



TRANSDERMAL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

The term "patches" refers to transdermal drug delivery systems (TDDS), which are dosage forms intended to apply a therapeutically effective quantity of medication to a patient's skin. To provide medicinal substances

The entire morphological, biophysical, and physicochemical characteristics of the human skin must be taken into account for systemic impacts. By improving patient compliance and avoiding first pass metabolism, respectively, transdermal administration offers a significant advantage over injectables and oral methods.

Transdermal delivery removes pulsed access into the systemic circulation and permits continuous injection of medications with brief biological half-lives in addition to providing controlled, continuous drug administration. This frequently results in unfavorable side effects. As a convenient resource for research scientists working on TDDS, the TDDS review papers offer important insights about transdermal drug delivery systems and its evaluation procedure. The pharmaceutical industry has become a trendier industry due to technological advancements. its assets. Convectional dose forms were used in the past, however new drug delivery systems are being used. Transdermal patches are among the most innovative new drug delivery technologies. The transdermal medication delivery system has the benefit of being a painless method of drug administration.

DEFINITION

A regulated way of delivering medicinal chemicals through the skin, mainly for systemic effects, is called a transdermal drug delivery system (TDDS). The medication avoids first-pass metabolism and sustains constant plasma drug concentrations for a long time by penetrating the skin's layers and entering the systemic circulation

ADVANTAGE

Avoidance of First-Pass Metabolism: By avoiding the liver's first-pass metabolism, medications administered topically have higher bioavailability

Controlled and Sustained Drug Release

TDDS can keep plasma concentrations constant for a long time, which lowers the need for frequent doses. Increased patient compliance is a result of less frequent dose and non-invasive, painless administration. Decreased adverse effects: Consistent plasma levels reduce the peaks and troughs that come with traditional oral dosage

Termination Ease

If side effects arise, drug administration can be instantly terminated by taking off the patch. Suitability for drugs with short half-lives: Effective plasma levels for medications that might normally need frequent dosage are maintained via continuous release from the patch

Convenient and Non-Invasive

TDDS is appropriate for long-term treatment because it does not involve needles or gastrointestinal discomfort.

DISADVANTAGE

Limited to potent drugs:: Due to the skin's restricted permeability, only medications with modest dosage requirements—typically less than 10 mg per day—are appropriate.

Skin barrier characteristics: Many medication molecules, particularly those that are hydrophilic or have a large molecular weight, are prevented from penetrating the stratum corneum, which serves as a significant barrier. Skin sensitization and irritation: Some patients may experience localized irritation, redness, itching, or allergic responses after using patches for an extended period of time.

Absorption variability: Disparities in skin moisture, thickness, and condition (e.g., age, application site, illness) can result in uneven drug absorption.

Adhesion issues: The delivery rate and therapeutic efficacy may be impacted by poor adhesion brought on by perspiration, bodily movement, or oily skin.



Components of transdermal patches

1 Polymer Matrix

- a) Molecular weight, chemical functionality of the polymer should be such that the specific drug diffuses properly and gets released through it.
- b) The polymer should be stable.
- c) The polymer should be nontoxic
- d) The polymer should be easily of manufactured
- e) The polymer should be inexpensive

Types of polymer: -

a) Natural polymers: , Gelatin, Waxes, Gum, Natural rubber, starch.

b) Synthetic Elastomers: silicone rubber, Nitrile, Neoprene.

c) Synthetic polymers: polyvinyl chloride, polyethylene, polyamide, epoxy

Drug

Penetration Enhancer

In direct contact with the release liner is the drug solution.

Enhancers increase fluidity and open up channels for drug diffusion by integrating themselves into the stratum corneum's lipid bilayers.

Terpenes and fatty acids, such as oleic acid, are examples.

interaction (protein modification) with keratin

Certain substances reduce the skin's barrier function by changing the keratin's structure in corneocytes.

For instance, DMSO and urea.

A rise in the partitioning of drugs

Enhancers boost the drug's partitioning and make it more soluble in the stratum corneum.

Surfactants

Amphiphilic compounds known as surfactants (surface-active agents) lower interfacial and surface tension.

They are typically employed in TDDS as:

Permeation enhancers are used to boost drug penetration by dissolving or fluidizing the lipids in the stratum corneum.

Solubilizers: to make the medication more soluble in the mixture.

Emulsifiers are used in TDDS that are emulsion- or microemulsion-based.

Stabilizers: to keep the patch matrix's medication distribution consistent.

Miscellaneous Chemicals: These comprise calcium thioglycolate, N, N dimethyl-m-toluamide, anticholinergic drugs, and urea, a moisturizing and keratolytic agent. Although some possible permeability enhancers have recently been developed, there is little information on their efficacy. These consist of soy casein, di-o-methyl- β -cyclodextrin, and eucalyptol

Other Excipient : excipients are essential for maintaining drug stability, permeability, adhesion, and controlled release in transdermal drug delivery systems (TDDS). In addition to the active pharmaceutical ingredient (API), a TDDS usually contains a number of excipients, including solvents, backing/lining materials, adhesives, plasticizers, polymers, and permeation enhancers.

A comprehensive list of excipients used in TDDS is provided below, along with citations to reliable pharmaceutical sources.1.

Polymers (also known as reservoir formers or matrix)

They regulate drug release and serve as the patch's structural core.

Examples

Methylcellulose, Eudragit RL/RS, 934 Carbopol

Permeation Enhancers

These improve the stratum corneum's ability to absorb drugs.



Examples: Oleic acid, DMSO, or dimethyl sulfoxide
Glycol propylene, Ethanol

Adhesives

Make sure the patch doesn't come loose from the skin.

Examples

PIB, or polyisobutylene
Adhesives with silicone

Linear

A zero-order kinetic model, in which the drug release rate is constant throughout time (a linear relationship between cumulative drug released and time), is what is meant by "linear release" if you were referring to a transdermal drug delivery system. Linear release, also known as zero-order release, refers to transdermal systems where the rate of medication release through the skin is constant over time and unaffected by drug concentration.

Examples

TDDS of the reservoir type, such as nitroglycerin and scopolamine patches.

Backing layer: Protect patch from external environment.

Factors Affecting Transdermal Bioavailability

The variables that impact transdermal bioavailability

The drug's absorption through transdermal methods is influenced by two main factors:

Physicochemical Factors:

Hydration of the skin: The permeability of the skin greatly increases when it comes into touch with water. The most crucial element boosting the penetration of skin. Thus, transdermal distribution is how humectants are used.

Temperature and pH: A ten-fold increase in medication penetration occurs with temperature changes. As the temperature drops, the diffusion coefficient drops as well.

The pH and pKa or pKb values determine how weak acids and weak bases dissociate. The drug concentration in skin is determined by the percentage of unionized drug. As a result, two crucial variables influencing medication penetration are pH and temperature.

Diffusion coefficient: The drug's diffusion coefficient determines its penetration. The characteristics of the drug, the diffusion medium, and their interactions determine the drug's diffusion coefficient at a constant temperature.

Drug Concentration in Transdermal Drug Delivery Systems: 1. The idea One of the main factors affecting drug flux—the rate at which a drug moves through the skin—is the concentration of the drug in a transdermal formulation or patch.

Biological Factors

Skin Condition: One of the most important physiological variables affecting transdermal bioavailability is skin health.

The primary barrier to drug penetration is the stratum corneum, the skin's outermost layer. The pace and degree of drug absorption from a TDDS can be considerably changed by any change in its lipid content, hydration, or integrity.

Comprehensive review on how barrier disruption (by disease or enhancers) alters transdermal permeability.

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Skin Age

The permeability and bioavailability of medications administered via transdermal systems are strongly influenced by the age of the skin, whether it is neonatal, adult, or geriatric.

The diffusion and absorption profile of transdermal medications is changed by age-related changes in skin structure, lipid composition, moisture, and barrier function.

Blood Flow

The pace and breadth of systemic absorption of medications delivered by transdermal delivery systems (TDDS) are significantly influenced by cutaneous blood flow.

Dermal blood circulation affects how quickly the absorbed medication is taken out of the absorption site and transferred into the systemic circulation, whereas the stratum corneum regulates the velocity of penetration through the skin.



TYPES OF TRANSDERMAL PATCHES

Single layer drug in adhesive

In this form, the medicine is present in the sticky layer. The adhesive layer is in charge of delivering the medication onto the skin in addition to holding the several layers together. A backing and a temporary liner encircle the adhesive layer.

Multi-layer drug in adhesive

This kind is comparable to the single layer as well, but it has an adhesive layer, a controlled release layer, and an immediate medication release layer. The drug's release is brought on by the sticky layer. Additionally, this patch features a temporary liner-layer with aon)

Vapour patch:going support

The purpose of the adhesive layer in this kind of patch is to both release vapor and hold the different layers together. Recently introduced to the market, vapor patches are frequently used to release essential oils during decongestion. Other kinds of vapor patches include also on the market that are used to lessen cigarette smoking circumstances and enhance sleep quality.

Reservoir System

This system embeds the drug reservoir between a rate-controlling membrane and an impermeable backing layer. Only the rate-controlling membrane, which may be non-porous or microporous, allows the drug to release. The drug may be in the form of a gel, suspension, solution, or dispersion within a solid polymer matrix within the drug reservoir compartment. It is possible to use hypoallergenic adhesive polymer as a drug-compatible outer surface polymeric membrane.

Matrix System

Drug-in-adhesive system: This kind of drug reservoir is created by dispersing the medication in an adhesive polymer, followed by the solvent casting or melting (for hotmelt adhesives) of the medicated adhesive polymer on an impermeable backing layer. For protection, unmediated sticky polymer films are placed on top of the reservoir.

ii. Matrix-dispersion system: In this kind, the medication is uniformly distributed within a matrix of hydrophilic or lipophilic polymers.

In a compartment made of a drug-impermeable backing layer, this drug-containing polymer disk is fixed to an occlusive base plate. To create a strip of adhesive rim, the adhesive is applied around the outside of the drug reservoir rather than on its face.

System of Microreservoirs

This kind of drug delivery device combines matrix-dispersion and reservoir technologies. The medication is initially suspended in a water-soluble polymer aqueous solution, and the solution is subsequently uniformly dispersed in a lipophilic polymer to create the drug reservoir. thousands of tiny, inaccessible drug reservoir spheres. Cross-linking agents are used to instantly cross-link the polymer in situ, stabilizing this thermodynamically unstable dispersion.

Methods of Preparation of TDDS

1 Polymer membrane permeation-controlled TDDs

The drug reservoir in this device is placed between a rate-controlling membrane and an impermeable backing layer. Only the rate-controlling membrane, which may be microporous or non-porous, allows the medicine to be released. The drug may be dissolved in a solid polymer matrix or present in the drug reservoir compartment as a solution, suspension, gel, or other form. It is possible to apply a thin layer of drug-compatible, hypoallergenic adhesive polymer to the polymeric membrane's outside (Figure 1). By altering the polymer composition, permeability coefficient, and thickness of the rate-controlling membrane, the rate of drug release from this kind of transdermal drug delivery system may be customized

2. Matrix diffusion controlled TDDS

Diffusion-controlled matrix TDDSThe medication is uniformly distributed inside a matrix of hydrophilic or lipophilic polymers. The drug-containing polymer disk is then attached to an occlusive base plate in a compartment made of a backing layer that is impermeable to drugs (Figure 3). The adhesive is applied around the perimeter of the drug reservoir to provide an adhesive strip rather than on the front of the reservoir (rim 9, 37). Figure 3 Diffusion-controlled matrix TDDSNitro Dur (nitroglycerine) is a once-daily angina pectoris medicine. 2.2.4 TDDS that is microreservoir controlled This drug delivery device combines matrix-dispersion and reservoir technologies. The drug is initially suspended in an aqueous solution of a water-soluble polymer, and then the drug is dispersed to create the drug reservoir.

3. Microreservoir controlled TDDS.

This drug delivery device combines matrix-dispersion and reservoir technologies. In order to create the drug reservoir, the drug is first suspended in an aqueous solution of a water-soluble polymer, and then the thermodynamically unstable dispersion is rapidly stabilized by instantly cross-linking the polymer in situ. As a result, a transdermal therapeutic system was created, with a medicated disc in the middle and an adhesive rim around it.



Evaluation of TDDS

The patch's thickness

Using a computerized device, the thickness of the drug-loaded patch can be measured at various spots. micrometer to measure the prepared patch's thickness (

Uniformity of Weight

Prior to testing, the created patches are dried for four hours at 60°C. A predetermined patch area must be sliced into several pieces and weighed using a digital balance. The standard weight and average

Folding Stamina

A predetermined length of strip is cut uniformly, then folded repeatedly until it breaks.

The value of folding endurance is determined by how many times the film could be folded in the same spot without breaking.

The percentage of Moisture Content

Each created film is weighed separately, then left at room temperature for 24 hours in a desiccator filled with fused calcium chloride. The films are then reweighed, and the percentage content of drugs A certain volume of a patch must be dissolved in an appropriate solvent. Next, the After passing the solution through a filter medium, the drug content is examined using the appropriate technology, such as UV or HPLC.

Polariscope Analysis

This test uses a polariscope to look at the drug crystals from the transdermal patch. To determine if the drug is present in a patch in crystalline or amorphous form, a certain surface arTest for peel adhesionThe force needed to remove an adhesive covering from a substrate in this test is known as the adherence of peel. One piece of tape is placed on a stainless steel plate or a preferred backing membrane. The tape is then pulled off the substrate at a 180° angle, and the force needed to do so is measured.

The Thumb-Tack Test

This test was used to determine the adhesive's tack properties. The relative tack quality is detected by merely pressing the thumb against the adhesive.ea of the piece is maintained on the object slide and examined for drug crystals.e moisture content is calculated using the formula below.

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