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Development and Evaluation of Antifungal Lacquer for Enhanced Transungual Drug Delivery

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Abstract: *Onychomycosis, a mycotic nail infection caused primarily by dermatophytes, yeasts, and non-dermatophyte molds, is an endemic condition in 5-10% of the world population. The tightly keratinous nature of the nail plate and its relatively slow growth rate constitute a significant barrier to effective drug delivery. Traditional treatment with oral antifungals and topical creams is often restricted by systemic toxicities, poor penetration of nails, and low patient compliance. Antifungal lacquers are a new choice with controlled drug delivery, sustained release, and improved patient compliance. The review paper outlines a critical overview of antifungal lacquer development, formulation strategy, mode of action, and clinical evaluation. It also discusses the issues of transungual drug delivery and brings in recent developments that have occurred in this field, e.g., nanotechnology and combination therapy.*

Key Words: *Antifungal, Drug, Formulation strategy, Clinical evaluation*

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1. Introduction

Onychomycosis is a chronic fungal infection that primarily affects the nail plate, nail bed, and perifungal tissues. It is one of the most common nail disease, accounting for as much as 50% of all nail pathology. The pathogenesis of the condition is caused by a broad variety of fungal pathogens, including dermatophytes (e.g., Trichophyton rubrum and Trichophyton mentagrophytes), yeasts (e.g., Candida albicans), and non-dermatophyte moulds (e.g., Scapularies and Aspergillus species). Onychomycosis is not only a cosmetic issue; it is also associated with significant morbidity in the form of pain, nail disfigurement, and functional impairment, which can severely interfere with a patient's quality of life. In severe forms, infection may lead to complications such as cellulitis, paronychia, and secondary bacterial infection, particularly in immunocompromised patients or in those with peripheral vascular disease (Gupta et al., 2015).

The incidence of onychomycosis is determined by a number of factors, such as age, geography, and comorbidities. The elderly are disproportionately represented, with research indicating as many as 20% of people over age 60 and 50% of those over 70 have the disease. This heightened vulnerability is due to age-related structural changes in the nail, compromised blood flow, and increased

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prevalence of comorbidities like diabetes and peripheral arterial disease. Diabetics are especially vulnerable because of compromised immunity and diminished peripheral sensation, which can cause delayed diagnosis and treatment. Immunocompromised individuals, like HIV/AIDS patients or chemotherapy patients, are also more likely to get fungal nail infections due to impaired immune mechanisms (Nair et al., 2018).

The traditional management of onychomycosis is through oral and topical antifungal therapy. Oral therapy with drugs like terbinafine and itraconazole is generally the gold standard of treatment due to their systemic availability and high efficacy rates. Terbinafine is an allylamine compound with excellent efficacy against dermatophytes with clinical trial cure rates of 70-80%. Itraconazole, being a triazole antifungal drug, is also widely popular and acts upon both the yeasts and the dermatophytes. They possess drawbacks as oral drugs as well. They manifest systemic side effects such as hepatotoxicity, gastrointestinal disturbances, and drug interactions, particularly among those receiving over one drug. Additionally, the protracted length of oral antifungal treatment (typically 3-6 months for nails of the fingers and 6-12 months for nails of the toes) may lead to poor adherence by the patient and greater side effects (Shivakumar et al., 2016).

Topical preparations, such as creams, ointments, and solutions, offer a less risky choice than oral preparations since they do not cause so many systemic side effects. However, their usefulness is usually limited by the natural impermeability of the nail plate. The nail plate is made up of closely packed keratin fibers surrounded by a lipid matrix and thus forms an impermeable drug barrier. Accordingly, topical solutions often fail to achieve therapeutic levels of drugs within the nail bed, the home of the fungal infection. This limitation has stimulated the development of new drug delivery systems that seek to enhance transungual penetration of drugs and optimize treatment effect (Murdan, 2002).

Antifungal lacquers are a potential remedy for the inadequacies of traditional topical therapies. The formulations are put directly onto the nail plate and, upon evaporation, leave a hard adhesive film. The medication is released in the form of a reservoir, which sustains the active antifungal component over a period of an extended duration of time. The process of prolonged release maintains therapeutic levels of the drug at the infected site, thus improving the prospects of effective treatment. In addition, penetration enhancers such as urea or salicylic acid are also included in antifungal lacquers, which destabilize the keratin matrix of the nail plate and facilitate increased drug permeation. Through delivery of prolonged release combined with enhanced penetration, antifungal lacquers reverse the biggest disadvantage of conventional topical preparations (Vejnovic et al., 2010).

Another significant advantage of antifungal lacquers is their ease of use, which increases patient compliance. Compared to oral medications that require daily administration and have risks of systemic side effects, antifungal lacquers are topically applied and typically less often (e.g., daily or weekly). This ease of use, accompanied by their site-of-action at the localized level and lower systemically available systemic toxicity, makes antifungal lacquers an appealing option for the treatment of patients presenting with mild-to-moderate onychomycosis. Further, novel formulations based upon nanotechnology, or combinations therapy, hold promise for enhancing both the efficacy and patient acceptability of antifungal lacquers (Gupta & Foley, 2015).

2. Challenges in Trans ungual Drug Delivery

The nail plate is a sophisticated, highly differentiated barrier structure responsible for protecting the fingertips and toes. It consists predominantly of densely packed keratin fibers embedded in a lipid matrix that produces an extremely impermeable drug entry barrier. It is this keratin-lipid two-part composition that gives the nail plate hardness and strength, yet simultaneously presents colossal impediments to drug delivery of antifungal medication for the cure of infections such as onychomycosis. We discuss further below the primary challenges that are associated with trans ungual drug delivery:

Physical Barrier: The Dense Keratin Network

The nail plate consists mainly of keratin, a fibrous structural protein in the form of a dense, cross-linked network. The network is responsible for the mechanical strength of the nail but also presents a physical barrier to the diffusion of drugs. The densely packed keratin fibers create a tortuous path that hinders the entry of drug molecules, particularly those with high molecular weight or poor solubility. For example, high molecular weight molecules struggle to penetrate the narrow intercellular channels between keratin fibers, and thus exhibit poor penetration. Poorly soluble drugs also have additional barriers, as they are unable to dissolve and diffuse effectively in the keratin matrix. Physical barrier is also reinforced by the stratified nature of the nail, with the dorsal, intermediate, and ventral layers possessing differential densities and orientations of keratin fibers, making penetration by drugs more difficult (Murdan, 2002).

Chemical Barrier: The Hydrophobic Nature of the Nail Plate

Apart from its physical structure, the chemical make-up of the nail plate is also a significant hindrance to drug delivery. The lipid matrix surrounding the keratin fibers confers on the nail a hydrophobic character, which resists penetration by hydrophilic (water-soluble) drugs. This hydrophobic character results from the presence of lipids such as cholesterol, ceramides, and fatty acids dispersed within the keratin network. Hydrophilic drugs, such as certain antifungals, struggle to partition into the lipid-filled nail plate, i.e., permeation is poor. Conversely, while lipophilic drugs more easily penetrate into the lipid matrix, they are prone to being trapped within the hydrophobic domains, i.e., they cannot easily penetrate into deeper layers of the nail or the nail bed. This combined barrier of maintaining drug solubility and permeability calls for careful formulation strategies to ensure optimal trans ungual delivery (Shivakumar et al., 2016).

Slow Nail Growth: Prolonged Treatment Durations

The nail plate itself grows at a mean rate of approximately 0.1 mm per day, and therefore a complete cycle of regrowth for the nail is 6-12 months for the fingernails and 12-18 months for the toenails. This slow growth rate has several implications in the management of onychomycosis. Fungal infection eradication requires the sustained release of drugs over extended periods of time to enable the newly growing nail to be free of infection. Antifungal agents must be effective in the nail plate over extended periods of time, and this necessitates controlled release systems. The long duration of therapy can lead to poor patient compliance, reducing the overall efficacy of the treatment. The sluggish rate of growth also leads to the improvements in nail appearance taking months, which deters patients from completing their treatment programs (Gupta et al., 2015).

Accessibility to Infection Site: Profound Fungal Pathogens

Fungal infections such as onychomycosis typically begin in the nail bed (the tissue underneath the nail plate) and spread to the nail plate subsequently. Such a deep-seated nature of the infection is a serious issue for drug delivery as antifungal drugs must pass through multiple layers to reach the infected area. The nail plate can be between 0.5 and 1 mm thick, and this is person- and location-specific, further deterring drug penetration. The fungal pathogens are also present in biofilm, which are protective groups of microorganisms covered in a matrix secreted by themselves. Biofilms are highly resistant to antifungal drugs and need higher doses of medication or combination therapy (Nair et al., 2018).

Other Challenges: Apart from the primary hurdles outlined above, several other complications render trans ungual drug delivery difficult. The nail surface is not perfectly smooth, but rather tends to be ridged, grooved, and otherwise imperfect in a manner that can prevent even application and absorption of topical formulations. In advanced onychomycosis, the nail plate may become thickened, brittle, or fractured, which further hinders the efficacy of topical treatment. These environmental parameters are humidity, temperature, and exposure to water, which influence the permeability and hydration of the nail, consequently affecting drug delivery (Murdan, 2002).

Overcoming the Barriers: Optimal Trans ungual Delivery Strategies

These barriers have been challenged by scientists coming up with innovative methods to enhance drug penetration through the nail plate. These are based on chemical penetration enhancers such as urea, salicylic acid, and thioglycolic acid that disrupt the network of keratin and facilitate the permeation of drugs. The hydration of the nail is a significant method by which water penetrating the nail plate softens the keratin fibers, which is more drug permeable. Nanocarrier systems, such as liposomes, micelles, and solid lipid nanoparticles, increase the solubility of drugs and facilitate deeper penetration into the nail plate and nail bed. Film-forming polymers, such as hydroxypropyl chitosan, create a tight film on the nail surface, allowing for sustained drug release and longer contact with the nail plate (Shivakumar et al., 2016).

3. Antifungal Lacquers: Innovative Formulation Strategies for Enhanced Transungual Drug Delivery

Antifungal lacquers are designed with the specific intention of overcoming the inherent challenges to transungual drug delivery such as the dense keratin matrix of the nail plate, its lipophilic nature, and the conservative nail growth rate. Such challenges generally limit the efficacy of conventional topical and systemic antifungal therapy. Antifungal lacquers bypass such challenges using advanced formulation concepts maximizing penetration, achieving sustained release, and improving patient compliance. The key components of antifungal lacquers include film-forming polymers, penetration enhancers, active antifungal agents, and advanced nanocarrier systems. All these contribute significantly to the enhancement of delivery of antifungal drugs to the nail bed and surrounding tissues.

Film-Forming Polymers: The film-forming polymers constitute the structural matrix of antifungal lacquers. They create a stable adhesive film on the nail surface that maintains the drug in close proximity to the nail for an extended period of time. This film not only enables extended release of the drug but also protects the nail from extraneous dirt particles. Some of the commonly used polymers include hydroxypropyl chitosan, polyvinyl alcohol

(PVA), and ethyl cellulose. Hydroxypropyl chitosan is a biodegradable, biocompatible polymer from chitin that exhibits excellent film-forming ability, nail adhesion, and enhancement of drug permeation. PVA is a water-synthetic soluble polymer that forms a hard, water-resistant film over the nail plate, supporting the sustained release of the drug. Ethyl cellulose is a water-repelling polymer that yields controlled release properties, forming a tough film that slows down the diffusion of the drug, yielding prolonged therapeutic concentrations at the site of infection (Vejnovic et al., 2010).

Penetration Enhancers: Penetration enhancers are required to increase the permeation of antifungal drugs through the nail plate. These drugs work by altering the nail structure, increasing its hydration, or disrupting the keratin matrix. By reducing the barrier function of the nail, penetration enhancers facilitate more extensive and effective drug delivery. Urea, salicylic acid, and thioglycolic acid are some of the most commonly employed penetration enhancers. Urea is a keratolytic agent that softens the nail plate by breaking disulfide bonds in keratin, rendering the nail more permeable and allowing for better drug penetration. Salicylic acid is a traditional keratolytic drug that reduces the barrier function of the nail by disrupting the keratin structure. Thioglycolic acid is a potent reducing agent that disrupts disulfide bonds in keratin to significantly enhance drug penetration (Shivakumar et al., 2016).

Active Antifungal Agents: Choice of antifungal agent is a key factor in determining the effectiveness of the lacquer. The agent must demonstrate spectrum activity against onychomycosis pathogens such as dermatophytes, yeasts, and non-dermatophyte molds. A few agents commonly used as antifungal agents in the lacquer preparations are ciclopirox, amorolfine, and terbinafine. Ciclopirox is an antifungal agent with a wide spectrum, having adjunctive anti-inflammatory and antibacterial activity. Ciclopirox blocks the enzymatic activity of fungi through the chelation of polyvalent cations, for example, iron and aluminum. Amorolfine is a morpholine analogue with inhibitory activity on ergosterol biosynthesis, an integral component of the fungal cell membrane. Terbinafine is an allylamine analogue with squalene epoxidase inhibitory activity, an enzyme necessary for ergosterol synthesis (Gupta et al., 2015).

Nanocarrier Systems: Recent advances in nanotechnology have transformed transungual drug delivery by facilitating the use of nanocarriers in antifungal lacquers. The drug solubility, stability, and penetration are enhanced using these systems, some of the chief limitations of conventional formulations. Liposomes, micelles, and SLNs are some examples of nanocarriers utilized in antifungal lacquers. Liposomes are phospholipid vesicles with drugs entrapped within their aqueous core or lipid bilayer that enhance drug delivery by incorporating into the nail plate and releasing the drug directly into the nail bed through fusion. Micelles are self-assembled structures generated by amphiphilic molecules that increase the solubilization of hydrophobic drugs by encapsulating them within their hydrophobic center. SLNs are solid lipid-based colloidal carriers with controlled release of the drug and enhanced drug permeation (Vejnovic et al., 2010).

Blend of Ingredients for Optimized Performance: The efficacy of antifungal lacquers depends on synergistic interaction of film-forming polymers, penetration promoters, active antifungal ingredients, and nanocarrier systems. For example, a lacquer made of

hydroxypropyl chitosan as the film-former, urea as the penetration promoter, ciclopirox as the active component, and liposomes as the nanocarrier system would have several advantages. Chitosan film holds the drug for a prolonged time period and enhances adhesion to the nail, urea dissolves keratin in the nail plate, thereby facilitating drug penetration, ciclopirox demonstrates wide-spectrum antifungal action, and liposomes enhance stability of the drug and facilitate drug penetration deep within the nail bed (Shivakumar et al., 2016).

Future Directions in Formulation Development: Ongoing work is focused on further refining development of antifungal lacquers. Central subjects of interest include combination therapies, smart drug delivery, and biodegradable polymers. Combination therapies administering antifungal drugs along with penetration enhancers or anti-inflammatory drugs enhance efficacy. Smart drug delivery such as pH-sensitive or heat-sensitive releases drugs by virtue of specific conditions in the region of infection. Biodegradable polymers are studied in order to boost sustainability and safety for lacquers (Gupta & Foley, 2015).

4. Drug Penetration Mechanisms

Antifungal lacquers are designed to disrupt the barrier function of the nail plate and ensure effective delivery of the drug to heal onychomycosis. Antifungal lacquers employ more than one mechanism for enhancing drug penetration and retention:

i. Controlled Release: Film-forming polymers (such as hydroxypropyl chitosan, polyvinyl alcohol) develop a firm film on the nail surface, facilitating drug release slowly. This delivers therapeutic levels at the infection site, reduces frequency of application, and improves patient compliance (Vejnovic et al., 2010).

ii. Nail Hydration: Lacquers provide moisture to the nail plate, loosening its tight keratin structure and improving permeability. Hydration forms pores at the microscopic level, improving drug diffusion and solubility, particularly of water-soluble drugs (Murdan, 2002).

iii. Chemical Penetration Enhancement: Penetration enhancers (e.g., urea, thioglycolic acid, salicylic acid) disrupt disulfide bonds in keratin, relaxing nail structure and increasing porosity. This allows drugs to penetrate into deeper layers and increases delivery of hydrophobic agents (Shivakumar et al., 2016).

iv.Occlusive Effect: The occlusive film developed by the lacquer acts as an occlusive medium, preventing the evaporation of moisture and enhancing drug retention. This enhances bioavailability of the drug at the infection site with extensive contact and adsorption (Gupta et al., 2015).

v.Synergistic Effects: They synergize with each other—hydration softens, penetration enhancers disrupt its structure, and sustained release ensures constant drug release. The occlusive effect enhances additional drug retention and efficacy (Nair et al., 2018).

vi. Nanotechnology: Nanocarriers (e.g., liposomes, micelles, solid lipid nanoparticles) increase the solubility, stability, and penetration of drugs. They provide controlled release and targeted delivery, enhancing the overall efficacy of antifungal lacquers (Vejnovic et al., 2010).

5. Evaluation of Antifungal Lacquers

Antifungal lacquers are found to be effective by a combination of in vitro, ex vivo, and in vivo experiments:

In Vitro Experiments: In vitro experiments establish drug release kinetics, nail penetration, and antifungal activity. Franz diffusion cells are one of the popular techniques used to quantify

drug permeation through excised nail plates, and antifungal susceptibility testing to identify the minimum inhibitory concentration (MIC) of the drug against fungal pathogens (Shivakumar et al., 2016).

Ex Vivo Studies: Ex vivo studies include the utilization of nails that have been excised from animals or human subjects to determine drug permeation and retention. Ex vivo studies provide important information on the capacity of the formulation to penetrate the nail plate (Murdan, 2002).

In Vivo Studies: In vivo studies, including clinical trials, test the patient compliance, safety, and efficacy of the lacquer. Key parameters are adverse effects, mycological cure rate (percentage of patients with negative cultures for fungi after treatment), and clinical cure rate (percentage of patients with complete resolution of clinical manifestations) (Gupta et al., 2015).

6. Clinical Efficacy and Safety

Antifungal lacquers have been a promising therapeutic choice for the treatment of mild to moderate onychomycosis, providing a non-invasive and patient-friendly alternative to systemic treatments. These products are formulated to provide high levels of antifungal agents directly to the nail plate and underlying tissue, reducing systemic exposure and related side effects. Clinical trials have long assessed the efficacy and safety of numerous antifungal lacquers, and the most researched agents include ciclopirox, amorolfine, and terbinafine.

Ciclopirox Lacquer: Ciclopirox lacquer (8% w/v) is an antifungal drug with broad spectrum of action, along with anti-inflammatory and antibacterial activities. It has been reported to attain mycological cure rates ranging from 29-36% following daily use for 48 weeks. Ciclopirox is effective because it chelates polyvalent metal cations, like iron and aluminum, that are needed for fungal enzymatic processes. This disrupts mitochondrial activity and prevents the growth of the fungus. The lacquer is used once daily on the affected nail and adjacent skin, and although the treatment time is extended, the lack of invasiveness enhances patient compliance over oral therapies. Ciclopirox lacquer is tolerable, with very few side effects of mild erythema or irritation at the site of application. Systemic absorption is minimal, lowering the incidence of systemic toxicity (Gupta et al., 2015).

Amorolfine Lacquer: Amorolfine lacquer (5% w/v), a derivative of morpholine, is another good topical therapy for onychomycosis. It has high nail penetration and long duration of antifungal action, with mycological cure rates of 40-50% in clinical trials. Amorolfine blocks two major enzymes in fungal ergosterol biosynthesis, viz. Δ14-reductase and Δ7-Δ8 isomerase. The dual blockade of these enzymes destroys the integrity of the fungal cell membrane, with resultant cell death. The lacquer is used once or twice a week, thus proving to be more convenient compared to daily applications. The long-lasting film on the nail surface provides controlled drug release, and the low systemic bioavailability reduces the risk of side effects. Amorolfine is tolerable, with local irritation or discoloration of the nail only rarely reported. The frequency of once or twice a week for application considerably enhances patient compliance, especially among busy individuals (Nair et al., 2018).

Terbinafine Lacquer: Terbinafine lacquer, an allylamine compound, is strongly active against dermatophytes, the major pathogenic fungi in onychomycosis. It has demonstrated quick penetration of the nails and significant antifungal activity, with mycological cure rates equaling oral terbinafine in several studies. Terbinafine works by inhibiting squalene

epoxidase, an important enzyme in the fungal ergosterol biosynthesis pathway, resulting in the accumulation of toxic squalene and ergosterol deficiency, which causes the death of fungal cells. It is generally applied weekly, making it one of the most convenient antifungals available. The weekly schedule is especially favored by patients with difficulty adhering to daily application schedules. Terbinafine lacquer is characterized by very few side effects, mainly restricted to minor local irritation, and systemic absorption is minimal, decreasing the risk of hepatotoxicity and other systemic side effects with oral terbinafine (Shivakumar et al., 2016).

Comparative Analysis: Although ciclopirox, amorolfine, and terbinafine lacquers were found to have clinical efficacy, their efficacy also depends on aspects like the offending pathogen, severity of disease, and compliance of the patient. Ciclopirox and amorolfine possess wider antifungal spectrums covering activity against yeasts and non-dermatophyte molds, whereas terbinafine is most potent against dermatophytes. With respect to frequency of application, the most convenient regimen is provided by terbinafine lacquer (weekly), with amorolfine (twice or once weekly) and ciclopirox (daily) following in order. Amorolfine lacquer has greater mycological cure rates (40-50%) than ciclopirox (29-36%), while terbinafine lacquer has potential in bringing about rapid and long-term clearance of fungus (Gupta et al., 2015).

Issues in Clinical Practice: Despite the benefits, antifungal lacquers are not without issues in clinical practice. The extended duration of treatment, usually 6-12 months, can influence the compliance of patients. Moreover, antifungal lacquers are most effective for mild to moderate infections, and serious or refractory cases can be treated with combination therapy using oral antifungals. The growth velocity of nails (0.1 mm/day) is slow, so visible recovery may take several months, which could be demoralizing to patients. To overcome such problems, ongoing work is concentrating on improving the drug delivery via incorporating penetration enhancers, nanocarriers, and newer polymers. Antifungal combination therapies comprising pairing antifungal drugs with keratolytics or anti-inflammatory drugs in combination are under research for possible synergy. Besides that, patient-focused formulations exhibiting greater aesthetics, rapid drying rate, and film retention for long time are in process to develop and improve the patient compliance (Nair et al., 2018).

7. Challenges and Future Perspectives

Notwithstanding the encouraging advances made in the creation of antifungal lacquers as treatments for onychomycosis, some issues currently exist that restrict their widespread use and potency. Resolution of these issues is paramount to achieving the maximal therapeutic potential and success of these products in a clinical setting. Future studies also need to target the development of ways to surmount these obstacles by using novel approach strategies to the formulation, seeking new antifungal drugs, and stringent clinical proof.

Challenges in the Development of Antifungal Lacquers: One of the main difficulties in antifungal lacquer development is their poor effectiveness in extreme or resistant cases of onychomycosis. In the treatment of mild to moderate infections, these lacquers have been found to be effective, but their penetration deep into the nail matrix and bed—where fungal pathogens tend to live—is still inadequate. More severe infections usually necessitate systemic antifungal drugs, like oral itraconazole or terbinafine, which are fraught with

hepatotoxicity, drug interactions, and other systemic toxicities. This highlights the need for better topical preparations that will be able to deliver therapeutic doses of antifungal drugs into deeper layers of the nail. Future research should aim at improving drug penetration and retention, possibly by using combination therapy or sophisticated drug delivery systems, including nanocarriers or penetration enhancers (Gupta et al., 2015).

Patient Compliance and Adherence: Patient compliance and adherence are also major challenges in the treatment of onychomycosis. Antifungal lacquers need to be applied frequently over periods ranging from several months to a year, depending on the infection severity and nail growth rate. Regimens of daily or weekly application might be a heavy burden for patients, resulting in poor compliance and poor treatment outcomes. Furthermore, the clinical improvement of the nail may take months, and this can lead to discouragement of patients to continue treatment. To overcome this, researchers seek ways to make application regimens easier to follow, including creating lacquers whose films last longer or that can be given less often. Patient education and support interventions can also be important in enhancing adherence (Shivakumar et al., 2016).

Regulatory Barriers: Regulatory barriers are another issue that makes the development and marketing of antifungal lacquers more difficult. The regulatory requirements demand significant preclinical and clinical data to prove the safety, efficacy, and quality of these preparations. This entails drug release kinetic studies, nail penetration, stability, and long-term safety studies. The specificity of transungual drug delivery also demands proprietary testing methodologies and endpoints, which can prolong approval to market and drive up expenses. Simplifying regulatory routes and setting up uniform guidelines for testing antifungal lacquers may speed up their development and delivery (Murdan, 2002).

Future Research Directions: In order to address these issues, future research will need to be directed towards maximizing formulation approaches, identifying new antifungal compounds, and carrying out large-scale clinical trials. Formulation science advancements have a high potential to enhance the efficacy and patient acceptability of antifungal lacquers. Major areas of emphasis are the synthesis of new film-forming polymers that improve adhesion, durability, and drug release characteristics. Intelligent polymers that sense pH or temperature changes may provide site-specific delivery of drugs to the infection area. Further, the discovery and optimization of chemical penetration enhancers like urea, salicylic acid, and thioglycolic acid can enhance drug permeation without causing tissue damage. Nanocarrier systems including liposomes, micelles, and solid lipid nanoparticles provide another means of improving the drug solubility, stability, and penetration along with controlled release (Vejnovic et al., 2010).

New Antifungal Agents: Finding and developing new antifungal agents with greater efficacy and safety profiles also remain important in overcoming the drawback of current therapies. Scientists are examining broad-spectrum antifungals that inhibit a wide variety of fungal pathogens, such as dermatophytes, yeasts, and non-dermatophyte molds. Mechanism-based therapy acting on new targets in fungi, such as fungal cell wall components or virulence factors, might break the resistance barrier and enhance efficacy. Natural products from plant extracts or essential oils are also under investigation for their

synergistic effect and low toxicity (Gupta & Foley, 2015).

Clinical Validation: Strong clinical validation is necessary to determine the long-term safety and efficacy of antifungal lacquers. Large-scale, multicenter, randomized controlled trials with heterogeneous patient populations should be the focus of future studies to assess the real-world performance of these products. Long-term follow-up studies are required to determine the durability of treatment effects and the risk of recurrence over long periods. Comparative trials that assess the safety and effectiveness of antifungal lacquers compared with current treatments, such as oral antifungals and other topical treatments, will also be essential (Nair et al., 2018).

Patient-Centric Design: Another key area of interest is patient-centric design improvement for antifungal lacquers. A faster drying time, better aesthetics, and odourless nature can improve acceptability and compliance. Shortening the total treatment period by enhancing nail growth or optimizing drug delivery is another primary objective. Combination regimens that match antifungal drugs with keratolytics or anti-inflammatory drugs may target several facets of the infection and enhance overall efficacy (Shivakumar et al., 2016).

8. Conclusion

Antifungal lacquers represent a significant advancement in the treatment of onychomycosis, offering targeted drug delivery, sustained release, and improved patient compliance. While challenges remain, ongoing research and development hold great promise for improving the efficacy and accessibility of these formulations. By addressing the limitations of traditional therapies, antifungal lacquers have the potential to revolutionize the management of onychomycosis and improve patient outcomes.

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