TRANSDERMAL DRUG DELIVERY SYSTEMS: A COMPREHENSIVE REVIEW ON CURRENT PROGRESS AND FUTURE PERSPECTIVES

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ABSTRACT

The transdermal drug delivery system (TDDS) is one of the controlled drug delivery systems, with the goal of delivering the drug via the skin at a predetermined and regulated rate. TDDS are adhesive drug-containing devices with a specific surface area that release a predetermined amount of drug to the surface of undamaged skin at a programmed rate until it enters the systemic circulation. The utilization of transdermal drug delivery systems (TDDS) has become a viable method of administering therapeutic substances through the skin barrier while avoiding the negative aspects of oral administration and invasive routes. This review provides an in-depth overview of the TDDS's fundamental ideas, modifications, clinical applications and challenges. It also examines forward to this rapidly evolving subject.

Mechanisms of penetration via the skin, formulation approaches, clinical success stories, recent advances, obstacles, and regulatory concerns are some of the significant topics that are mentioned. The main objective of this study is aimed at providing insights into the revolutionary promise of transdermal delivery of medications in contemporary treatment by reviewing existing information and highlighting future directions.
KEYWORDS: Transdermal drug delivery, skin permeation, transdermal patches, micro-needles, iontophoresis, therapeutic applications, tdds components.

INTRODUCTION

The skin, which is the body's most significant organ, functions as a formidable defence to drug penetration because of its complex structure and protective procedures, affords equal possibilities and hurdles for drug administration.

Transdermal drug delivery methods are emerging as a promising alternative to conventional delivery routes, offering numerous advantages such as enhanced compliance among patients, controlled release kinetics, and the reduction of first-pass metabolism.

However, TDDS utilizes a wide range of approaches to overcome these barriers, including passive diffusion, chemical enhancers, physical approaches such as microneedles, and cutting-edge technologies such as iontophoresis and sonophoresis. These techniques make it easier to transfer medications past the stratum corneum and into the systemic circulation, resulting in precise dosages for treatment.

The article aims to present an in-depth survey of transdermal drug administration, beginning with a deeper look into the mechanisms behind skin penetration and proceeding to the latest advancements and its applications in the field.

Basic Components of TDDS

1. Polymer matrix

Polymers form the backbone of TDDS, controlling the drug's release from the device. A polymer matrix can be created by dispersing a medication in a liquid or solid-state synthetic polymer basis. The polymers utilized in TDDS should be biocompatible and chemically
compatible with the medication and other system components, such as penetration enhancers and PSAs.

Furthermore, they should distribute a medicine consistently and effectively throughout the product's stated shelf life while being safe.

2. Membrane
A membrane can be sealed to the backing to create a pocket that encloses the drug-containing matrix, or it can be employed as a single layer in the patch assembly. The membrane's diffusion qualities are employed to regulate the availability of the medicine and/or excipients to the skin.

Ethylene vinyl acetate, silicone rubber, polyurethane, and other materials are commonly employed as rate-controlling membranes.

3. Drug
To successfully construct a TDDS, the medicine should be carefully chosen. Transdermal patches have numerous advantages over medications that undergo considerable first-pass metabolism, pharmaceuticals with a limited therapeutic window, or drugs with a short half-life that promote noncompliance due to frequent dosing. Some medicines that are appropriate for TDDS include Nicardipine hydrochloride, Captopril, Atenolol, Metoprolol tartrate, Clonidine, Indapamide, Propranolol hydrochloride, Carvedilol, Verapamil hydrochloride, and Niterdipine.

4. Permeation enhancers
One long-standing strategy to increasing TDD involves the use of penetration enhancers (also known as sorption promoters or accelerants), which improve the permeability of the SC in order to achieve higher therapeutic levels of the drug candidate.

Penetration enhancers interact with structural components of the SC, changing barrier functions and resulting in enhanced permeability. Three channels are proposed for drug penetration via the skin: polar, non-polar, and polar/non-polar. The enhancers function by changing one of these routes. The key to modifying the polar route is to create a change in protein structure or solvent swelling.
5. **Pressure-sensitive adhesives**

PSAS is a substance that adheres to a substrate, in this case skin, with light force and leaves no residue upon removal. They create interatomic and intermolecular attractive forces at the interface, assuming that intimate contact is established. To achieve this level of touch, the material must be able to deform with light pressure, hence the phrase "pressure sensitive". Adhesion involves a liquid-like flow that wets the skin surface when pressure is applied, and when the pressure is released, the adhesive sets in that state. When a PSA's surface energy is lower than that of the skin, it wets and spreads on it. After the initial adhesion, the PSA/skin relationship can be developed by stronger interactions (e.g., hydrogen bonding), which will depend on skin characteristics and other parameters.

Widely used PSA polymers in TDDS are polyisobutylene-based adhesives, acrylics and silicone-based PSAs, hydrocarbon resin, etc.

6. **Backing laminates**

Backings are chosen for appearance, flexibility, and occlusion; thus, while constructing a backing layer, the material's chemical resistance is the most crucial factor to consider. Excipient compatibility should also be examined because prolonged contact between the backing layer and the excipients may cause the additives to leach out of the backing layer or allow excipients, drugs, or penetration enhancers to diffuse through the layer.

The most comfortable backing will have the lowest modulus or great flexibility, good oxygen transfer, and a high moisture vapor transmission rate. Backing materials include vinyl, polyethylene, polyester, aluminium, and polyolefin films.

7. **Release liner**

During storage, the patch is coated with a protective liner, which is removed and discarded before applying the patch to your skin. Because the liner has direct contact with the TDDS, it should be chemically inert. A release liner is often constructed out of a base layer that can be non-occlusive (e.g., paper fabric) or occlusive (e.g., polyethylene, polyvinyl chloride), as well as a release coating layer made of Silicon or Teflon. Other materials utilized for TDDS release liners include polyester foil and metalized laminates.

8. **Other excipients like Plasticizers and Solvents**

Drug reservoirs are prepared using a variety of solvents, including chloroform, methanol,
acetone, isopropanol, and dichloromethane. Plasticizers including dibutyl phthalate, triethyl citrate, polyethylene glycol, and propylene glycol lend flexibility to the transdermal patch.

**Mechanisms of transdermal drug delivery**

1. **Passive diffusion**
   This is an especially usual mechanism in which medications travel from a higher concentration (in the drug formulation) to a lower concentration (in the skin layers and bloodstream) with no help of external force. The drug molecules penetrate the stratum corneum, which is the outermost layer of the skin, and then permeate into the epidermis and dermis before reaching the bloodstream.

2. **Reservoir systems**
   In this method, a drug reservoir is enclosed between a membrane that is permeable and an adhesive substrate. The drug is released from the reservoir in a controlled manner, dissipates via the layer of skin, and enters the bloodstream.

3. **Iontophoresis**
   It is a process that makes use of a small amount of electric current to propel charged molecules through the skin's barrier. The electric current influences the skin's permeability, allowing medicines to penetrate more easily.

Iontophoresis is highly efficient for delivering major compounds that cannot passively diffuse through the skin.

4. **Sonophoresis**
   It involves the application of ultrasound waves to the surface of the skin in order to temporarily interrupt the stratum corneum, allowing drugs to penetrate more easily. This method is often employed when combined with other transdermal delivery methods to increase medication consumption.

**Technologies in transdermal drug delivery**

1. **Patches**
   Transdermal patches are perhaps the most popular kind of transdermal delivery of medication. These patches generally consist of a drug-containing reservoir or matrix of nicotine, lidocaine or estradiol that is placed to the skin. They provide a controlled release of prescription drugs over a period of time, resulting in steady plasma levels.
2. Microneedle arrays

Microneedles are very small, surgical syringes which produce micropores in the stratum corneum, allowing drugs to penetrate deeper layers of the skin. They can be either solid or hollow, while they provide a painless and potent means of transdermal drug delivery.

3. Liposomes and Nanoparticles

These are lipid or polymer carriers that encompass medicinal compounds. They can improve drugs solubility, stability, and skin permeability. These delivery methods can be adjusted to target particular skin layers or cells.

4. Hydrogel-Based systems

Hydrogels are networks of three dimensions that are composed of hydrophilic polymers which can absorb huge volumes of water. They generate a humid environment that promotes drugs penetration through the skin and enhance patient comfort.
Advantages of TDDS
TDDS is harmless, enabling painless administration and more effective patient compliance, notably in youth and geriatric populations. Moreover, transdermal patches allow prolonged pharmaceutical release over a longer period of time, which results in stable plasma concentrations and lessened dose frequency.

This not only enhances the therapeutic effect but also minimizes fluctuations in levels of medication, lessening the chances of undesirable effects.

Clinical Applications and Success stories
Transdermal administration of drugs has been proven to oversight chronic pain, cardiovascular problems, hormone imbalances, and neurological disorders. For example, nicotine patches have altered the process of smoking cessation therapy, whilst hormone replacement patches provide a handy choice for menopausal women. Furthermore, TDDS has been shown to be successful in the delivery of analgesics, antiemetics, and anti-inflammatory drugs, which improves patient outcomes as well as quality of life.

Challenges and Limitations
Despite its apparent advantages, transdermal delivery of drugs confronts multiple challenges, such as limited drug permeability for larger molecules, variability in skin permeability between individuals, and the possibility of allergic reactions or hypersensitivity with particular formulations. Also, legal obstacles and manufacturing difficulty hinder the widespread implementation of TDDS. In order to solve the aforementioned issues, researchers, doctors, and regulatory organizations need to collaborate together to optimize formulation design, maximize delivery efficiency, and safeguard safety for patients.
Recent Advancements and Future perspectives

The latest advances in TDDS technology have brought about in the development of novel formulations and delivery strategies with the objective of further enhancing drug absorption, prolonging patch wear time, and enabling targeted distribution to specific tissues. Nanotechnology-based techniques, such as lipid nanoparticles and membrane systems, show potential for improving drug dissolution and skin penetration. In addition, incorporating smart sensors and microfluidic devices into transdermal patches allows for real-time monitoring of physiological parameters as well as customized drug delivery, bringing in a new era of personalized health care.

CONCLUSION

Transdermal drug delivery technology represents a safe, effective, and patient-friendly compliance, alternative to traditional medication methods. With endured research and technical advancements, the future holds tremendous potential for TDDS in terms of delivering a diverse range of medications, boosting treatment outcomes, and enhancing patient well-being. By overcoming current obstacles and unleashing the full potential of this special method, we are able to usher in a new era of customized and personalized healthcare.

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