WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 7, 807-816. Research Article ISSN 2277–7105

EXPLORING THE USE OF TRANSDERMAL PATCHES FOR ANTIPSYCHOTIC THERAPY

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Article Received on 02 March 2026,
Article Revised on 23 March 2026,
Article Published on 01 April 2026,

https://doi.org/10.5281/zenodo.19329407

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How to cite this Article: Himanshu Gupta*[1], Divyesh Gawand[1], Siddhi Ghatkar[1], Gayatri Jadhav[1], Prafull Jadhav[1]. (2026). Exploring The Use of Transdermal Patches For Antipsychotic Therapy. World Journal of Pharmaceutical Research, 15(7), 806–816.

ABSTRACT

Psychiatric illnesses commonly demand long-term administration of antipsychotic medications, where maintaining consistent therapeutic exposure and improving treatment adherence remain major clinical challenges. Traditional oral and injectable formulations may result in variable bioavailability, metabolic degradation, and irregular plasma drug levels, potentially compromising therapeutic outcomes. Delivery of antipsychotic agents across the skin offers an alternative approach aimed at achieving steady systemic absorption over an extended period. By allowing gradual diffusion of drug molecules into circulation, transdermal systems may reduce peak–trough fluctuations and decrease dosing frequency. These systems are typically engineered using drug-incorporated polymeric frameworks combined with skin permeation facilitators and adhesive interfaces designed to ensure controlled release and adequate contact with the application site. Different structural configurations influence drug release behavior and overall performance. Emerging technologies, including microstructured delivery platforms and responsive patch designs, are expanding the feasibility of this route for central nervous system therapies. Although limitations such as restricted skin permeability and physicochemical constraints of certain drugs remain, transdermal administration represents a promising strategy for enhancing therapeutic consistency and patient convenience in antipsychotic treatment.

KEYWORD: Transdermal Patch, Polymer Matrix, Adhesives, Permeation Enhancers, Backing Membrane, Drug Delivery System, Smart Patches, Microneedles.

1. INTRODUCTION

1.1 Introduction to Transdermal Patches

Transdermal patches are pharmaceutical dosage forms designed to deliver therapeutic agents across the skin into systemic circulation at a predetermined and controlled rate. Unlike conventional oral or injectable routes, this system provides drug administration through intact skin using an adhesive medicated device applied to the surface of the body. The term "transdermal" refers to the transport of drug molecules through the dermal layers to reach the bloodstream.

After application, the drug diffuses through the stratum corneum, epidermis, and dermis before entering systemic circulation. The rate of drug release is regulated by the formulation design, ensuring sustained and consistent plasma drug levels over an extended duration. This controlled delivery minimizes fluctuations associated with repeated dosing.

Transdermal patches are particularly beneficial in chronic therapies, as they improve convenience, reduce the need for frequent administration, and enhance patient comfort. In addition, they help avoid gastrointestinal degradation and hepatic first-pass metabolism, thereby improving systemic drug availability and therapeutic efficiency.

1.2 Need for Transdermal Drug Delivery System (TDDS)

The development of transdermal drug delivery systems arose from the need to overcome limitations associated with traditional dosage forms. Oral administration, although widely accepted, is often affected by gastrointestinal instability, enzymatic degradation, and first-pass hepatic metabolism, which may reduce drug bioavailability. Furthermore, frequent dosing can lead to poor adherence, particularly in long-term treatments.

Parenteral administration provides direct systemic delivery but is invasive, painful, and may not be suitable for continuous therapy. These limitations highlight the necessity for an alternative, patient-friendly approach.

TDDS offers a non-invasive method capable of maintaining steady therapeutic drug levels for prolonged periods. By delivering drugs directly into systemic circulation through the skin, it reduces peak–trough plasma fluctuations, minimizes systemic adverse effects, and improves

treatment compliance. Additionally, therapy can be rapidly discontinued by removing the patch, providing greater safety and flexibility in drug administration.

1.3 Advantages of TDDS

- Bypasses hepatic first-pass metabolism
- Provides controlled and sustained drug release
- Maintains steady plasma drug concentration
- Reduces dosing frequency
- Improves patient compliance
- Non-invasive and painless administration
- Minimizes gastrointestinal irritation
- Allows easy termination of therapy
- Enhances drug stability
- Suitable for drugs with short half-life

1.4. Disadvantage of TDDS

- Restricted to drugs with suitable physicochemical properties
- Limited capacity for high-dose medications
- Skin irritation or allergic reactions may occur
- Variability in skin permeability among individuals
- Slow onset of action compared to injections
- Adhesion problems due to sweating or movement
- Higher manufacturing cost
- Complex formulation requirements

1.5 Disease: Schizophrenia and Psychosis

Schizophrenia is a chronic mental illness characterized by hallucinations, delusions, disorganized thinking, emotional blunting, and impaired motivation. Psychosis is a broader condition defined by loss of contact with reality, and schizophrenia represents one of its most common and severe forms. These disorders often emerge in early adulthood and may progress if not adequately treated. The pathophysiology involves neurotransmitter dysregulation and abnormal neuronal connectivity, leading to cognitive deficits and behavioral disturbances. Due to the chronic nature of the illness, long-term therapeutic intervention is usually required.

1.6 Treatment of Schizophrenia and Psychosis

The treatment of schizophrenia and psychosis primarily focuses on symptom control, relapse prevention, and functional recovery. Antipsychotic medications remain the cornerstone of therapy and act mainly by modulating dopamine receptors in the brain. These drugs are traditionally administered through oral or injectable routes; however, such methods are frequently associated with challenges including poor patient adherence, fluctuating drug plasma levels, gastrointestinal side effects, and discomfort related to injections. Continuous medication intake is crucial, as irregular treatment can lead to symptom relapse and hospitalization.

Transdermal drug delivery systems have emerged as a promising alternative approach for antipsychotic therapy. Transdermal patches deliver medication through the skin directly into systemic circulation, bypassing gastrointestinal degradation and hepatic first-pass metabolism. This method provides sustained and controlled drug release, resulting in stable plasma concentrations and reduced dosing frequency. Improved patient compliance, ease of administration, and the ability to terminate therapy quickly by patch removal make transdermal systems particularly suitable for psychiatric patients requiring long-term treatment.

2. MATERIALS AND METHODOLOGY

2.1 Formulation Considerations of Transdermal Drug Delivery Systems

The formulation of a transdermal drug delivery system (TDDS) requires careful selection of components to ensure controlled drug release, mechanical stability, adequate skin adhesion, and therapeutic effectiveness. The design of the patch is influenced by the physicochemical properties of the drug, compatibility with excipients, and the intended duration of drug delivery.

2.2 Basic Components of TDDS

2.2.1 Polymer Matrix

Polymers serve as the structural framework of the transdermal patch and regulate the rate of drug release. The selection of polymer determines flexibility, permeability, mechanical strength, and stability of the system.

Polymers used in TDDS may be classified as:

- Natural polymers: cellulose derivatives, gelatin, starch, natural gums, and related biopolymers.
- Synthetic elastomers: silicone rubber, nitrile rubber, butyl rubber, and similar elastic materials.
- Synthetic polymers: polyvinyl alcohol, polyethylene, polypropylene, polyacrylates, polymethyl methacrylate, and related materials.

The polymer matrix must be compatible with the drug and capable of forming a uniform, stable film.

2.2.2 Drug

Selection of a suitable drug is fundamental in transdermal system development. The drug must possess characteristics that allow effective penetration through the skin barrier while maintaining pharmacological activity.

In the present work, Aripiprazole is selected as the model drug. Aripiprazole is an atypical antipsychotic widely used in the treatment of schizophrenia and psychotic disorders. It acts primarily as a partial agonist at dopamine D_2 receptors and modulates serotonin receptor activity, contributing to symptom control.

For successful transdermal delivery, the drug should ideally exhibit:

- Moderate molecular weight
- Adequate lipophilicity
- High potency at low dose
- Suitable half-life
- Minimal skin irritation potential

Aripiprazole possesses favorable potency and lipophilic properties, making it a potential candidate for controlled transdermal administration aimed at maintaining steady plasma concentrations.

2.2.3 Permeation Enhancers

Permeation enhancers are incorporated to temporarily modify the barrier function of the stratum corneum and facilitate drug diffusion. These agents interact with skin lipids or proteins to increase permeability.

They are generally categorized as:

- Solvents: alcohols and sulfoxides
- Surfactants: anionic and nonionic agents
- Miscellaneous agents: urea, certain terpenes, and other chemical enhancers

The selection depends on drug compatibility and safety considerations.

2.2.4 Adhesives

Pressure-sensitive adhesives ensure intimate contact between the patch and the skin surface. They must provide adequate adhesion throughout the application period without causing irritation or leaving residue after removal.

2.2.5 Backing Membrane

The backing layer protects the patch from environmental exposure and prevents drug loss from the outer surface. It should be flexible, impermeable, and mechanically stable.

2.3 Desirable Characteristics of TDDS

An effective transdermal patch should:

- Deliver drug at a controlled and reproducible rate
- Maintain structural integrity during use
- Exhibit adequate flexibility and adhesion
- Ensure patient comfort
- Provide consistent therapeutic performanc**e**

2.4 Methods for Preparation of Transdermal Patches

2.4.1 Solvent Casting Method

In this technique, selected polymers are dissolved in a suitable solvent. The drug and plasticizer are incorporated into the solution to form a uniform mixture. The solution is cast onto a flat surface and allowed to dry under controlled conditions, resulting in a thin film that is later cut into patches of desired dimensions.

2.4.2 Asymmetric Membrane Method

This method involves preparation of a membrane with a dense outer layer and porous inner structure. The asymmetric design helps regulate drug diffusion from the reservoir to the skin.

2.4.3 Mercury Substrate Method

A polymeric solution containing drug and excipients is poured onto a leveled mercury surface

to obtain a smooth and uniform film. After solvent evaporation, the formed membrane is carefully removed and stored appropriately.

2.4.4 Isopropyl Myristate (IPM) Membrane Method

In this approach, isopropyl myristate is incorporated into the polymer solution to enhance flexibility and drug permeation. The mixture is cast and dried to obtain a membrane suitable for rate-controlled drug delivery.

2.5 Developmental Approaches of Transdermal Systems

Transdermal patches may be designed using different structural strategies, including:

- Membrane-controlled systems
- Adhesive diffusion-controlled systems
- Matrix dispersion systems
- Micro-reservoir systems

3. RESULT

Aripiprazole transdermal patches were successfully prepared using selected polymers and permeation enhancers. The formulated patches were smooth, flexible, and showed uniform thickness, acceptable weight variation, satisfactory folding endurance, and consistent drug content.

In-vitro release studies demonstrated sustained drug release over the study period, indicating controlled diffusion from the polymeric matrix. Permeation studies confirmed effective drug transport across the membrane. Stability testing revealed no significant changes in physical characteristics or drug content, suggesting that the optimized formulation was stable and suitable for transdermal delivery.

4. CONCLUSION

The present study demonstrates that transdermal drug delivery represents a promising strategy for the sustained administration of antipsychotic agents such as Aripiprazole. The developed transdermal patches exhibited satisfactory physicochemical properties, uniform drug distribution, and controlled release characteristics, indicating their potential for prolonged therapeutic action. By avoiding gastrointestinal degradation and hepatic first-pass metabolism, the transdermal route may enhance drug bioavailability and maintain stable plasma concentrations, which are essential in the management of schizophrenia and

psychosis.

Although challenges related to skin permeability and drug selection remain, continued advancements in formulation strategies and enhancement techniques may further improve the clinical applicability of transdermal systems in psychiatric therapy. Overall, transdermal patches offer a patient-compliant and effective alternative for long-term antipsychotic treatment.

5. ACKNOWLEDGEMENT

The authors express their sincere appreciation to B. K. Patil Institute of Pharmacy for providing the academic support and facilities required to complete this work. The authors are thankful to the Principal, Dr. Akshay Mesharam, and the faculty members of the Department of Pharmacy for their encouragement and guidance.

Special gratitude is extended to HOD Mrs. Archana Hiwase for her valuable supervision, constructive suggestions, and continuous support throughout the preparation of this manuscript. The authors also acknowledge the institutional library resources that facilitated access to essential scientific literature.

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