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Transdermal Drug Delivary System

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ABSTRACT
Many noninvasive administrations have recently e merged as alternatives to conventional needle inject ions.The transdermal drug delivery system (TDDS) , which has a low rejection rateremarkable ease of a dministration, and remarkable patient convenience and persistence, is the most alluring of all.TDDS m ay be useful not only in the pharmaceutical industr y but also
in the skin care industry, which includes cosmetics. Because this method focuses on local administration, it can prevent local drug concentration accumulation and nonspecific drug distribution to tissues that are not the medication's target. There has been a lot of research on techniques to overcome the various physicochemical properties of the skin that hinder transdermal delivery. In this review, we enumerate the several types of TDDS methodologies now in use and critically analyze their unique advantages and disadvantages, characterization methods, and potential.Research on these alternative ways has advanced, demonstrating the high efficiency of TDDS, and it is expected that these technologies will be used in many different industries.

KEY WORDS- Skin, Transdermal route, Microneedle, Polymeric needles, Drug delivery

I. INTRODUCTION

The skin, or cutaneous membrane, is what covers the body's outside.It is the largest organ in the body, making up approximately 16% of the total weight and area of the adult body, with an area of two square meters and a thickness of 0.5 mm on the eye lids, which are composed of two distinct layers.[1]

Outer- Epidermis, Inner – Dermis

The subcutaneous layer, located beneath the dermis, is not a component of the skin. This layer, also referred to as the hypodermis, is made up of adipose and areolar tissue. The skin is anchored to the sub Q layer, which is connected to the underlying tissues and organs, by fibers that stretch from the dermis. In addition to storing fat, the sub Q layer has big blood vessels that supply the skin.It also contains lamellated (Pacinian) corpuscles, which are pressure-sensitive nerve terminals.[1]

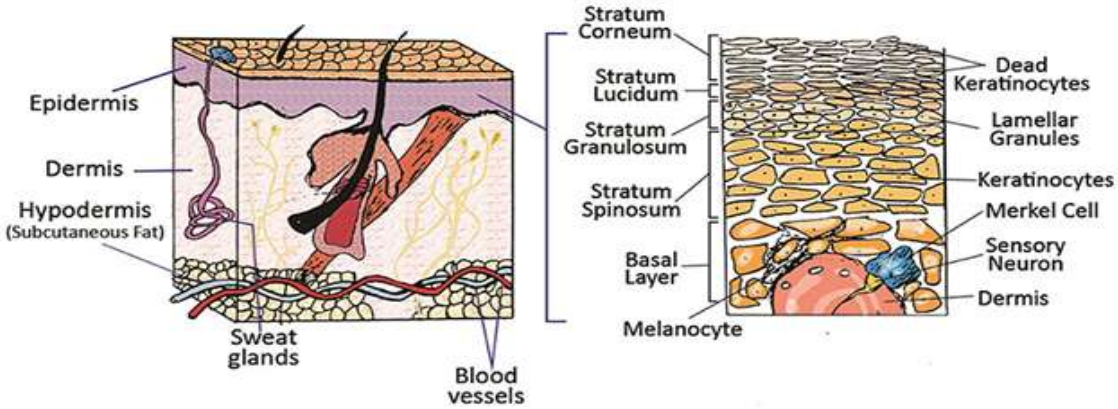

Fig.1 – Skin layer structure

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An additional method of administering medications through the skin layer is transdermal drug delivery [2, 3]. Before the medication reaches the intended location, it passes through the skin and enters the bloodstream, where it circulates throughout the body[2,3]. Oral administration systems have many drawbacks despite these benefits, including low drug stability in the gastrointestinal tract and susceptibility to first pass metabolism. For example, medication degradation may result from exposure to the stomach's acidic environment or from an enzymatic response [4].

Because transdermal drug delivery methods avoid first-pass metabolism and may modulate drug intake rate over an extended period of time, they are advantageous in the management of skin conditions [5]. Due to the skin's abundance of blood and lymphatic vessels, which are closely related to the rest of the body, the unique physiological structure of the skin offers a great opportunity to transport therapeutic agents to the skin for the treatment of illness [6].

The stratum corneum (SC), which serves as the skin's first layer of protection and restricts drug absorption, is the biggest obstacle to the transdermal transfer of active substances. This will drastically lower the therapeutic agent delivery's efficacy and restrict the kinds of medications that can be absorbed through the skin. In comparison to current transdermal drug delivery strategies, there have been a number of studies conducted recently on microneedles that penetrate the superficial skin barrier (SC) while avoiding contact with significant nerves and capillaries in the epidermis. This approach offers a more effective and rapid drug delivery method. The new method combines patch systems with traditional injection. Transdermal delivery of the medication eliminates the discomfort and intrusiveness associated with traditional method in medicine [7]

- **Basic Component of Transdermal Patch**

Transdermal patches are usually made up of many layers with the purpose of delivering the medication into the bloodstream through the skin. A medicated patch's fundamental components are shown in Figure 1. Depending on the medication being administered and the intended rate of drug release, the patch's precise shape and composition may change. The patch's outermost layer, known as the backing layer, shields the inner layers from the elements. Typically, a flexible, waterproof substance like polyethylene or polypropylene is used to create this layer. The purpose of the adhesive layer is to adhere and maintain the patch's position on the skin. Usually, it is composed of a skin-friendly, hypoallergenic adhesive that is robust. Drugs that are absorbed through the skin are found in the drug layer. It is designed to release the medications gradually and at a steady pace. The rate at which the medications are released from the patch is managed by the rate-controlling membrane. Typically, semi-permeable materials are used to create membranes, which enable regulated medication passage through the membrane. The patch and adhesive are shielded by the linen. Prior to being put to the skin's surface, the patch needs to be taken off[8].

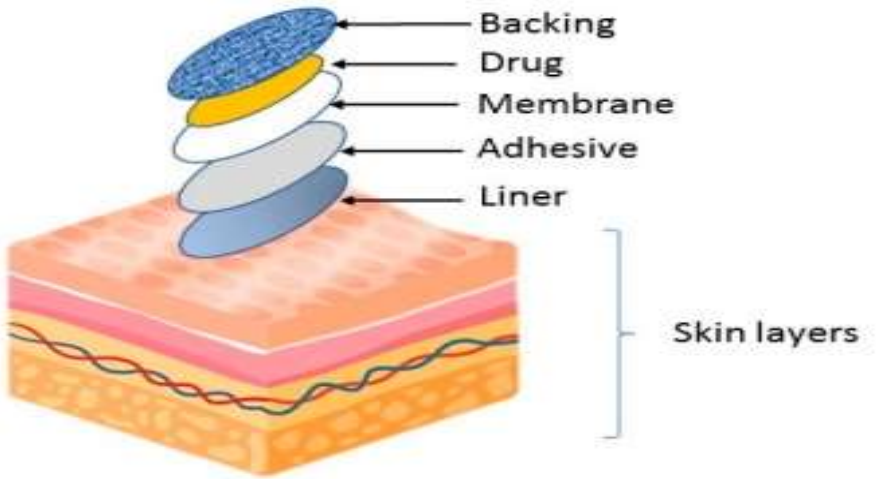

Fig.2- Basic Component of Transdermal Patch

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- **GENERATION OF TRANSDERMAL DRUG DELIVARY**

As seen in fig. 3, there are three generations of transdermal medication delivery. The original generation of transdermal drug delivery systems used patches, and only a very small number of drug candidates were suitable for patch formulation. These candidates had to meet certain requirements, including having the right molecular weight, hydrophilicity, and low dosage efficacy [9]. To expand its use in transdermal drug delivery, a skin permeability improvement approach was used to the second generation of TDDS. Iontophoresis, chemical enhancers, and non-cavitational ultrasonography were among the techniques of improvement. However, these techniques are not able to enhance the distribution of drug molecules through SC or shield the deeper tissues from any physiological damage [10].

The third generation of delivery methods included the introduction of novel chemical enhancers, electroporation, thermal ablation, microneedles, cavitational ultrasound, and microdermabrasion. These methods improved the ability of biotherapeutics and large molecules to permeate the outer corneum layer, leading to increased efficacy of transdermal delivery in human clinical trials [11].

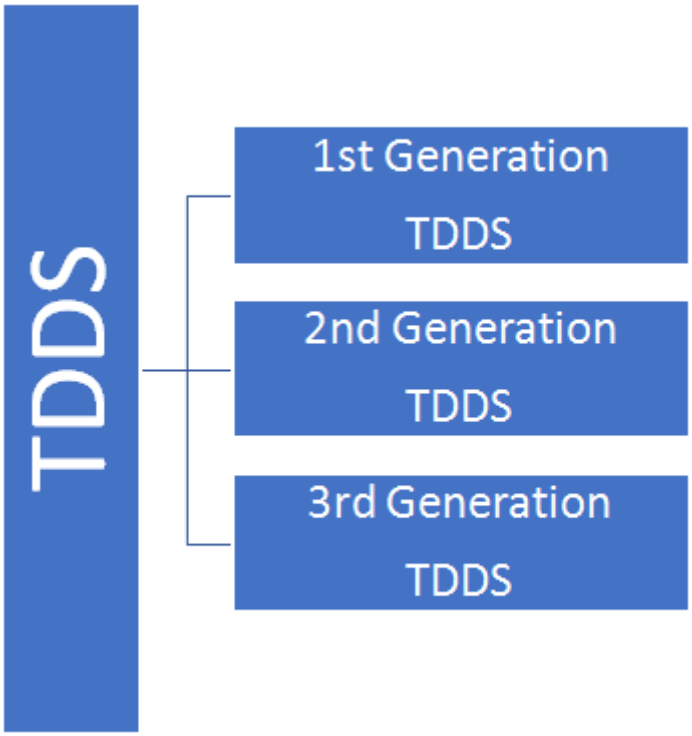

Fig.3-GENERATION TDDS

- **Comparison of transdermal delivery systems**

Not only do over 100 medications come in cream and ointment form, but 19 medications or drug combinations are currently delivered through FDA-approved transdermal delivery systems. The majority of these first-generation delivery methods mainly depend on the right pharmacological characteristics that allow for skin absorption without appreciably enhancing skin penetration. However, the area is moving toward transdermal administration of hydrophilic compounds, macromolecules, and vaccines thanks to advancements made possible by second- and third-generation transdermal delivery technologies. The majority of enhancement techniques raise skin permeability without adding to the transdermal transport's driving force. Chemical enhancers are an exception, as they have the ability to both increase drug solubility and disturb the structure of the stratum corneum, increasing the drug concentration-gradient driving force. Another exception is the use of solid microneedles for coating and encapsulation or hollow needles for infusion, which allow microneedles to penetrate the skin in addition to piercing it. Iontophoresis and

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electroporation are two methods of electrical drug administration that primarily work to drive pharmaceuticals into the skin and disturb the stratum corneum structure, respectively, even though they can also impact skin permeability and generate an electrical driving force. Iontophoresis may be especially helpful when combined with another technique that raises skin permeability since it offers a transport driving force. Prior research on these combination enhancing tactics has been done in the literature[12].

- **Annual Global Publication on Transdermal Drug Delivery**

From 2000 to 2022, 7815 papers pertaining to transdermal drug delivery research were retrieved from Scopus. The yearly publications on TDD that are produced are displayed in (fig4). Global annual publications grew from 131 in 2000 to 659 in 2022, with a greatest increase in 2020 (+28.8%), likely as a result of the worldwide pandemic emergency. The average annual growth rate was 6.4%. The scientific community has redirected research initiatives to identify creative ways and prevent and combat COVID-19 in response to the worldwide health emergency. The gathered information is consistent with the theory that this crisis has caused a sharp rise in biomedical research output, including TDD. In contrast, the quantity of articles published stagnated for a while in some years. This occurrence may be explained by a brief shortage of funds for research and development. Research can be expensive, and it can be challenging for researchers to complete their work without sufficient funding. For instance, the rise in global output ceased in the 2010s following the global financial crisis that was set off by the 2008 bankruptcy of Brother Lehman Bank, and this was initially seen in trade. Global exports of products and services, which had been rising for decades, sharply decreased in comparison to the expansion of the economy [13]. The succeeding years may have seen a rise in TDD publications as a result of these approvals. When more active compounds for transdermal delivery have received approval, the same result has been shown [14].

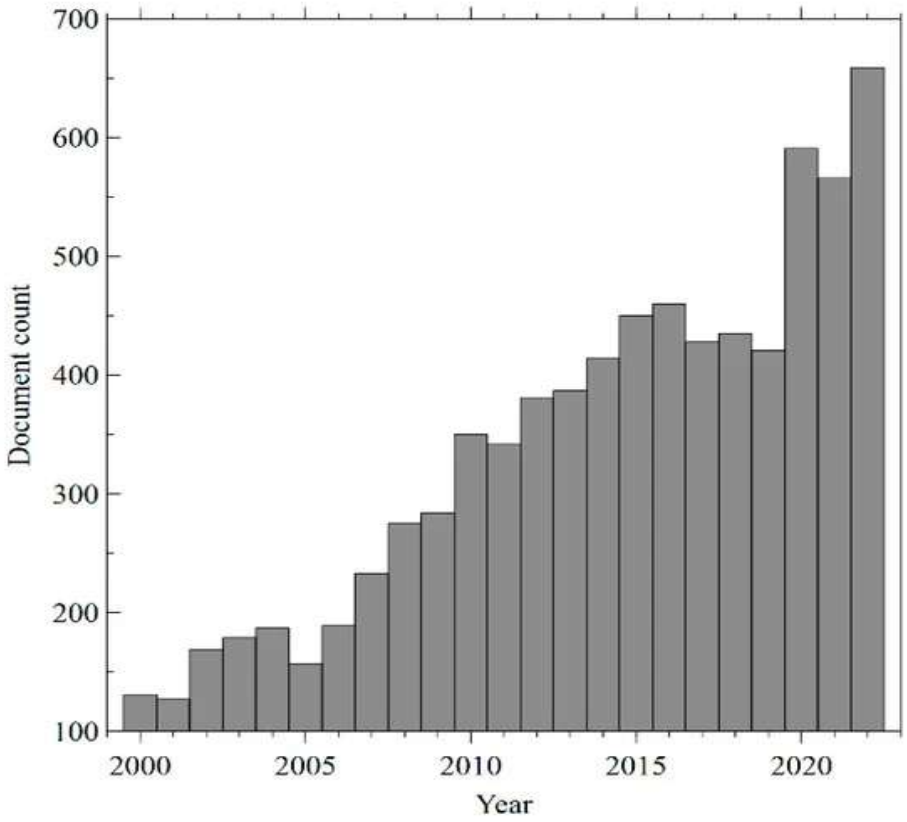

Fig.4- Number of papers per year

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