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Review Article

Transdermal Drug Delivery System: A Review

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ABSTRACT

The development of the transdermal drug delivery system aimed to address the issues related to oral drug consumption.These systems usually involve applying medicated adhesive patches on skin to deliver medication directly into the bloodstream for targeted treatment. One significant advantage of these patches is their ability to release medication in a controlled manner , either through a porous membrane over a medication reservoir or via melting by body temperature, thin medication layers within the adhesive.This article seeks to explain the pros, cons, and important components of the transdermal drug patches , including polymers, permeation enhancers, backing laminates, and adhesives. Assessment criteria cover various aspects like chemical properties, adhesive effectiveness, and results from in vivo and in vitro studies. Recent advances in this area show a growing interest in transdermal delivery due to its potential to minimize side effects when compared to the other methods of administration.

INTRODUCTION

Transdermal drug delivery systems (TDDS) are self-contained forms of medication that release drugs through the skin at a controlled rate into the bloodstream1,2. This method is effective for both local and systemic delivery of drugs. TDDS are designed to transport an effective dose of drug through the skin, avoiding issues like reduced effectiveness from liver metabolism3. The goal of TDDS is to optimize drug absorption while minimizing retention and metabolism in the skin4. This delivery method ensures consistent drug release and avoids sudden spikes in drug levels that can cause side effects. Innovative drug delivery systems, including TDDS, have become popular for their benefits5.

TABLE 1: Example of patches and their uses

PATCH	USES
Nicotine patches	Smoking cessation
Nitroglycerine	Angina pectoris

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Scopolamine	Motion sickness
Rotigotine	Parkinson's disease

ADVANTAGES OF TDDS :

1. TDDS is a drug delivery method employing a patch to steadily deliver medication into the bloodstream, circumventing issues associated with other dosage forms6.
2. This approach ensures a steady concentration of medication for effective treatment. It is a useful option for patients who cannot take medications orally, especially for those with gastrointestinal problems or who are unable to swallow7.
3. TDDS also offers an alternative for patients who are nauseous or unconscious8.
4. It helps maintain a consistent drug level in the blood, similar to intravenous infusion, and can be easily removed in case of toxicity9.
5. This method is convenient for drug administration, bypasses the first-pass metabolism, reduces systemic drug interactions, extends drug action duration, and can be self-administered10.

DISADVANTAGES OF TDDS11 :

1. Many hydrophilic drugs face difficulty in passing through the skin or do so at a slow rate, which can impact the effectiveness of the drug.
2. Skin patches may lead to issues like itching, swelling, or redness. The strength of the skin's barrier can differ depending on factors like age or location on the body. There is a possibility of irritation at the application site.
3. Using this drug delivery method might be costly and is more suitable for long-term conditions rather than sudden ones.

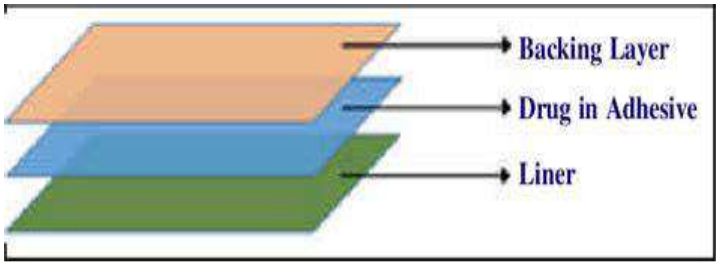
TABLE 2 : Properties and range of transdermal patch

PROPERTIES	RANGE
Shelf life	Shelf life should be up to 2.5 years
Patch size	Size should be less than 40cm^2
Dose frequency	Once a daily – once a week
Appearance	Should be clear or white colour
Packaging properties	Should be easily removable of release liner
Skin reaction	Should be non-irritating
Release properties	Should have consistent pharmacokinetic and
Packaging properties	Pharmacodynamics profiles over time
	Should be easily removable of release liner

TYPES OF TRANSDERMAL PATCHES12,13

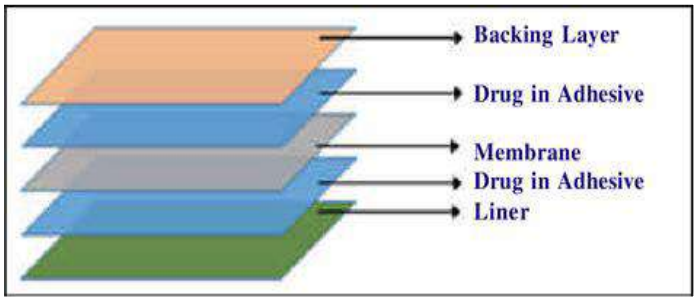
1. SINGLE-LAYER DRUG IN ADHESIVE

The drug-in-adhesive system contains the drug within the adhesive layer, which serves to hold the layers together, attach it to the skin, and aid in drug release. This adhesive layer is covered by a removable liner and a backing.



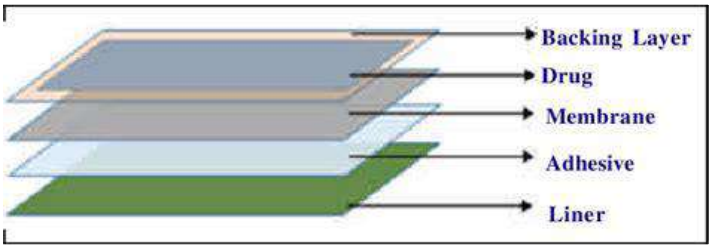
2. MULTI-LAYER DRUG IN ADHESIVE :

The multi-layer drug-in-adhesive patch resembles the single-layer system in terms of drug release, but it sets itself apart by incorporating multiple adhesive layers for drug delivery. In the multi-layer type of patch, there are typically multiple layers of drug-in-adhesive, with adhesive layers separating the drug layers. It also includes a removable liner layer and a backing, akin to the single-layer patch.



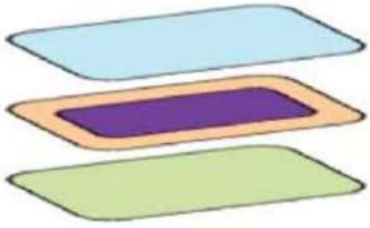
3. RESERVOIR :

The distinctive feature of the reservoir transdermal system compared to other drug-in-adhesive systems is its incorporation of an independent drug reservoir, typically in the form of a liquid compartment containing a drug solution or suspension. This drug reservoir is isolated by the adhesive layer and supported by a backing layer. Unlike other systems, the reservoir system releases the drug at a consistent rate known as a zero-order pattern.



4. MATRIX :

The matrix system incorporates a layer of medication composed of a semi-solid matrix that holds drug content. In this formulation, the adhesive layer covers part of the drug layer.



Drug matrix-in-adhesive

5. VAPOUR PATCH :

These adhesive patches not only bind the layers but also assist in vapor emission. They are a recent product intended for the release of essential oils over 6 hours and are primarily used for clearing congestion. Controlled-release vapor patches are also on the market to enhance sleep and reduce smoking habits.

COMPONENTS OF TRANSDERMAL PATCHES 14,15,16 :

Compents of transdermal patches are:

1. Polymers
2. Drug
3. Permeation enhancers
4. Excipient’s

1. **Polymers:**

The polymer matrix plays a crucial role in controlling drug release from patches. It can be either in matrices or reservoirs form, playing a key role in drug dispersion. Polymers need to meet certain criteria such as consistency, compatibility with drugs, safety, and skin-friendly characteristics. Various examples of polymers include natural polymers like cellulose derivatives, as well as synthetic elastomers and polymers.

EXAMPLES :

Natural Polymers:

Cellulose derivatives, natural proteins, shellac, starch, waxes, zein etc.

Synthetic Elastomers:

Acrylonitrile, butyl rubber, hydrin rubber, neoprene, nitrile, silicone poly siloxanes, rubber and styrene butadiene rubber.

Synthetic Polymers:

Polyamide, polyacrylate, polyethylene, polypropylene, polyurea, etc.

2. **Drug :**

Transdermal drug delivery is beneficial for drugs with specific characteristics such as a narrow therapeutic window or extensive first-pass metabolism.

3. **Permeation enhancers :**

Permeation enhancers help to increase drug permeability by interacting with its structural components, thus enhancing therapeutic levels.

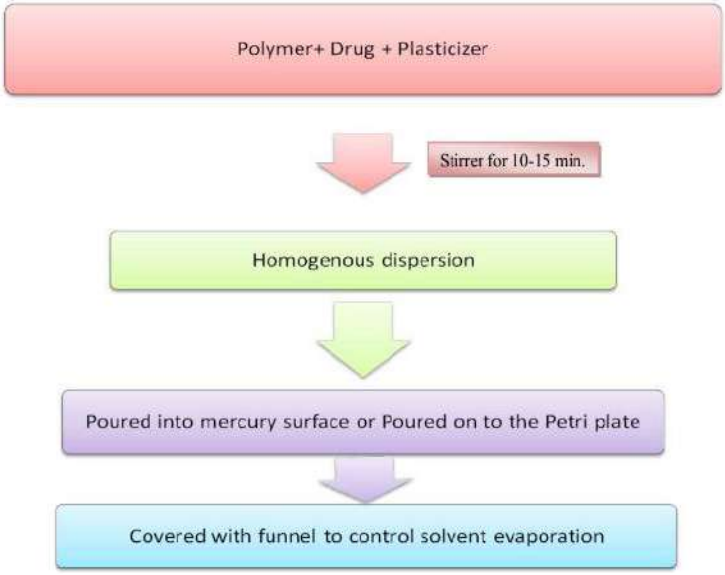
4. **Excipient's :**

Excipients, including adhesives and backing laminate, are essential components of transdermal patches.Adhesives need to be tacky, long-lasting, skin-friendly, and should not alter drug release patterns.

EXAMPLE :

Polyisobutylene, acrylics, and silicones.

Backing laminate should be flexible, allow for oxygen and moisture transmission, and prevent leaching or diffusion of components. Examples of backing membranes include metallic plastic laminates and adhesive foam pads.



EVALUATION PARAMETERS :

Evaluation of the patches involves assessing various parameters such as :

- Physicochemical properties,
- Adhesive characteristics,
- In vitro evaluation
- In vivo assessment.
- Physiochemical evaluation includes17,18 :

1. **Measurements of thickness:**

to determine the depth of the patch at various points using a micrometer. The mean and variability are estimated.

2. Weight variation:

10 patches selected at random are weighed. The average weight of the patches and the estimated standard deviation are determined.

3. Folding endurance of the patches:

Folding endurance is gauged by the film's folding capacity, which refers to the number of times the film can be folded at a particular area until it breaks, thus yielding the folding endurance value.

Evaluation of adhesives focuses on factors like :

1. Peel adhesion:

Peel adhesion is defined as the force needed to detach an adhesive coating from the test substrate. The molecular weight of an adhesive polymer, the nature and amount of adhesive, and the constituents of the polymer affect the adhesion properties of the polymers the test is carried out by placing the patch over the substrate and measuring the force required to pull it out at an angle of 180◦. The test is passed if there is no residue left on the substrate19.

2. Tack properties :

Tack refers to the adhesive polymer's capability to adhere to the substrate upon the application of minimal pressure.Tack properties can be assessed by following tests:

- **Thumb tack test :**

The adhesive is applied over the thumb and the force needed to remove it from the thumb is measured.

- **Rolling ball test:**

The adhesive is placed in an upward-facing direction and a stainless steel ball is allowed to travel over it along its length. The more adhesive, the shorter is the distance covered by the ball.

- **Peel tack test:**

The adhesive is applied onto the substrate and the force needed to separate the bond between the adhesive and the substrate is measured while removing the adhesive from the substrate at a speed of 90 inches/min at an angle of 90°.

3. Shear strength properties:

Shear strength or creep resistance is the measurement of cohesive strength of an adhesive polymer. Shear strength is assessed through the time taken for pulling an adhesive-coated tape from a stainless steel plate upon the application of a certain weight to the adhesive.20,21,22.

- In vitro studies help understand the skin permeation mechanisms of drug molecules using devices like:

1. Franz diffusion cell23.

- In vivo evaluation involves testing on 24:

1. Animal models,
2. Human volunteers,
3. Biophysical models

CONCLUSION:

In recent times, the use of transdermal patches has increased due to their efficacy and reduced side effects. Various research is conducted on transdermal drug delivery because of increased use by patients. This system is preferred for patients who cannot swallow and unconscious patients. Various techniques are developed to enhance it for better absorption into systemic circulation. This article provides information on transdermal drug delivery systems and evaluation parameters.

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