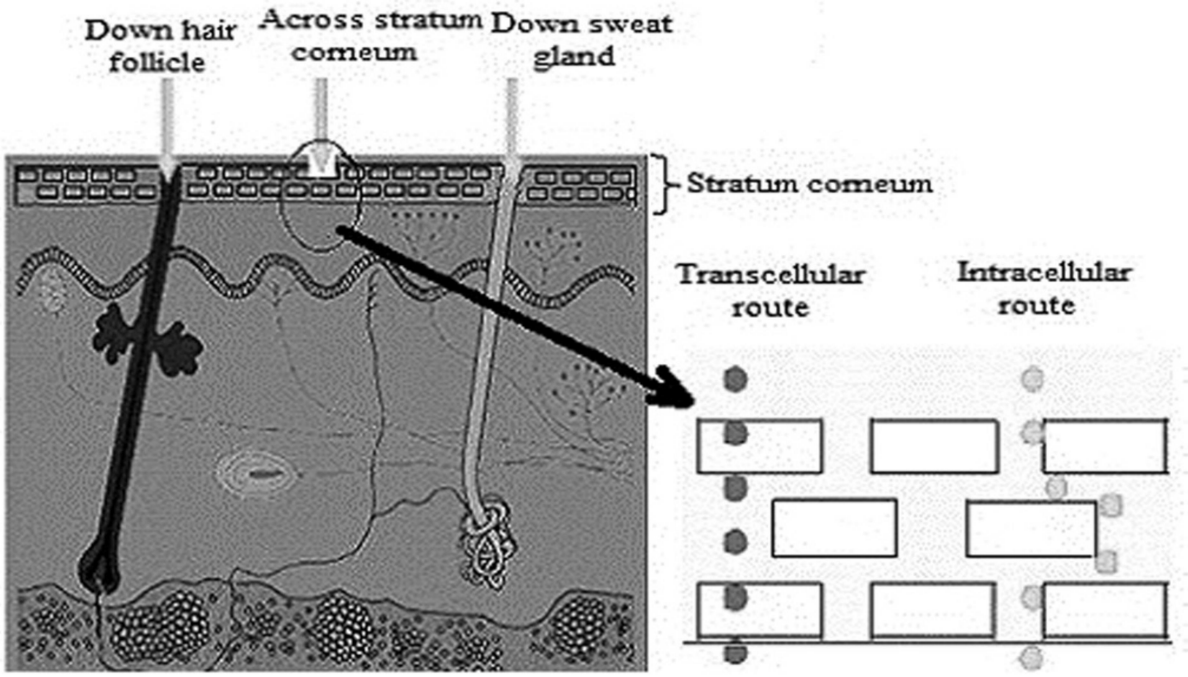

Figure 1.2 Drug penetration pathways across skin.[29]

Common Factors affecting transdermal drug delivery system:

Biological factors:

a) Skin : The skin serve as a resistance barrier for many chemical compounds.

b) Circulation: Changes in the blood circulation can influence the transdermal drug delievery system.

c) Skin texture: Drug penetration depends upon skin thickness, density & nature of skin.

d) Metabolic process: The metabolic process of the skin regulates the drug permeability factor.

Physicochemical factors:

a) Hydration or Aquation: As the skin hydration increases, permeability of drug also increases.
b) Temperature and pH: As the temperature & pH varies, permeation of drug also increases.
c) Diffusion constant: Drug perforation depends on diffusion coefficient & its properties
d) Drug potency: Higher the drug potency, higher drug will be more across the barrier.
e) Molecular weight: Drug penetration is inversely proportional to molecular weight.

As we know, oral drug delivery system and injection therapies have low permeability into stratum corneum. Therefore, it requires transdermal route that allow drug release at optimal rate. Recently, some novel physical enhancement techniques seemed to enhance transdermal drug delivery system e.g., iontophoresis & sonophoresis.[30]

Recent technology used in transdermal drug delivery system:

- Iontophoresis
- Sonophoresis

Iontophoresis: It is also termed, as ion transfer is the introduction of substances into the body for therapeutic purposes by means of a low voltge direct current. According to recent studies, iontophoresis promote transdermal drug penetration by increasing permeability of the stratum corneum for producing therapeutic effects. The basic mechanism of iontophoresis is that when therapeutic current is applied to a solution (containing drug in ionic form), electrolysis occurs & brings about movement of positive charged ions towards the negative pole and the negatively charged ions towards the positive pole. Then, it will pass through the skin and into the tissues and form compounds in the blood stream.

Phonophoresis: In this method of transdermal drug delivery, the drug is driven by therapeutic ultrasound. Phonophoresis is defined as the migration of particles of drug into deeper layer of the skin and subcutaneous tissues under the influence of the ultrasound. The therapeutic effects produced in the tissues are caused both by ultrasound and the nature of drug that is applied. The basic mechanism is that drug molecules administered into the target tissue through electrolysis processes to release therapeutic compounds in blood circulation for producing therapeutic effects.[31]

CONCLUSION: The use of iontophoresis & phonophoresis therapeutic approaches has been explored to a great extent although skin permeability & depth of penetration caused by iontophoresis & phonophoresis are different. Regardless, both these promising approaches are being used to a greater extent, and come up with new prospective in clinical settings.

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