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A Review on Transungal Patch for Effective Treatment on Nail Infection

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A B S T R A C T

Transungual drug delivery presents a promising, targeted strategy for the treatment of nail conditions such as onychomycosis and nail psoriasis, effectively overcoming the limitations associated with traditional oral and topical therapies. The distinctive architecture of the nail creates substantial obstacles to drug penetration owing to its girth, limited permeability, and dense keratin composition. Recent progress in drug formulation—including the development of transungual patches, permeation enhancers, and nanocarrier systems—has enhanced the delivery of drugs to the nail bed and matrix, where the majority of pathologies are located. Transungual patches, in particular, offer sustained adhesion, regulated drug delivery, and improved patient adherence. Their efficacy and safety are assessed through a comprehensive analysis of physical, mechanical, and biological parameters, including uniformity of thickness and weight, folding endurance, tensile strength, surface pH, moisture content, drug content, drug release profile, permeation studies, antifungal activity, and stability. Although laboratory results are promising, additional clinical studies are necessary to refine the patch design, improve nail adhesion, and confirm its effectiveness and applicability in real-world applications.

Keywords: Transungual Drug Delivery, Nail Patches, Onychomycosis, Nail Disorders, Controlled-Release Systems,

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INTRODUCTION

Transungual drug delivery administers medications through the nail to facilitate targeted treatment of nail disorders. Due to the nail's durability and limited permeability, this approach presents significant challenges. Enhancing topical delivery for conditions such as onychomycosis and nail psoriasis can decrease reliance on systemic therapies, reduce adverse effects, and lower the risk of recurrence. Compared to oral treatments, topical therapies exhibit fewer systemic effects, reduced drug interactions, and are appropriate for patients who are unable to receive systemic medications. Local adverse effects are uncommon and generally moderate; however, limited nail penetration frequently hampers the achievement of effective drug concentrations.The nail unit, a sophisticated keratinized structure located at the fingertips and toenails, serves to provide both protection and sensory function. Key components encompass the nail plate matrix, nail bed, hyponychium, and eponychium. Well-vascularized and forming early in gestation, nails may be impacted by a variety of disorders at any age, most commonly resulting from infection, but also arising from metabolic, inflammatory, or malignant origins. Treatment presents difficulties due to patient adherence, recurrence, and the nail's inherent barriers to drug penetration.[1,2,3]

ANATOMY OF NAIL

The nail is a distinctive, hydrogel-like barrier composed of numerous keratin filaments interconnected by disulfide bonds. It is about 100 times thicker than the stratum corneum, making it the body's toughest structure. Fingernails grow steadily at about 0.1 mm per day, while toenails grow more slowly, with full regeneration requiring 4–6 months for fingernails and 8–12 months for toenails. Structurally, the nail consists of 25 layers of delicate, non-living, keratinized cells, each approximately 0.01 mm in thickness. The nail plate originates from the matrix, is held by lateral pleats, and protects the nail bed, separating from it at the hyponychium. The nail plate is thin, elastic, rigid, transparent, and convex. Its cells are interconnected through intercellular junctions, desmosomes, and membrane-coating granules. Its low lipid content and unique keratin composition give the nail a hydrogel-like behavior, distinct from other body barriers.

a) **Nail Plate:**The nail plate is the visible, protective component of the nail, approximately 0.25 to 0.6 mm in thickness, composed of 25 layers of toughened, keratinized cells. It is tri-laminar, adheres firmly to the nail bed with corresponding ridges, and its form and thickness provide enhanced strength, particularly to toenails.The lunula located near the base serves as an indicator of nail growth.[4,5]
b) **Nail Bed:**A thin layer of epidermis beneath the nail plate, the nail bed facilitates nail growth and is securely connected to the underlying bone. It lacks oil glands and hair, producing distinctive keratin; ridges on both the nail bed and plate facilitate smooth forward movement.
c) **Perionychium:**Encircles the nail plate on both the lateral and proximal aspects. The cuticle, originating from the proximal perionychium, serves as a barrier to infection. The lateral portion supports the nail, whereas the proximal portion safeguards the matrix and provides increased UV protection.
d) **Hyponychium:**Situated beneath the distal border of the nail, it establishes a barrier that prevents the entry of pathogens and foreign matter. It is important for infection prevention and medication absorption.
e) **Eponychium:**It guards against infection and environmental harm and is also referred to as the cuticle. It should be kept because removing it raises the danger of infection.
f) **Nail Matrix:**It is essential to nail growth and repair and is located behind the cuticle, where new nail cells are produced.
g) **Nail Root:**The lunula delineates the visible boundary of the nail root, or germinal matrix, which is situated beneath the epidermis behind the nail and contributes to nail thickness.[6-10]

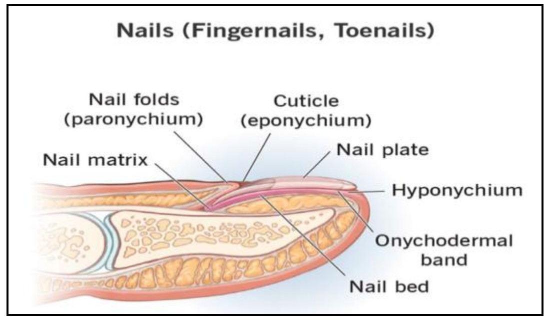

Figure 1: Parts of Nails (Fingernails, Toenails)

NAIL RELATED DISORDERS

Nail disorders, which affect about 10% of people with skin problems, include discolouration, atrophy, inflammation, and brittleness. They are more common in older people. Poor circulation, long-term disorders like diabetes, tumors, changes in how the body works, and a weak immune system are all possible causes.Nails can show signs of systemic disease and make life harder by causing pain, making it hard to move, and making social situations uncomfortable.

Onychomycosis: The widespread fungal infection known as onychomycosis causes coloring, thickness, and detachment (onycholysis) of the nail unit, which includes the nail plate, matrix, and bed. More than half of nail diseases are caused by it. New therapeutic and diagnostic methods are available, and laboratory confirmation prior to treatment is advised. About 90% of toenail infections and 75% of fingernail infections are caused by dermatophytes, particularly Trichophyton rubrum and T. mentagrophytes. About 10% of cases are caused by non-dermatophyte molds, such as Aspergillus and Fusarium, whereas yeasts, such as Candida albicans, are less prevalent and mainly afflict people with impaired immune systems. About 5.5% of people worldwide suffer with onychomycosis, which is more common in adults, the elderly, and people with risk factors such tinea pedis, chronic paronychia, nail damage, immunodeficiency, diabetes, and poor grooming. Males are more likely to have toenail onychomycosis, whilst females are more likely to have fingernail Candida infections. Direct contact leads to fungal invasion, and the nail's susceptibility is increased by its ineffective cell-mediated immunity. Keratin is broken down by fungal enzymes, which makes infection easier. The clinical subtype is determined by the invasion site and type, and biofilm formation is a contributing factor to antifungal resistance. The following are the five forms:

- **Distal Lateral Subungual Onychomycosis:** Starting in the hyponychium, it spreads under the nail plate, causing discolouration and thickness. This is the most frequent type of nail infection.
- **White Superficial Onychomycosis:**It presents itself as white patches on the surface of the nail, which can be removed with ease.

- **Proximal Subungual Onychomycosis:** Starts close to the cuticle and spreads away from it; this condition is observed in immunodeficient people.
- **Endonyx Onychomycosis:** Only the nail plate is affected, with milky areas and no separation.
- **Total Dystrophic Onychomycosis**: The nail is completely destroyed, which is often the last stage of other kinds.[11]

The following are the most prevalent nail conditions, description, symptoms, and their causesare shown in table 1.

Table 1: Detailed Description of Nail Diseases, their Causes and Symptoms[12-20]

No.	Condition	Description	Symptoms	Causes / Risk Factors
1.	Paronychia	Infection or inflammation of the nail folds; can be short-term or long-term.	Swelling, redness, pain, tenderness, pus formation	Bacterial infection (acute), chronic moisture exposure, irritants, trauma
2.	Nail Psoriasis	The nail matrix and bed are affected when psoriasis affects the nails.	Pitting, fissures, yellow-red discoloration, thickening, nail loosening	Psoriasis, autoimmune factors, genetic predisposition
3.	Onychogryphosis	Excessive nail thickening accompanied by aberrant curvature resembling a claw.	Thick, elongated, curved nails	Aging, trauma, poor circulation, neglect, systemic disease
4.	Koilonychia (Spoon nails)	Nails that are abnormally thin, concave, and flipped upside down.	Spoon-shaped nails, brittleness	Iron deficiency anemia, infancy, endocrine disorders, genetics
5.	Pseudomonas Infection	Bacterial infection of the nail unit by Pseudomonas aeruginosa.	Green discoloration, softening, nail detachment	Moist environment, artificial nails, prolonged occlusion
6.	Fungal / Yeast Infection	A nail infection caused by dermatophytes, yeasts, or molds respectively.	Onycholysis, discoloration, thickening, sub-nail debris	Poor hygiene, moisture, immunosuppression, diabetes
7.	Tinea Unguis	A nail plate-specific kind of onychomycosis.	Nail hypertrophy, brittleness, discoloration, nail loss	Dermatophyte fungal infection, aging, occlusive footwear
8.	Onychatrophia	Degeneration and thinning of the nail plate.	Nail thinning, nail shedding	Trauma, systemic illness, nutritional deficiencies
9.	Onychorrhexis	Longitudinal splitting and brittleness of nails.	Fragile nails, ridges, nail breakage	Solvent exposure, aging, heredity, dehydration
10.	Leuconychia	White discoloration of the nail plate.	White spots or patches	Minor trauma to nail matrix, systemic illness
11.	Beau's Lines	Transverse grooves due to temporary arrest of nail growth.	Horizontal depressions across nail	Severe illness, chemotherapy, malnutrition, stress
12.	Subungual Hematoma	Blood accumulation beneath the nail plate.	Pain, red-black discoloration	Trauma, crush injuries
13.	Melanonychia	Pigmented discoloration of nail plate.	Brown or black longitudinal bands	Benign melanocytic activation, drugs, melanoma
14.	Pterygium	Scar tissue growth from proximal nail fold onto nail plate.	Nail distortion, nail loss	Lichen planus, trauma, scarring disorders
15.	Pterygium Inversum Unguis	Adherence of hyponychium to the underside of the nail.	Pain, difficulty trimming nails	Connective tissue disorders, allergies
16.	Vertical Ridges	Longitudinal ridges on nail surface.	Visible ridges, rough texture	Aging, dehydration, reduced nail lipids
17.	Nail-Patella Syndrome	Genetic disorder affecting nails and skeletal system.	Nail hypoplasia, absent cuticles, skeletal defects	Autosomal dominant inheritance

Figure 2: Types of Onychomycosis

FACTORS AFFECTING BARRIERS IN DRUG DELIVERY THROUGH THE NAIL

a) **Molecule Size:** Drugs with larger molecules have a shorter ability to penetrate the nail.
b) **Lipophilicity (HLB Value):** The permeability of a substance is increased by moderate lipophilicity and hydration, while it is decreased by extremely non-polar solvents. This is referred to as the HLB value.[21]
c) **Ionization:** Non-ionized medicines have a higher rate of permeation compared to ionized medications.[22]
d) **The nature of the vehicle:** Water-based vehicles hydrate and inflate the nail, which increases the number of pores in the nail.
e) **Dorsal Layer:** The very topmost layer is the primary barrier; removing it (either through the use of chemicals or enzymes) allows for more medication to enter the body.
f) **Keratin Binding:** When medications attach to nail keratin, it can reduce their penetration, particularly when we are talking about ionic drugs.
g) **Formulation Effects**: The solubility of the medicine, the hydration of the nail, and the penetration are all affected by the pH, the solvent, and the permeation enhancers (such as DMSO).[23,24]

TRANSUNGUAL DRUG DELIVERY SYSTEM (TUDDS)

Nail disorders, including onychomycosis, nail psoriasis, onycholysis, and chronic paronychia, are prevalent, persistent, and aesthetically troubling ailments that substantially impact quality of life. Systemic antifungal therapy utilizing agents such as terbinafine, itraconazole, or fluconazole is efficacious; nonetheless, it has risks of hepatotoxicity, potential drug-drug interactions, and necessitates prolonged treatment durations, particularly in elderly and taking multiple medicines patients. Topical dermatological formulations, including creams and ointments, exhibit minimal efficacy on nails due to their quick removal and inability to penetrate the dense barrier of the nail plate.

The transungual drug delivery system has been designed to address these restrictions by facilitating targeted drug delivery through the nail plate to the nail bed and matrix, where infections or pathologies typically reside. The human nail is a highly keratinized, hydrophilic barrier primarily formed of hard keratin, characterized by numerous disulfide linkages, minimal lipid content, and a compact, crosslinked structure, rendering it significantly less permeable than the stratum corneum. Nevertheless, advancements in formulation science, such as permeation enhancers, nanocarriers, and device-based enhancements, currently make TUDDS a promising alternative or complement to oral therapy for nail disorders.

Transungual delivery presents numerous advantages over systemic administration: elevated drug concentrations at the infection site, limited systemic exposure and toxicity, decreased likelihood of medication–drug interactions, and potentially enhanced adherence owing to localized topical treatment.

TYPES OF TRANSUNGUAL DRUG DELIVERY SYSTEMS

The transungual drug delivery systems can be classified according to the route and technology used:

1. **Systemic therapy targeting nail structures:** Oral antifungals penetrate the nail through the nail matrix and capillaries of the nail bed, although they experience restricted drug concentration at the nail plate and considerable systemic side effects.
2. **Conventional topical formulations on the nail surface:**
   - Creams, ointments, and gels, simple to administer but exhibit inadequate residence duration and restricted penetration through the nail.
   - Medicated nail lacquers are film-forming polymeric solutions that generate a drug depot on the surface of the nail and hydrate the nail, thereby increasing the rate of diffusion. Some examples of these lacquers include ciclopirox, amorolfine, econazole, and luliconazole lacquers.
3. **Advanced topical transungual systems:**
   - Pharmaceutical nail lacquers including permeability enhancers (thiols, urea, salicylic acid, organic solvents, surfactants) to disrupt or plasticize keratin.
   - Transungual patches (polymeric films or adhesive patches laden with drugs).
   - Nanocarrier systems, including as liposomes, nanoemulsions, polymeric nanoparticles, and nanofibers, are engineered to enhance medication loading and penetration through the nail plate.
4. **Device-based and physical enhancement approaches**

These involve nail plate abrasion, microneedling, iontophoresis, laser ablation, and photodynamic therapy, which may be integrated with topical preparations (lacquer or patch) to enhance ungual flow.

Transungual Patch

A transungual patch is a specific adhesive drug delivery method applied to the nail, designed to maintain extended contact with the nail plate and distribute the medicine in a regulated manner. A transungual patch often comprises:

- A polymeric matrix or reservoir containing a medication (e.g., acrylate, polyvinylpyrrolidone, cellulose derivatives).
- A pressure-sensitive adhesive coating designed to bond with the rigid, hydrophilic nail surface.

- A backing membrane that is either occlusive or semi-occlusive, which regulates medication release and minimizes water loss, and
- A release liner detached during the application process.

Transungual patches can be made as multi-layer systems (drug reservoir + rate-controlling membrane) or as matrix-type single-layer films. When applied to the nail surface, they create a tight bond, hydrate the nail, and diffuse the medication to the nail bed underneath. Compared to nail lacquers and other topical treatments, the patch platform has the following advantages:

- Prolonged residence time, adhesion maintained for several hours to days without removal.
- Improved dose accuracy, established surface area and drug loading for each patch.
- Potential for controlled or modified release, achievable through adjustments to polymer composition and thickness.
- Safeguarding the formulation against mechanical removal and environmental exposure.

Researchers have looked into ciclopirox olamine, terbinafine, and other antifungals in experimental nail patch systems. Palliyil and Lebo developed a ciclopirox patch that markedly enhanced drug accumulation in the nail plate and nail folds in comparison to reference lacquer. New medicated nail patches have also been made for onychomycosis that have good mechanical qualities, adhesion, and in-vitro release.[24-27]

MECHANISM OF DRUG PENETRATION THROUGH THE NAIL PLATE

Patch-based transungual drug delivery is a complex, diffusion-driven method that allows for the targeted and prolonged distribution of medications into the underlying nail bed and matrix through the dense, keratin-rich nail plate. The nail's distinctive structure creates both opportunities and obstacles for efficient drug transport, in contrast to transdermal delivery, where the stratum corneum serves as the primary barrier.

1. Patch Adhesion and Nail Occlusion

The patch's pressure-sensitive adhesive makes sure that the drug-loaded matrix stays in close contact with the nail surface for a long time after it is applied. The occlusive backing layer keeps moisture in and helps the nail plate stay hydrated. More hydration leads to:

- Keratin fibers swell
- Aqueous pores expand
- Nail plate porosity increases
- Hydrated nails allow drugs to penetrate at rates that are 2–5 times higher than dry nails.

2. Drug Release from the Polymeric Matrix

The medication is mixed with a polymeric matrix inside the patch.When it gets wet, the polymer expands and relaxes, and the drug molecules mostly move through diffusion. The kind and viscosity of the polymer, the amount of plasticizers, the thickness of the patch, and the drug's solubility in the polymer all affect how quickly the medication is released. This makes it possible for the medicine to be delivered to the nail surface over a period of hours or even days.

3. Drug Partitioning into the Hydrated Nail Plate

The drug, particularly the unionized portion, is driven to partition into the keratin network of the nail by the concentration gradient that is created between the patch and the nail.Hydration improves medication absorption by increasing keratin's free volume and intercellular space.

4. Diffusion Across the Keratinized Nail Plate

Diffusion across the tightly packed keratin network of the nail is the primary rate-limiting process. Drug molecules move through:

- Intercellular aqueous microchannels;
- Transcellular routes (thru keratin fibers)

Fick's first law of diffusion governs this process, according to which the concentration gradient (ΔC), partition coefficient (K), diffusion coefficient (D), and nail thickness (h) all affect drug flux (J):

$$J = D \cdot K \cdot \Delta C/h$$

Unlike the skin, the nail behaves more like a hydrated hydrogel than a lipid membrane.

5. Role of Chemical Permeation Enhancers

Transungual patches frequently utilize chemical enhancers to promote medication absorption.

a) **Disulfide bond cleavage:** Compounds such as thioglycolic acid, sulfites, and mercaptans disrupt S–S bonds in keratin, thereby relaxing the rigid structure.

b) **Keratolytic effect:** Urea and salicylic acid soften the nail plate and diminish the diffusion pathway.

c) **Hydration and solvent action:** Compounds including polyethylene glycol (PEG), ethanol, and propylene glycol enhance water content and medication solubility in the nail.

6. Patch Reservoir Effect and Sustained Drug Release

In contrast to nail lacquers, which have the potential to dry up, patches act as an ongoing medication reservoir.They guarantee sustained and reliable drug administration throughout the nail by maintaining a steady drug gradient and offering controlled or even zero-order release kinetics.

7. Drug Accumulation in the Nail Bed and Matrix

The medication builds up in the nail bed and matrix after going through the nail plate. These are important places for fungal infections like onychomycosis. Long-lasting drug levels at these locations:

- Stop the production of ergosterol
- Make fungal cell membranes less stable

8. Lateral Diffusion and Intra-Nail Reservoir Formation

Drugs can spread laterally within the nail plate in addition to vertically, creating a reservoir that redistributes the active agent to untreated areas. Even if the patch only covers a portion of the nail, this enables efficient full-nail therapy.

9. Post-Removal Drug Action (Depot Effect)

The medicine contained in the moistened nail continues to diffuse gradually when the patch is removed, while drug distribution from the surface stops. The therapeutic advantage is prolonged and persistent antifungal activity is provided by this post-application depot effect. [28-32]

METHODS OF TRANSUNGUAL PATCH PREPARATION

There are many ways to make medicated patches and films that let medications through the nail.The method you choose can affect not only how strong and sticky the patch is, but also how much drug it can hold, how soon the drug is released, and how even the patch looks.

1. Solvent Casting / Film Casting Method

Solvent casting is the most used method for nail films and patches because it's simple and homogenous.The medication is dissolved in a volatile solvent such ethanol, isopropanol, acetone, or a water–alcohol combination. A clear or homogenous solution or dispersion is made by adding and mixing film-forming polymers (such as Eudragit® acrylate copolymers, PVP, or HPMC), plasticizers (PEG, DBP, or glycerol), and permeation enhancers. This solution is poured into glass molds, Petri dishes, or backing membranes and dried under regulated temperature and humidity to evaporate the solvent. Peel and cut dried film into patches of specific sizes and medication dosages.

Thickness, weight fluctuation, flexibility (folding endurance), tensile strength, surface pH, medication content, lab test release, nail sample penetration, and antifungal activity are usually examined.Palliyil and Lebo employed solvent casting to make ciclopirox nail patches and found that more than 80% of the medication was released within two hours, with substantially higher drug deposition in and around the nail than commercial lacquers. Similar methods have worked for ciclopirox, terbinafine, and other antifungal patches and films.

2. Hot-Melt Extrusion / Melt Casting Method

When polymers and lipophilic (fat-loving) excipients are heated above their melting or glass transition temperature, they become a liquid mass. A hot-melt extruder or a heated plate is used to mix the medication and other ingredients together. After that, the liquid mixture is spread out into a thin film on a backing layer and cooled until it hardens then, it is cut into patches. This approach doesn't use any solvents, which is great for medications that don't like moisture.However, the temperature needs to be carefully managed so that drugs that can't withstand heat don't break down.

3. Lamination and Multi-Layer Patch Fabrication

Multi-layer or reservoir-type patches are laminated with backing films and perhaps a rate-controlling membrane after the drug-loaded matrix or adhesive is created by solvent casting or mixing.Drug-in-adhesive or drug-loaded matrix films are usually made. An occlusive backing sheet like aluminized polyester is attached to one side, and the adhesive side has a detachable protective lining. Patches of laminate are trimmed to size. This method is used in commercial transdermal patches and is currently being used in nail patch research because it lets researchers optimize medication release and mechanical or adhesive qualities separately.

4. Other and Emerging Techniques

Newer methods are also being explored for making nail films and patches:

- **Electrospinning:** This method makes nanofiber mats that can be used as nail patches or overlays.

- **In situ film-forming systems:** They are cast or sprayed right onto the nail, and as the solvent dries, they produce a thin, sticky coating.
- **Hybrid systems:** In this case, nanocarriers (small delivery vehicles) are spread out in a film-forming matrix to improve drug loading and penetration.

Systematic evaluations of anti-onychomycotic (antifungal) transungual patches reveal a lack of solid clinical data despite encouraging laboratory and ex-vivo results.Before these items are widely used in clinical settings, more work is required to improve cosmetic acceptance, increase adherence on the curved nail surface, and guarantee patient ease of use.

Encourage the removal of nails.[33-37]

PHYSICAL METHODS

Techniques for physical improvement are being extensively investigated to improve transungual medication delivery by mechanically breaking the nail barrier.

1. **Nail Abrasion:** Mechanical filing or abrasion diminishes nail thickness, establishing direct routes for drug penetration.
2. **Microneedling and Fractional Laser:** These techniques generate microchannels or micropores in the nail plate, promoting improved drug absorption by circumventing the keratinized barrier.
3. **Iontophoresis:** It's employs a gentle electrical current to facilitate the transdermal delivery of charged drug molecules through the nail, whereas ultrasound enhances drug transport by sonic cavitation and microstreaming. These may be integrated with drug-infused patches or lacquers for a synergistic effect.

PERMEATION PROCESS IN A TRANSUNGUAL PATCH

The comprehensive procedure for medication penetration from a transungual patch comprises multiple stages:

1. Release of the drug from the polymeric patch matrix into a thin liquid film on the nail surface.
2. Distribution of the medication within the moistened nail plate.
3. Diffusion of the pharmaceutical agent through the keratin matrix.
4. Distribution throughout the nail bed and matrix, where fungal infections frequently inhabit in onychomycosis.

EVALUATION PARAMETERS OF TRANSUNGUAL PATCHES

1. Thickness Uniformity

During the process of producing a transungual patch, one of the first things that researchers observe is the degree to which the thickness of the patch is uniform. The significance of this measurement lies in the fact that a patch with a uniform thickness ensures that the medicine is distributed evenly throughout the matrix. This measurement is often performed at many spots using a digital micrometer or screw gauge. A drug diffusion rate that is reliable over the nail plate may be maintained with the help of such uniformity, which ensures that each application yields predictable outcomes. The uneven thickness of the patch, on the other hand, can cause certain areas of the patch to release an excessive amount or an insufficient amount of medication, which may result in the treatment being less effective or even hazardous.It is for this reason that it is essential to maintain a constant patch thickness in order to provide predictable therapeutic effectiveness.

2. Weight Uniformity

The weight of each patch must to be uniform, just like the thickness of an individual patch. Through the process of individually weighing patches and computing the average, researchers are able to guarantee that the medicine and other components are dispersed uniformly throughout the patches. There are difficulties in the mixing or manufacturing process if there are significant variances in weight. On the other hand, maintaining a consistent weight is necessary for achieving dose precision and repeatability from batch to batch.

3. Folding Endurance

The folding endurance test is a test of flexibility and mechanical durability that determines how many times a patch can be folded at the same point before it breaks. Patches that have a high folding endurance will not break or fall apart when being handled, packaged, or while patients are going about their everyday lives.In light of the fact that the patch must be able to tolerate continuous movement and stress, this feature is of significant importance.

4. Tensile Strength and Percent Elongation

The percentage of elongation discloses how far a patch can stretch before it breaks, whereas the tensile strength indicates the amount of force that must be applied in order to break a patch when it is stretched. It is crucial to strike the appropriate balance between strength and flexibility. A patch should be thick enough to prevent it from tearing, but it should also be elastic enough to fit securely over the curved surface of the nail without becoming loose.

5. Surface pH

The percentage of elongation discloses how far a patch can stretch before it breaks, whereas the tensile strength indicates the amount of force that must be applied in order to break a patch when it is stretched. It is crucial to strike the appropriate balance between strength and flexibility. A patch should be thick enough to prevent it from tearing, but it should also be elastic enough to fit securely over the curved surface of the nail without becoming loose.

6. Moisture Content

The patch is weighed both before and after it has been stored in a desiccator in order to assess the amount of moisture that it contains. This parameter is significant because it has an impact on the patch's capacity to maintain its stability, flexibility, and susceptibility to the growth of microorganisms. A patch that has too little moisture can become brittle, while an excessive amount of moisture can cause the medicine to become contaminated or degrade. The key to producing a product that is both stable and effective is to find the correct moisture balance.

7. Moisture Uptake

In order to determine how much water a patch is capable of absorbing, it is placed in a humid environment and its weight growth is recorded throughout the process.The nail may become more hydrated as a result of increased moisture intake, which makes it simpler for the medicine to permeate the nail. On the other hand, if the patch takes in an excessive amount of moisture, it may become unstable, lose its adherence, or swell to an extreme degree.

8. Drug Content Uniformity

A patch is placed in a humid atmosphere and its weight development is recorded throughout the procedure in order to ascertain how much water it is capable of absorbing. For this purpose, the patch is placed in the environment.It is possible that the nail may become more hydrated as a result of increased moisture intake, which will make it easier for the medication to penetrate the nail. On the other hand, if the patch is exposed to an excessive amount of moisture, it may become unstable, lose its ability to stick to the skin, or swell to an extremely high degree.

9. In-Vitro Drug Release Study

Through the use of apparatus such as the Franz diffusion cell, in-vitro release studies are carried out with the purpose of predicting the manner in which the medication will really be administered. The results of these researches contribute to the determination of the pace and pattern of drug release, including whether it is direct, delayed, or sustained. For the purpose of gaining a better understanding of the underlying release mechanism, the release data are subjected to additional analysis utilizing kinetic models (such as zero-order, first-order, or the Higuchi model).

10. Ex-Vivo Transungual Permeation Study

In order to determine how well the medicine is able to pass through the nail plate, this test makes use of genuine nail samples taken from either humans or animals. These investigations, which are mounted on a Franz diffusion cell, assist in the calculation of parameters such as flux and permeability coefficient, as well as the evaluation of the effectiveness of penetration enhancers in the formulation.

11. Adhesion Strength (Peel Adhesion Test)

Adhesion strength quantifies the force required to detach the patch from the nail. Moderate adhesion is essential: insufficient adhesion may result in detachment, while excessive adhesion might cause injury or damage to the nail upon removal.

12. Nail Hydration and Swelling Study

Researchers can evaluate hydration and edema by measuring nail weight or thickness prior to and following patch administration. Enhanced hydration expands the keratin matrix, facilitating routes that promote more efficient drug diffusion, which is essential for optimal transungual administration.

13. Antifungal Activity Study

The antifungal efficacy of the patch is often evaluated by the agar diffusion method, which assesses its capacity to inhibit organisms such as Candida albicans or Trichophyton rubrum. A distinct zone of inhibition surrounding the patch indicates that the medication retains its efficacy post-incorporation into the patch.

14. Nail or Skin Irritation Study

The patch undergoes testing on nails or skin to identify any indications of irritation, erythema, or edema, ensuring its long-term safety. This stage verifies that the formulation is mild and appropriate for patients.

15. Stability Studies

At last, stability studies conducted in accordance with ICH requirements evaluate the patch under diverse storage circumstances. Parameters like as appearance, drug content, adhesion, and drug release are assessed throughout time to forecast shelf life and guarantee that the patch stays safe, effective, and stable until its expiration date.[38,39,40,41,42]

CONCLUSION

Transungual drug delivery methods, notably medicated nail patches, are a novel and effective approach to overcoming the inherent obstacles of treating nail illnesses. These devices reduce systemic side effects while increasing local efficacy by providing regulated medication release, increased nail penetration, and improved patient adherence. To ensure consistent performance and safety, transungual patches must be carefully designed and evaluated in terms of their physical, mechanical, and biological qualities. While laboratory and early clinical findings are promising, further study and optimization are required to translate these technologies into widely used therapeutic options for nail ailments.

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