WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Transdermal Drug Delivery System

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ABSTRACT:-

The transdermal drug delivery system (TDDS) is a sort of controlled drug delivery system that sends medicine via the skin at a defined and controlled rate. It has a lot of good things about it, like a longer therapeutic effect, less side effects, improved bioavailability, better patient compliance, and a simple method to quit taking the drugs. Most substances can't get through the stratum corneum, which is regarded to be the barrier that slows down their transdermal entry. Drugs can enter the body in three main ways: through the appendageal, transcellular, and intercellular channels. When providing medications this method, you should think about the person's age and skin condition, as well as the physicochemical and ambient conditions. The polymer matrix, membrane, drug, penetration enhancers, pressure-sensitive adhesives, backing laminates, release liner, and other basic pieces of TDDS are all very significant.

Key words:- Penetration enhancer, adhesives, systemic blood circulation , bioavailability

INTRODUCTION

Patches or transdermal drug delivery systems (TDDS) are dosage forms intended to apply a therapeutically effective quantity of medication to a patient's skin. The morphological, biophysical, and physicochemical characteristics of the human skin must all be taken into account when delivering medicinal substances through it for systemic effects. By improving patient compliance and preventing first pass metabolism, transdermal administration offers a significant advantage over injectables and oral methods. [1] The application of transdermal patches in pharmaceuticals has been somewhat restricted, as only a limited number of drugs—mainly certain cardiac medications like nitroglycerin and hormones such as estrogen—have shown effective absorption through the skin. These patches utilize a specially designed membrane to regulate how quickly the drug, typically in liquid form within a reservoir, is absorbed into the bloodstream through the skin. A standard transdermal drug delivery system generally includes several key components: the drug either dissolved or suspended in a reservoir or an inert polymer matrix, an outer protective backing made from materials like foil, plastic, or paper, and a pressure-sensitive adhesive that secures the patch to the skin. This adhesive is initially covered by a release liner that must be removed before application. Examples of medications delivered using transdermal patches include nicotine, scopolamine, lidocaine, estrogen, and nitroglycerin. [2] Transdermal drug delivery offers significant advantages over oral and injectable methods by enhancing patient compliance and bypassing the first-pass effect of liver metabolism. [3]

TRANSDERMAL PATCH:

A transdermal patch is a medicated adhesive device that is put on the skin and is meant to administer a certain amount of medicine into the bloodstream at a steady and controlled rate.

SKIN & DRUG PERMEATION:

The goal of transdermal drug delivery systems (TDDS) is to provide systemic medication through the application of drugs to intact skin. To achieve this effectively, it is crucial to examine the structural and biochemical characteristics of the skin, particularly those aspects that contribute to its barrier function and influence the rate at which drugs are absorbed into the body. The skin is one of the largest organs, covering around 2 square meters in an average adult. The main layers of the skin, from deepest to outermost, include the fatty subcutaneous layer (hypodermis), the connective tissue-rich dermis, and the stratified, vascularized epidermis. This multi-layered organ receives about one-third of the blood circulating in the body. The epidermis, which is the outermost layer, is about 150 µm thick and forms from a dynamic population of basal epithelial cells.(4)

ADVANTAGES:-

1. Hepatic first-pass metabolism, along with salivary and intestinal metabolic processes, is bypassed.
2. Drugs that cause gastrointestinal irritation or have poor absorption can be effectively delivered through the skin.
3. The release of the drug is controlled, ensuring a predictable and extended therapeutic effect.

4. The need for injections, along with their associated pain, risks, and inconvenience, is eliminated. The release of the drug is more sustained compared to oral extended-release systems.
5. Transdermal patches allow for self-administration and provide a continuous, sustained release of the medication.
6. The transdermal system minimizes fluctuations in drug concentration, avoiding peak and trough levels, and offers longer dosing intervals, often extending over multiple days.

DISADVANTAGES:-

1. Currently, only small, lipophilic (fat-soluble) drugs can be effectively delivered through the skin.
2. Transdermal drug delivery is generally not suitable for ionic (charged) drugs.
3. Skin irritation may occur due to one or more components in the formulation.
4. The binding of the drug to the skin could potentially lead to a sudden release of the drug (dose dumping).(5)

TYPES OF TRANSDERMAL DRUG DELIVERY SYSTEM:

a) Single Layer Drug-in-Adhesive:

n this configuration, the drug is incorporated directly into the adhesive layer. The adhesive controls the drug's release onto the skin and holds the patch's many components together.

b) Multi-Layer Drug-in-Adhesive:

Similar to the single-layer technique, this type contains both an immediate-release and a controlled-release layer within the adhesive. It also has a temporary liner to sustain the structure of the patch and a permanent backing layer.

c) Reservoir System:

This technique holds the medication in a reservoir that is positioned between an impermeable backing layer and a rate-controlling membrane. The medication is exclusively given through this membrane, which can be either micro-porous or non-porous. The medicine could be dispersed throughout a solid polymer matrix, gel, suspension, or solution in the reservoir. The external adhesive layer, which is often made of hypoallergenic polymer and helps ensure drug compatibility, securely adheres the patch to the skin. [7]

d) Matrix system:

i. Drug-in-Adhesive System:

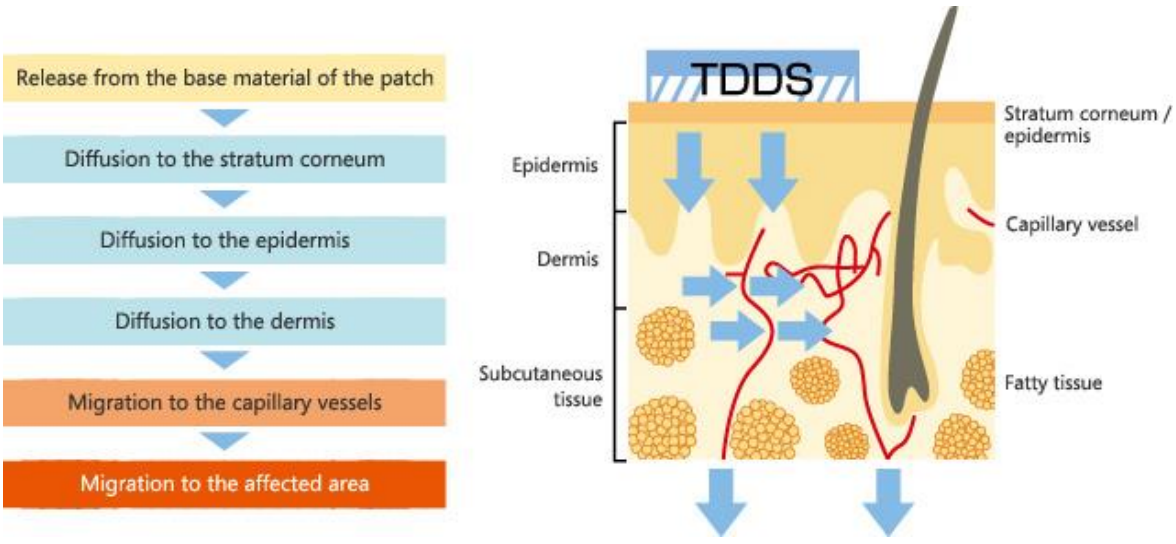
Drug-in-Adhesive System: to create a drug reservoir, a pharmaceutical is combined with a polymer that adheres to it. The mixture is subsequently applied to an impermeable backing layer using solvent casting or melting techniques. The reservoir's top is covered with a non-medicated sticky polymer layer to hold the patch in place.

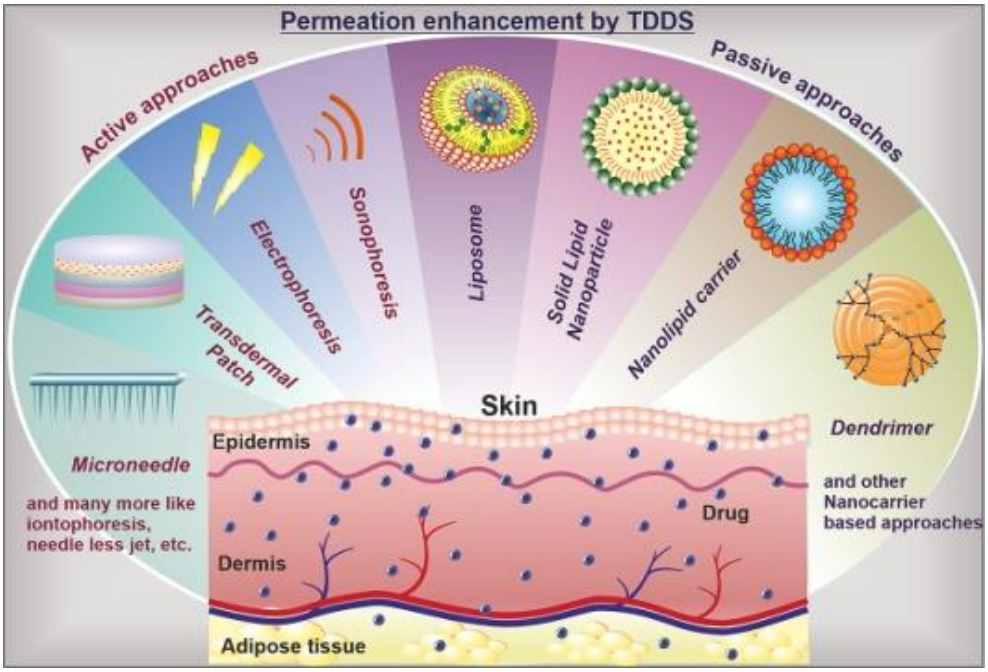
ii. Matrix-Dispersion System:

In this technique, the drug is evenly distributed throughout a hydrophilic or lipophilic polymer matrix. The drug-infused polymer is then shaped into a medicated disc that has a specific size and thickness. This disk is mounted on an occlusive base plate made of a backing layer that is resistant to medicines.

e) Micro Reservoir System:

This system releases the medicine from microscopic drug reservoirs in a zero-order method to maintain consistent drug levels. It includes elements of reservoir and matrix-dispersion systems. The drug is mixed with an aqueous solution of a water-soluble polymer, which is subsequently dispersed into a lipophilic polymer employing high-shear mechanical force to produce millions of microscopic drug reservoirs. [7]





BASIC COMPONENT OFTDDS:[8]

- **Backing Films:**

Transdermal patches cannot work or be effective without backing films. They protect the active layer, maintain system stability, and control skin penetration and tolerance based on their level of occlusion or breathability. To prevent incompatibilities, the release liner should be completely inert to all of the chemicals in the patch.

- **Release Liners:**

To release liners, an anti-adherent material is used. Their primary function is to protect the patch during packing, and they are removed just prior to the transdermal drug delivery system (TDDS) being placed to the skin. Release liners are essential to the stability, safety, and efficacy of the patch. Selecting the appropriate release liner for the patch is essential.

- **Penetration Enhancers:**

Certain chemical substances with comparable capabilities but differing structures are known as penetration enhancers. They let the active substance to pass through the skin more efficiently by significantly increasing its rate of penetration

VARIOUS METHODS FOR PREPARATION TDDS: [9]

A. Asymmetric TPX membrane method:

To create a prototype patch, a heat-sealable polyester film (type 1009, 3M) can be utilized as the backing membrane. This membrane will be 1 cm in diameter and concave.

B. Circular teflon mould method:[10]

A solution of polymers in various ratios is made using an organic solvent. The required amount of medication is dissolved using half of the solvent, and the enhancers are dissolved in different proportions using the other half. The drug-polymer solution is then mixed with a plasticizer called di-N-butyl phthalate. The slurry is stirred for 12 hours before being put into a circular Teflon mold. The mold is placed on a level surface and covered with an inverted funnel to regulate solvent evaporation, which is carried out in a laminar flow hood with an airspeed of 0.5 m/s. The solvent is allowed to evaporate for a full day. The dried films are then stored for an additional twenty-four hours at 25±0.5°C in a desiccator with silica gel to remove any remaining moisture and reduce the effects of aging. These films are evaluated a week after they are prepared.

C. By using IPM membranes method:[11]

The medication is dispersed in a solution of water and propylene glycol, coupled with carbomer 940 polymer, and the combination is stirred for 12 hours using a magnetic stirrer. A buffer with a pH of 7.4 can be used to create a gel solution after neutralizing the dispersion, particularly if the drug is not very soluble in water

D. Mercury substrate method:[12]

Using this method, the drug is dissolved in a polymer solution that also includes a plasticizer. The mixture is dumped onto a level surface to allow the solvent to evaporate after being stirred for 10 to 15 minutes to ensure homogeneity

E. EVAC membranes method:[13]

To build the desired transdermal therapeutic system, rate-controlling barriers such as polyethylene (PE), ethylene-vinyl acetate copolymer (EVAC) membranes, and a 1% carbopol reservoir gel can be employed.

FACTORS AFFECTING TRANSDERMAL DRUG DELIVERY[14]

• Skin condition -[14]

Some substances, such acids and alkalis, can get through the skin's barrier cells despite the skin's natural ability to act as a barrier. Different solvents, such as methanol and chloroform, break down the stratum corneum's thick structure by removing its lipid content, creating artificial channels that facilitate the passage of pharmaceuticals.

Skin Age:

It has been observed that children's and adults' skins are generally more permeable than those of the old, however this difference is not statistically significant. Children are particularly susceptible to negative effects due to their larger skin surface area relative to body weight. Strong drugs including steroids, boric acid, and hexachlorophene have had major adverse consequences in children.

Physicochemical factors:-

• Hydration of skin-[15]

Saturating the skin with water causes the tissues to swell, wrinkles to disappear, and the permeability to improve, which facilitates the penetration of drug molecules.

Temperature and pH of the Skin:

The pace at which medications penetrate the skin is affected by variations in skin pH. As the temperature decreases, the diffusion coefficient decreases, slowing down drug penetration. However, by helping to maintain a consistent temperature, wearing the right clothing lowers fluctuations in skin temperature and drug penetration rates. In terms of pH, only unionized molecules may easily penetrate the lipid layers of the skin. Weak acids and bases dissociate to varying degrees depending on the pH of the surrounding environment and the pKa or pKb values of the substances.

Environmental factors:

Sunlight:

Because sunlight thins blood vessel walls, even minor wounds in areas exposed to the sun can cause bruising. Additionally, pigmentation alterations like freckles or solar lentigines are frequent sun-induced skin changes.

Cold Season:

During the colder months, skin often becomes dry and irritated. The skin may react by creating extra oil to counteract the drying effects of the weather. Drinking plenty of water keeps the skin hydrated and healthy-looking, even though applying a good moisturizer can help lessen the symptoms of dry skin.

• Air pollution-

: Dust can cause acne or patches by clogging pores and increasing the quantity of bacteria on the skin's surface. It can also potentially hinder the skin's capacity to absorb treatments. Furthermore, invisible chemical pollutants in the air might disrupt the skin's natural barrier function.

EVALUATION PARAMETERS:

1.Thickness of patch:

The thickness of the pharmaceutical patch is measured at various points using a digital micrometer. The average thickness and standard deviation are then calculated to ensure uniformity in the thickness of the prepared patch. The thickness of the patch typically ranges from 0.12 to 0.25 millimeters. [16]

2) Interaction studies:

Excipients are essential components in practically all pharmacological dosage formulations. One factor that affects a formulation's stability is how well the medication and excipients work together. To ensure product stability, the medication and excipients must be compatible, which calls for identifying any potential chemical or physical interactions.

Weight Uniformity:

The generated patches must be dried at 60°C for four hours prior to testing. A certain portion of the patch is then taken out of different places, and each piece is weighed using a digital balance to assess weight homogeneity.

4) Skin Irritation Study:

Skin irritation and sensitization tests can be performed on healthy rabbits that weigh an average of 1.2 to 1.5 kg. After cleaning the rabbit's 50 cm^2 dorsal area, the fur is shaved off. After cleaning the skin's surface with rectified spirit, the representative composition is applied. The patch should be removed after a day, and any irritation of the skin should be examined. [17]

5) Stability studies:

Stability studies are to be conducted according to the ICH guidelines by storing the TDDS samples at 60±5% ,40±0.5°c and 75±5% RH for 6 months.[18]

RESULTS:-

Two possible advantages of TDDS in medication delivery are improved bioavailability and patient compliance. However, a comprehensive evaluation of the drug's characteristics, formulation design, and potential skin responses is necessary to optimize therapy outcomes.

CONCLUSION:-

The transdermal drug delivery system (TDDS), which is utilized to transmit hydrophilic and hydrophobic active ingredients to medications, is discussed in this study in helpful depth. TDDS, the most recent drug delivery technique, is a practical and effective use case.

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