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## RECENT ADVANCES IN TRANSDERMAL PATCHES

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### ABSTRACT

Transdermal drug delivery systems (TDDS) have gained significant attention in the field of pharmaceuticals due to their ability to provide a controlled and sustained release of drugs through the skin, thereby bypassing the oral route and its associated challenges. The primary objective of transdermal delivery is to enhance patient compliance by offering a non-invasive and painless mode of drug administration. Various techniques, such as patches, gels, and micro/nanoemulsions, have been developed to facilitate efficient drug permeation through the skin barrier. This review highlights the mechanisms underlying transdermal drug delivery, emphasizing the importance of formulation techniques, skin permeation enhancers, and the selection of appropriate drug candidates. Additionally, the review discusses challenges related to skin permeability, drug stability, and regulatory approval, underscoring the need for continuous research and innovation in formulation technologies. Furthermore, the impact of transdermal drug delivery on specific therapeutic areas, including pain management, hormone replacement therapy, and cardiovascular diseases, is explored. Looking forward, this examines emerging trends such as microneedle-based systems, smart patches, and personalized transdermal therapies, providing a glimpse into the future of drug delivery. As TDDS continue to evolve, they hold the promise of revolutionizing healthcare by improving patient outcomes, ensuring precise drug dosing, and minimizing adverse effects, ultimately leading to enhanced overall quality of life for patients.

**Keywords:** Sustained release, Non-invasive, Drug permeation, Pain management, Hormone replacement

## INTRODUCTION -

In the realm of modern medicine, the development of innovative drug delivery systems has significantly improved patient care and treatment outcomes. Transdermal drug delivery has emerged as a groundbreaking method for administering therapeutic compounds through the skin, offering numerous advantages over traditional routes such as oral ingestion or injections. This article explores the intricacies of transdermal drug delivery systems, highlighting their mechanism of action, advantages, challenges, and promising future prospects. The field of pharmaceutical technology has witnessed significant advancements in recent years, leading to the development of novel drug delivery systems [1]. Among these systems, transdermal drug delivery has emerged as a promising approach for administering therapeutic agents through the skin. Transdermal patches, a key component of transdermal drug delivery systems, offer numerous benefits, including improved patient compliance, enhanced therapeutic efficacy, and minimized side effects. This article aims to provide a comprehensive overview of transdermal drug delivery systems, focusing on transdermal patches. We will explore their history, classification, advantages, disadvantages, and discuss several drugs commonly administered using transdermal patches [1, 2].

Transdermal drug delivery involves the absorption of medications through the layers of the skin for systemic distribution within the body. The human skin, comprising the outermost layer called the stratum corneum, acts as a formidable barrier, protecting the body from external factors. However, it also possesses a unique property—permeability, which allows for the passage of certain molecules. Leveraging this property, transdermal drug delivery systems deliver therapeutic compounds in a controlled manner, ensuring optimal drug release and absorption [3].

### Layers of Transdermal Patches-

The layers typically include:

- 1. Backing Layer:** This layer, located at the bottom, provides structural integrity to the patch and protects the drug formulation from external factors.
- 2. Drug Reservoir:** The drug reservoir contains the medication, which may be in the form of a liquid, gel, or solid matrix. The reservoir is responsible for storing the drug and controlling its release rate.
- 3. Membrane:** The membrane separates the drug reservoir from the adhesive layer and plays a crucial role in regulating the rate at which the drug is released from the patch.
- 4. Adhesive Layer:** The adhesive layer ensures proper attachment of the patch to the skin, providing stability and allowing for controlled drug delivery [4].

**Mechanism of Action:**

The stratum corneum, the outermost layer of the skin, serves as the primary barrier for drug penetration. It consists of closely packed dead skin cells embedded in a lipid-rich matrix. Transdermal drug delivery systems employ various strategies to overcome this barrier:

**1.Enhancing Permeability:** Methods like chemical enhancers, iontophoresis (use of electrical current), and sonophoresis (use of ultrasound) can temporarily disrupt the

stratum corneum, facilitating drug penetration.

**2.Drug Solubility:** The drug must be formulated in a manner that promotes solubility in the skin and allows it to diffuse across the various layers.

**3.Controlled Release:** The transdermal system controls the release rate of the drug to maintain a therapeutic concentration in the bloodstream over an extended period. This ensures a constant drug level, reducing the need for frequent dosing [4, 5].

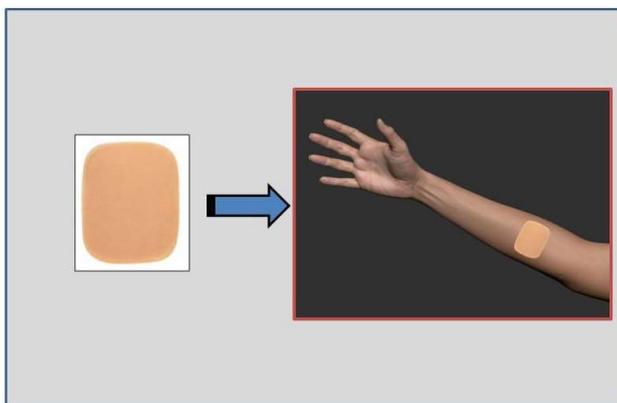


Figure: 1.1 Transdermal Patch Applied on Hand

**HISTORY -**

The history of transdermal drug delivery systems, specifically transdermal patches, can be traced back several decades. The concept of delivering medications through the skin for systemic absorption has evolved over time, leading to significant advancements in the field. Here is a brief overview of the history of transdermal drug delivery systems:

**1960s:**

The idea of transdermal drug delivery began to take shape in the 1960s. Early experiments involved the use of skin patches with reservoir systems for the delivery of drugs such as scopolamine and nitroglycerin. These early patches faced challenges in maintaining drug stability and controlling drug release rates.

**1970s:**

In the 1970s, the first commercial transdermal patch was introduced. In 1979,

the FDA approved the scopoderm patch for the prevention of motion sickness. This marked a significant milestone in transdermal drug delivery, demonstrating the viability and potential of the technology.

#### **1980s:**

The 1980s saw the development of more transdermal patches for various therapeutic indications. In 1981, the Transderm-Nitro patch, delivering nitroglycerin for angina treatment, was approved by the FDA. The release of the Estraderm patch for hormone replacement therapy in 1985 further expanded the application of transdermal patches.

#### **1990s:**

During the 1990s, the field of transdermal drug delivery continued to advance, and more patches were introduced. In 1991, the FDA approved the Duragesic patch, which delivered the potent opioid analgesic fentanyl for managing chronic pain. This marked a significant breakthrough in transdermal delivery for high-potency drugs.

#### **2000s and Beyond:**

The 2000s witnessed further advancements in transdermal patch technology. The development of novel adhesive formulations and permeation enhancers allowed for improved patch adhesion and enhanced drug permeation. This resulted in the introduction of patches for diverse therapeutic areas, including smoking cessation (nicotine

patches), hormone therapy, pain management, and cardiovascular disorders.

In recent years, there has been increasing interest in developing innovative transdermal patch technologies. These include microneedle patches, which use microscopic needles to enhance drug delivery efficiency and expand the range of drugs that can be delivered transdermally.

Today, transdermal patches have become an established and widely accepted drug delivery method. They offer numerous advantages, such as controlled drug release, convenience, and improved patient compliance. Ongoing research continues to focus on optimizing patch design, enhancing drug permeation, and expanding the range of drugs that can be effectively delivered through the skin. The history of transdermal drug delivery systems showcases the evolution of this technology from early experimental stages to its current state as a reliable and effective drug administration method, offering promising prospects for the future of healthcare [6].

#### **TYPES-**

Transdermal drug delivery systems offer several different types, each with its unique characteristics and applications. Here are some of the prominent types of transdermal drug delivery systems:

##### **1. Matrix Patches:**

Matrix patches are the most common type of transdermal drug delivery systems. They

consist of a drug-containing matrix dispersed in an adhesive polymer. The drug is uniformly distributed throughout the matrix, and the adhesive layer helps the patch adhere to the skin. The drug diffuses through the matrix and then permeates the skin for systemic absorption. Matrix patches are versatile and can deliver a wide range of drugs, including small molecules, hormones, and analgesics [7].

## 2. Reservoir Patches:

Reservoir patches have a distinct drug reservoir separate from the adhesive layer. The drug reservoir is a compartment that contains the drug formulation, and it is typically surrounded by a semipermeable membrane. The membrane controls the drug release rate from the reservoir, allowing for a more precise and controlled release profile. Reservoir patches are often used for drugs with complex release kinetics or those requiring high loading dose [8].

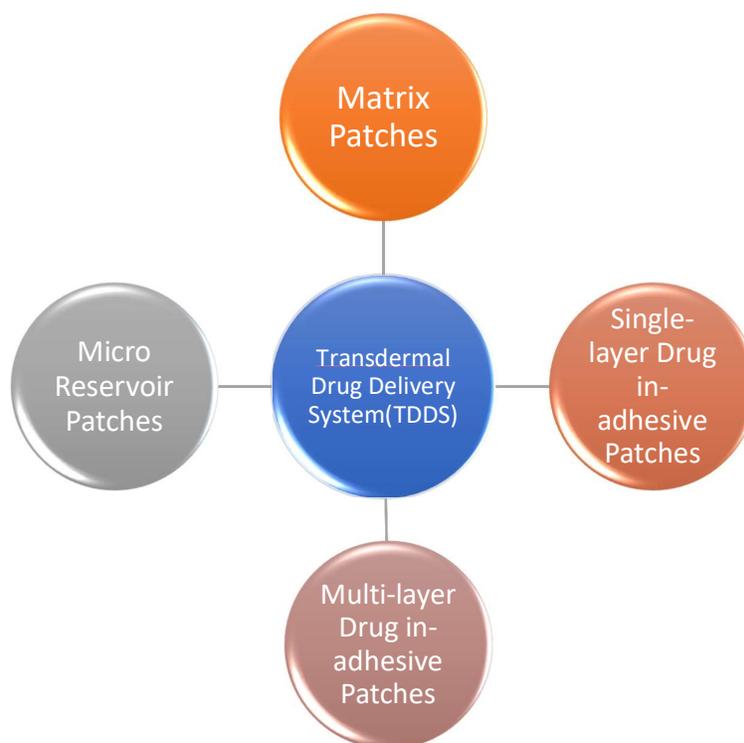


Figure 2: Types of Transdermal Drug Delivery

## 3. Microreservoir Patches:

Micro reservoir patches are a variation of reservoir patches where the drug reservoir consists of multiple micro reservoirs. These

micro reservoirs are encapsulated within a polymer matrix or contained within a microneedle array. Micro reservoir patches provide more precise control over drug

release and allow for the delivery of a larger volume of drugs, including those with poor solubility or high molecular weight. They also offer the potential for controlled release of multiple drugs simultaneously [9].

#### **4. Drug-in-Adhesive Patches:**

In drug-in-adhesive patches, the drug is directly dispersed within the adhesive layer of the patch. The adhesive layer acts as both the drug reservoir and the adhesive for attachment to the skin. This type of patch offers simplicity in design and manufacturing and can accommodate a wide range of drug types. Drug-in-adhesive patches are commonly used for delivering drugs with low doses or drugs requiring frequent dosing intervals [10].

#### **5. Active Transdermal Patches:**

Active transdermal patches incorporate additional components to enhance drug permeation through the skin. These components can include permeation enhancers, which help temporarily disrupt the stratum corneum barrier, or technologies such as iontophoresis, which use electrical currents to facilitate drug transport across the skin. Active transdermal patches are particularly useful for drugs with poor skin permeability or high molecular weight [11].

#### **6. Dissolving Microneedle Patches:**

Dissolving microneedle patches utilize an array of microscopic needles to painlessly penetrate the outer layer of the skin. These microneedles are made from biocompatible

materials and can be loaded with drug formulations. Once inserted into the skin, the microneedles dissolve, releasing the drug into the skin layers for systemic absorption [12-13]. Dissolving micro needle patches offer improved drug delivery efficiency and are suitable for delivering a wide range of drugs, including vaccines and biologics. Each type of transdermal drug delivery system has its advantages and limitations, and the selection depends on the specific drug, therapeutic requirements, and patient needs. Continued research and technological advancements are expanding the range of transdermal delivery options, providing new opportunities for efficient and patient-friendly drug administration [14-15].

#### **ADVANTAGES -**

Transdermal drug delivery systems offer several advantages compared to conventional routes of drug administration:

**1. Non-Invasive:** Transdermal delivery avoids the discomfort associated with injections and eliminates the risk of infections or needle-related injuries [16].

**2. Prolonged Drug Action:** The controlled release of drugs allows for sustained therapeutic concentrations in the bloodstream, resulting in improved patient compliance and convenience [17].

**3. Avoidance of First-Pass Metabolism:** Drugs absorbed through the skin bypass the

liver, reducing the risk of metabolism and enhancing bioavailability [18].

**4.Minimized Side Effects:** By delivering drugs directly into the systemic circulation, transdermal systems minimize side effects associated with gastrointestinal irritation or local tissue reactions [19-20].

**5.Potential for drug withdrawal** or patch replacement in case of adverse reactions [21].

#### DISADVANTAGES-

1.Limited drug permeability through the skin, restricting the use of certain drug.

2.Skin irritation or sensitization at the application site.

3.Difficulties in delivering high molecular weight drugs.

4.Variations in drug absorption due to factors like skin thickness, hydration, and perfusion [22].

Table1.1: Method of preparation of few drugs along with their doses [23]

S. No.	Drug Name	Method Of Preparation	Dose
1.	Nitroglycerine	Matrix dispersion method	0.2-0.8mg/hour
2.	Fentanyl	Solvent casting method	12-100mcg/hour
3.	Estradiol	Reservoir system with rate control	25-100 mcg/day
4.	Nicotine	Drug-in-adhesive patch	7-21mg/day
5.	Lidocaine	Matrix system with penetration enhancers	5-700 mg/patch

#### OUTCOMES -

Transdermal drug delivery systems offer various outcomes, including:

**1.Prolonged Drug Action:** Transdermal patches provide a controlled and sustained release of medications, ensuring a prolonged therapeutic effect.

**2.Steady Blood Levels:** These systems maintain consistent drug levels in the bloodstream, leading to stable therapeutic outcomes and improved efficacy.

**3.Reduced Dosing Frequency:** Patients often require fewer doses compared to oral medications, enhancing convenience and improving adherence to the treatment plan.

**4.Minimized Side Effects:** By avoiding sudden peaks and troughs in drug

concentration, transdermal delivery can reduce the occurrence of adverse effects.

**5.Improved Patient Comfort:** Transdermal patches are non-invasive and easy to apply, enhancing patient comfort and compliance, especially for individuals who fear needles or have difficulty swallowing pills.

**6.Targeted Therapy:** Transdermal patches can deliver drugs directly to the affected area, providing localized treatment for conditions like pain, inflammation, or skin disorders.

**7.Enhanced Bioavailability:** Transdermal delivery bypasses the gastrointestinal system, avoiding degradation of drugs in the stomach or liver, leading to increased bioavailability for certain medications.

**8. Flexibility in Dosage Adjustment:**

Dosage adjustments can be made by altering patch size or wearing multiple patches, allowing for personalized and flexible treatment regimens.

It's important to note that the effectiveness of transdermal drug delivery can vary based on the specific drug, the formulation of the patch, and individual patient factors [24].

**CRITICAL REVIEW –****Table 1.2: Detailed Outcome of Patented Drug Patches [25]**

S. No.	Patent No.	Title of Patent	Inventors	Outcomes
1.	US20030235610	Liposomes containing biologically active compounds	Scott McLean, William Campbell	Reduces pain, inflammation, and infections
2.	US20140328898	Nano-Liposomal Formulations and methods of use	Renee Hood, Eric Kendall, Donald Lad Devoe, Julia Cole, Finkel, Zenaide Quezado, Mariana Mafra Junqueira	Containing nanoparticles loaded with NSAIDs for safe and effective delivery
3.	US20030180250	Compositions and complexes containing a macro molecular compound as potential anti-inflammatory agents	Abhay Chauhan, Prakash Diwan, Narendra JAain, Kondapuram Raghavan	Complexing a NSAID with a branched macromolecular polymeric structure called dendrimer for enhanced transdermal delivery
4.	US20090263486	Nanoparticle- stabilized capsule formulation for the treatment of inflammation	Clive Allan Prestidge, Spomenka Simovic	Nanoparticles- stabilized capsules loaded with indomethacin and their utility in transdermal therapeutics
5.	CA2923064	Transdermal composition for treating pain	Moheb Maalaway	Loading an NSAID into ethosomes and their efficacy to reduce in-vivo inflammation in animals

**FUTURE PROSPECTIVES –**

The future of transdermal drug delivery systems holds promising prospects for advancements in Technology, formulation design, and expanded applications. Here are some potential future perspectives for transdermal drug delivery:

**1. Enhanced Drug Permeation:**

Researchers are continuously exploring new techniques and technologies to improve drug permeation through the skin. This includes the development of novel permeation enhancers, use of physical techniques like microneedles and

ultrasound, and the utilization of nanotechnology-based delivery systems. These advancements aim to enhance the skin's permeability and allow for efficient delivery of a broader range of drugs [26].

**2. Personalized Medicine:**

Transdermal drug delivery systems have the potential to enable personalized medicine approaches. Tailoring drug delivery to an individual's specific needs, such as adjusting dosage or release rate, can enhance therapeutic outcomes and minimize side effects. This could be achieved through the integration of sensors, wearable devices, and feedback

mechanisms to monitor drug levels and optimize treatment regimens [27].

### **3. Biologics and Macromolecules:**

Currently, transdermal delivery of large molecules, such as biologics and macromolecules, is challenging due to their size and complexity. However, ongoing research focuses on developing innovative strategies to overcome these barriers. This includes the use of advanced delivery systems like microneedles, nanocarriers, and physical enhancement techniques to facilitate the delivery of biologics through the skin [28].

**4. Combination Therapies:** Transdermal drug delivery systems can provide opportunities for combination therapies, where multiple drugs or therapeutic agents can be delivered simultaneously through a single patch. This approach can enhance treatment effectiveness, improve patient compliance, and simplify medication regimens [29].

**5. On-Demand Drug Delivery:** Future transdermal systems may incorporate technologies that allow for on-demand drug delivery in response to specific triggers or signals. For example, responsive systems that release drugs in response to changes in temperature, pH, or biomarkers can provide personalized, dynamic drug delivery tailored to the patient's condition [30].

**6. Continuous Monitoring:** Transdermal patches can be integrated with sensors to

monitor physiological parameters, drug levels, or biomarkers. This real-time monitoring capability can enable healthcare professionals to track treatment efficacy, adjust dosages, and intervene promptly if necessary [31].

### **7. Pediatric and Geriatric Applications:**

Transdermal drug delivery systems offer advantages for pediatric and geriatric populations. Future developments may focus on optimizing formulations and patch design specifically for these patient groups, considering their unique physiological characteristics and needs.

It is important to note that while these future prospects hold significant potential, their realization may require extensive research, technological advancements, and regulatory considerations. Nonetheless the evolving landscape of transdermal drug delivery holds immense promise in improving treatment outcomes, patient comfort, and overall healthcare delivery [32].

### **CONCLUSION -**

Transdermal patches have significantly transformed the field of drug delivery, offering a convenient and effective alternative to traditional methods of medication administration. Through this innovative technology, patients now have access to a non-invasive, painless, and consistent way of receiving medications, which has revolutionized the treatment of various medical conditions [33].

The widespread adoption of transdermal patches can be attributed to their several advantages. They provide a controlled release of medication, ensuring a steady and continuous absorption rate into the bloodstream. This controlled delivery not only enhances the effectiveness of the treatment but also reduces the risk of side effects associated with rapid fluctuations in drug levels. Additionally, transdermal patches offer improved patient compliance, especially for individuals who struggle with swallowing pills or need long-term medication management. The ease of use and minimal interference with daily activities make transdermal patches a preferred choice for many patients and healthcare providers alike.

Furthermore, transdermal patches have opened avenues for personalized medicine by allowing for customized dosages and tailored drug delivery schedules. This individualized approach to treatment has the potential to optimize therapy outcomes and minimize adverse reactions, thereby improving the overall quality of life for patients.

As research and development in the field of transdermal drug delivery continue to advance, we can anticipate even more breakthroughs. These developments may include enhancements in patch technology, enabling the delivery of a broader range of medications, including biologics

and vaccines. Additionally, ongoing research may lead to the creation of patches that can monitor vital signs, detect specific biomarkers, or deliver multiple drugs simultaneously, further expanding their applications in healthcare.

In conclusion, transdermal patches represent a remarkable achievement in the pharmaceutical industry, offering a patient-friendly, efficient, and precise method of drug delivery. With their numerous benefits and potential for future innovations, transdermal patches continue to shape the landscape of modern medicine, ensuring better treatment options and improved outcomes for patients around the world.

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