



Trans Dermal Drug Delivery System

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Abstract

Transdermal Drug Delivery Systems (TDDS) represent an innovative method for administering medications via the skin, offering steady and prolonged therapeutic effects. This thesis delves into the underlying mechanisms, formulation strategies, component materials, and modern advancements in TDDS. Emphasis is on route and first-pass hepatic metabolism, TDDS can enhance systemic drug availability. Additionally, the thesis evaluates current use cases, challenges, and emerging trends in the field.

Keywords: Transdermal Drug Delivery; Controlled Drug Release; Skin Permeation; First-Pass Metabolism Avoidance; Drug Formulation Strategies

Introduction: Transdermal drug delivery systems provide an innovative route for systemic administration of therapeutics by facilitating absorption through the skin. This non-invasive approach offers several benefits over oral and injectable routes, notably the avoidance of gastrointestinal degradation and hepatic first-pass metabolism, leading to enhanced bioavailability of certain drugs.

These systems are particularly advantageous for compounds with low oral bioavailability, short half-lives, or those requiring steady plasma concentrations. Drugs such as fentanyl, nicotine, and nitroglycerin have been successfully delivered through transdermal patches.

History: The origins of transdermal therapy date back to ancient times when herbal pastes and oils were applied topically to treat various ailments. These early practices laid the conceptual groundwork for modern transdermal drug delivery, although they lacked scientific validation.

Following this success, transdermal systems were developed for cardiovascular treatments and chronic pain relief. Drugs like nitroglycerin, fentanyl, and clonidine soon followed, demonstrating the practicality of transdermal patches for long-term management of diseases requiring steady drug plasma levels.

With advances in polymer chemistry, nanotechnology, and biocompatible materials in the 2000s, TDDS evolved into a robust field that spans pharmaceuticals, dermatology, and biomedical engineering. Today,

transdermal patches are widely used for administering hormones, analgesics, cardiac drugs, and vaccines, and the field continues to grow through interdisciplinary research and innovation.

Advantages:

1. **Non-invasive administration:** TDDS avoids needles and the digestive system, reducing discomfort and improving safety, especially for patients afraid of injections.
2. **Improved patient compliance:** With reduced dosing frequency often once daily or even weekly TDDS enhances adherence to treatment regimens.
3. **Controlled drug release:** Patches can maintain a consistent plasma drug level over extended periods, minimizing fluctuations and peak-related side effects.
4. **Convenience and discretion:** Patches are portable, easy to use, and allow patients to maintain a routine without frequent dosing or medical supervision.
5. **Applicability in special populations:** Particularly beneficial for geriatric and pediatric patients or individuals with swallowing difficulties.

Disadvantages:

1. **Skin irritation:** Some formulations may cause contact dermatitis or allergic reactions due to adhesives or excipients.
2. **Limited drug candidates:** Only drugs with specific properties low molecular weight (<500 Da), sufficient potency, and suitable lipophilicity are viable for transdermal delivery.
3. **Slow onset of action:** TDDS is generally unsuitable for drugs requiring rapid therapeutic effects, as drug permeation through the skin takes time.
4. **Higher manufacturing cost:** TDDS requires advanced materials and technologies, which can increase production expenses compared to tablets or capsules.
5. **Variability in skin permeability:** Differences in skin thickness, hydration, and environmental exposure can affect absorption and bioavailability.

Key physicochemical properties influencing passive diffusion include:

- **Molecular weight:** Ideal candidates are under 500 Da.
- **Lipophilicity:** A log P (partition coefficient) between 1 and 3 enhances solubility in both lipid-rich and aqueous environments.
- **Melting point:** Lower melting points (<200C) are preferred for sufficient solubility at skin temperature.
- **Active Enhancement Techniques:-** For drug that do not readily permeate the skin, active delivery techniques are employed to temporarily disrupt the stratum corneum or increase drug mobility.
- **Iontophoresis:** Uses a mild electric current to enhance the delivery of charged drugs.
- **Electroporation:** Applies short high-voltage pulses to create temporary aqueous channels in the lipid bilayers.
- **Sonophoresis:** Uses ultrasound waves to disrupt lipid structures in the skin.
- **Microneedles:** Physically breach the stratum corneum to allow direct entry of drug molecules into deeper layers.

Types of TDDS

- 1. Single-Layer Drug-in-Adhesive Systems:** In this type of TDDS, both the adhesive layer and the drug layer are integrated. The drug is embedded within the adhesive material, which also serves as the medium for controlled release.
- 2. Multi-Layer Drug-in-Adhesive Systems:** Similar to single-layer systems, multi-layer drug-in-adhesive systems consist of multiple adhesive layers, each potentially containing different amounts of the drug. A membrane separates each layer to ensure a controlled release profile, offering more precise drug delivery.
- 3. Drug Reservoir-in-Adhesive Systems:** These systems consist of a distinct drug reservoir separated from the skin by an adhesive layer. The reservoir, often liquid or gel-based, provides zero-order drug release, meaning that the drug is delivered at a constant rate, independent of concentration.

Classification of TDDS Based on Technology:

- **Conventional or Passive TDDS:-** These systems rely solely on the natural diffusion of drug molecules across the skin barrier. The release of the drug is governed by its physicochemical properties, including molecular weight, solubility, and lipophilicity.
- **Active TDDS:-** Active transdermal systems utilize external energy or mechanical assistance to enhance skin permeability and allow delivery of drugs that would otherwise be poorly absorbed.
- **Sonophoresis (Phonophoresis):** Uses ultrasound waves to temporarily disrupt the lipid matrix of the stratum corneum, facilitating drug passage.
- **Microneedles:** These are tiny projections that painlessly puncture the outer skin layers to create microchannels, allowing drugs including proteins and vaccines to bypass the stratum corneum barrier.

Physicochemical Evaluation:

- **Thickness and weight uniformity:** Each patch must be evaluated for consistent thickness and uniform weight distribution, which reflect proper manufacturing practices and dosing consistency.
- **Drug Content Uniformity:** Ensures each patch delivers the intended drug dose. This is typically tested by dissolving the patch in a suitable solvent and analyzing the extract using techniques like UV spectroscopy or HPLC.

Skin Barrier Function: The stratum corneum, the outermost layer of the skin, acts as a strong barrier to drug penetration. Although permeation enhancer and techniques like microneedles can improve delivery, they may cause irritation or compromise skin integrity if not carefully controlled.

Additionally, variations in skin physiology due to factors like age, site of application, hydration, and disease state can lead to inconsistent absorption profiles.

Regulatory and Stability Concerns:

- **Strict requirements:** Transdermal products must meet rigorous safety, efficacy, and skin tolerability standards.
- **Stability issues:** Drugs sensitive to temperature, light, or humidity may degrade more easily in patch formulations.

Vaccine and Gene Delivery: Microneedle patches are being explored for painless, needle-free vaccination, which is particularly valuable in pandemic preparedness and mass immunization campaigns. Additionally, transdermal delivery of gene therapies and nucleic acids is gaining interest as a non-invasive alternative to traditional injection routes.

Summary: Transdermal Drug Delivery Systems (TDDS) provide a non-invasive method for administering drugs through the skin directly into systemic circulation. These systems bypass the gastrointestinal tract and first-pass metabolism, offering controlled and sustained drug release with improved patient compliance. Modern systems use advanced materials like polymers, adhesives, and permeation enhancers to optimize delivery. Several FDA-approved TDDS products exist for pain management, hormone replacement, and neurological conditions. Recent advances include smart patches integrated with biosensors, stimuli-responsive delivery systems, and wearable devices for real-time monitoring.

Conclusion: TDDS have emerged as a powerful alternative to conventional drug administration routes, offering non-invasive, controlled, and patient-friendly delivery of a wide range of therapeutic agents. By circumventing the gastrointestinal tract and hepatic first-pass metabolism, TDDS enhances drug bioavailability and supports sustained plasma concentrations features especially valuable in chronic and long-term therapies.

Despite these advances, the field continues to face challenges, including skin barrier limitations, restricted drug suitability, and potential for local skin reactions. However, ongoing research in biocompatible materials, stimuli-responsive systems, and personalized medicine is rapidly addressing these barriers.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship and publication of this article.

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