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A COMPREHENSIVE REVIEW ON TRANSDERMAL PATCHES FOR ANTIFUNGAL DRUG DELIVERY

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ABSTRACT

Fungal infections are very common and often need long-term treatment, but oral antifungal medicines can cause side effects and may not always give consistent results. Because of this, transdermal drug delivery systems (TDDS) are becoming an attractive alternative. Transdermal patches deliver medicine through the skin at a controlled rate, avoid first-pass metabolism, reduce stomach-related problems, and improve patient comfort and compliance. This review explains the basic design of antifungal transdermal patches, including reservoir, matrix, and drug-in-adhesive systems, along with the role of polymers, plasticizers, and penetration enhancers in improving patch performance. It also discusses commonly used antifungal drugs such as azoles, allylamines, and polyenes, and the challenges related to their skin permeability. Modern approaches like microneedles, iontophoresis, and nanocarriers are highlighted as promising methods to enhance drug delivery. In addition, important evaluation methods such as thickness testing, drug release studies, permeation studies, and stability testing are described. Overall, antifungal transdermal patches offer a safe, convenient, and effective way to treat fungal infections, although more research is still needed to overcome limitations like skin irritation and limited drug loading.

INTRODUCTION

Transdermal preparations have been explored extensively as an alternate drug delivery method for a variety of active chemicals. Transdermal application can stop the first-pass effect, which has fewer adverse effects than oral formulations. Transdermal preparations allow medications to enter the body through the skin and have systemic effects. One formulation used to address potential issues with plant extract-based treatment is a transdermal medication delivery method. Certain medicines require intricate processes to synthesize plant extracts. Additionally, the majority of their active ingredients have poor penetration, such they are broken down in the liver and become unstable in extremely acidic situations. A transdermal patch made of polymers is an illustration of a transdermal medication delivery device. The most crucial components for creating patch matrices that measure the rate of medication release as a gauge of treatment effectiveness are polymers. A transdermal patch is a medicated adhesive patch that is applied to the skin to deliver medications percutaneously into the bloodstream at a predetermined dosage. Plasticizers are one of the patch components that influence its elasticity and stability. Plasticizers are low molecular weight liquids or resins that reduce secondary bonds in polymer chains and instead creating ones with polymer chains. Polymer materials can have their resting times extended and their toughness and flexibility increased by adding plasticizers. However, it is anticipated that hardness and tensile strength will decline. Incorporating plasticizers into transdermal drug delivery systems can enhance the patch formulation's qualities and appearance, lower the polymer glass transition temperature, avoid cracks, boost flexibility, and achieve the mechanical qualities required for transdermal patches.[1]

In recent years, there has been a growing interest in creating innovative medication delivery systems for Current pharmaceutical compounds have been revitalized. In addition to improving the drug's performance in terms of safety and efficacy, the creation

of a novel delivery system for already-existing drug molecules significantly increases patient compliance and the overall therapeutic benefit. One Transdermal Drug Delivery Systems (TDDS) are self-contained, discrete dose forms, sometimes referred to as "patches." Deliver the medication to the systemic circulation through the skin at a regulated rate when patches are applied on unbroken skin. TDDS are dose forms made to apply a therapeutically effective dosage of medication to a patient's skin. The primary goal of a transdermal drug delivery system is to administer medications via the skin to the systemic circulation at fixed rate with little variation between and within patients. Transdermal administration is now one of the most promising ways to provide drugs. It lessens the strain that the oral route often places on the liver and digestive system. It improves patient compliance, reduces negative drug side effects from brief overdoses, and is convenient for transdermal medications that only need to be applied sparingly.[2]

Benefits of TDDS

- Transdermal medicine provides a continuous drug infusion over a long duration.
- The transdermal patch can be removed at any time to stop the drug input.
- The streamlined drug schedule results in enhanced patient compliance and decreased inter- and intra-patient variability.
- These systems allow for self-administration.
- They can be applied to medications with limited therapeutic windows.
- Reduced frequency of dosage due to a longer duration of action By removing the application from the skin's surface, drug therapy can be quickly stopped.

Disadvantages of TDDS[3]

- When using one or more of the system's components, some patients have contact dermatitis at the application site, which requires stopping.
- Before deciding to manufacture a transdermal product, clinical need must also be thoroughlyconsidered.
- The skin's barrier function varies within an individual, between individuals, and with age.
- Many medications, particularly those with hydrophilic properties, penetrate the skin too slow.
- Erythema, itching, and localized edema may result from the medication, adhesive, or other excipients in the patch formulation
- The skin's barrier function varies within an individual, between individuals, and with age.

Limitations of TDDS[4]

- Due to system components, some patients get contact dermatitis at the application site.
- The skin's barrier function varies depending on the site, individual, and age.
- The number of drugs that can be administered in this way is limited by poor skin permeability.
- A high drug level cannot be achieved by this system.
- Transdermal drug delivery is limited to potent drugs.
- It cannot deliver drugs in a pulsatile manner.
- Tolerance-inducing drugs or those (like hormones) that chronopharmacological management are not suitable candidates.
- It requires a significant lag time.

Properties of TDDS

- A sufficient solubility in water and fat is required for improved medication penetration.
- Good therapeutic activity requires an optimal partition coefficient, therefore a medication with a low melting point (<200°C) is preferred.

The saturated solution's pH should be between 5 and 9.

Types of TDDS[5]

(i) Reservoir system

Structure[6]

A reservoir patch contains:
Backing layer (protective outer layer)
Drug reservoir (liquid or gel form of drug
Rate-controlling membrane
Adhesive layer
Protective liner (removed before use)

How It Works

The drug is stored in a liquid/gel reservoir and released slowly through a semi-permeable membrane. The membrane controls the release rate.

Examples

Nitroglycerin patches (for angina)
Scopolamine patches (motion sickness)

Advantages[7]

Precise, controlled drug release
Suitable for potent drugs
Long duration of action

Disadvantages[8]

Risk of dose dumping if membrane breaks
More complex manufacturing
Thicker than other type

(ii) Matrix systems without a rate-controlling membrane

Structure[9]

Backing layer
Drug uniformly dispersed in polymer matrix
Adhesive
Release line

How It Works[10]

The drug is embedded in a polymer matrix. It diffuses slowly from the matrix into the skin.

Examples
Nicotine patches
Hormone replacement patches

Advantages[11]
Simpler design
Lower risk of dose dumping
Flexible and comfortable

Disadvantages[12]
Less precise control than reservoir type
Drug release depends on matrix properties

(iii) Drug-in-Adhesive transdermal patch[13]
Structure[14]
The drug is directly incorporated into the adhesive layer.

Types
Single-layer drug-in-adhesive
Multi-layer drug-in-adhesive

How It Works
When applied to the skin, the drug diffuses directly from the adhesive into the bloodstream.

Examples[15]
Fentanyl patches
Nicotine patches (many modern ones)

Advantages
Thin and comfortable
Easy to manufacture
Good patient compliance

Disadvantages[16]
Limited drug loading capacity
Possible skin irritation

Antifungal Drugs Used in Transdermal Systems[17]
➢ **Azoles**[18]
Mechanism: Inhibit ergosterol synthesis by blocking lanosterol 14α-demethylase.

Examples
- Fluconazole
- Ketoconazole
- Luliconazole
- Clotrimazole
- Posaconazole

Advantages
- Broad spectrum
- Good safety profile

Challenges
- Variable permeability
- Potential hepatotoxicity (systemic)

➢ **Allylamines**
Example: Terbinafine

Mechanism
- Inhibits squalene epoxidase
- Causes toxic squalene accumulation

Advantages
- Fungicidal activity
- Effective against dermatophytes

➢ **Polyenes**[19]
Example: Amphotericin B

Mechanism
- Binds ergosterol
- Forms membrane pores

Challenges
- High molecular weight
- Poor permeability
- Systemic toxicity

Penetration Enhancement Techniques
➢ **Chemical Enhancers**[20]
- Alcohols
- Fatty acids (oleic acid)
- Surfactants
- DMSO

➢ **Physical Enhancers**
- Microneedles
- Iontophoresis
- Sonophoresis
- Electroporation

➢ **Nanotechnology Approaches**[21]
- Lipid-based carriers
- Polymeric nanoparticles
- Transfersomes
- Ethosomes

Evaluation and Characterization of Antifungal Patches
7.1 Physicochemical Evaluation[22]
- Thickness
- Weight uniformity
- Folding endurance
- Moisture content
- Drug content uniformity
- Surface pH

7.2 Mechanical Properties[23]
- Tensile strength
- Elasticity
- Adhesion strength

7.3 In Vitro Drug Release
- Franz diffusion cell
- Release kinetics modeling:
  - Zero order

- First order
- Higuchi model
- Korsmeyer-Peppas model

7.4 Ex Vivo Permeation Studies[24]

- Animal skin (rat, pig)
- Human cadaver skin

Measured parameters

- Flux (µg/cm²/hr)
- Permeability coefficient
- Lag time

7.5 Antifungal Activity

- Zone of inhibition
- MIC determination
- Time-kill studies
- Biofilm inhibition studies

7.6 Stability Studies

- ICH guidelines
- Temperature & humidity conditions
- Drug degradation monitoring

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