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A REVIEW ARTICLE ON FUNCTI ONAL NANO-SYSTEMS FOR TRANSDERMAL DRUG DELIV ERY AND SKIN THERAPY

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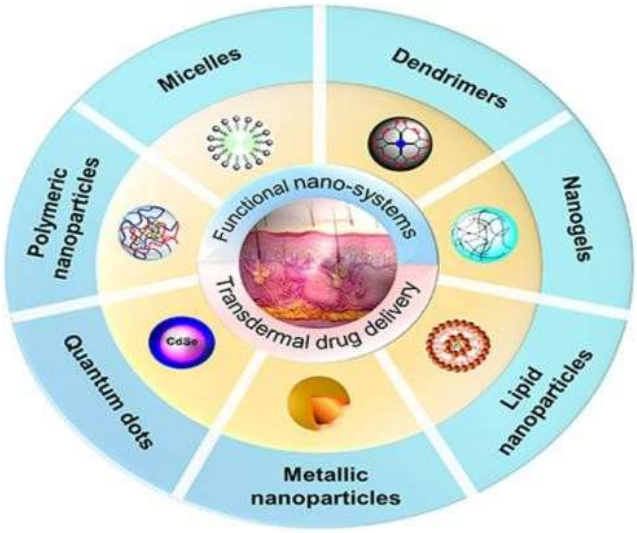
ABSTRACT

The largest organ in the body, the skin is also where many drugs are administered. Compared to conventional distribution methods, transdermal medication administration systems provide a number of advantages. Its therapeutic effects are both systemic and localized. It is essential to comprehend the kinetics, physiochemical characteristics, and drug transport pathway in order to get optimal efficacy. A few benefits of these systems include avoided hepatic first-pass metabolism, controlled plasma drug levels, and decreased dose frequency. The potential of physical approaches to reduce pain is a significant benefit that can be leveraged for efficient illness care.The concepts of various physical methods for facilitating transdermal medication distribution were the main emphasis of this work. Among these are needleless injections, ultrasound, photomechanical waves, iontophoresis, electrophoresis, and microneedles.

Keywords: Transdermal, Microneedle, Ultrasound, Facilitate Transdermal Drug Delivery.

I. INTRODUCTION

Oral and parenteral routes are the most often used for medication administration; most small molecule pharmaceuticals are typically administered orally. Predetermined dosages, mobility, and patient self-administration are benefits of the oral route. These factors make taking medication orally still the most practical option. However, due to size-limited transport across the epithelium and fast breakdown in the stomach, the majority of therapeutic peptides or proteins are not given orally. Therefore, injections are the main method of giving macromolecules. However, injections have several drawbacks, including the need for a professional administrator and their intrusive nature, which can cause pain and lower patient acceptance and compliance.



Transdermal drug delivery (TDD)

TDD is a painless way to apply a medication formulation to healthy, unbroken skin in order to administer the medicine systemically. Without building up in the dermal layer, the medication first enters the stratum corneum before moving on to the deeper layers of the epidermis and dermis. A medication can be absorbed systemically by the dermal microcirculation once it has reached the dermal layer. TDD offers a number of benefits over other traditional medication delivery methods. Many placement possibilities for transdermal absorption on the skin are made possible by the skin's enormous surface area and ease of access. Moreover, medications have more consistent pharmacokinetic profiles with fewer peaks, which reduces the possibility of harmful side effects.

Because fewer doses are required, it can increase patient compliance. Patients who depend on self-administration

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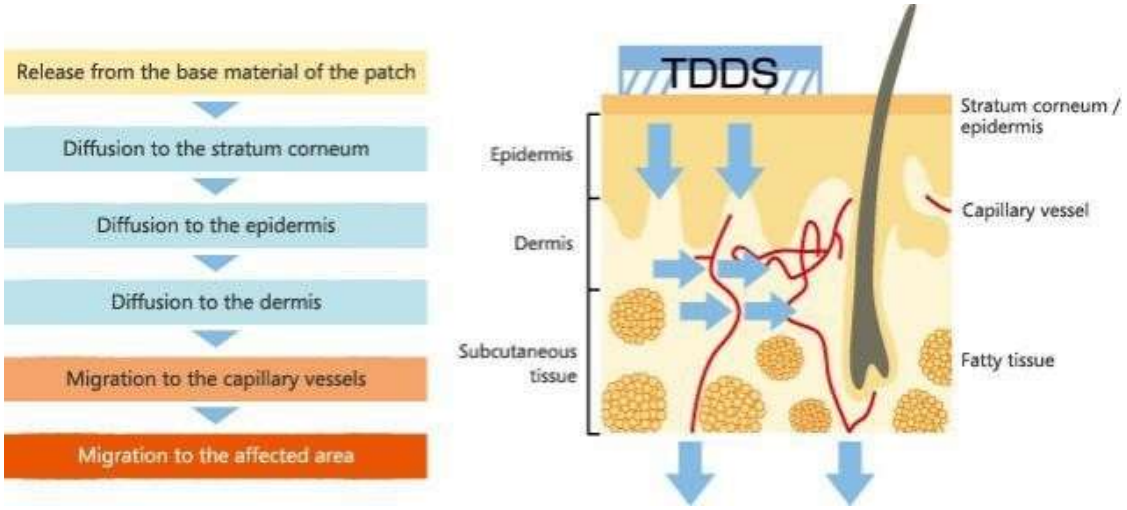
or who are asleep or vomiting can also benefit from it. TDD improves bioavailability by avoiding pre-systemic metabolism.



Advantages of transdermal drug delivery system

- Enhance drug absorption and keeps drug concentration in the blood steady for a predetermined amount of time. Simple to expand.
- There are several medications that can be purchased as transdermal patches.
- Enhances adherence from patients.
- Less variation both within and between patients.
- Reduces the amount of medication needed.
- Reduces adverse effects on the gastrointestinal system (GI).
- In the event of toxicity or side effects, stopping the medication is simple.
- If a patient is unconscious, medication administration may be necessary.
- Having a comparatively wider application range than the nasal or buccal cavities. Avoiding drug exposure that could cause enzymatic breakdown, gastrointestinal discomfort, hepatic first- pass metabolism, and the gastrointestinal tract (GIT).

Disadvantages of transdermal drug delivery system

- Ionic medicines and/or pharmaceuticals cannot be delivered via transdermal drug delivery methods.
- Transdermal delivery is not suitable for drugs larger than 500 Daltons.
- It cannot raise the concentration of the medication in the blood or plasma. Itching, erythema, and skin irritation are possible side effects.
- It is unable to send medications in a pulsating manner.
- The patient has discomfort during long-term adherence.
- Sufficient solubility in the hydrophilic and hydrophobic phases and a log P between 1 and 3 are required to pass through the SC and the underlying aqueous layer.
- Medications cannot enter the bloodstream whether their partition coefficient is high or low. This kind of drug delivery device is better suited for candidates with lower doses.

Fundamentals of transdermal delivery

- **Skin biology**

The skin, which makes up 16% of an average person's total body mass, is the largest and most accessible organ in the body, covering 1.7 m^�. The skin's primary purpose is to act as abarrier of defense between the body and the outside world, keeping out germs, toxins, allergies, ultraviolet (UV) radiation, and water loss. The three primary layers of skin are the dermis, which is the middle layer, the hypodermis, which is the innermost layer, and the epidermis, whichh is the outermost layer and contains the stratum corneum.

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A. Epidermis

The outermost layer of skin, known as the epidermis, varies in thickness, measuring around 0.8 mm on the soles of the feet and palms of the hands. Below the stratum corneum, the viable epidermis is sometimes referred to as the epidermal layers. It is composed of multi-layered areas of epithelial cells. Around 95% of the cells in the epidermis are keratinocytes; melanocytes, Langerhans cells, and Merkel cells are among the other cells that make up the epidermal layers.The outermost layer of the epidermis is called the stratum corneum. Its low hydration of 15%–20% and extremely high density (1.4 g/cm3 in the dry state) may contribute to its barrier qualities as it is in direct contact with the outside world.

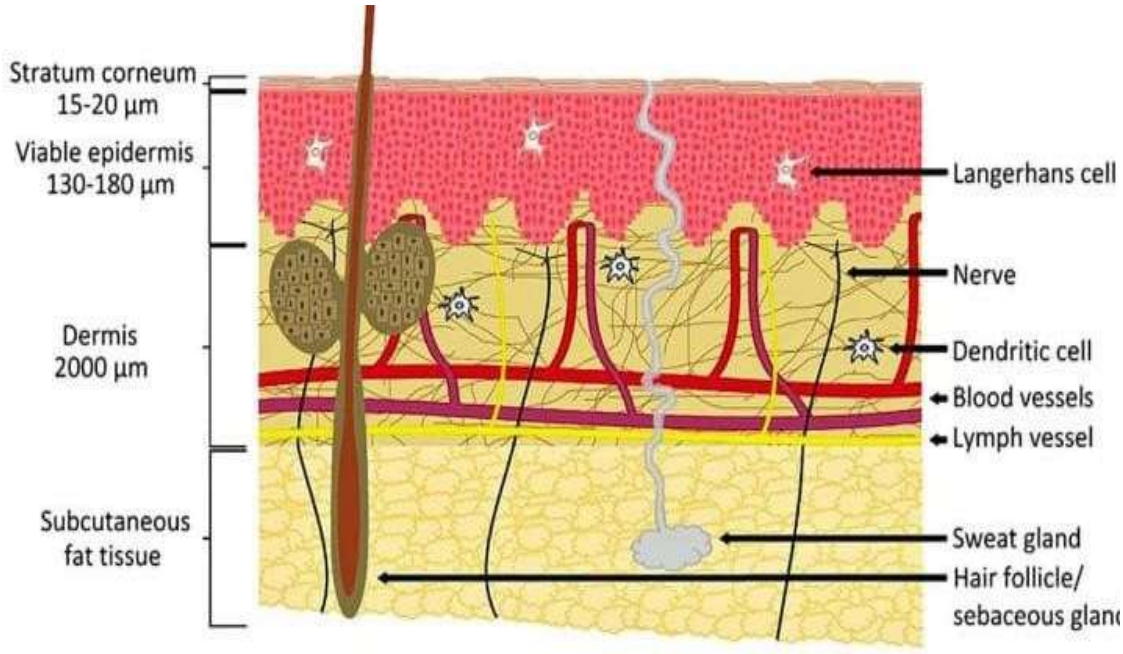
The majority of the cells of the s"ratu' corneum are made up of 20% lipid and 70% insoluble keratins. Keratin in the corneocytes is linked to water in the stratum corneum.

B. Dermis

The dermis, which gives the skin its strength and elasticity, is about 2-3 mm thick and is made up of 70% collagenous and elastin fibers. The dermis's blood vessels supply the epidermis and dermis with nourishment. The dermis layer also contains lymphatic veins, nerves, and macrophages.

C. Hypodermis

The deepest layer of the skin, known as the hypodermis or subcutaneous layer, is made up of a network of fat cells. It serves as the layer of contact between the skin and the body's underlying tissues, including the bones and muscles. Thus, the primary roles of the hypodermis are heat insulation, protection from physical shock, and support and conductance of the skin's vascular and neurological impulses. About half of the body's fat is made up of fat cells that dwell in the hypodermis; the two main cell types in the hypodermis are macrophages and fibroblasts.



Routes of transdermal permeation

There are three ways that the transdermal medication can enter the bloodstream through the skin (above figure).

1) The Transappendageal route.
2) The Transcellular route.
3) The Intracellular route.

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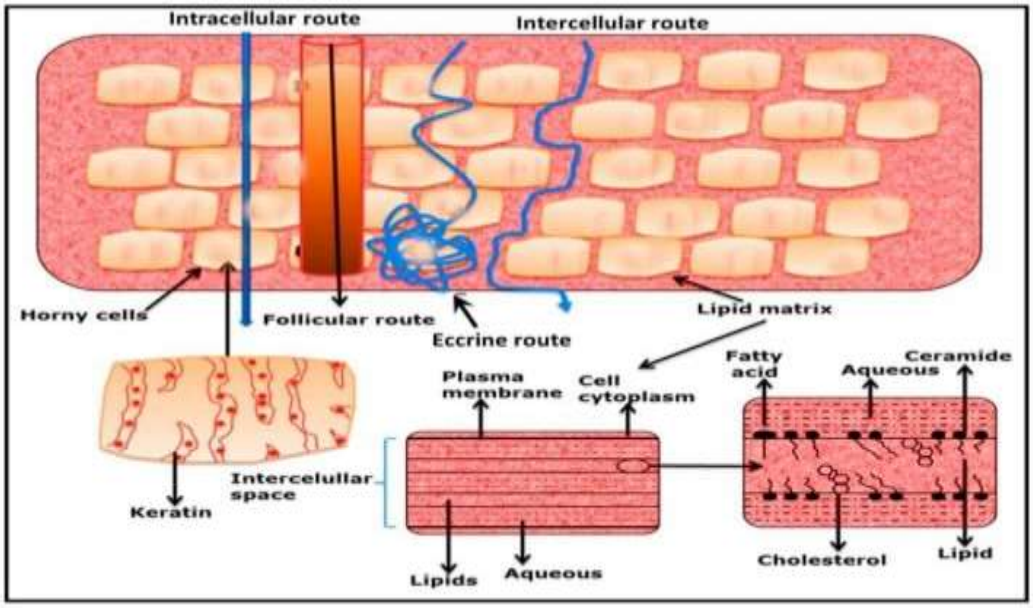

1. Trans-appendageal route

The name for this is the SHUNT path. Sweat and sebaceous glands allow for penetration over the hair follicles. The way across the SC is made apparent by the existence of these appendages. The number, volume, and opening breadth of follicles are important parameters in the transportation of medicines through appendages.

2. Transcellular route

Despite being the fastest route, drug molecules encounter many difficulties because they have to pass through both hydrophilic and hydrophobic structures. In order to pass through the corneocytes and partition into them, a candidate must do so. This is the pathway via which small lipophilic compounds can enter cell membranes following partitioning. The partitioning of hydrophilic compounds in the cell membrane Is restricted; yet, if the molecules are tiny in size and/or employ receptor-mediated transporters, they may be able to pass via this channel.

3. Intracellular route

The paracellular pathway is another name for this path. This pathway allows hydrophilic medicines to diffuse; nevertheless, a smaller particle size is ideal for this pathway. Tight connections are present, which restricts the diffusion of medicines.

II. CONCLUSION

The purpose of this analysis was to provide readers with a comprehensive understanding of the different physical techniques used in transdermal medication delivery methods to promote penetration. These techniques differ from the chemically based method as well. The pharmaceutical business is becoming more and more reliant on transdermal drug administration technology as medical technologies advance. The use of electromechanical, acoustics, sound, friction, microneedle amplification, and heating strategies for the preparation and design of new products, such as 3D printing of transdermal medications, enhanced performance patches, and quick and non-invasive infusion applications, are some of the new approaches that are being used to develop and commercialize transdermal drug delivery technologies. These approaches are helping to change the landscape.

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