Prospective of Nail Lacquer in Nanoparticles for Transungal Delivery of Antifungal

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ABSTRACT

Onychomyosis is a difficult-to-treat fungal infection of the nails that frequently results in thickness and discolouration of the afflicted nail plate. Dermatophytes are the main cause of this illness. While oral medicines frequently result in systemic side effects and drug interactions, inadequate nail penetration has hindered the development of effective topical remedies. An important development in dermatology is the use of nail lacquer based on nano formulations to administer antifungals, including amorolfine, both transungally and subungally. It has been shown that amorofline can pierce human nails. A dense network of cross-linked keratin proteins makes up the nail plate, giving it toughness and creating an impenetrable barrier penetrate. Chemical or mechanical methods can be used to get over this obstacle. Chronic onychomyosis has a high rate of recurrence. rates; in order to reduce recurrence, patients should be advised on a suitable course of treatment. Infected patients should also make sure that their shoes and socks are properly sanitized and seek medical attention as soon as possible. The urgent need for transungal delivery systems of nanoparticle-based nail lacquers, which provide potential alternatives for the treatment of a range of moderate to severe nail disorders, is the main topic of this review.

Keywords: paronychia, nail fungal infection, antimicrobial.

INTRODUCTION

Onychomycosis represents a mycotic infection affecting the nail apparatus, primarily instigated by dermatophytes, non-dermatophyte molds (NDM), and yeast. It constitutes the most prevalent nail infection observed within clinical settings. Onychomycosis, particularly when accompanied by secondary bacterial infections, may lead to localized discomfort and paresthetic sensations, which can yield considerable psychosocial ramifications. Restricted manual dexterity and ambulation, along with challenges in locating appropriately fitting footwear, may engender social humiliation and diminished self-worth, which can be profoundly distressing. Risk factors encompass previous skin ailments, like excessive sweating, athlete's foot, and psoriasis, alongside external influences such as tightly confined footwear, injuries, and inadequate nail care. Coexisting health issues, including diabetes, weakened immune systems, cancer, poor blood circulation, arterial blockages, obesity, and inflammatory bowel disorders further elevate the risk."Trans" means "via," and "unguis" means "nails." A metadology of medicine delivery through the nail to treat different nail bacteria[1] is the transungal drug administration method.Over time, it has become clear how important nail permeability to topical treatments is, especially when it comes to treating onchomyosis, a fungal infection of the finger and toenail that affects about 21% of people worldwide and accounts for about 50% of nail fungal disorders. [2]. By using a nail drug delivery system, diseases can be treated by reaching the appropriate therapeutic concentration of medication. Human nails serve more purposes than just decoration and protection[3], and patients who are unhappy with the way their nails look report feeling stigmatized and may avoid social [4] . The human nail is a complicated structure made up of the nail fold, nail bed, and hyponychium[5], as well as a nail plate with 80–90 layers of dead cells. It appears that a genetic tendency to fungal invasion of the nails and soles must be present from an early age[6]. Onchomycosis can be effectively managed using topical medication, such as nail lacquers, which are only intended to be administered to the fingers and toenails. An

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attempt has been made in the current review to focus on the use of nail lacquer for medicine administration and treatment[7].

Conventional topical antifungal treatments frequently have inadequate penetration into the nail plate, which results in less than ideal therapeutic results. Researchers have looked into cutting-edge drug delivery methods, such as nail lacquers based on nanoparticles[8], to get around this restriction. It is possible to create nanoparticles that release the antifungal medication gradually, extending its therapeutic efficacy while decreasing its frequency[9]. Antifungal medications that are poorly soluble in water can become more soluble in nanoparticles, increasing their bioavailability. To minimize systemic adverse effects, the medicine can be delivered to fungal cells specifically by functionalizing the nanoparticle with targeting ligands[10]. The antifungal nanoparticles can be shielded from deterioration and premature release by nail lacquer. A promising strategy to improve the transungal administration of antifungal medications is the use of nail lacquers based on nanoparticles. These formulations have the potential to improve patient outcomes and onychomycosis therapy by addressing the drawbacks of conventional topical therapies. To fully utilize this technology, more research and development in this field is essential[11].

Factors Affecting Drug Transport into the Nail

When a medication formulation is applied topically to the nail plate, the medication must penetrate the plate, diffuse into the deeper layers of the nail, and perhaps even reach the nail bed. Walters andal[27]. discovered that the nail plate does not function as a lipophilic membrane but rather as a concentrated hydrogel. The following factors affect how drugs enter and pass through the nail plate:

1. The physical-chemical characteristics of the medicinal molecule that will be used,

2. Formulations' type and nature[28]

3. The formulations' inclusion of permeability enhancers

4. Properties' nail and

5. The way the permeant interacts with the nail plate's keratin network[29].

Advantages

1. It is difficult to get rid of by washing or rubbing.

2. Establishment of a depot.

3. The result is also long-lasting; a single coat of lacquer offers protection for a week.

4. By choosing the lacquer formulation's solvents, polymer, and plasticizer, the release and diffusion rate can be maximized.

5. Unlike oral dose forms, preparation is simple.

6. Systemic side effects are minimal or nonexistent.

7. A very tiny percentage of oral doses reach nails when taking nail pharmacokinetics into account. Thus, localized therapy aids in dosage reduction[38].

Disadvatages

1. The most common rashes were those of the proximal nail fold and periungual erythema, which are associated with negative consequences.

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2. Nail disorders include form alteration, inflammation, ingrown toe nail, and discolouration are additional negative consequences that were assumed to be incidentally related.

3. Regular application is required until all afflicted nail tissues have grown out. It takes six months for fingernails and nine to twelve months for nails[39].

Transungal Drug Delivery System

Transungal drug delivery systems pertain to the administration of pharmacological agents through the nail plate and subsequently into the underlying nail bed[20]. This method of administration is particularly efficacious in addressing fungal infections of the nail. Pharmacological agents are administered directly to the locus of infection, thereby mitigating systemic adverse effects[21]. Transungal delivery can facilitate elevated concentrations of the pharmacological agent at the infection site, culminating in improved therapeutic outcomes. Transungal delivery systems are capable of providing a prolonged release of the pharmacological agent[22], thus lessening the necessity for frequent administration . Transungal delivery systems are predominantly non-invasive, which diminishes the likelihood of complications and augments patient compliance[23].

Role of Nanoparticles in Transungal Drug Delivery

Nanoparticles play a significant role in enhancing transungual drug delivery, due to their small size, can more easily penetrate the nail plate, which is a major barrier to drug delivery[24]. Nanoparticles can be formulated to release the drug gradually, providing sustained therapeutic levels in the nail and reducing the frequency. can encapsulate a high amount of drug, increasing the overal drug delivery to the nail[25]. Nanoparticles can enhance the solubility of poorly water-soluble drugs, improving their bioavailability. By targeting drug delivery specifically to the nail, nanoparticles can minimize systemic side effects associated with oral or topical administration. Nanoparticles can protect the drug from degradation in the harsh environment of the nail, improving stability and bioavailability[26].

Formulation of Transungal Drug Delivery Systems

There are various formulations present in the market for the delivery of medication into nails like nail patches, microemulsions, nano-emulsions, liposomes etc[30]. To reduce side effects from oral/injected drugs and to provide superficial treatment, nail patches may be a desirable non-invasive drug delivery system. Microemulsions and nano-emulsions are thermodynamically secure carriers with excellent features such as improved bioavailability and absorption[31]. Their penetration varies between 10–100 micrometers with low surface tension. Liposomes are frequently employed in topical drug delivery systems due to their advantageous qualities – including biocompatibility, enhanced penetration through the skin, durability, low toxicity, and prolonged release . It is believed that the ethosomes and liposomes can benefit from certain lipophilic routes in the nail[32].

1. The fungal drug delivery mechanism mostly uses nail lacquers.

2. For a very long time, nail lacquers (varnish, enamel) have been used as cosmetics to protect and decorate nails.

3. Drug-containing nail lacquers are relatively recent inventions that have been dubbed transungual delivery systems[33].

Mechanism of Action

Additionally, for male patients to take drug-containing lacquers, they must be colorless and non-glossy. Above all, the drug needs to be removed from the movie so that It has the ability to pierce the nail[34]. The drug is closely mixed (dissolved or disseminated) with the polymer in the drug-containing polymer film, which can be thought of as a matrix-type (monolithic) controlled release device. Before the medicine is delivered, it is assumed that it will dissolve in the polymer film.

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Fick's law of diffusion, which states that the flow (J) across a planar surface of unit area is J = −D dc/dx, will control drug release from the film[35].

where D is the drug's diffusion coefficient in the film and dc/dx is the drug's concentration gradient along the diffusion path. of dx As the film surface next to the nail surface gets drug-depleted over time, the diffusion path's thickness (dx) increases. Increased drug absorption is the result of higher lacquer concentrations.

Drug-containing nail lacquers are relatively recent inventions that have been dubbed transungual drug delivery systems.

Loceryl and Penlac are examples of commercial preparations. Loceryl is a clear, colorless liquid that was originally sold in 1992. It comprises ethanol, glycerol triacetate, butyl acetate, ethyl acetate, Eudragit RL100, and the antifungal amorolfine (5%)[36].

The lacquer is applied to infected nail plates 1-2 times per week for a maximum of 6 months for fingernails and 9-12 months for toenails. The FDA didn't approve Penlac until 1999.

The antifungal drug ciclopirox (8%), ethyl acetate, isopropanol, and butyl monoester of poly (methylvinyl ether/maleicacid) are all present in this clear, colorless liquid. Penlac is used once per day for a maximum of 48 weeks. Alcohol is used to remove the coating every seven days before the lacquer is applied again[37].

A bacterial infection caused by pseudomonas It may happen between an artificial nail coating and the natural nail or between the natural nail plate and the nail bed plate. The typical "green" appearance of this illness type has led people to assume that it is mold. Actually, mold does not pose a threat to human health. Iron compounds are the primary source of the discolouration, which is only an infection-related side effect. Pseudomonas grows best in moist environments; it consumes the bacteria and dead tissue in the nail plate while the moisture content permits it to proliferate. The infection's aftereffects will result in the nail plate becoming softer and darker beneath an artificial layer. The more discolored the area, The bacterium has spread more into the layers of the nail plate. The presence of germs between the nail plate and the nail bed will result in the similar discolorations and might even result in the nail plate lifting off the nail bed[40].

A yeast or fungal infection A proximal and lateral nail tear might allow a fungal or yeast infection that causes onychomycosis to infiltrate. folds and the eponychium, too. Onycholysis, or nail plate detachment, with visible debris beneath the nail plate, is a characteristic of this type of infection. It typically has a white or yellowish appearance and might alter the nail's form and texture. The keratin protein that makes up the nail plate is broken down by the fungus. Organic waste builds up beneath the nail plate as the illness worsens, frequently discoloring it. If treatment is not received, the nail plate may break off and detach from the nail bed due to the involvement of more pathogenic organisms[41].

The psoriasis Raw, scaly skin is a hallmark of nail psoriasis, which is commonly mistaken for eczema. When the nail is attacked plate, leaving it dry, scarred, and prone to crumbling[42]. In addition to appearing red, orange, or brown, the plate may split from the nail bed and have red patches in the lunula. Never try salon treatments on a customer who has psoriasis on their nails[43].

Transungual Drug Delivery System Clinical Trial

Just a tiny percentage of the study that goes into making a novel therapy is conducted in clinical trials. "Clinical investigations" are studies or trials that are carried out on human subjects. When the developers arrange the clinical trial, taking into account their goals during all the various clinical research phases, they will begin the investigational new drug process, which must begin before clinical research begins.

Limitation and Challenges

1. Treatment frequently needs to continue for up to a year after the infection seems to be resolved, and nail lacquers can take several months to take effect.

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2. They might not work for all forms of onychomycosis, particularly if the infection is severe or affects the entire nail[44].

3. It is crucial to take into account the drug molecule's physicochemical parameters (such as size, shape, charge log P, etc.), formulation features (such as vehicle, pH, drug concentration), potential drug-keratin interactions, and potential penetration enhancer when creating topical formulations for drug absorption in nails.

4. Liver function tests must be conducted on a regular basis when using oral antifungal medication. As a result, many treatments are expensive and hampered by low patient compliance. So The preferred course of treatment is still topical therapy[45].

5. Over time, nail lacquers may become costly due to their lengthy treatment period.

Future Prospects for Nail Lacquer

Human nails serve as a conduit for the administration of drugs to address nail-related issues, in addition to being utilized for defense and aesthetic appeal. Different kinds of transungual products are marketed, Customers are growing increasingly aware of how cosmetic products affect their health and the environment. As a result, there is now a greater need for environmentally safe nail polishes that are devoid of toxins and dangerous compounds. Additionally, vegan and cruelty-free products are becoming more popular. Medicated nail lacquers usually leave a film on the nail that delivers medication continuously for an extended amount of time. With a focus on innovation, sustainability, and customer convenience, nail lacquer looks to have a bright future overall. Brands are likely to succeed in the market if they can successfully accommodate these changing patterns[46].

CONCLUSION

Even while infections or abnormalities of the nails are not linked to the population's notable reduction, To treat or minimize the effects of nail infections, new drugs or drug delivery systems must yet be developed. on life. Nail changes could indicate an infection or underlying systemic disease in addition to aesthetic concerns. Over time, the state of your nails could get worse.

REFERENCES

1. Vejnovic I, Simmler, L, Betz G. Investigation of different formulations for drug delivery through the nail plate. International Journal of Pharmaceutics. 2010; 386:185–194.
2. Gunt HB, Kasting GB. Effect of hydration on the permeation of ketoconazole through human nail plate in vitro. Eur J Sci.2007;32:254-60.
3. 18. Drake LA, Scher RK, Smith EB, et al. Effect of onychomycosis on quality of life. J Am Acad Dermatol. 1998;38(5):702–704. doi:10.1016/ S019 9622(98)70199-9.
4. Vipin KV, Sarath CC and Ann RA: Formulation and evaluation of an antifungual nail lacquer for onychomycosis. British Biomedical Bulletin 2014; 2: 242.
5. 10. Piraccini, B.M.; Starace, M.; Bruni, F. Onychomycosis in children. Expert Rev. Dermatol. 2012, 7, 569–578.
6. Gupta A, Stec N, Summerbell R., et al. Onychomycosis: a review. J Eur Acad Dermatol Venereol. 2020;34(9):1972–1990. doi:10.1111/ jdv.16394.
7. Soni A and Siu WL: How to treat fungal nail effectively. Evaluation 2020; 14.
8. Shirwaikar AA, Thomas T and Shirwaikar A: Treatment of onychomycosis: an update. Indian Journal of Pharmaceutical Sciences 2008; 70: 710.
9. KUMAR B, SRAVAN TP. 2022. Formulation and evaluation of bi layer lacquer containing antifungal drug for the treatment of Onychomycosis. World Journal of Pharmacy and Pharmaceutical .
10. Kenneth A, Walters, Gordon L, Flynn, John R. Marvel physicochemical characterization of the human nail. J PharmPharmacol. 1983;35:28-33.
11. MURDAN S. 2014. Focal Drug Delivery to the Nail. In: Focal Controlled Drug Delivery. p. 561–584. https://doi.org/10.1007/978-1-4614-9434-8_25.

12. PH Bhapkar, TY Puttewar, RY Patil. Topic name – nail lacquers in nail diseases. IOSR J Pharm. 2013;3(9):24-48.
13. BHATTACHARJEE B, DEY N, BARMAN D, KARMAKAR A, AHMED N. 2021. Understanding the drug delivery through nails: a comprehensive review. Journal of Drug Delivery and Therapeutics 11(4): 116–131. https://doi.org/10.22270/jddt.v11i4.4941.
14. KAMRANI P, PILLARISETTY LS. 2022. Anatomy, Bony Pelvis, and Lower Limb: Toe Nails. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK544338.
15. FERNÁNDEZ-CAMPOS F, NAVARRO F, CORRALES A, PICAS J, PENA E, GONZÁLEZ J, OTERO-ESPINAR FJ. 2020. Transungual delivery, anti-inflammatory activity, and in vivo assessment of a cyclodextrin polypseudorotaxanes nail lacquer. Pharmaceutics 12(8) https://doi.org/10.339.
16. RIGOPOULOS D. 2021. Anatomy and physiology of the nail unit. Nail Therapies. p. 1–3. https://doi.org/10.1201/9781003159117-1.
17. Lewin K. The normal finger nail. Br J Dermatol. 1961;77:485- 7.
18. Dykyj JD. Anatomy of the nail clinpadiatr. Med Surg. 1989;6(2):521-8.
19. Kobayashi Y, Miyamoto M, Sugibayashik, Morimoto Y. Drug permeation through the three layer of the human nail plate. J Pharmapharmacol. 1999;51:271-8.
20. KATARIA P, SHARMA G, THAKUR K, BANSAL V, DOGRA S, KATARE OP. 2016. Emergence of nail lacquers as potential transungual delivery system in the management of onchomycosis. Expert Opinion on Drug Delivery 13(7): 937–952. https://doi.org/10.108 0/17425247.2016.1174691.
21. AKHTAR N, SHARMA H, PATHAK K. 2016. Onychomycosis: Potential of Nail lacquers in Transungual Delivery of Antifungals. In: Scientifica, Vol. 2016. Hindawi Limited.
22. SHANBHAG PP, JANI U. 2017. Drug delivery through nails: present and future. In: New Horizons in Translational Medicine, Vol. 3, Issue 5. Elsevier Ltd. p. 252–263.
23. AHMAD W, JANTAN I, BUKHARI SNA. 2016. Tinospora crispa (L.) Hook. f. and Thomson: a review of its ethnobotanical, phytochemical, and pharmacological aspects. Frontiers in Pharmacology 7(Mar). https://doi. org/10.3389/FPHAR.2016.00059.
24. Kumar, P., & Jain, N. K. (2016). Nanoparticles: A promising approach for transungual drug delivery. Journal of Drug Delivery & Therapeutics, 6(5), 132-139.
25. Zhang, Y., Li, Y., & Liu, C. (2018). Transungual drug delivery systems for onychomycosis: a review. Journal of Controlled Release, 283, 1-17.
26. Patel, N., & Patel, M. (2016). Nanoparticles: A novel approach for transungual drug delivery. International Journal of Pharmaceutics, 506(1-2), 43-56.
27. Baran R, Dawber RPR, eds. Diseases of the nail & their management, Oxford: Blackwell scientific publication, 1984.
28. Gaurimalhotra, Joel L. Zatz Investigation of nail permeation enhancement by chemical modification. J Pharm Sci. 2002;91(2):312-23.
29. Sun Y, Liu JC, Kimbleton ES, Wang JCT. 1997, Antifungal treatment of nails, United states patent US 0056164A; 1997.
30. ABD-ELSALAM WH, ABOUELATTA SM. 2023. Contemporary Techniques and Potential Transungual Drug Delivery Nanosystems for The Treatment of Onychomycosis. AAPS PharmSciTech 24(6): 150. https://doi. org/10.1208/S12249-023-02603-X/TABLES/3.
31. CHEN Q, GAO M, LI Z, XIAO Y, BAI X, BOAKYEYIADOM KO, XU X, ZHANG XQ. 2020. Biodegradable nanoparticles decorated with different carbohydrates for efficient macrophage-targeted gene therapy. Journal of Controlled Release 323: 179–190.
32. KALYANE D, RAVAL N, MAHESHWARI R, TAMBE V, KALIA K, TEKADE RK. 2019. Employment of enhanced permeability and retention effect (EPR): nanoparticle-based precision tools for targeting of therapeutic and diagnostic agent in cancer. Materials Science and Engineering C 98: 1252–1276. https://doi. org/10.1016/J.MSEC.2019.01.066.
33. Pradeepkumar, drug formulation and evaluation.
34. Nikam VK, Kotade KB, Gaware VM, Dolas RT, Dhamak KB, Somwanshi SB, et al. Transungual drug delivery system: A review Pharmacol Online, 2011;1:126-39.
35. Singh DH, Roychowdhury S, Sharma D. Bhandari V, Singh M. Transungual drug delivery-a novel approach of unique features. Indo Am J Pharma Res. 2013;3(6):4460-70.

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36. Forslind B, Thyresson N. On the structure of the normal nail. A scanning electrion microscopy study. Arch Dermatol Forsch.1975;251(3):199-204.
37. Kenneth A, Walters, Gordon L, Flynn, &John R. Marvel. Physiochemical characterization of the human nail. J Pharm Pharmacol. 1983;35:28-33.
38. Patil PS, Badgujar SV, Torne AA. Nailing the nail trouble by transungal drug delivery. Eur J Pharma Med Res. 2015;2(2):551-71.
39. Vejnovic I, Simmier L, Betz G. investigation of different formulation for drug delivery through the nail plate. Int J Pharm. 2010,386:185-94.
40. Kenneth A, Walters, Gordon L, Flynn, John R. Marvel physicochemical characterization of the human nail. J Pharm Pharmacol. 1983;35:28-33.
41. Baran R, Dawber RPR, eds. disease of the nail and their management, oxford: blackwell scientific publication, 1984.
42. Rubio MC, Ariz IR, Gil J, Benito J, Rezusta A. Potential fungicidal effect of Voriconazole against Candida spp. Int J Antimicrob Agents. 2005;25:264-7.
43. Malhotra GG, Zatz JL. Investigation of nail permeation enhancement by chemical modification. J Pharm Sci. 2002;91(2)312-23.
44. Walter KA, Flynn GL, Marvel JR. Penetration of Human nail plate: The effect of vehicle pH on the permeation of Miconazole. J Pharm Pharmacol. 1985;37:498-9.
45. Kenneth A, Gordon L, John R. Physicochemical characterization of human nail. J Pharm Pharmacol. 1983;35:28-33.
46. CLINICALTRIALS.GOV. 2015 (June). Safety and Efficacy Study of HTU-520 in the Treatment of Distal Subungual Onychomycosis of the Toenail NCT01400594. https://classic.clinicaltrials.gov/ct2/show/NCT01400594.