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Review Article

A Overview of the Transdermal Drug Delivery System

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ABSTRACT

The skin offers an accessible & convenient site for the administration of medication. The transdermal drug delivery system has been a safe &effective drug delivery system, it aims to deliver the drug through the skin at a predetermined rate and controlled rate. If a drug has the right mix of physical chemistry and pharmacology, transdermal delivery is a remarkably effective route of administration. The transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose & medication through the skin & into the bloodstream. Often, this promotes healing to an injured area of the body. An advantage of the TDDS route over other types of medication delivery such as oral, topical, and IV is that the patch provides a controlled release of medication into the patient. Due to the large advantages of TDDS, many new researches are going on today to incorporate newer drugs via this system.

INTRODUCTION

The transdermal drug delivery system has been in existence for a long time, in the past the most commonly applied system was topically applied creams and ointments for dermatological disorders [1]. Transdermal drug delivery not only provides controlled, constant administration of the drug but also allows continuous input of the drug with a short biological half-life & eliminates pilsed entry into the systemic circulation [2].

DEFINITION: A Transdermal patch, also known as a skin patch, is a Medicated adhesive patch that is applied to the skin and is used to deliver an amount of medication into the circulation [3].

ADVANTAGES AND DISADVANTAGES

Advantages:

[1]. Self-medication is possible
[2]. A side effect is reduced
[3]. Plasma drug concentration becomes maintained [4]
[4]. Extendable drug action

Disadvantages:

[1]. Chances of an allergic reaction

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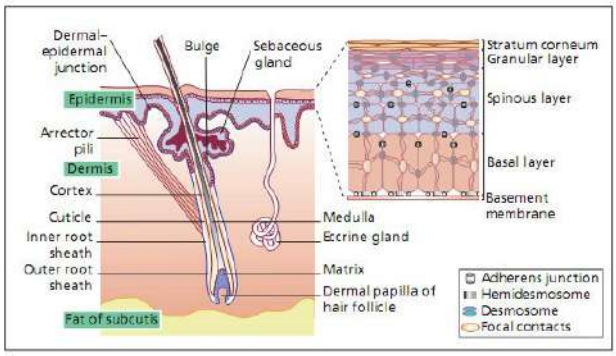
[2]. High molecular drugs can not attain a therapeutic level

ANATOMY AND PHYSIOLOGY OF SKIN



Skin is the largest organ, 16% of total body length 1.5-2.0 m & weight 6-10%. Skin is made up of different layers of cells. Human skin are of two types SKIN (non-hairy) and hair-bearing skin has both hair follicles & sebaceous gland.

Layers of Skin:

Epidermis: Epidermis is the stratified squamous, keratinizing epithelium. The thickness of the palm is 0.06mm, on the eyelid 8% melanocytes are present, and 905 keratinocytes

Four layers of epidermis

i) Stratum Basale
ii) Stratum granulosum
iii) Stratum corneum
iv) Stratum spinosum

Dermis: Dermis is the layer of 3.0- 5.0 mm thick layer % made by lattice connective tissue, containing veins, lymph vessels & nerve vessels that reach inside 2.0mm of skin surface & give sink condition to most atoms entering the skin.

Hypodermis: Fat subcutaneous tissue underpins the dermis and epidermis. Control temperature gives wholesome & mechanical security. It acts as an absorber and act like insulates the body to prevent heat loss.

MECHANISM OF TRANSDERMAL PERMEATION

- Permeation of drug by feasible epidermis.
- Sorption through stratum corneum.
- Take up the drug moiety through the capillary system in the dermal pupillary layer.

Function of Skin:

- Protection – it is a primary physical barrier that the human body has against the external environment, protection from microorganisms [6].
- Sensation – to pain, temperature, touch & deep pressure
- Mobility – allowing smooth movement of the body
- Endocrine/exocrine activity – the biochemical process involved in vitamin D production i.e., essential for calcium absorption and normal metabolism

Whereas, exocrine activity releases water, urea & ammonia & skin secretes like sweat & pheromones, etc.

- Immunity – provides immunity against pathogens
- Regulations of temperature- help in thermal regulation

TRANSDERMAL DRUG DELIVERY SYSTEM

Basic components of TDDS:

Polymer Matrix: Polymer controls the release of the drug from the device

[1] The molecular weight, glass transition temperature & chemical functionality of the polymer should be such that the specific drug diffuses properly & gets released through it.
[2] It should be stable, non-reactive & Inexpensive
[3] Nontoxic & non-antagonistic to the host
[4] Mechanical properties of the polymer should not deteriorate excessively when large possible useful polymers for devices are

- Natural polymer
- Synthetic polymer
- Synthetic elastomers

Drug-: A drug can be chosen with great concentration which can have both

physiochemical properties as well as biological properties

Permeation Enhancer: A Compound that promotes skin permeability by altering the skin as a barrier to flex a desired penetrant**.** The flex, of the drug across the skin can be written as: -

J=D dc/dx

Properties of permeation enhancer:

- Controlled & reversible enhancing action
- Chemical & physical compatibility c- drug & often pharmaceutical excipients
- Should not cause loss of body fluid, electrolytes

Other endogenous materials:

- The polymer should be stable
- Polymer should be nontoxic
- The polymer should be easily manufactured
- A large number of active agents are incorporated into it
- Odorless, colorless, economical & cosmetically acceptable

Other excipients: Solvents are used as chloroform, methanol, acetone & isopropanol to prepare drug reservoir**s.** e.g.- transdermal patches is also used.

[1]. **Pressure Sensitive Adhesive:** PSA is a material that helps in maintaining contact between the transdermal system and skin surface. It is removable from smooth surfaces without leaving residue e.g.- polyacrylamides, polyisobutylene, and silicon-based adhesives [8].

- It is based on patch design& drug formulation.

[2]. **Backing laminates:** It is chemical resistant & excipients may be compatible because of prolonged contact between the backing layer& excipients, drug, or penetration enhancer through the layer.

Release liner: During storage, patches are covered by a protective layer that is removed & discarded before the application of the patch to the skin. However, liner is in intimate contact with the delivery system, it should comply with specific requirements regarding chemical inertness & permeation to the dry, permeation enhancer & water [9].

TRANSDERMAL SYSTEMS CAN BE DIVIDED INTO TWO LAYER SYSTEMS:

- The single-layer drug in adhesive
- The multi-layer drug in adhesive

The single-layer drug in adhesive: In this type of patch, the adhesive layer not only serves to adhere the various layers together, along with a system to the skin but is also responsible for releasing the drug

Multi-layer drug in adhesive: This patch is similar to a single-layer system in that both adhesive layers are also responsible for the release of the drug.

Reservoir: The single as well as multi-layer drug in an adhesive system. The reservoir transdermal system has a separate drug layer, drug layer is a liquid compartment containing a drug solution or suspension separated by an adhesive layer.

Matrix: Drug layer of a semisolid matrix containing a drug solution or suspension. The adhesive layer in this patch surrounds the drug layer [7].

ROUTE OF DRUG PENETRATION ACROSS SKIN:

Three potential entry macro routes to the viable tissue-

- Via sweat gland
- Across continuous stratum corneum [Diffusion]
- Through the hair follicle then the associated sebaceous gland.

There are two possible routes of drug penetration:

- Trans epidermal pathways
- Trans appendageal pathways

Drug penetration across the liquid skin, namely the trans epidermal & Trans appendageal pathway. The transdermal pathway involves the passage of

molecules through stratum corneum, multilayer & multicellular barriers. Trans epidermal penetration can be termed intra or inter-cellular. The intracellular route through corneocytes, terminally differentiated keratinocytes, allows the transport of hydrophilic or polar solutes. The trans-appendageal route involves- the passage of molecules through the sweat gland & hair follicle.

KINETICS OF TRANSDERMAL DRUG DELIVERY:

Percutaneous absorption of molecules is very important. Percutaneous absorption is the penetration of substances in various layers of skin.

Percutaneous absorption of molecules is a step-in process involving:

- **Penetration:** When a substance enters the skin layer.
- **Portioning:** The partitions from stratum corneum into aqueous or soluble viable epidermis.
- **Diffusion:** Viable epidermis & into the upper dermis.
- **Permeation:** Molecule penetrates from one layer to another.
- **Absorption:** Substance uptake & into the systemic circulation.

Step 1: [Penetration] Drug entry into a skin layer.

Step 2: [Petitionary] From skin layer into aqueous viable the upper dermis.

Step 3: [Diffusion] Drug permeation from one layer into another.

Step 4: [Permeation] Uptake of a drug into the systemic circulation.

Step 5: [Absorption] Drug reaches to designed site for action.

FACTOR AFFECTING TRANSDERMAL PERMEABILITY

Parameter	Factors
Formulation	Boundary layer Thickness Temperature Geometry of system Polymer
	Vehicles Porosity of membrane
Skin	Species Condition of skin (healthy, diseased, pre-treated, secretion)
Adhesion	Size/shape Cohesiveness
Bio-pharmaceutical	The half-life of the drug Pharmacological blond level [6]

FORMULATION OF TRANSDERMAL PATCH

1) Membrane permeation-controlled system: Multilaminate processes, such as Transdermal Nitro, can be used in these systems. Three substrates are kept together by two layers of drug-containing glues in these items. The medicine is first transformed into the physical/chemical form needed for inclusion into the final product. To obtain a homogeneous mixture. The drug adhesive component and excipients are combined with a solvent. These adhesive compositions are applied as a thin coating to moving objects and then dried to eliminate the solvent. The dried adhesive film and other layers are then laminated together to produce a five-layer product, that includes a release linear contact adhesive control membrane, a drug, and a backing substrate. The finished dosage form is then printed and die-cut from the lamination. Individual foil pouches are then used to package the punished product. The item is automatically put into to continuously moving web of pouch stock that is sealed around the dosage form after inspection [10].

2) Adhesive dispersion type system: That system can be divided into the following parts.

- **Preparation of individual matrix:** To make a standard or stock solution, the raw ingredients are dissolved into an organic solvent. The matrix solution is then made by combining the stock solution with the chemical listed in the formulation. The active substance is mixed with additional chemicals.

- **Coating of individual matrix layer:** Coating the solution creates a distinct layer. Using a coating machine to remove the solvent from smooth paper or film. This machine is made up of two parts.
- **Coating unit:** Coating solvent-based composition onto the suitable web. Depending on the matrix solution viscosity, flow ability, and surface tension.
- **Drying unit:** Closed to the outside and immediately attached to the drying machine to prevent evaporation of the solvent and active ingredients. Bypassing the coated web through a drying channel with a transport system such as a cranked shaft or a conveyor belt, the solvent from the adhesive spot is evaporated.

3) Matrix diffusion-controlled system: The medications are suspended in an insoluble hydrophobic matrix that is stiff and nonswellable. Insoluble polymers like PVC and fatty compounds are employed for stiff matrices. The drug is usually kneaded using a solution of PVC in an organic solvent for plastic material, and the granular waxy matrix is made by distributing the drug in molten fat. A swellable matrix system is useful for maintaining the release of extremely water-soluble drugs after the granules have been compacted into tablets. These matrices are generally made of hydrophobic gums, which are generally natural or synthetic. The medicine and the gums are granulated together and crushed into tablets using a solvent such as alcohol. The simultaneous absorption of water and desorption of medication from such initially dehydrated hydrogel is accomplished by the swelling diffusion process. The gum expands, and the drug diffuses out of it.

4) Micro-sealed dissolution-controlled system or encapsulation: The microencapsulation procedure coats or encapsulates the drug particle with a slowly dissolving solution such as cellulose, PEGs, and wax. The resultant pellets can be placed in firm gelatin capsules. The solubility and thickness of the coating can range from 1 to 200 microns [11].

MARKETED PRODUCTS OF TDDS

TDD products are continuing to provide actual therapeutic value to patients all across the world. In the United States, more than 35 TDD products have been approved for sale, and roughly 16 active components have been approved for usage in TDD products across the world.

Product Name	Drug	Manufacturer	Indications
Androderm	Testosterone	GlaxoSmithKline	Hypogonadism in Males
Catapress-TTS	Clonidine	Alza/boehinger ingelhein	Hypertension
Alora	Estradiol	Theratech	Post menstrual syndrome
Climara	Estradiol	3m pharmaceutical/berlex labs	Postmenstrual syndrome

CONCLUSION

Transdermal drug delivery system & its evaluation process details as a ready reference for the research for the scientists who are involved in TDDS. It has great potential, being able to be used for both hydrophobic & hydrophilic acting substances into promising deliverable drugs.

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