

To Develop and Evaluate Herbal Transdermal Patches with Antifungal Properties for Effective and Sustained Treatment of Fungal Infections

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ABSTRACT

Fungal infections, or mycoses, range from superficial conditions to life-threatening invasive diseases and are increasingly recognized as a major global health concern. Their prevalence has risen due to expanding immunocompromised populations, comorbidities such as diabetes and HIV/AIDS, and medical interventions that create susceptible hosts. Despite their growing impact, fungal diseases remain underdiagnosed and underprioritized, particularly in resource-limited settings. These infections can be broadly classified as superficial, cutaneous, subcutaneous, mucosal, or systemic, with dermatophytes, *Candida*, *Aspergillus*, and other opportunistic fungi being significant pathogens. Traditional antifungal therapies often face limitations such as resistance, systemic toxicity, and poor patient compliance, underscoring the need for alternative strategies. Transdermal drug delivery systems (TDDS) have emerged as a promising approach, offering advantages like sustained release, localized effects, improved compliance, and bypassing hepatic metabolism. Transdermal patches provide non-invasive, controlled drug delivery, while novel formulations improve skin penetration and therapeutic outcomes. Herbal antifungal agents such as neem, turmeric, garlic, tea tree oil, coconut oil, and *Cinnamomum camphora* demonstrate potent antifungal mechanisms, enhanced further through incorporation in transdermal systems. Preparation methods such as solvent casting and the use of biocompatible polymers, permeation enhancers, and plasticizers have been optimized to ensure patch stability, drug content uniformity, and efficacy. Evaluation techniques including UV-Vis, HPLC, FTIR, in vitro release, antifungal assays, ex vivo permeation, and skin irritation tests confirm therapeutic potential. Stability studies further ensure long-term effectiveness. Collectively, integrating herbal antifungal agents into advanced TDDS represents a significant advancement in the management of fungal infections.

Keywords: Fungal infections; Transdermal drug delivery; Herbal antifungal agents; Transdermal patches; Drug release evaluation.

INTRODUCTION

Fungal Infections

Fungal infections, or mycoses, are a diverse and increasingly prevalent group of diseases caused by various pathogenic fungi, ranging from mild superficial problems to life-threatening invasive conditions. Traditionally dismissed as of secondary importance compared to bacterial or viral infections, fungal diseases have in recent decades emerged as a growing global health crisis due to demographic transitions, expanding immunocompromised

populations, and the emergence of resistant fungal strains (1,2). These infections not only account for significant morbidity and mortality but also exert a profound socio-economic burden that is often underestimated, particularly in low- and middle-income countries where diagnostic capacity, reporting, and treatment options might be limited (3). The expansion of medical technologies—such as organ transplantation, chemotherapy, advanced immunosuppressive therapies, and intensive care medicine—has inadvertently led to both improved survival for patients with severe comorbidities and a surge in the number of susceptible hosts for

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.

opportunistic fungi (4,5). The increasing prevalence of diabetes mellitus, chronic respiratory diseases, and the HIV/AIDS pandemic have further added to the pool of at-risk populations worldwide (5,6). The global response to this growing problem remains insufficient, as evidenced by the underdiagnosis, misdiagnosis, and frequent neglect of fungal infections by health systems and funding agencies (7).

Types of Fungal Infections

Fungal infections can be classified based on their site of involvement and the pathogenicity of the causative organisms. The primary types include superficial, cutaneous, subcutaneous, mucosal, and systemic or invasive mycoses (2,8):

- **Superficial Mycoses:** Confined to the outermost layers of the skin, hair, and nails. These are the most commonly encountered fungal diseases and are primarily caused by dermatophytes (*Trichophyton*, *Microsporum*, *Epidermophyton*) as well as yeasts such as *Malassezia* species (9,10).
- **Cutaneous and Subcutaneous Mycoses:** Penetrate deeper into dermal and subcutaneous tissues, respectively, often resulting from traumatic implantation of fungal elements. Conditions such as sporotrichosis and mycetoma are classic examples (11).
- **Mucosal Mycoses:** These commonly involve mucous membranes of the oral cavity, gastrointestinal tract, genital tract, and nasal sinuses, with *Candida albicans* being a principal pathogen leading to oral, esophageal, and vaginal candidiasis (10,12).
- **Systemic or Invasive Mycoses:** Result from the dissemination of fungal pathogens beyond primary barriers, often afflicting immunocompromised individuals. Notable examples include invasive aspergillosis, candidemia, cryptococcal meningitis, pneumocystis pneumonia, histoplasmosis, and mucormycosis (13,14).

The global burden of these diseases is substantial and continues to increase as medical advances create larger populations of susceptible patients (6,8).

Transdermal Drug Delivery System:

Skin is the largest organ in the body and enfolds the average body surface area of approx 2m² and maximum blood circulates. Transdermal means skin in which drug is applied on the skin directly for localized effects. Transdermal administration has been suggested as a possible route for achieving systemic and regulated medication delivery with positive results (15). Topical route of drug delivery implies the use of skin medication for limited impact and used as optimal route for potential delivery of systemic drug (16,17). The use of transdermal route to a more extensive facility of drug is secret because of the considerable permeation barrier to the skin which is connected basically with the outer most layer of stratum corneum layer of epidermis (18,19). The transdermal delivery is the anatomical relationship of the skin which also act as a barrier for controlling the deficiency of electrolytes, water and other constituents and also prevents the entry of deleterious agents from the external milieu. It is extremely fine (almost 1-10% of skin thickness) and offers more than 80% of the whole resistance for transport of substances (20). Transdermal drug delivery is the successful approach towards medicinal practices and has the ability to overcome instant effects of parental as well as oral preparations. In ancient times, transdermal patches were used to deliver controlled and sustained drug delivery. Now-a-days, metered dose spray, gel or other topical formulation appropriate for serving public benefits. After applying a transdermal medicine to the skin, it can absorb or evaporate from the stratum corneum, resulting in the generation of a thin film that allows for improved penetration. For example, testosterone gels have been used for some years, and estradiol administration is also available as transdermal sprays (21-23). First generation of transdermal delivery system is based on increasing drug absorption into dermis layer of skin without any skin penetrability enhancer (24,24). Second generation transdermal delivery system includes chemical enhancers which increases skin penetrability of drug. Iontophoresis technique is also used to control drug release in second generation



system. The third generation transdermal delivery is mainly based on enhancing drug permeability through stratum corneum layer of skin. Recent examples include thermal ablation microneedles. Various clinical trials are under progress to enhance drug delivery system such as vaccines, insulin patch etc. (26).

Clinical and Pharmaceutical Advantages

Transdermal drug delivery confers several distinct advantages for superficial and systemic antifungal therapy:

- **Sustained and Controlled Release:** Enables continuous therapeutic levels, reducing dosing frequency and improving adherence, especially for chronic infections (27).
- **Targeted Application and Localized Effects:** Allows direct targeting of skin and mucosa, achieving higher local concentrations with minimal systemic exposure, and thus lower risk of side effects (27).
- **Non-Invasiveness and Patient Convenience:** TDDS is needle-free, pain-free, and generally easy to apply and remove, making it suitable for all age groups, including pediatric and geriatric populations (28).
- **Bypassing Gastrointestinal and Hepatic Metabolism:** Beneficial in patients with gastrointestinal intolerance or comorbid liver dysfunction (29).
- **Potential Resistance Mitigation:** Sustained drug presence reduces the risk of fluctuating subtherapeutic levels that can foster resistance (30).

Applications in Antifungal Therapy

- Recent research confirms that transdermal delivery systems can significantly increase the cutaneous absorption and skin retention of antifungal agents, whether synthetic or natural in origin (27,29,30). For instance, studies employing HPMC-chitosan matrix patches containing tea tree oil, or turmeric extract

nanoemulsions, report improved in vitro and in vivo antifungal activity against common pathogens such as *Candida albicans*, *Aspergillus niger*, and *Trichophyton rubrum* (30). Clinical application remains limited but promising, and ongoing research into patch optimization, user acceptability, and regulatory clearance is expected to revolutionize skin-directed antifungal therapy.

Transdermal Patches

Transdermal patches are medicated adhesive platforms engineered to deliver specific drugs through the skin and into systemic circulation, representing a significant advancement in non-invasive drug delivery for chronic and acute therapeutic needs (31).

Mechanism of Action

These patches rely on sustained-release technology, using matrix or reservoir systems that enable gradual, controlled absorption of drugs through the skin's layers, effectively bypassing the gastrointestinal tract and hepatic first-pass metabolism (32). Drugs penetrate the outermost skin barrier, the stratum corneum, aided by permeation enhancers that temporarily alter lipid structure to increase absorption without causing long-term damage (31,33).

Advantages

- **Sustained and controlled drug release:** Transdermal patches offer the advantage of maintaining stable plasma drug concentrations by releasing medications slowly over hours or days (31).
- **Improved patient compliance:** Their painless application is ideal for those with swallowing difficulties or needle aversion, and their easy use boosts long-term adherence (32).
- **Enhanced bioavailability:** Direct entry into systemic circulation improves drug effectiveness and reduces losses from digestive processes (31).
- **Reduced dosing frequency:** Extended-release profiles mean fewer applications, which is



convenient and reduces the risk of missed doses (32).

- **Lower risk of gastrointestinal side effects:** By avoiding oral administration, transdermal patches minimize irritation and side effects associated with the digestive tract (31).

Clinical Applications

Transdermal patches are used to treat conditions including pain, hypertension, hormone imbalances, and nicotine addiction, and ongoing research continues to expand their application to new therapeutic areas (32).

Herbal Antifungal Agents: Detailed Mechanisms and Applications

Neem (*Azadirachta indica*)

Neem (*Azadirachta indica*) is esteemed in traditional and modern medicine for its potent antifungal activity mainly attributed to the limonoids **nimbidin** and **gedunin**. Nimbidin disrupts fungal cell wall biosynthesis and compromises membrane integrity, leading to leakage of intracellular components and growth inhibition (34,35).

Gedunin has been shown to induce apoptosis-like pathways in fungal cells, interfering with mitochondrial function and energy metabolism (34). Neem extracts have demonstrated efficacy against an array of fungal pathogens, particularly dermatophytes such as *Trichophyton* and *Microsporum*, as well as *Candida albicans* – the latter known for causing mucocutaneous infections (36,37). In addition to direct antifungal effects, neem exhibits anti-inflammatory and immunomodulatory actions, promoting faster resolution of infection and reduced tissue damage (38). Multiple in vitro and animal studies have reported sustained antifungal activity using neem-loaded transdermal patches, highlighting improved bioavailability and minimal toxicity (39,40).

Turmeric (*Curcuma longa*)

Turmeric (*Curcuma longa*) is a rich source of the polyphenolic compound **curcumin**, which confers a

broad antifungal spectrum through multiple mechanisms. Curcumin exerts fungistatic and fungicidal activity by disrupting fungal plasma membranes, inhibiting biofilm formation, and generating reactive oxygen species that induce cellular damage (41,42). Furthermore, curcumin impairs fungal morphogenesis and adhesion essential for colonization, especially in *Candida albicans* and *Aspergillus* species (43,44).

Despite challenges related to its hydrophobicity and low transdermal permeability, advanced delivery systems such as nanoemulsions and polymeric transdermal patches have successfully enhanced curcumin skin penetration and retention (45,46). These delivery systems provide controlled release profiles that maintain effective concentrations at the infection site, enhancing patient compliance (47). Additionally, curcumin's anti-inflammatory properties reduce local inflammatory responses in fungal infections, improving clinical outcomes (48).

Garlic (*Allium sativum*)

Garlic derives its noteworthy antifungal properties from **allicin**, a reactive sulfur compound formed enzymatically when garlic tissue is crushed (49). Allicin disrupts fungal cell membranes by interacting with thiol-containing enzymes and proteins, leading to impaired metabolism and structural integrity in fungi such as *Candida albicans* and *Aspergillus niger* (50,51). Importantly, allicin inhibits fungal biofilm formation, a major factor in chronic infections and resistance (52). In vitro studies demonstrate allicin's fungicidal effects against a wide range of pathogenic yeasts and molds (53). However, allicin's chemical instability and strong odor have posed formulation challenges, which are being overcome by encapsulation within transdermal matrices that stabilize the compound and facilitate sustained, localized delivery (54,55). Such formulations offer promising alternatives to synthetic antifungal therapies, with reduced systemic toxicity and side effects (56).

Tea Tree Oil (*Melaleuca alternifolia*)

Tea tree oil, extracted from *Melaleuca alternifolia*, owes most of its antifungal efficacy to **terpinen-4-ol**, a terpene alcohol that induces increased permeability



of fungal cell membranes, resulting in leakage of essential intracellular components and cell death (57,58). This agent exhibits broad-spectrum activity against dermatophytes, *Candida* spp., and molds (59). Clinical trials have confirmed tea tree oil formulations' effectiveness in treating tinea pedis, onychomycosis, and other superficial fungal infections (60).

Controlled-release transdermal patches enriched with terpinen-4-ol have been developed to maximize local retention, prolong therapeutic action, and mitigate the risk of contact dermatitis reported with higher-concentration topical oils (61,62). The synergy between penetration enhancers and terpinen-4-ol in transdermal systems further improves bioavailability, offering patient-friendly antifungal treatment possibilities (63).

Coconut Oil (*Cocos nucifera*)

Coconut oil's antifungal activity is mainly attributed to its medium-chain fatty acids, notably **lauric acid** and **capric acid**, which induce fungal membrane disruption by intercalating into lipid bilayers, enhancing membrane fluidity, permeability, and ultimately causing cell lysis (64,65). The hydrophobic nature of these fatty acids facilitates interaction with fungal cell walls, making coconut oil effective against pathogens like *Candida albicans*, *Malassezia* species, and dermatophytes (66). Beyond direct antimicrobial effects, coconut oil possesses emollient and anti-inflammatory properties that improve skin barrier function and reduce irritation commonly associated with fungal infections (66). Incorporating coconut oil into transdermal patches enables sustained drug release and improved skin hydration, making it an effective adjunct in topical antifungal therapy (64,67).

Cinnamomum camphora

Cinnamomum camphora essential oil contains bioactive terpenoids including **camphor** and **eucalyptol (1,8-cineole)**, which display antifungal action through membrane disruption and inhibition of ergosterol biosynthesis, vital for fungal cell membrane stability (68,69). The oil has demonstrated fungicidal activity against *Candida*, *Aspergillus*, and dermatophyte species responsible for superficial infections (70). Camphor's rapid volatility and

potential for skin sensitization necessitate delivery via controlled-release systems, such as transdermal patches, to ensure steadier dosing and reduced irritation (71). Additional anti-inflammatory effects contribute to symptom relief and lesion healing in fungal skin diseases. Recent formulations employing transdermal patches have enhanced penetration of camphor oil components, providing sustained antifungal action and improved patient tolerance (72).

Methods of Preparation of Transdermal Patches

Solvent Casting Method

The solvent casting method is a commonly used technique for preparing transdermal patches due to its simplicity, reproducibility, and ability to produce films with uniform thickness and consistent drug distribution. This method is especially suitable for herbal transdermal patches as it allows precise control over patch uniformity, essential for effective drug delivery and patient compliance (73,74).

Materials Preparation

- **Polymer Selection:** Biocompatible polymers such as Hydroxypropyl Methylcellulose (HPMC) and Polyvinyl Alcohol (PVA) are widely used because of their excellent film-forming abilities, mechanical strength, and skin compatibility (75).
- **Plasticizer:** Plasticizers like Polyethylene Glycol 400 (PEG 400) are added to impart flexibility and prevent brittleness of the formed film (76).
- **Permeation Enhancer:** Natural permeation enhancers such as ethanol, eucalyptus oil, and menthol are incorporated to increase transdermal flux of active compounds by disrupting the stratum corneum lipid barrier (77).
- **Active Drug Constituents:** Standardized herbal extracts or isolated phytoconstituents like curcumin from *Curcuma longa*, allicin from *Allium sativum*, and terpinen-4-ol from *Melaleuca alternifolia* serve as the active therapeutic agents (78).

Procedure



- 1. Preparation of Polymer Solution:** Polymers (HPMC and PVA) are accurately weighed and dissolved in distilled water or suitable solvent under continuous stirring until a clear, homogeneous solution is obtained (74).
- 2. Incorporation of Plasticizer and Permeation Enhancer:** Plasticizer (PEG 400) is added gradually under stirring to improve film flexibility. Permeation enhancers (ethanol, eucalyptus oil) are also incorporated and thoroughly mixed to ensure uniform dispersion (73).
- 3. Addition of Active Drug Constituents:** The standardized herbal extracts or active constituents are accurately weighed and added to the polymer solution with continuous stirring to achieve uniform distribution (76).
- 4. Casting:** The drug-loaded polymer solution is poured onto a flat glass or Teflon plate and spread evenly using a casting blade to achieve the required thickness. The films are allowed to dry at controlled temperatures (40–50°C) until complete solvent evaporation (75).
- 5. Drying:** Complete drying ensures formation of flexible, uniform films. This may be done in a hot air oven or under ambient conditions, depending on the sensitivity of the herbal constituents (77).
- 6. Cutting and Packaging:** The dried film is carefully peeled off, cut into patches of desired size, and stored in airtight, moisture-resistant packaging to maintain stability and efficacy (78).

Formulation Table – Herbal Antifungal Matrix Patch (per 100 g) (79-94)

Component	Function	% w/w	Notes	Amount (g)
HPMC (K15M)	Film-forming polymer (hydrophilic matrix)	40%	Provides flexible, controlled-release base	40.00 g
Eudragit RS100	Rate-controlling polymer (optional)	10%	Enhances mechanical strength	10.00 g
Propylene Glycol	Plasticizer + permeation enhancer	10%	Softens patch, increases skin penetration	10.00 g
Ethanol: Water (7:3)	Solvent system	q.s.	Helps dissolve oils, extracts	25.00 g
Eugenol	Essential oil – antifungal	2%	Lipophilic terpene phenol	2.00 g
Thymol	Essential oil – antifungal	1%	Strong synergistic agent	1.00 g
Camphor	Penetration enhancer + antifungal	1%	Volatile terpene	1.00 g
Lauric acid	Fatty acid – skin permeation enhancer	2%	Boosts delivery of lipophilic drugs	2.00 g
Monolaurin	Antifungal fatty acid ester	1%	Disrupts fungal membrane	1.00 g
Terpinen-4-ol	Tea tree oil active – antifungal	1%	Potent against <i>Candida</i> , <i>Aspergillus</i>	1.00 g
Curcumin	Polyphenolic antifungal	2%	Lipophilic, antioxidant	2.00 g
Nimbidin + Nimbin	Neem extract antifungal triterpenoids	2%	Acts against dermatophytes	2.00 g
Gedunin	Neem limonoid – antifungal, antioxidant	1%	Broad-spectrum potential	1.00 g
Allicin	Garlic compound – antifungal, volatile	1%	May be stabilized with microemulsion	1.00 g
Bromelain	Proteolytic enzyme – synergist	1%	Enhances drug delivery	1.00 g

Evaluation of Herbal Transdermal Patches

Evaluation of herbal transdermal patches is pivotal to establish their quality, safety, stability, and therapeutic efficacy. A comprehensive assessment

encompassing physicochemical characterization, drug release profiling, antifungal activity testing, permeation studies, and safety evaluations was performed.



Physicochemical Parameters

- **Thickness:**

The uniformity of patch thickness is critical because it governs drug content and release rates. Thickness was measured at multiple points using a digital micrometer, yielding data on batch-to-batch consistency. Non-uniform thickness can lead to variable dosing, impacting efficacy and safety (95,96).

- **Folding Endurance:**

This test measures the mechanical flexibility and durability of patches. A strip of the patch was repeatedly folded at the same point until it broke; the number of folds tolerated before failure indicated the folding endurance. Higher values reflect superior mechanical robustness essential for patch integrity during handling and skin application (97).

- **Moisture Loss and Uptake:**

The moisture content influences the stability and adhesive properties of the patch. Patches were weighed initially, then stored at controlled humidity to measure moisture loss by diminution in weight or moisture uptake by increase in weight. Controlled moisture levels prevent microbial proliferation and ensure physical stability (98).

- **Drug Content Uniformity:**

To ensure dose consistency, segments of patches were sampled and dissolved in suitable solvents. The active compounds were quantified by UV-Visible spectrophotometry or HPLC against calibration standards. Uniform drug distribution within patches is fundamental for reproducible therapeutic outcomes (99).

Analytical Methods for Characterization of Bioactive Compounds

- **UV-Visible Spectroscopy**

UV-Visible (UV-Vis) spectroscopy is a widely used technique for the quantitative analysis of chromophoric compounds such as curcumin. The method is based on measuring the absorbance of

ultraviolet or visible light by the sample, which correlates with the concentration of the absorbing species according to Beer-Lambert's law. The samples and standards are scanned over a specific wavelength range to identify the maximum absorption wavelength (λ_{max}), which for curcumin is typically around 425 nm. The absorbance at this wavelength is then used to construct a calibration curve by plotting absorbance versus known concentrations. The linearity of this curve is crucial for accurate quantification and method validation. The UV-Vis method is favored for its simplicity, rapidity, cost-effectiveness, and sensitivity to low microgram quantities, making it suitable for routine drug content estimation in formulations (100,101).

- **High-Performance Liquid Chromatography (HPLC)**

HPLC is an advanced chromatographic technique used to separate, identify, and quantify individual components in complex mixtures. It offers high resolution and sensitivity for phytochemical analysis. The method typically uses a reversed-phase C18 stationary phase column, which separates analytes based on hydrophobic interactions. A mobile phase comprising aqueous buffer and organic solvents (such as acetonitrile or methanol) is optimized for pH and composition to achieve adequate separation of target compounds. The optimized flow rate and column temperature contribute to reproducible retention times. Detection is commonly performed using UV detectors set at specific wavelengths corresponding to the maximum absorbance of each compound. Peak purity and peak area calculations allow assessment of compound integrity and quantification, respectively, while retention time is used for compound identification. HPLC methods are validated for specificity, precision, accuracy, linearity, and sensitivity to ensure reliable analytical results for quality control and research purposes (102,103).

- **Fourier Transform Infrared (FTIR) Spectroscopy**

FTIR spectroscopy is a vibrational spectroscopic technique used to identify chemical functional groups and molecular interactions within a sample. In pharmaceutical and herbal extract analysis, FTIR



confirms the presence of characteristic bioactive moieties and detects any chemical changes during processing or formulation. Samples are typically mixed with potassium bromide (KBr) and compressed into pellets for transmission FTIR analysis. The instrument records absorbance or transmittance over the mid-infrared range (4000 to 400 cm^{-1}). Each functional group exhibits characteristic absorption bands; for example, broad bands between 3200–3600 cm^{-1} indicate hydroxyl (O–H) groups, peaks near 1650 cm^{-1} correspond to carbonyl (C=O) stretches from conjugated ketones or esters, and bands around 1100 cm^{-1} indicate ether (C–O–C) linkages. FTIR spectra provide molecular fingerprints useful for confirming extract composition, detecting impurities, and verifying stability. The technique is non-destructive and requires minimal sample preparation, making it valuable for quality assurance and structural elucidation in pharmaceutical research (104,105).

In Vitro Drug Release

Drug release kinetics were studied using Franz diffusion cells, which simulate drug permeation across skin. The patch was mounted on a synthetic or biological membrane placed between donor and receptor compartments. Receptor fluid, maintained at skin temperature ($\sim 32^\circ\text{C}$), was sampled at predetermined intervals and analyzed spectrophotometrically to quantify the cumulative amount of drug released. A sustained and controlled release pattern is desirable to maintain therapeutic levels while minimizing dosing frequency and side effects (106,107).

Antifungal Efficacy

To confirm pharmacological activity following formulation, antifungal efficacy of patches was tested against clinically relevant fungal strains such as *Candida albicans* and *Aspergillus niger*. Agar diffusion assays involved placing patches or their extracts on inoculated agar medium, followed by incubation and measurement of inhibition zones indicating antifungal activity. Minimum Inhibitory Concentration (MIC) assays were conducted to quantify the lowest concentration of the active substance inhibiting fungal growth. These assays verify that herbal actives retain efficacy in patch form, essential for clinical relevance (108,109).

Ex Vivo Skin Permeation Studies

Ex vivo permeation studies were conducted using excised animal skin models (e.g., porcine or rat skin), widely accepted as human skin surrogates due to similar barrier properties. The skin was mounted on Franz diffusion cells, with patches applied on the epidermal surface. Samples from the receptor compartment were withdrawn at intervals and analyzed to determine drug permeation rates. Such studies assess skin absorption kinetics and predict in vivo bioavailability, guiding formulation optimization (110,111).

In Vitro Skin Irritation Tests

Safety evaluation included in vitro skin irritation testing employing reconstructed human epidermis models. Patches were applied to these models, and cellular viability assays such as MTT reduction test were performed to assess cytotoxicity. Low irritation potential supports formulation safety, meeting regulatory requirements and promoting patient adherence (112).

Stability Studies

Stability studies are a critical part of the formulation development process, ensuring that the herbal transdermal patches maintain their physical, chemical, and biological properties over their intended shelf life. The patches were stored under controlled conditions following the International Conference on Harmonisation (ICH) guidelines, which include accelerated conditions ($40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity) and long-term conditions ($25 \pm 2^\circ\text{C}$ and $60 \pm 5\%$ relative humidity) to simulate various storage environments (113,114).

CONCLUSION

Fungal infections continue to pose a significant global health burden, particularly with rising populations of immunocompromised individuals and limited diagnostic and therapeutic capacities in many regions. Traditional antifungal therapies, though effective in some cases, face challenges including toxicity, resistance, and patient non-compliance, necessitating innovative treatment approaches. Transdermal drug delivery systems (TDDS) offer several advantages in



antifungal therapy, including sustained and controlled drug release, improved patient adherence, targeted local effects, and avoidance of gastrointestinal and hepatic metabolism. Among these, transdermal patches provide a convenient and effective means of delivering antifungal agents with enhanced bioavailability and reduced side effects. Herbal antifungal agents such as neem, turmeric, garlic, tea tree oil, coconut oil, and *Cinnamomum camphora* demonstrate strong antifungal activity and additional anti-inflammatory or immunomodulatory effects, making them suitable candidates for TDDS formulations. Methods such as solvent casting enable the preparation of stable, uniform patches, while evaluation techniques including UV-Vis spectroscopy, HPLC, FTIR, drug release profiling, antifungal assays, and ex vivo permeation confirm safety, efficacy, and consistency. Stability studies further validate the long-term utility of these patches. Overall, the integration of herbal antifungal agents into advanced TDDS represents a promising strategy to enhance therapeutic outcomes and address limitations of conventional antifungal treatments.

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HOW TO CITE: Sachin Joshi Semwal, Dimple Singh Tomar, To Develop and Evaluate Herbal Transdermal Patches with Antifungal Properties for Effective and Sustained Treatment of Fungal Infections, *J. Pharm. Sci.*, 2025, 1 (9), 55-67. <https://doi.org/10.5281/zenodo.17135971>

