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Transnail drug delivery device:A prominent approach for Onychomycosis therapy

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ABSTRACT

Onychomycosis is often challenging therapeutically and demands a multipronged approach both in terms of systemic as well as topical delivery. The conventional treatment modalities available for onychomycosis are marred with challenges such as low permeation, infection reoccurrence and resistance development. Henceforth, the current article explores the concept of a Transnail drug-delivery device as a promising tool offering high clinical potential and aesthetic suitability against onychomycosis.

Keywords: Onychomycosis, Transnail, Nail Lacquer, *Trichophyton rubrum*

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1. Introduction

Onychomycosis is a locoregional fungal affliction of toes and finger nails mainly caused by dermatophyte *Trichophyton Rubrum; Microsporium; Epidermophyton genere* and Non-dermatophytes such as *Candida spp.*, *Aspergillus spp.,* and *Fusarium spp*. The surface of the nail inflicted with onychomycosis are highly mutilated, distorted and disfigured as presented in Figure 1 often resulting in immense pain and reduced quality of a patient's life (1). Onychomycosis estimates for about 50% of global nail diseases prominently due to fungal dermatophyte *Trichophyton rubrum* (2).

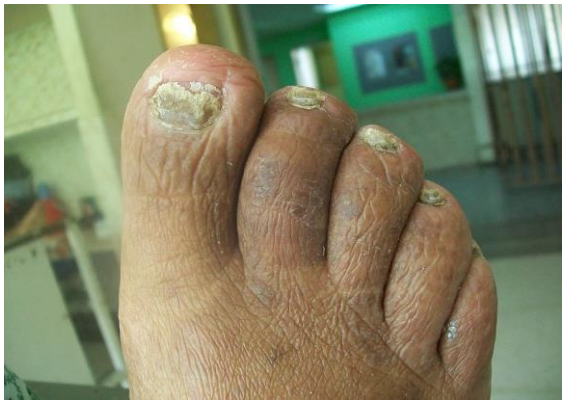

Figure 1. Surface of the human nails infected with Onychomycosis (3)

Onychomycosis Risk Factors

The primary or most common risk factors for onychomycosis are psoriasis or trauma, immuno-suppression, diabetes, peripheral arterial diseases, advancing age and sports activities. The secondary or least common risk factors include frequent nail trauma, family history, genetic factors, common bathing facilities and occlusive footwear as presented in Figure 2. (a, b.)

Though the condition and cases of onychomycosis are highly invasive and prevalent it still requires a broader attention of patients and their surrounding individuals because if remains untreated onychomycosis has the potential to lead to the ulceration of feet and legs (4).

Onychomycosis Global Challenges

The most prevailing obstructions related to onychomycosis treatment are low permeation rate through dense keratinized nail plate, Constant recurring or infection relapse and resistance development subsequently leading to low therapeutic efficacy and ineffectiveness of various topical and systemic antifungal based formulations therefore, type of onychomycosis, degree of infection, severity of nail involvement and components of nail (Nail plate, bed and matrix) affected are the primary parameters in determining effective treatment option for onychomycosis such as either topical or systemic or combination therapy (4, 5).

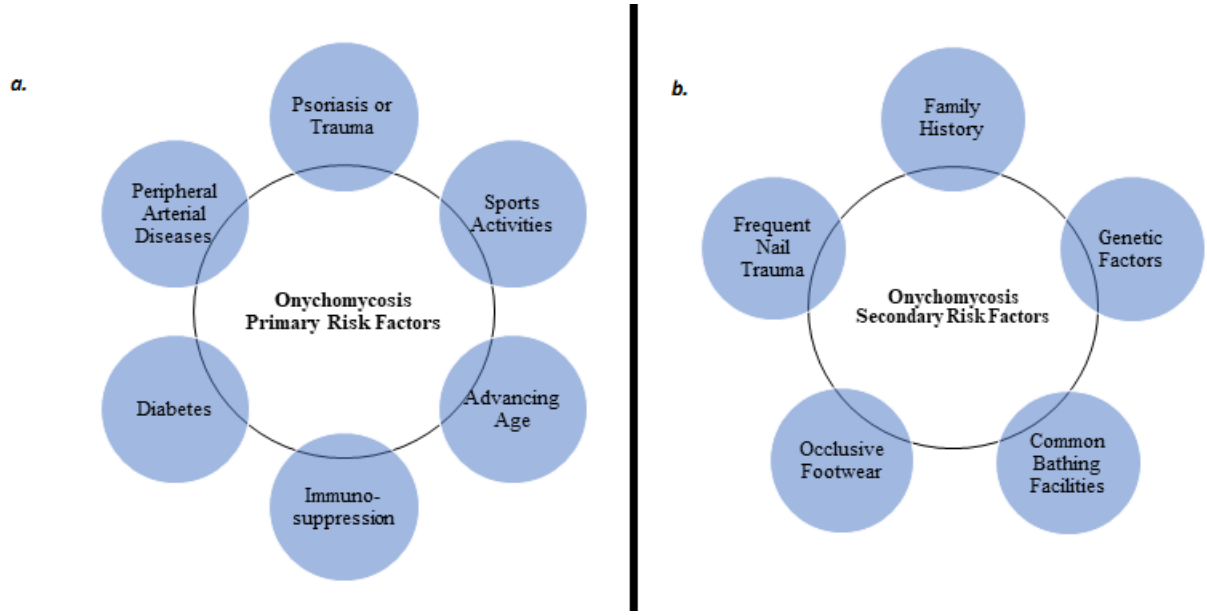

Figure 2. A schematic representation of onychomycosis ***a***. primary risk factors; ***b.*** secondary risk factors

Types of Onychomycosis

The four major types of onychomycosis; Distal lateral subungual onychomycosis (DLSO); Superficial white onychomycosis (SWO); Proximal subungual onychomycosis (PWO) and Total dystrophy onychomycosis (TDO) are generally classified on the basis of pattern and the infection sites (6).

Among the four aforementioned types DLSO is the most common form of onychomycosis under which causative fungus originates from the hyponychium, skin under the free edge of the nail and penetrates into the nail matrix infecting the nail plate distally and laterally along with underside of the nail bed (7). SWO affects the nail plate superficially accompanying the formation of white patches. PSO is the least common infection under which fungus penetrates through the nail matrix forming whitish lunula (8, 9) and TDO or candida onychomycosis inflicts the entire nail and is mainly observed in patients with chronic candidiasis (7).

2. Transnail Drug-Delivery Device

In recent times onychomycosis has emerged as a complex and difficult to treat nail fungal infection due to impediments of a conventional treatment, inadequate success of systemic therapy and lack of locally acceptable antifungal drug-delivery system. Side effects often preclude the systemic drug use and therefore exploration of Transnail i.e. through the nail drug-delivery device is highly necessary as they propose to offer a handful of positive attributes such as easy preparation, improved adhesion, low drug interactions; systemic adverse effects and easy removal. However, the presence of *alpha*-keratin and lanosterol-14*a*-demethylase obstructs the delivery and maintenance of therapeutically active formulations into deeper nails layers (10, 11).

Taking cue from the aforesaid challenges a wide range of pharmaceutically active transnail preparations such as nail lacquers, solutions and films have been developed as a novel drug-delivery platform for the treatment of a difficult to treat disease, onychomycosis. Nail lacquers is a viscous and translucent polish primarily prepared by mixing API and film-forming polymers in a suitable organic solvent that are volatile in nature. After the evaporation of a solvent layer, the API-polymer layer forms a protective film over the nail plate. As the lacquer application is topical drug does not reach the systemic circulation surpassing adverse reactions and interactions in the body. Nail lacquers purportedly reduces incidence of infection relapse in initial steps as drug by pass delivery from nail bed via matrix circulation (4). However, low permeation of drug into dense keratinized nail layers has served as a major demerit of a potential nail lacquer, to overcome this barrier the use of permeation enhancers such as urea, glycolic acid, thioglycolic acid was increased and have yielded suitable results as well. Permeation enhancers works by the mechanism of cleavage as presented in Figure 3. *T*hey break or cleaves the di-sulphide linkages of alpha-keratin, protein present in human nails often considered as a toughest biological material. Following the cleavage of di-sulphide linkages new pores are formed thus, enhancing permeation of API in nails (10).

Nail lacquers are widely exploited in recent years as either water-soluble or water-insoluble. Water soluble lacquers are highly acceptable as they offer strong adhesion over the surface of a nail thereby, promoting larger amount of drug release into the nail plate. The primary disadvantages of a water-based lacquers are easy or non-voluntary removal upon contact with water therefore, they require frequent applications which often becomes a tedious process for patients. Water-insoluble lacquers though provide a sustained release with longer stay, the problem of their periodic removal with organic solvent causes pain and skin irritation making it non-compliant to patients. Therefore, for an effective Transnail activity a combination of water insoluble and water-soluble nail lacquers has been evaluated and proposed to dictate improve adhesion, drug release and occlusion properties (8).

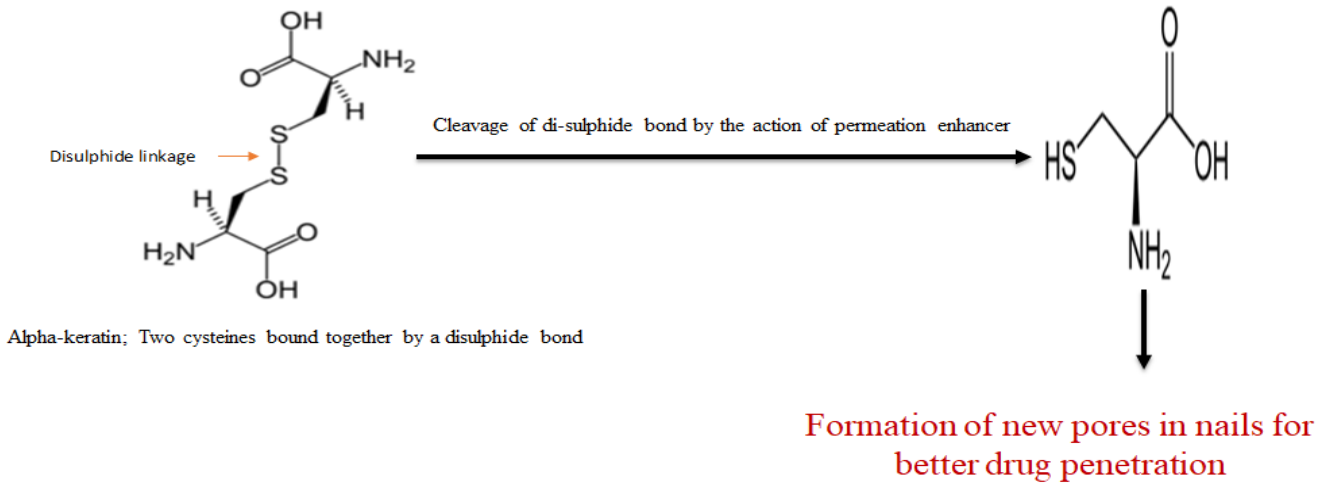

Figure 3. A schematic representation of a purported mechanism of permeation enhancers.

Hasan *et al.* in 2017 has developed a transungual Duple Nail Lacquer (DNL) for onychomycosis therapy. The proposed DNL is an amalgamation of two lacquer layers; first layer is hydrophilic and second layer is hydrophobic in nature. As discussed earlier hydrophilic layer supports covering; adhesion and promotes drug release whereas, hydrophobic layer provides occlusion and integrity to the first layer. The purported DNL is fabricated by employing luliconazole (azole-imidazole) as an API (12). As per literature, the azole class of anti-fungal drugs targets lanosterol 14 α-demethylase, enzyme necessary to convert lanosterol to ergosterol in fungal cell membrane. Following the depletion of ergosterol fungal membrane disrupts inhibiting the growth of fungal cell as represented in ***Figure 4.***

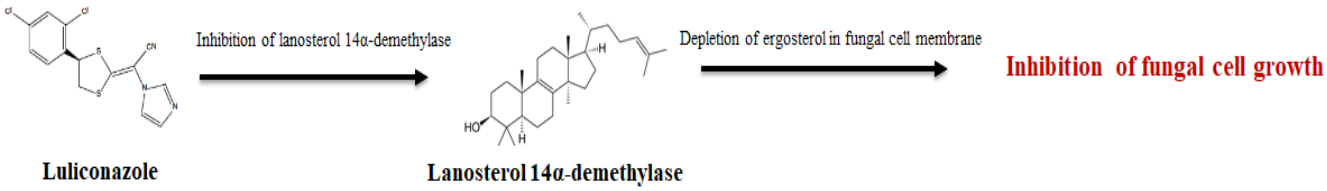

Figure 4. A schematic representation of a purported mechanism of Luliconazole.

The combination of permeation enhancers with newer anti-fungal agents have yielded suitable results and have proposed to target the two major barriers in the path of a transnail delivery.

3. Conclusion

Owing to the high prevalence and reporting rate of onychomycosis over the last few decades a pursuit of attaining viable solution for its treatment has also increased thus shifting the focus of worldwide researchers on the development of novel preparations which offers localised action, cosmetic acceptability, sustained release and a high degree of patient compliance.

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Conflict of interest

The authors declare that there are no conflicts of interest, financial or otherwise.

References

1. Murdan S, Hinsu D and Guimier M. A few aspects of transonychial water loss (TOWL): inter-individual, and intra-individual inter-finger, inter-hand and inter-day variabilities, and the influence of nail plate hydration, filing and varnish. Eur J Pharm Biopharm. 2008; 70:6849. DOI: 10.1016/j.ejpb.2008.05.018
2. Elewski BE. Onychomycosis: pathogenesis, diagnosis, and management. Clin Microbiol Rev. [Internet]. 1998 [cited 2018 Oct 20]; 11(3):415-29.
3. Onychomycosis.JPG [Internet]. 2009 Jun 27 [cited 2018 Oct 18]. Available from: https://commons.m.wikimedia.org/wiki/File:Onychomycosis.JPG
4. Gupta AK, Simpson FC. New pharmacotherapy for the treatment of onychomycosis: an update. Expert Opin Pharmacother. 2015; 16(2):227-36.
5. Iorizzo M, Piraccini BM, Tosti A. Today's treatments options for onychomycosis.J Dtsch Dermatol Ges. 2010; 8(11):875-9.
6. Onychomycosis nailed Leelavathi M, Noorlaily MN. Onychomycosis nailed. Malays Fam Physician. 2014; 9(1):2-7.
7. Alley MR, Baker SJ, Beutner KR and Plattner J. Recent progress on the topical therapy of onychomycosis. Expert Opin Investig Drugs. 2007; 16:157-67.

8. Shivakumar HN, Juluri A, Desai BG and Murthy SN. Ungual and transungual drug delivery. Drug Dev Ind Pharm. 2012; 38:901-11.
9. Murdan S. Drug delivery to the nail following topic1al application. Int J Pharm. 2002; 236:1-26.
10. Akhtar N, Sahu S, Pathak K. Antifungal potential of tolnaftate against Candida albicans in the treatment of onychomycosis: development of nail lacquer and ex vivo characterization. PBR. 2016; 2(3):1-2. DOI: 10.18869/acadpub.pbr.2.3.1
11. Hussan SD, Santanu R, Devina S, Vishal B, Manmohan S. Transungual drug delivery-a novel approach of unique features. Am. j. pharm. Res. 2013; 3(6).
12. Hasan N, Singh M, Sulaiman S, Nandy S, Dudeja M, Ali A, Iqbal Z. Design, development and optimization of a transungual duple nail lacquer for onychomycosis therapy. Journal of the J Eur Acad Dermatol Venereol. 2018 Jun; 32(6): e250-1.