Journal of Drug Discovery and Health Sciences

journal home page : https://jddhs.com/index.php/jddhs/index

Review Article

Therapeutic Implication of the Transdermal Patches in Treatment of the Chronic Diseases

Amita Singh Yadav, Shubham Bhatt*, Krishna Verma, Deepika Shukla, Deepika Gupta

Maharishi School of Pharmaceutical Sciences, MUIT, Lucknow, U.P., 226013, India.

ARTICLE INFO

Article history:
Received: 02 May, 2025
Revised: 19 May, 2025
Accepted: 11 June, 2025
Published: 30 June, 2025

Keywords:
Transdermal patches, Therapeutic efficacy, Pharmacokinetics, Pharmacodynamics, Personalized medicines, Chronic disease.

DOI:
10.21590/jddhs.02.02.07

ABSTRACT

The evolving landscape of drug delivery systems has ushered in innovative approaches that transcend the limitations of conventional routes. Among these, transdermal drug delivery systems (TDDS) have emerged as a promising platform, offering a non-invasive and patient-compliant alternative for the management of chronic diseases. This review aims to explore the therapeutic implications of transdermal patches, particularly focusing on their role in ensuring sustained drug release, improving pharmacokinetics, and enhancing therapeutic efficacy. The primary objective of this review is to critically evaluate the design, types, mechanisms, and clinical applications of transdermal patches in the treatment of long-term conditions such as hypertension, diabetes, cardiovascular disorders, hormonal imbalances, and chronic pain. The purpose is to provide a comprehensive understanding of how these systems minimize first-pass metabolism, reduce dosing frequency, and improve patient adherence—factors crucial in managing chronic illnesses that require consistent therapeutic levels over prolonged durations. Recent advancements such as microneedle-enhanced delivery, iontophoresis, and nanoparticle-incorporated patches have significantly broadened the scope of TDDS, enabling the delivery of large molecules, peptides, and biologics. This review also discusses the selection criteria for polymers and permeation enhancers, challenges in skin permeability, and regulatory considerations involved in the development of transdermal systems. TDDS represent a transformative strategy in chronic disease management by offering controlled, targeted, and safe drug delivery. Their growing relevance in personalized medicine and potential integration with smart wearable technologies make them a focal point in future pharmaceutical innovation and clinical practice.

INTRODUCTION

Chronic diseases are long-lasting health conditions that often require ongoing medical attention and management over extended periods. These include cardiovascular disorders, diabetes mellitus, chronic respiratory diseases, arthritis, and neurological disorders, among others. The prevalence of chronic illnesses has risen dramatically worldwide, largely due to aging populations, sedentary lifestyles, and unhealthy dietary habits. According to the World Health Organization, chronic diseases account for nearly 71% of all global deaths, posing significant socio-economic burdens and healthcare challenges. One of the critical hurdles in managing chronic diseases is ensuring consistent and effective therapeutic levels of medications while minimizing side effects and enhancing patient compliance. *(Bhatt et al. 2021)* Chronic diseases such as cardiovascular disorders, diabetes mellitus, chronic respiratory conditions, and cancers represent the leading causes of morbidity and mortality worldwide. According to the World Health Organization (WHO, 2023), non-communicable diseases (NCDs) account for approximately 74% of all global deaths, with over 41

***Corresponding Author:** Shubham Bhatt

Address: Maharishi School of Pharmaceutical Sciences, MUIT, Lucknow, U.P., 226013, India.

Email ✉**:** shubhatt521@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

million people dying annually—many of whom are under the age of 70. This rising burden is particularly concerning in low- and middle-income countries (LMICs), where healthcare infrastructure often struggles to manage long-term disease care effectively. Additionally, the global shift in lifestyle behaviors—including physical inactivity, unhealthy diets, and tobacco use—has exacerbated the prevalence and severity of chronic conditions. The increasing incidence not only overwhelms healthcare systems but also imposes significant economic strains on families and governments alike, necessitating sustainable, patient-friendly, and cost-effective therapeutic solutions. *(Han et al. 2015)*

Conventional drug delivery systems, such as oral and parenteral routes, often present limitations in the management of chronic diseases. These include issues such as first-pass metabolism, gastrointestinal degradation, poor bioavailability, frequent dosing, and invasive administration. Consequently, there has been a continuous search for alternative drug delivery systems that can overcome these challenges while providing controlled and sustained drug release. Among these alternatives, transdermal drug delivery systems (TDDS) have emerged as a promising approach. TDDS are designed to deliver drugs across the skin and into the systemic circulation, offering several advantages over traditional methods. These include improved patient compliance due to non-invasive application, steady plasma drug concentrations, bypassing hepatic first-pass metabolism, and reduced dosing frequency. Since the first transdermal patch (scopolamine) was approved in the late 1970s, there has been a significant evolution in transdermal technology, enabling its application in a wide range of therapeutic areas including hypertension, angina, chronic pain, hormone replacement therapy, and neurological conditions like Parkinson's disease. *(Schoellhammer et al. 2014)*

Traditional drug delivery systems such as oral tablets, capsules, and parenteral injections, while widely used, present several limitations when managing chronic diseases. Issues such as first-pass metabolism, fluctuating plasma drug levels, poor patient compliance due to frequent dosing, and invasive administration routes compromise therapeutic outcomes, especially for conditions requiring long-term management. Conventional systems often fail to ensure steady-state drug concentrations, a crucial factor in chronic therapy. In contrast, novel drug delivery systems (NDDS) have emerged as transformative approaches to optimize drug bioavailability, minimize side effects, and enhance patient adherence. Among these, transdermal drug delivery systems (TDDS)—especially in the form of transdermal patches—offer significant clinical advantages. As highlighted in recent studies by *Sharma et al. (2023) and Li & Zhang (2022),* transdermal patches bypass hepatic first-pass metabolism, provide controlled and sustained drug release, and improve patient convenience through non-invasive application. The global market for transdermal patches has witnessed steady growth, fueled by innovations in polymer technology, permeation enhancers, and microneedle systems, making them a viable alternative for long-term drug administration in chronic disease therapy. *(Donnelly et al. 2012)*

In order to advance therapeutic treatment, this generation of delivery systems largely focuses on improving the dispersion of small molecules for localized and other systemic applications. Delivering macromolecules, however, is less successful. Transdermal delivery techniques of the third generation are made to specifically target the stratum corneum and its effects. More effective transdermal transport is the outcome of this stratum corneum barrier breakdown, which protects deeper tissues. *(Valenta et al. 2004)* In 1979, the US FDA approved the first transdermal motion sickness patch, called Transdermal-SCOP, which contained scopolamine as its active ingredient. Nowadays, the transdermal administration method is the most efficient approach to deliver drugs like fentanyl, lidocaine, oestradiol, and other combination patches with several different medications. Drugs can be delivered to the skin's reasonable epidermis and possibly dermal tissue for a local therapeutic impact using transdermal drug delivery systems (TDDS). At the same time, a fairly large portion of the drug is transferred through the systemic blood circulation. *(Kretsos & Kasting, 2007)*

The integration of TDDS into chronic disease management protocols not only enhances pharmacokinetic and pharmacodynamic profiles but also aligns with the broader goal of personalized medicine, particularly in aging populations with polypharmacy concerns. Therefore, exploring the potential and challenges of transdermal patches in treating chronic conditions is both timely and critical in the context of modern pharmaceutics. *(Santos et al., 2018)*

Concept of Transdermal Drug Delivery System (TDDS)

The transdermal drug delivery system (TDDS) represents a sophisticated and non-invasive method of administering therapeutic agents through the skin into systemic circulation. Unlike traditional routes such as oral or parenteral administration, TDDS provides a controlled and sustained release of drugs over extended periods, bypassing the hepatic first-pass metabolism and minimizing gastrointestinal degradation. The system typically consists of a medicated patch adhered to the skin, engineered to deliver specific dosages of a drug at a predetermined rate. *(Sa'adon et al., 2019)* The human skin, especially the stratum corneum, presents a significant barrier to drug permeation; thus, the formulation and technology behind TDDS must be optimized to ensure adequate drug flux. Various mechanisms, including passive

diffusion and enhancement techniques like iontophoresis, microneedles, and chemical enhancers, have been employed to improve transdermal permeability. TDDS offers several clinical advantages such as improved patient compliance, ease of administration, and the possibility of terminating drug delivery simply by removing the patch. This delivery system is particularly beneficial in the management of chronic diseases, where long-term medication with steady plasma levels is essential for therapeutic success. *(Donnelly et al., 2012)*

Anatomy and Physiology of the Skin Relevant to Drug Delivery

The human skin, being the largest organ of the body, plays a pivotal role not only in protecting against external insults but also in regulating temperature, hydration, and metabolic processes. For transdermal drug delivery systems (TDDS) such as patches, understanding the skin's anatomical and physiological barriers is essential to optimize drug permeability and therapeutic efficacy, especially in chronic disease management. *(Tuan-Mahmood et al., 2013)*

Structure of Skin

The skin is the body's largest organ, made of water, protein, fats and minerals. Our skin protects your body from germs and regulates body temperature. Nerves in the skin help you feel sensations like hot and cold. *(Zahra et al. 2023)* The skin is composed of three primary layer which are shown in Table 1.

The three main layers of the skin are the dermis, hypodermis (subcutaneous tissue), and epidermis. The most important barrier to drug penetration among these is the stratum corneum (SC), the outermost layer of the epidermis. The dead, flattened keratinocytes (corneocytes) that make up the SC are around 10–20 µm thick and encased in a lipid matrix that includes free fatty acids, cholesterol, and ceramides. *(Ramarao et al. 1998)* The "brick and mortar" paradigm is frequently used to explain this structure, with lipids serving as the "mortar" and corneocytes as the "bricks." Most medications' main rate-limiting barrier is the stratum corneum, which only permits molecules with specific physicochemical characteristics to pass through, usually having a molecular weight of less than 500 Da, a log P between 1 and 3, and moderate lipophilicity. *(Lee et al. 2011)*

Table 1: Three primary layers of the skin

Layer	*Sub-components*	*Function*
Epidermis	Stratum corneum-Viable epidermis	Acts as a primary barrier for drug penetration
Dermis	Papillary dermis-Reticular dermis	Provides vascular network for drug absorption
Hypodermis	Adipose tissue-Connective tissue	Offers insulation and structural support

Beneath the stratum corneum lies the viable epidermis, which contains metabolically active cells such as keratinocytes, Langerhans cells, and melanocytes. While it is more hydrophilic than the SC and plays a limited role in barrier function, it can enzymatically metabolize certain drugs through enzymes like esterases and cytochrome P450 isoforms, potentially influencing drug bioavailability. The next major layer is the dermis, a vascularized and innervated connective tissue layer measuring approximately 1–2 mm in thickness. It contains a dense network of blood vessels, lymphatics, and nerves, allowing systemic absorption of drugs that have successfully permeated through the upper layers. Once a drug reaches the dermis, it is rapidly absorbed into the systemic circulation, making it a key target layer for transdermal therapeutic systems. Additionally, the dermis can act as a reservoir, holding drugs temporarily before systemic release. *(Suh et al. 2014)*

The hypodermis, or subcutaneous tissue, lies beneath the dermis and is composed primarily of adipose (fat) tissue and connective tissue. Although it does not directly influence drug permeation, it plays an essential role in thermoregulation, mechanical protection, and depot storage of lipophilic drugs, thereby affecting their distribution and pharmacokinetics once they are systemically absorbed. *(Minghetti et al. 1999)* Besides the transepidermal route, drugs can also be absorbed through appendageal pathways, which include hair follicles, sebaceous glands, and sweat glands. These structures, although covering less than 0.1% of the total skin surface, can serve as shunt pathways and facilitate rapid drug absorption, particularly for nanoparticles, ionized molecules, or lipophilic agents. Hair follicles, in particular, have been explored as drug reservoirs, capable of enhancing localized as well as systemic delivery. *(Peasah et al. 2013)*

Several physiological factors influence transdermal drug absorption. These include skin hydration, which enhances permeability by swelling the corneocytes and loosening the lipid matrix, and skin temperature, which can increase diffusion coefficients and dermal blood flow. The skin's pH, typically ranging between 4.5–6.0, can affect drug ionization, solubility, and hence, permeability. *(Guyot et al. 2000)* Moreover, regional variations in skin thickness (e.g., thinner skin behind the ears vs. thicker skin on palms and soles) also affect permeation rates, necessitating strategic site selection for patch application as shown in Table 2.

These anatomical and physiological parameters is crucial when developing transdermal patches for chronic diseases such as hypertension, diabetes, hormonal imbalances, and chronic pain, where long-term, consistent drug plasma levels are desired. Modern transdermal systems incorporate chemical enhancers, microneedles, iontophoresis, or sonophoresis to overcome the barrier function of the stratum corneum and facilitate effective delivery of both small molecules and macromolecules.

Table 2: Factors affecting the Drug Delivery System

Factor	*Relevance to drug delivery*
Skin hydration	Increases permeability by swelling corneocytes
Skin temperature	Enhances diffusion and blood flow
pH of skin	Acidic (4.5–6.0); affects ionization and solubility of drugs
Enzymatic activity	May lead to prodrug activation or drug metabolism
Regional variation	Thinner skin (e.g., behind ears, scrotum) allows higher permeability; thicker skin (e.g., palms, soles) resists penetration

(Iwase et al., 2000) The skin's complex structure and selective permeability present both challenges and opportunities in transdermal drug delivery. A thorough understanding of skin anatomy and physiology provides the foundation for designing optimized transdermal patches capable of achieving sustained, non-invasive, and patient-friendly drug delivery for long-term treatment of chronic illnesses. *(Phatale et al., 2022)*

Types of Transdermal Patches

Transdermal drug delivery systems (TDDS) are designed to deliver therapeutic agents through the skin for systemic circulation. The efficacy of these systems, particularly in managing chronic diseases, is largely dependent on the type of transdermal patch used. Based on design and drug-release mechanism, transdermal patches are classified into the following major types as shown in Table 3.

Reservoir Type Transdermal Patch

Reservoir patches consist of a drug-containing reservoir sandwiched between a rate-controlling membrane and an impermeable backing layer. In order to increase efficacy, the medicine is frequently combined with excipients or penetration enhancers and kept in the reservoir in a gel or solution form. To adhere the patch to the skin, an adhesive coating is put on the membrane's exterior. The drug is released in a zero-order kinetic manner, providing a constant and controlled drug delivery rate over a prolonged period. This makes it ideal for managing chronic conditions requiring steady plasma concentrations, such as angina (nitroglycerin), hypertension (clonidine), and chronic pain (fentanyl). *(Syam et al. 2019)*

Key advantages of this type include precise drug release and protection of the drug within the reservoir. However, it carries a potential risk of dose dumping if the rate-controlling membrane is damaged, and the design can be bulky and less flexible for patient use.

Matrix Type Transdermal Patch

In matrix-type patches, the drug is uniformly dispersed or dissolved within a polymeric matrix, which also serves as the platform for drug release. This matrix is placed between a backing layer and an adhesive layer, which may be coated across the entire surface or just around the perimeter. The drug release follows first-order kinetics, meaning that the release rate declines over time as the drug concentration in the matrix decreases. These patches are widely used due to their simplicity in manufacturing, flexibility, and reduced risk of dose dumping. Examples include nicotine patches (for smoking cessation), estradiol patches (for hormone replacement therapy), and buprenorphine patches (for chronic pain). Matrix systems offer less precision in controlling drug release compared to reservoir systems. Additionally, drug loading is limited based on the compatibility with the polymer used. *(Abhange et al. 2022)*

Adhesive Dispersion Type Transdermal Patch

Adhesive dispersion patches incorporate the drug directly into the pressure-sensitive adhesive (PSA), which serves both to deliver the drug and adhere the patch to the skin. A backing layer covers the top, while a release liner is removed just before application.

The drug diffuses through the skin directly from the adhesive layer, typically following first-order or non-linear release kinetics, depending on the drug's characteristics. These patches are especially useful for delivering low-dose medications over shorter durations, such as scopolamine for motion sickness or lidocaine for localized pain relief. These patches are appreciated for their easy and cost-effective design, better skin contact, and high patient compliance. However, they suffer from limited drug-loading capacity and may face stability issues, as the drug is in continuous contact with the adhesive medium. *(Brown et al. 2005)*

Table 3: Different types of transdermal patches and its properties

Type	*Drug Distribution*	*Release Kinetics*	*Advantages*	*Limitations*	*Examples*
Reservoir	Enclosed in a reservoir	Zero-order	Precise control, long duration	Dose-dumping risk, bulky	Fentanyl, Nitroglycerin
Matrix	Uniformly dispersed in matrix	First-order	Simple, flexible, lower cost	Less precise control	Buprenorphine, Estradiol
Adhesive dispersion	Incorporated in adhesive layer	First-order/ non-linear	Easy to manufacture, good skin contact	Limited drug load, stability issues	Scopolamine, Lidocaine
Micro-reservoir	Micro-reservoirs in matrix	Controlled/ sustained	Combined benefits of reservoir & matrix	Complex formulation	Hormonal therapy, Chronic pain relief

Micro-Reservoir Type Transdermal Patch

The micro-reservoir patch is a hybrid system that combines the properties of both reservoir and matrix patches. In this system, the drug forms microsized reservoirs within a polymeric matrix, usually by suspending or dispersing the drug using specialized techniques. The patch also contains a backing membrane and a release liner. Drug release from micro-reservoir patches is sustained and controlled, as it involves diffusion from the micro-reservoirs into the matrix, followed by penetration into the skin. This system is ideal for drugs with narrow therapeutic indices or those requiring long-term and stable release, such as in hormonal therapy and chronic pain management. *(Maurya, V. B., 2019)* Key benefits include better control over release rates and combining the advantages of both matrix and reservoir systems. However, the manufacturing process is complex, requiring precise control of reservoir size and uniform distribution throughout the patch. *(Costa et al. 1997)*

Each type of transdermal patch offers unique design and pharmacokinetic features, making them suitable for different classes of chronic diseases. Reservoir patches provide constant release and are suited for critical conditions but pose safety risks. Matrix patches offer a balance between efficacy and simplicity. Adhesive dispersion patches are easy to apply and cost-effective, while micro-reservoir systems are ideal for controlled, sustained release with better therapeutic outcomes. Choosing the appropriate transdermal patch depends on multiple factors including drug properties, desired release profile, disease type, and patient convenience. *(Wester et al. 1980)*

Advantages and Limitations of Transdermal Patches

An alternative to conventional oral and parenteral routes, transdermal drug delivery systems (TDDS) are a major improvement in controlled drug administration. Several pharmacokinetic and therapeutic benefits are offered by transdermal patches, which transfer medications through the skin and straight into the bloodstream. The formulation and practical use of these systems must take into account their inherent limits, as is the case with all drug delivery systems. *(Long et al. 2022)*

Advantages

Bypass of first-pass metabolism

One of the most significant benefits of transdermal patches is their ability to bypass hepatic first-pass metabolism. When drugs are taken orally, they often undergo significant biotransformation in the liver before reaching systemic circulation, which reduces their bioavailability. Transdermal delivery avoids this route, thus enhancing bioavailability. For instance, nitroglycerin patches used in angina pectoris allow the drug to enter systemic circulation directly, maintaining therapeutic levels without hepatic degradation. *(Long et al. 2022)*

Controlled and sustained release

Transdermal patches are designed to release the active pharmaceutical ingredient (API) at a controlled rate over an extended period, minimizing fluctuations in plasma drug concentrations. This controlled release helps maintain drug levels within the therapeutic window, improving efficacy and reducing toxicity. An example is the fentanyl transdermal patch, which provides analgesia for up to 72 hours in chronic pain management, reducing the need for frequent dosing. *(Long et al. 2022)*

Improved patient compliance

Transdermal patches are non-invasive, painless, and easy to use, which leads to better patient adherence, especially in chronic disease management. Patients with swallowing difficulties or gastrointestinal issues particularly benefit from this mode of delivery. The scopolamine patch for motion sickness, applied behind the ear, exemplifies a user-friendly, long-acting option that improves compliance in travel-related nausea. *(Long et al. 2022)*

Reduction in systemic side effects

Because transdermal systems maintain a steady-state concentration of the drug, they minimize the peaks and troughs associated with oral dosing, which can lead to adverse effects. Additionally, the avoidance of gastrointestinal exposure reduces local side effects such as irritation or ulceration. For example, clonidine patches used in hypertension offer a smoother pharmacological profile with fewer central nervous system side effects compared to oral formulations. *(Long et al. 2022)*

Limitations

Limited to potent drugs

The skin has a limited absorption capacity, which restricts transdermal delivery to drugs that are effective at low doses (typically less than 10 mg per day). Drugs requiring high plasma concentrations are often unsuitable for patch delivery. For instance, antibiotics or drugs with high therapeutic doses (like metformin) are impractical for transdermal systems due to dose size and permeability issues. *(Kumar et al. 2022)*

Skin irritation and allergic reactions

Long-term patch use might cause local side effects include allergic dermatitis, erythema, and itching. These responses could be brought on by the adhesive, the medication, or other excipients that were added to the patch. Some patients who use nicotine patches, for instance, suffer skin irritation that makes it necessary to stop using them or to alter application sites regularly. *(Kumar et al. 2022)*

Barrier properties of the stratum corneum

A major obstacle to medication penetration is the stratum corneum, the skin's outermost layer. Only lipophilic medications with a low molecular weight—typically less

than 500 Da—are able to effectively pass over this barrier. Large molecular weight and hydrophilic medications, such as many peptides and proteins, have trouble passing through the skin without the aid of chemical penetration enhancers, microneedles, or iontophoresis. *(Kumar et al. 2022)*

While transdermal patches offer a promising and patient-friendly route for drug delivery with numerous clinical advantages, their success is dependent on careful drug selection, formulation optimization, and addressing challenges such as skin permeability and local tolerability. The continued development of novel transdermal technologies may help overcome current limitations and expand the range of drugs suitable for this route. *(Witika et al., 2021)*

Selection Criteria for Drugs and Formulation Aspects

Effective drug penetration across the skin barrier necessitates the strategic selection of drug candidates and formulation component optimization in the design and development of a transdermal drug delivery system (TDDS). Because the stratum corneum, the skin's outermost layer, is a major barrier to drug transport, only medications with particular physicochemical characteristics can be transported through this route. *(Al Hanbali et al., 2019)* Critical selection criteria and formulation considerations are listed below.

Physicochemical Properties of Drugs Suitable for TDDS

Drugs intended for TDDS must fulfill certain physicochemical prerequisites to permeate through the skin effectively:

Molecular weight

Ideally, the drug should have a molecular weight below 500 Da. Larger molecules typically encounter difficulty penetrating the stratum corneum. *Example*: Fentanyl (MW ~336.5 Da) is a potent opioid analgesic with successful transdermal formulations.

Solubility

Drugs must possess adequate solubility in both lipophilic and hydrophilic media to cross various skin layers and dissolve in systemic circulation. A balance between aqueous and lipid solubility is crucial.

Lipophilicity (Log P)

The optimal Log P (partition coefficient) value ranges between 1 and 3, enabling effective partitioning into the lipid-rich stratum corneum and subsequent migration into the aqueous viable epidermis.

Example: Nicotine (Log P ~1.17) effectively penetrates the skin and is available as transdermal patches for smoking cessation. *(DeMerlis et al. 2003)*

Dose requirement

Drugs administered via TDDS should require low daily doses (typically <10 mg/day) due to the limited flux through the skin. *Example*: Clonidine (0.1 mg/day) used for hypertension meets this criterion and is marketed in patch form.

Role of Permeation Enhancers

Permeation enhancers are essential components of TDDS formulations that transiently increase the skin's permeability, allowing drugs to diffuse across the stratum corneum without permanent damage.

- These agents function by disrupting lipid structure, altering protein conformations, or increasing drug solubility within the skin layers.
- Common classes include Fatty acids (e.g., oleic acid), Alcohols (e.g., ethanol, propylene glycol), Surfactants (e.g., sodium lauryl sulfate) & Terpenes (e.g., menthol, limonene). Ethanol is widely used as a solvent and enhancer in the TDDS of nitro-glycerine, enhancing its flux across the skin. *(Alkilani et al. 2015)*

Formulation Components: Backing Layer, Adhesive Layer, and Release Liner

A well-designed TDDS involves multiple structural layers, each serving a specific function to support drug delivery and ensure patient compliance. *(Prausnitz et al. 2008)*

Backing layer

This is the outermost protective layer that prevents drug loss and environmental contamination. It must be impermeable, flexible, and compatible with other layers. *Example*: Polyester film is commonly used for its strength and inertness.

Adhesive layer

This layer is responsible for maintaining contact with the skin and, in drug-in-adhesive systems, may also serve as the drug reservoir. It must provide long wear time, skin compatibility, and uniform drug release. *Example*: Acrylate or silicone-based adhesives are preferred due to minimal skin irritation.

Release liner

This is the removable layer that protects the adhesive surface during storage. It must not interact with the drug or adhesive and is usually made of siliconized polyester or polypropylene film.

Evaluation Parameters of TDDS

A comprehensive evaluation of TDDS is essential to ensure product quality, efficacy, and safety. These include both in vitro and in vivo assessments:

In Vitro Evaluation

- Drug content uniformity
- Thickness and weight variation
- Tensile strength and folding endurance

- Moisture content and uptake
- In vitro drug release (using Franz diffusion cells)
- Skin permeation studies with excised animal or human skin

Example: Franz diffusion cell studies can determine the flux of drugs like diclofenac from different patch formulations.

In-vivo Evaluation

- Skin irritation or sensitization studies (using rabbit or human volunteers)
- Pharmacokinetic studies to determine Cmax, Tmax, AUC
- Bioavailability and bioequivalence studies
- Stability testing under ICH guidelines

Example: Fentanyl patches have undergone rigorous in vivo testing for steady-state plasma levels in pain management. Selection of drug candidates for TDDS hinges on a thorough understanding of their physicochemical characteristics, while formulation aspects such as permeation enhancers and structural components play a vital role in optimizing therapeutic outcomes. A robust evaluation framework ensures safety, efficacy, and consistent performance, paving the way for the successful development of transdermal therapeutics. *(Peddapalli et al. 2018)*

Application of Transdermal Patches in Chronic Diseases

Transdermal drug delivery systems (TDDS) have emerged as a significant innovation in the management of chronic diseases as shown in Table 4, offering sustained therapeutic effect, improved patient compliance, and avoidance of first-pass hepatic metabolism. Their non-invasive nature and capacity for controlled drug release make them especially advantageous for long-term treatments. Below are key chronic conditions where transdermal patches have been successfully applied. *(Wokovich et al. 2006)*

Cardiovascular Disorders

Transdermal nitroglycerin patches are widely used in the management of angina pectoris, a condition characterized by reduced myocardial oxygen supply. Nitroglycerin, a potent vasodilator, helps alleviate chest pain by dilating coronary arteries and decreasing cardiac workload. The transdermal system delivers a controlled dose over 12–24 hours, thus minimizing the frequency of dosing and enhancing patient adherence. For instance, commercial products like *Minitran*® and *Nitro-Dur*® offer varying strengths tailored to patient needs. *(Lee et al., 2015)*

Pain Management

Fentanyl transdermal patches are a cornerstone in chronic pain management, particularly in cancer patients. Fentanyl, a highly potent opioid analgesic, is released steadily over 72 hours, ensuring consistent plasma drug levels. This bypasses gastrointestinal issues associated with oral opioids and reduces the need for frequent dosing. Marketed products such as *Duragesic*® and *Fentanyl Sandoz*® exemplify successful commercial transdermal opioid therapy for severe pain conditions. *(Teodorescu et al. 2019)*

Diabetes Mellitus

Although still largely in the experimental and developmental phase, transdermal insulin patches aim to offer non-invasive delivery of insulin in diabetes mellitus. Innovative techniques, such as microneedle arrays, iontophoresis, and chemical enhancers, are being explored to overcome the skin's barrier and enable the effective delivery of macromolecular insulin. For instance, a microneedle patch developed by researchers at MIT and the University of North Carolina has shown promising results in animal models, demonstrating controlled insulin release based on glucose levels. *(Nokhodchi et al., 2003)*

Parkinson's Disease

Rotigotine, a non-ergoline dopamine agonist, is used in the treatment of Parkinson's disease via a transdermal system known as *Neupro*®. The patch delivers a steady dose of medication over 24 hours, aiding in the management of motor symptoms and reducing fluctuations associated with oral dopaminergic therapy. It simplifies the treatment regimen and is particularly beneficial for patients with swallowing difficulties, a common issue in advanced Parkinson's disease. *(Prajapati et al. 2011)*

Hormonal Disorders

Hormone Replacement Therapy (HRT) via transdermal patches is widely accepted for managing menopausal symptoms and androgen deficiency. Estrogen patches (e.g., *Climara*®, *Vivelle-Dot*®) help alleviate vasomotor symptoms and prevent postmenopausal osteoporosis. Testosterone patches (e.g., *Androderm*®) are used in hypogonadism to maintain physiological hormone levels and restore libido, energy, and mood. The transdermal route offers more stable hormone levels and minimizes hepatic side effects seen with oral formulations. *(Haimhoffer et al., 2021)*

Hypertension

Clonidine, a centrally acting α2-adrenergic agonist, is administered via a transdermal patch (*Catapres-TTS*®) to manage high blood pressure. It delivers medication consistently for up to 7 days, thus reducing blood pressure variability and improving compliance, especially in elderly or multi-drug patients. Ongoing research is focused on incorporating other antihypertensives, such as β-blockers and calcium channel blockers, into transdermal systems. *(Głąb et al., 2021)*

Smoking Cessation

Nicotine transdermal patches are among the most common and effective tools in smoking cessation programs. Brands

Table 4: Marketed transdermal patches for chronic disease

Disease	*Drug*	*Type of patch*	*Brand name*	*Duration*
Hypertension	Clonidine	Matrix	Catapres-TTS	7 days
Pain	Fentanyl	Reservoir	Duragesic	72 hrs
Parkinson's	Rotigotine	Matrix	Neupro	24 hrs
Hormone Therapy	Estradiol	Adhesive dispersion	Estraderm	3-4 days

like *NicoDerm CQ*® and *Habitrol*® deliver controlled doses of nicotine over 16 to 24 hours, reducing withdrawal symptoms and cravings. The convenience and gradual reduction protocol make it easier for users to quit smoking without abrupt cessation, improving success rates. *(Thakur et al., 2024)*

Recent Advances and Innovations

Recent advancements in transdermal drug delivery systems (TDDS) have revolutionized the way therapeutic agents are administered, offering controlled, painless, and non-invasive alternatives to conventional drug delivery routes. One of the most promising innovations is the microneedle patch, which incorporates microscopic needles to painlessly penetrate the stratum corneum and deliver drugs directly into the dermis. These patches enhance bioavailability and are particularly useful for macromolecules like insulin and vaccines—for instance, microneedle-based influenza vaccines have shown promising results in clinical trials. Another notable advancement is the use of iontophoresis and sonophoresis. Iontophoresis utilizes a mild electric current to drive charged drug molecules across the skin, while sonophoresis employs ultrasonic waves to disrupt the skin barrier, enhancing the permeability of both hydrophilic and lipophilic drugs. These methods have shown success in delivering peptides, proteins, and anti-inflammatory agents such as dexamethasone. *(Hadžiabdić et al. 2021)*

A significant leap in personalized therapy comes from smart transdermal systems integrated with sensors. These systems can monitor physiological parameters like skin temperature, hydration, and drug plasma levels in real time, allowing for feedback-controlled drug release. For example, glucose-responsive patches embedded with biosensors can adjust insulin release based on blood glucose levels, thereby improving diabetic care. Furthermore, the integration of 3D printing technology has enabled the development of customized transdermal patches tailored to individual patient needs. *(Suksaeree et al., 1996)* This innovation allows for precise control over patch geometry, drug dose, and release kinetics, significantly enhancing therapeutic outcomes. For instance, 3D-printed patches loaded with captopril have been successfully fabricated for personalized hypertension management. Collectively, these innovations reflect a paradigm shift in TDDS, pushing the boundaries of precision medicine, patient compliance, and therapeutic efficiency. *(Latif et al. 2022)*

CONCLUSION

Transdermal patches have revolutionized the delivery of drugs for chronic diseases by offering a non-invasive, patient-friendly, and controlled-release alternative to conventional dosage forms. Their ability to bypass hepatic first-pass metabolism, maintain steady plasma drug concentrations, and enhance patient compliance makes them a promising therapeutic strategy for long-term disease management. This delivery system is particularly beneficial in conditions requiring sustained drug levels such as hypertension, diabetes, chronic pain, hormone replacement therapy, and neurodegenerative disorders. Recent innovations in patch design—such as microneedle-assisted systems, iontophoretic and sonophoretic enhancement techniques, and smart patches embedded with biosensors—have addressed the limitations associated with drug permeability and skin irritation. The integration of nanotechnology and stimuli-responsive materials has further enabled the delivery of large, hydrophilic, or unstable molecules, including peptides and biologicals, expanding the scope of transdermal therapeutics. The development of personalized transdermal systems using 3D printing and digital health platforms signifies a future where drug therapy can be tailored based on individual pharmacokinetics and disease dynamics. Such innovation not only ensures better therapeutic outcomes but also minimizes adverse effects and improves the quality of life for patients with chronic illnesses. However, challenges such as interpatient variability in skin permeability, formulation instability, limited drug selection, and high development costs must be addressed through continued research, regulatory support, and interdisciplinary collaboration. It represents a cutting-edge advancement in chronic disease therapy. With ongoing technological progress and a deeper understanding of skin physiology, these systems hold the potential to become a mainstay in chronic disease management, supporting the transition towards more effective, personalized, and patient-centric care. Future efforts must focus on overcoming current barriers and expanding the clinical utility of this promising drug delivery platform.

REFERENCES

1. Han, T., & Das, D. B. (2015). Potential of combined ultrasound and microneedles for enhanced transdermal drug permeation: a

review. European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Für Pharmazeutische Verfahrenstechnik e.V, 89, 312–328. https://doi.org/10.1016/j.ejpb.2014.12.020.

2. Schoellhammer, C. M., Blankschtein, D., & Langer, R. (2014). Skin permeabilization for transdermal drug delivery: recent advances and future prospects. Expert Opinion on Drug Delivery, 11(3), 393–407. https://doi.org/10.1517/17425247.2014.875528.
3. Donnelly, R. F., Singh, T. R. R., Morrow, D. I., & Woolfson, A. D. (2012). Microneedle- Mediated Transdermal and Intradermal Drug Delivery. Wiley.
4. Kretsos, K., & Kasting, G. B. (2007). A geometrical model of dermal capillary clearance Mathematical Biosciences, 208(2), 430–453. https://doi.org/10.1016/j.mbs.2006.10.012.
5. Donnelly, R. F., Singh, T. R. R., Garland, M. J., Migalska, K., Majithiya, R., McCrudden, C. M., Kole, P. L., Mahmood, T. M. T., McCarthy, H. O., & Woolfson, A. D. (2012). Hydrogel- forming microneedle arrays for enhanced transdermal drug delivery. Advanced Functional Materials, 22(23), 4879–4890. https://doi.org/10.1002/adfm.201200864.
6. Tuan-Mahmood, T.-M., McCrudden, M. T. C., Torrisi, B. M., McAlister, E., Garland, M. J., Singh, T. R. R., & Donnelly, R. F. (2013). Microneedles for intradermal and transdermal drug delivery. European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences, 50(5), 623–637.
7. Lee, J. W., Gadiraju, P., Park, J.-H., Allen, M. G., & Prausnitz, M. R. (2011). Microsecond thermal ablation of skin for transdermal drug delivery. Journal of Controlled Release: Official Journal of the Controlled Release Society, 154(1), 58–68.
8. Suh, H., Shin, J., & Kim, Y.-C. (2014). Microneedle patches for vaccine delivery. Clinical and Experimental Vaccine Research, 3(1), 42–49. https://doi.org/10.7774/cevr.2014.3.1.42.
9. Peasah, S. K., Azziz-Baumgartner, E., Breese, J., Meltzer, M. I., & Widdowson, M. (2013). Influenza Cost and Cost-Effectiveness Studies globally-A Review. Vaccine, 31, 5339–5348.
10. Phatale, V., Vaiphei, K. K., Jha, S., Patil, D., Agrawal, M., & Alexander, A. (2022). Overcoming skin barriers through advanced transdermal drug delivery approaches. Journal of Controlled Release: Official Journal of the Controlled Release Society, 351, 361–380. https://doi.org/10.1016/j.jconrel.2022.09.025.
11. Syam, S. (2019). Transdermal patches fabricated from hyaluronic acid for the enhanced skin penetration of therapeutic entities. Journal of Drug Delivery & Therapeutics, 9(1), 252–256.
12. Abhange, O. A., Shaikh, K. U., & Bawage, S. B. (2022). Recent advances in transdermal drug delivery systems: a review. Biomat Res, 3, 1162–1170.
13. Brown, M. B., & Jones, S. A. (2005). Hyaluronic acid: a unique topical vehicle for the localized delivery of drugs to the skin. Journal of the European Academy of Dermatology and Venereology: JEADV, 19(3), 308–318. https://doi.org/10.1111/j.1468-3083.2004.01180.x.
14. Maurya, V. B., Kumar, V., & Kumar, R. (2019). An overview on Transdermal drug delivery system. Journal of Drug Delivery and Therapeutics, 9(4-A), 773–778. https://doi.org/10.22270/jddt.v9i4-a.3570
15. Wester, R. C., & Noonan, P. K. (1980). Relevance of animal models for percutaneous absorption. International Journal of Pharmaceutics, 7(2), 99–110. https://doi.org/10.1016/0378-5173(80)90054-x
16. Long, M. O., Guijing, L. U., & Xiping, O. (2022). Formulation and development of novel control release transdermal patches of carvedilol to improve bioavailability for the treatment of heart failure. Saudi J Biol Sci, 29(1), 266–272.
17. Kumar, S. (2022). Preparation and evaluation of matrix type of transdermal patches containing anti -diabetic drug. Indian J Pharm Pharmacol, 9(1), 29–34.
18. Al Hanbali, O. A., Khan, H. M. S., Sarfraz, M., Arafat, M., Ijaz, S., & Hameed, A. (2019). Transdermal patches: Design and current approaches to painless drug delivery. Acta Pharmaceutica (Zagreb, Croatia), 69(2), 197–215. https://doi.org/10.2478/acph-2019-0016.
19. Alkilani, A., McCrudden, M. T., & Donnelly, R. (2015). Transdermal drug delivery: Innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. Pharmaceutics, 7(4), 438–470. https://doi.org/10.3390/pharmaceutics7040438.
20. Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. Nature Biotechnology, 26(11), 1261–1268. https://doi.org/10.1038/nbt.1504.
21. Peddapalli, H., Ganta, R. P., & Boggula, N. (2018). Formulation and evaluation of transdermal patches for antianxiety drug. Asian J. Pharm, 12, 127–136.
22. Wokovich, A., Prodduturi, S., Doub, W., Hussain, A., & Buhse, L. (2006). Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Für Pharmazeutische Verfahrenstechnik e.V, 64(1), 1–8.
23. Hadžiabdić, J., Šejto, L., Rahić, O., Tucak, A., Hindija, L., & Sirbubalo, M. (2021). Transdermal patches as noninvasive drug delivery systems. In IFMBE Proceedings (pp. 395– 402). Springer International Publishing.
24. Latif, M. S., Al-Harbi, F. F., Nawaz, A., Rashid, S. A., Farid, A., Mohaini, M. A., Alsalman, A. J., Hawaj, M. A. A., & Alhashem, Y. N. (2022). Formulation and evaluation of hydrophilic polymer-based methotrexate patches: In vitro and in vivo characterization. Polymers, 14(7), 1310. https://doi.org/10.3390/polym14071310.
25. Bhatt, P., Trehan, S., Inamdar, N., Mourya, V. K., & Misra, A. (2021). Polymers in drug delivery: An update. In *Applications of Polymers in Drug Delivery* (pp. 1–42). Elsevier.
26. Valenta, C., & Auner, B. G. (2004). The use of polymers for dermal and transdermal delivery. European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft Für Pharmazeutische Verfahrenstechnik e.V, 58(2), 279–289. https://doi.org/10.1016/j.ejpb.2004.02.017
27. Yewale, C., Tandel, H., Patel, A., & Misra, A. (2021). Applications of Polymers in Drug Delivery. Polymers in Transdermal Drug Delivery, 131–158.
28. Santos, L. F., Correia, I. J., Silva, A. S., & Mano, J. F. (2018). Biomaterials for drug delivery patches. European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences,118,49–66.
29. Sa'adon, S., Abd Razak, S. I., Ismail, A. E., & Fakhruddin, K. (2019). Fabrication of dual layer polyvinyl alcohol transdermal patch: Effect of freezing-thawing cycles on morphological and swelling ability. Procedia Computer Science, 158, 51–57. https://doi.org/10.1016/j.procs.2019.09.027.
30. Zahra, F. T., Quick, Q., & Mu, R. (2023). Electrospun PVA fibers for drug delivery: A review. Polymers, 15(18), 3837. https://doi.org/10.3390/polym15183837.
31. Teodorescu, M., Bercea, M., & Morariu, S. (2019). Biomaterials of PVA and PVP in medical and pharmaceutical applications: Perspectives and challenges. Biotechnology Advances, 37(1), 109–131. https://doi.org/10.1016/j.biotechadv.2018.11.008.
32. Lee, I.-C., He, J.-S., Tsai, M.-T., & Lin, K.-C. (2015). Fabrication of a novel partially dissolving polymer microneedle patch for transdermal drug delivery. Journal of Materials Chemistry. B, Materials for Biology and Medicine, 3(2), 276–285. https://doi.org/10.1039/c4tb01555j.
33. Nokhodchi, A., Shokri, J., Dashbolaghi, A., Hassan-Zadeh, D., Ghafourian, T., & Barzegar- Jalali, M. (2003). The enhancement effect of surfactants on the penetration of lorazepam through rat skin. International Journal of Pharmaceutics,250(2), 359–369. https://doi.org/10.1016/s0378-5173(02)00554-9.
34. Prajapati, S. T., Patel, C. G., & Patel, C. N. (2011). Formulation and evaluation of transdermal patch of Repaglinide. ISRN Pharmaceutics, 2011, 1–9. https://doi.org/10.5402/2011/651909.
35. Haimhoffer, Á., Vasvári, G., Trencsényi, G., Béresová, M., Budai, I., Czomba, Z., Rusznyák, Á., Váradi, J., Bácskay, I., Ujhelyi, Z., Fehér, P., Vecsernyés, M., & Fenyvesi, F. (2021). Process optimization for

the continuous production of a gastroretentive dosage form based on melt foaming. AAPS PharmSciTech, 22(5). https://doi.org/10.1208/s12249-021-02066-y.
36. Głąb, M., Drabczyk, A., Kudłacik-Kramarczyk, S., Duarte Guigou, M., Makara, A., Gajda, P., Jampilek, J., & Tyliszczak, B. (2021). Starch solutions prepared under different conditions as modifiers of chitosan/poly (aspartic acid)-based hydrogels. Materials, 14(16), 4443. https://doi.org/10.3390/ma14164443.
37. Thakur, N., Goswami, M., Deka Dey, A., Kaur, B., Sharma, C., & Kumar, A. (2024). Fabrication and synthesis of thiococlchicoside loaded matrix type transdermal patch. Pharmaceutical Nanotechnology, 12(2), 143–154. https://doi.org/10.2174/22117385116
38. Suksaeree, J., Prasomkij, J., Panrat, K., & Pichayakorn, W. (1996). Cross-Linked Poly(ethylene glycol) Networks as Reser-voirs for Protein Delivery. J. Appl. Poly. Sci, 8, 459–466.
39. Costa, P. (1997). Design and Evaluation of a Lorazepam Transdermal Delivery System," Drug Dev. Drug Dev. Ind. Pharm, 23(10), 939–944.
40. Ramarao, P., & Diwan, P. V. (1998). Formulation and In Vitro Evaluation ofPolymeric Films of Diltiazem Hydrochloride and Indomethacin forTransdermal Administration. Drug Dev. Ind. Pharm, 24(4), 327–336.
41. Minghetti, P. (1999). Dermal Patches for the Controlled Release of Mi-conazole: Influence of the Drug Concentration on the Technical Characteristics. Drug Dev. Ind. Pharm, 25, 679–684.
42. Guyot, M., & Fawaz, F. (2000). Design and In Vitro Evaluation of AdhesiveMatrix for Transdermal Delivery of Propranolol. Int. J. Pharm, 204, 171–182.
43. Iwase, H., Sudo, J., Terui, J., Kakuno, K., Watanabe, T., Takayama, K., & Nagai, T. (2000). Transdermal absorption of L-dopa from a new system composed of two separate layers of L- dopa and hydrogel in rats. Drug Development and Industrial Pharmacy, 26(7),755–759. https://doi.org/10.1081/ddc-100101294.
44. Witika, B. A., Mweetwa, L. L., Tshiamo, K. O., Edler, K., Matafwali, S. K., Ntemi, P. V., Chikukwa, M. T. R., & Makoni, P. A. (2021). Vesicular drug delivery for the treatment of topical disorders: current and future perspectives. The Journal of Pharmacy and Pharmacology, 73(11),1427–1441. https://doi.org/10.1093/jpp/rgab082.
45. DeMerlis, C. C., & Schoneker, D. R. (2003). Review of the oral toxicity of polyvinyl alcohol (PVA). Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association, 41(3), 319–326. https://doi.org/10.1016/s0278-6915(02)00258-2.

HOW TO CITE THIS ARTICLE: Yadav, A.S., Bhatt, S., Verma, K., Shukla, D., Gupta, D. Therapeutic Implication of the Transdermal Patches in Treatment of the Chronic Diseases. J. of Drug Disc. and Health Sci. 2025;2(2):107-116. **DOI:** 10.21590/jddhs.02.02.07