A REVIEW ON TRANSDERMAL DRUG DEIVERY SYSTEM

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Abstract

Transdermal route of drug delivery can achieve local and systemic therapeutic effects. Transdermal drug delivery is an attractive substitute for oral drug administration as it bypasses first pass metabolism, gastrointestinal effects and, moreover, it can overcome the poor patient compliance associated with other drug delivery routes. Transdermal drug delivery is self-administered, allowing the drug to pass through intact skin over a controlled period of time to achieve a local or systemic. The microneedle-based transdermal medication delivery technology is advantageous since it avoids the stratum corneum barrier. It is possible to classify microneedles based on the material they are made of (solid, coated, dissolving, etc.). Transdermal drug delivery (TDD) is discussed in this review, as well as the factors that can effect TDD, the substances utilized in the formulation of TDDS, drug penetration, and various formulation processes.

***Keywords**: TDDS, Macro-needles, absorption, bioavailability*

Introduction

Because the stratum corneum (SC) of the skin is impermeable to most biopharmaceuticals and small molecule biotherapeutic medicines, TDD has been limited. Figure 1a shows the skin's anatomy. The hydrophobic characteristic of the skin's outer layer limits percutaneous distribution to transdermal patches and ointments. Because the skin is such a versatile biological barrier, the pharmacokinetic properties of drugs treated topically vary greatly (Fig 1a). The SC is the rate-limiting phase in the process of cutaneous penetration or transdermal absorption. Passive diffusion transports products to the viable epidermis (Fig 1b). Pharmaceutical companies and researchers are working hard to develop a safe and effective drug delivery method [1]. Transdermal medication administration can have both local and systemic therapeutic benefits. Transdermal medication delivery avoids first-pass metabolism,

gastrointestinal side effects, and poor patient compliance[2]. Transdermal medication administration can be utilised to achieve a local or systemic effect. Transdermal medication delivery techniques avoid difficulties such first-pass hepatic metabolism, enzymatic digestion, acidic drug breakdown, and gastrointestinal discomfort. This approach also has patient compliance, cheap costs, and regulated medication release[3]. Transdermal medication delivery devices are used to treat skin problems, angina pectoris, pain, stopping smoking, and neurological disorders like Parkinson's disease[4].

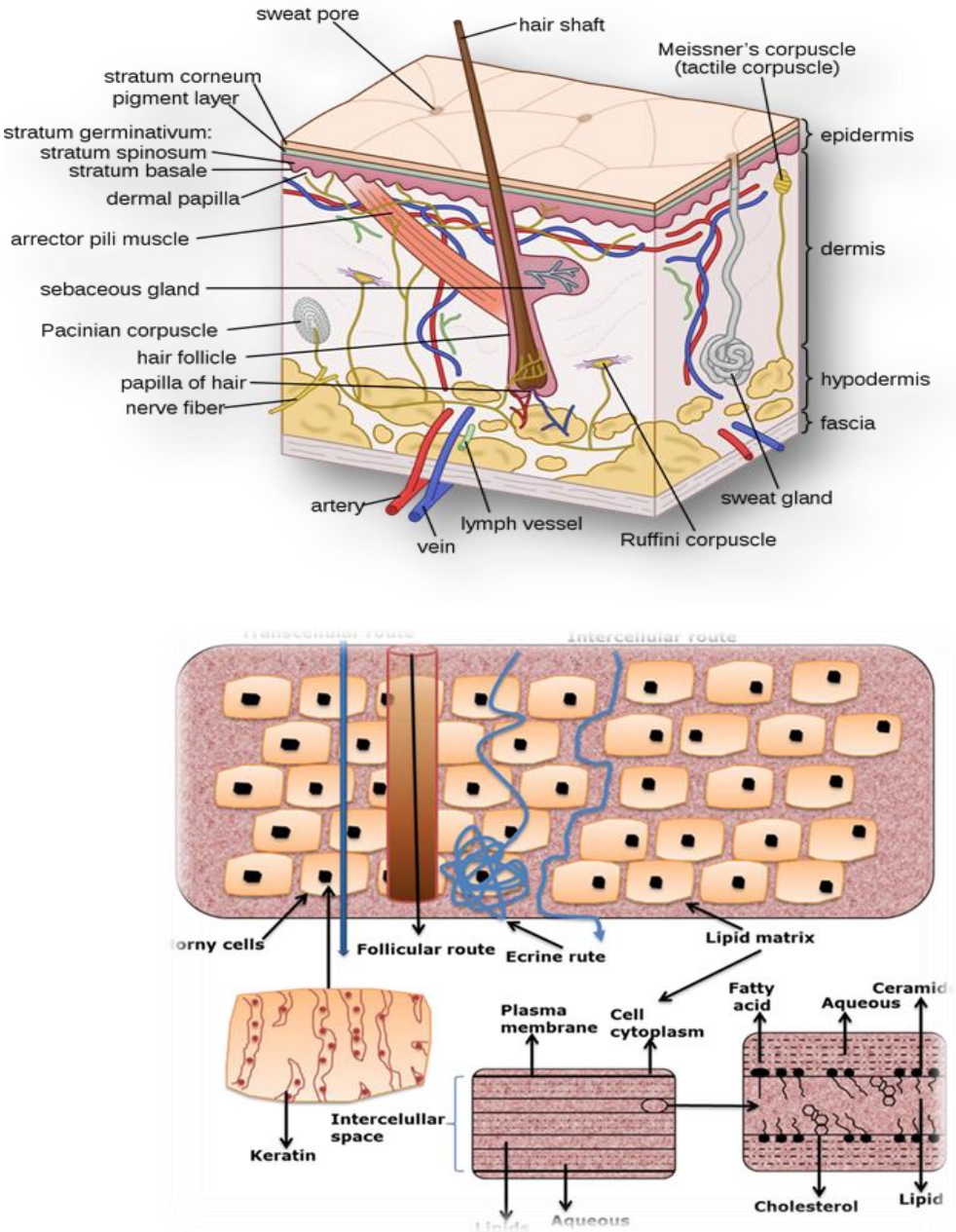

Fig: 1a Anatomy of Human Skin, 1b Routes of Percutaneous of Absorption

Types Of Trans-dermal drug delivery System

1. Reservoir system;
2. Matrix system;
3. Microresevior system;

Single-layer Drug-in-Adhesive

This system's adhesive layer contains the drug, making it unique. The adhesive layer in this sort of patch not only holds the layers together, but also releases the medicine through the skin. It has a temporary lining and a backing. The drug is mixed directly into the complexion adhesive before applying it to the epidermis[5].

Multi-layer Drug-in-Adhesive

The multilayer system is similar to the single layer system, but it adds a second layer of medicine in adhesive, generally separated by a membrane (but not in all cases). Drugs are released from the reservoir on two layers: immediate and controlled. With a removable liner and a fixed backing. The amount of drug released depends on the membrane permeability and drug molecule diffusion[6].

Reservoir

Comparatively, the reservoirs transdermal system features a unique drug layer. The sticky layer separates the drug layer from the solution or suspension. A drug reservoir is totally confined inside the shallow compartment molded from drug-impermeable metallic plastic lamination. This patch is supported by the background layer. This system's release rate is zero.

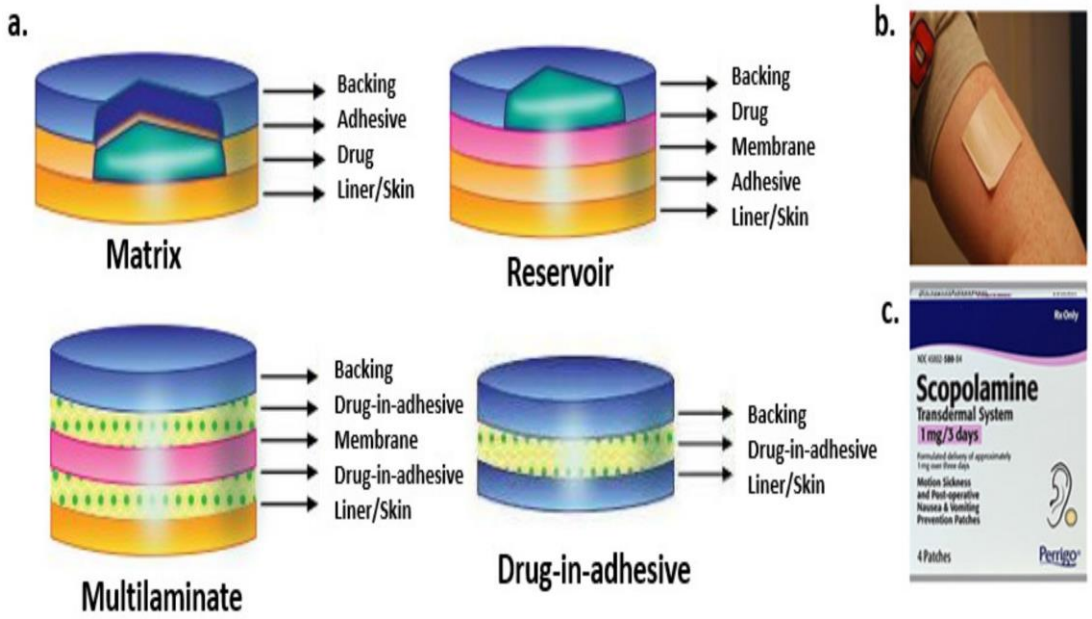

Fig: 1 Parts of Trans-dermal Patches

Advantages of transdermal route of drug administration [7]

- Maintains constant blood levels of a drug for a long time.
- The skin can give drugs, avoiding the pH changes that occur in the digestive system.
- The medication enters the bloodstream without first passing through the liver (though the skin is metabolically active).
- It is feasible to self-govern.
- The transdermal patch can be removed at any moment.

- A simplified prescription regimen improves patient compliance, reduces side effects, and reduces patient variability.
- Unlike parenteral medication, transdermal patches do not require needles.
- A transdermal patch delivers the same therapeutic effect as an oral pill, but at a lower dose.
- Intravenous infusion has numerous similarities.
- Patients who feel dizzy or sick may prefer this method.

Disadvantages of transdermal route of drug administration[7-8]

- The chemicals in patches can cause skin irritation, erythema, and possibly contact dermatitis.
- Lipophilic pharmaceuticals can only pass the stratum corneum efficiently, so they must have favourable physicochemical properties. The systemic circulation of hydrophilic medicines is unachievable without re-formulation.
- Due to the skin's impermeability, only strong drugs can be utilised in transdermal patches.
- A daily intake of 5mg is allowed.
- Body temperature and other factors affect skin barrier function, therefore it varies from person to person or generation to generation.
- Adhesives may not adhere well to all skin types, causing irritation.
- Transdermal delivery cannot achieve high blood/plasma concentrations.
- Ionic medications cannot be transdermally delivered.
- Patch fall-offs may go unnoticed.

Factors affecting transdermal permeability[9]:

The stratum corneum's transdermal permeability can be categorised into three major groups:

- The penetrants' physicochemical composition
- Drug delivery systems' physicochemical qualities
- Skin disorders, both normal and abnormal

(A) Penetrants physicochemical properties:

Skin absorption is preferable for drugs with high water and lipid soluble partition coefficients. The TPC and PC are connected (TP Coefficient). The pH of the skin and medication delivery devices affects ionogenic drug dissociation and transdermal permeability.

Surface permeability is determined by the concentration of chemicals that can flow through the skin's surface via passive diffusion.

(B) Delivery of drugs systems' physical and chemical qualities:

Transdermal penetration increases with ease of medication release from the delivery method. The interfacial partition coefficient (IPC) influences the rate of medication release from delivery systems into skin tissue. Pharmaceutical delivery systems When a medicine molecule is absorbed through the skin, the drug delivery system's makeup matters. Moisture, mixing with skin lipids, and other sorption-promoting events can change the stratum corneum's permeability, as can medication release rate.

(C) This includes skin physiology and pathology:

The horny layer, which acts as a depot or reservoir for some medications, might impact drug permeability through the skin. The lipid film formed by sebaceous gland and epidermal cell lipid production on the skin surface maintains this barrier function. Skin hydration can enhance permeability up to 8-fold.

The external temperature increased the skin penetration of salicylate and glucosteroids tenfold from 10^0 to 37^0 C.

Transdermal medication delivery techniques are divided into several different categories[10-11]:

Some of the most common types of transdermal medication delivery systems are as follows:

- Controlled permeability of polymer membranes
- Controlled diffusion in the polymer matrix
- Controlled by a gradient in the drug reservoir
- Controlled disintegration of micro-reservoirs
- Laminated structure filled with a liquid
- Laminate construction with adhesives on the peripherals
- Laminated solid-state structure
- The aforementioned subclasses

The six categories below describe how TDDS releases drugs [12].

- matrices
- Suspension in a matrix
- The final option is porous suspension.
- Membrane before solution
- Membrane upstream suspension
- Laminated membrane downstream

- **Basic Components of TDDS[13-14] :**

Both matrices and liquid reservoir patches have components. As you can see, the classes have some similarities and variances. Among those they share are

- Films with a soundtrack
- Liner Release
- Pressure-sensitive adhesive
- The active ingredient
- Permeation boosters
- Ingredients
- Microporous or semi-permeable membranes
- Toilet materials

Backing Films-

The TDDS uses backing films for both setup and operation (in their pouches). Depending on whether it is an occlusion or a breathability film, it protects the active layer and helps maintain system stability. Due to the vast variety of compounds, the release liner must be absolutely inert to the components. It must be printable, comfy, and well-adhesive, with

excellent affinity. Resins, polyethylene (high and low density), saran, polyesters, PVC, and nylon are used as release liners.

Release Liners:

Anti-adhesive coating on a release liner (typically a film). A release liner protects the system while in the package and is removed just before TDDS attachment to the skin. Release liners are critical to the product's stability and performance. So the releasing liner must be chosen carefully. A bad release liner reduces the patch's shelf life by making it difficult to remove. The most common release liners are paper, plastic film, and composite films. The most popular coatings are silicones and fluoropolymers.

Pressure-Sensitive Adhesives:

These molecules operate as a matrix for all active components (additional additives and permeation enhancers) while also helping the patch stick to the user's skin. The most popular PSAs are rubber-based, followed by emulsion polymers or hot melts, and acrylic solutions or emulsion polymers. Each glue family has subgroups that give the formulator freedom. The choice of adhesives is critical to the final product's performance.

Acrylics:

- Functional groups or not
- Linked or not
- Hot melts or emulsions
- Silicone Adhesives:
- Amine-compatible
- Amine-compatible Rubbers:
- Tickers
- X-linkers
- Instability-inducing agents

Penetration Enhancers

Chemically varied, permeation enhancers all have one thing in common: they improve skin penetration by several times. This is important because most actives don't enter the skin in sufficient quantities from a small area. Compounds are occasionally necessary to get desired results.

Analyse of transdermal drug delivery methods

Pharmacokinetics of Excipients To make a stable product, the drug and excipient must agree. The drug-excipient interaction will alter the final formulation's stability and bioavailability (s). If the excipients are fresh, they must be mixed with the active component first. It's vital to grasp how things fit together. FTIR, UV, and chromatographic techniques are utilised to compare their physicochemical properties such as dosage, melting point, number of waves, and maximum absorbance.

The average thickness and standard deviation of the patch are calculated using a digital micrometre.

The value of weight uniformity [15]: Test the patch after four hours at 60°C. Weigh each patch piece after it has been cut up. The average weight can be used to compute the standard deviation of the various weights.
Folding strength: A strip is sliced and refolded. Fold this strip until it snaps. The amount of breaks in the film determines its bending durability.

Percent Water content: Water content is calculated by removing dry weight from the starting weight and dividing the result by dry or total weight, depending on the reporting method.

Permeability of water vapour: Since the thickness of all films is known in this study, the calculation of water vapour permeability is derived by multiplying permeance by thickness. Water vapour transmission was measured and adjusted using several calculation methods.

Peel test for stickiness: The peel adhesion test evaluates the force required to separate two bonded pieces. The test result is usually stated as N (force to de-bond) / 25mm or 50mm depending on the specimen width.

Culture permeation studies: In vitro permeation studies often use side-by-side diffusional cells to outline permeation mechanisms, however they are less useful in predicting skin permeation in the real world.

Stability studies: Environmental factors can affect product quality, hence stability studies are done in the life sciences, chemical, and food and beverage industries. Environmental conditions can impact shelf life and formulation viability.

Conclusion

Transdermal medication delivery targets a specific spot. TDDs generally serve to maintain skin health by preventing or treating skin diseases. An innovative transdermal patch, nano emulsion, or nano solution that increases bioavailability and reduces skin infection. This review provides comprehensive information on skin components, mechanism, benefits, techniques, and evaluation factors of TDDS. Transdermal drug administration isn't new, and it's not restricted to patches. Recent technical advancements and medication integration into the site of action without breaching the epidermal membrane have made it the preferred drug absorption route. It may one day eliminate the need for needles to administer a wide spectrum of medications.

Conflict of Interest: Authors declare that they have no conflict of Interest

Acknowledgement: Authors are special thanks to Mr. Jitender Joshi; Chancellor and Prof. (Dr.) Dharam Buddhi; Vice Chancellor Uttaranchal University-Dehradun for encourage to publish this review work.

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