IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 15, Issue 6 Series. I (June 2025), PP. 11-16
www.iosrphr.org

Advances In Transungual Drug Delivery Systems for The Treatment of Onychomycosis

Dr.P.Premkumar *kalpanashree.k,sowmiyajayarani.s,Sarbunishabegam
SAVEETHA COLLEGE OF PHARMACY (SIMATS), SAVEETHA UNIVERSITY ,THANDALM,CHENNAI
Received 25 June 2025; Accepted 11 July 2025

ABSTRACT:
Onychomycosis is one of the common nail diseases worldwide and it is a fungal infection that chiefly involves the nails on fingers and toes. Secondary to dermatophytes but caused by yeasts and non-dermatophyte moulds as well. Though not lethal, they erode the quality of life of the affected patients due to pain and discomfort, unsightly nails, and the consequent social repercussions. Since I was comparing the prevalence in two populations, I had to get the estimates for the prevalence in the two groups separately from the literature: The prevalence rises with age and depends on risk factors such as immunosuppression, diabetes and working in wet conditions for a long time.
Onychomycosis which affects keratinized nail tissue manifests through change in colour, thickness, brittleness and onycholysis.However, histological examination, fungal culture, and potassium hydroxide examination remain the hallmarks of diagnosis today. Some of the recent advancements that affect the diagnostic accuracy include dermoscopy and polymerase chain reaction. The management involves the use of antifungal agents whether local and oral for serious infections and local for mild fungal infections. When immunotherapy is not effective, combination treatments are seen to have a better effect. Non-surgical methods including laser therapy and photodynamic therapy are relatively new and less invasive, though increased research is needed for standardization of treatment modalities.

I. INTRODUCTION:

Onychomycosis, also known as tineaunguium, is a common fungal infection affecting fingernails or toenails. It causes discoloration, thickness, and detachment from the nail bed. Treatment is challenging due to its chronic and recurrent nature (1). The incidence has been increasing globally due to aging populations, immunosuppressive treatment use, and lifestyle choices. About 5-20% of people worldwide are affected, and the prevalence increases with age. Onychomycosis can cause discomfort, bacterial infections, and functional impairment, primarily as a cosmetic issue (2,3).

The infectious nail disease onychomycosis represents the most common condition affecting half of all patient consultations. Studies show that the infection occurs more frequently in men whereas prevalence tends to rise as individuals age. Approximately 40% of elderly people develop the condition(4). The risk of developing onychomycosis increases for people who have diabetes mellitus as well as peripheral arterial disease and those who have HIV or are taking immunosuppressive medications. Anthropophilic dermatophytes Trichophytonrubrum and Trichophytonmentagrophytesvar(5).interdigital lead to most infections of the nail however non-dermatophyte molds cause either main infections or a second set of infections. Scientific data shows that fungal nail infections known as onychomycosis affect between 10% to 15% of the world's population(6).

Roughly 10% of affected nails contain Fusarium spp., Acremonium spp., Alternaria spp., and Neoscytalidium sp. along with dermatophyte fungi. Nails can become infected with three types of fungi including Candida albicans and Candida parapsilosis and yeasts. The prevalence of onychomycosis targets toenails over fingernails and occurs with dry-type plantar tineapedis infections. The diagnosis of onychomycosis in children depends on laboratory-confirmed fungus testing to identify nail-entry methods because treatment approaches vary based on infection type(7,8).

This fungal nail infection occurs in 0.5% to 2.6% of children primarily affecting their toenails. Acquisition of the fungus happens indirectly from family members or occurs through skin exposure to

environmental contamination and nail-trauma injuries. Evidence shows that both fungal nail and sole infections require genetic vulnerability which must develop before childhood (9,10).

CLINICAL FEATURES:

1] Distal and Lateral Subungual Onychomycosis:

Past the nail entry point fungi move towards the centre and penetrate the nail unit plate. The fungal infection known as distal and lateral subungual onychomycosis (DLSO) typically emerges from tineapedis damage and mainly targets great toenails. A yellow-white nail plate shows signs of hyperkeratosis and when detached it produces onycholysis. Nail discolorations from onycholysis affect a minority of cases (7). The nail condition known as Dermatophytoma features subungual hyphae and scale accumulation that leads to Black Nail Pigmentation (fungal melanonychia) following an infection by Melanoides form of Trichophytonrubrum or related melanin-producing fungus. Onychomycosis primarily develops due to infections with non-dermatophyte fungi that cause periungual irritation. DLSO may trigger nail psoriasis or traumatic onycholysis while diffuse hyperkeratosis and traumatic onycholysis stand as alternative diagnoses to DLSO (11). Excision and systemic treatment are required when dermatophytes trigger this DLSO manifestation.

2]White Superficial Onychomycosis:

White patches on toenails indicate superficial onychomycosis which experts link to fungal infections primarily driven by Trichophytonmentagrophytes and Roseo-griseumCephalosporium and Aspergillusterreus and Fusariumoxysporum group members(12,13). In superficial onychomycosis fungal infections avoid triggering inflammation yet can develop across any nail plate segment. The fungus shows saprophytic behaviour while growing inside living tissue despite its capacity for "in-vivo" development. With differential diagnoses being trauma-induced toenail leukonychia and an extended nail polish use, tineapedisinterdigitalis is often caused by T. interdigitale(7).

Category	Details
Disease	Onychomycosis – fungal infection of fingernails/toenails caused by dermatophytes, yeasts, and non-dermatophyte molds.
Impact Patients	Not lethal but reduces quality of life due to pain, discomfort, unsightly nails, and social effects.
Prevalence Factors	Increases with age; higher in individuals with immunosuppression, diabetes, or prolonged wet exposure.
Clinical Signs	Nail discoloration, thickening, brittleness, and onycholysis (detachment from the nail bed).
Diagnostic Methods	Standard: Histology, fungal culture, KOH (potassium hydroxide) prep. Recent advances: Dermoscopy, polymerase chain reaction (PCR).
Treatment	Mild: Topical antifungals. Severe: Oral + topical antifungals. Combination therapies when monotherapy is insufficient.
Non-surgical Options	Laser therapy, photodynamic therapy (PDT) – newer, less invasive treatments, but need more research for standardization.
Drug Delivery Advances	Enhancing drug penetration through nail plate using penetration enhancers, lacquers, Nano carriers, iontophoresis, microneedles.

3] Topical Subungual Onychomycosis:

A 36-year-old female received a diagnosis of proximal subungual onychomycosis from Microsporumcanis which attacked her left thumb and little fingernails. Onychomycosis affected both the nail of her left thumb and her pinky finger by causing the nail plates to thin out until they fell apart. Pathological examination of the 2-mm nail biopsy demonstrated fungal elements throughout the nail plate with fungal hyphae occurring primarily in the central area of the nail. The nail bed exhibited no inflammatory signs and no markers indicated immunodeficiency during testing. The two-month oral terbinafine therapy achieved complete fungal clearance with total recovery of the patient's infection.

4] Endonyx onychomycosis:

Three patients with Trichophytonsoudanense onychomycosis exhibit an Endonyx nail invasion, characterized by a diffuse milky-white discoloration of the affected nail without hyperkeratosis or onycholysis. The nail plate surface and thickness are normal, and the pathology contrasts between the presence of fungal hyphae in the nail

plate and the absence of fungal elements in the nail bed. The endonyx pattern of nail infection is specific to T. soudanense nail invasion and may reflect its high affinity to hard keratins (14).

5] Total Dystrophic Onychomycosis:

A common fungal nail infection called onychomycosis shows rare cases of yeast and non-dermatophyte mold involvement. Scientists discovered first-reported Aspergillusclavatus fungus causing onychomycosis in a 32-year-old lady with nail psoriasis. The patient needed 200 mg of daily itraconazole treatment to combat the antifungal-resistant isolate. Medical records show neither A. clavatus nor any drug-resistant strains of this species have been detected in onychomycosis cases.

Tabulated Summary of Onychomycosis

Aspect	**Details**
Etiological Agents	-**Primary**:Dermatophytes - **Secondary**: Yeasts and non-dermatophyte moulds
Epidemiology	-Prevalence increases with age - Higher in immune compromised patients, diabetics, and those working in moist environments
Clinical Manifestations	- Nail discoloration - Increased nail thickness - Brittleness - Onycholysis (nail detachment)
Impact on Quality of Life	- Pain and discomfort - Aesthetic issues - Social stigma
Diagnostic Methods	- Potassium hydroxide (KOH) examination - Fungal culture - Histological examination - **Recent Advances**: Dermoscopy, PCR
Treatment Options	- **Topical antifungals**: for mild infections - **Oral antifungals**: for severe infections - **Combination therapy** for better efficacy
Emerging Therapies	- Laser therapy - Photodynamic therapy *Note: Require further standardization and research*

DIAGNOSIS OF ONYCHOMYCOSIS:

Nail disease experts report that onychomycosis represents the most frequent nail disorder affecting half of all nail conditions. Among all onychomycoses (15)Trichophytonrubrum and Trichophytonmentagrophytes account for more than 90% of dermatophage-related infections.

Trichophytonrubrum andTrichophytonmentagrophytes. All four primary clinical signs include superficial and complete dystrophic onychomycosis alongside proximal subungal and distal subungal manifestation (16). Onychomycosis frequency depends on three primary factors alongside hereditary influences together with individual habits and existing medical conditions(17). Fungal nail infections show independent associations with peripheral vascular disease and diabetes and acquired immunodeficiency syndrome (18).

The condition's complex epidemiology requires precise diagnosis combined with correct therapy and explicit patient(19) education for effective treatment. The epidemiology of fungal nail infections shows connections to both illness and lifestyle decisions (20).

TREATMENT:

1] TOPICAL TREATMENT:

Topical antifungal agents are relatively restricted by poor penetration of the nail unit and high recidivism. In the severe cases of onychomycosis, thereby – systemic antifungal therapy, debridement, or nail avulsion may also be effective in reducing the time necessary for therapy, and increase the proportion of cured patients (21,22). Polishes can successfully treat WSO and DLSO, which involve less than 50% of the distal nail, and usually takes six to twelve months of treatment. This makes ciclopirox 8% and Amorolfine 5% potential candidates to

be used in non-water-soluble nail lacquers; ciclopirox is however applied daily. Amorolfine has both fungistatic and fungicidal properties against yeasts, molds, and dermatophytes (23). It should be used as a first-line treatment of distal-lateral subungual onychomycosis involving up to two nails and dermatophyte onychomycoses that is not limited to the proximal matrix portion of the nail.

Amorolfine is a topical antifungal preparation used for distal and lateral subungual onychomycosis involving up to two nails in mild cases or for onychomycosis with no matrix implication (24). It has ant-inflammatory activity, anti-allergic effect and fungicide and is used daily. Two are ciclopirox 8% in non-water-soluble lacquers and ciclopirox in water-soluble lacquer that enhances the nails' permeability.

Two new topical antifungal agents, tavaborole 5 percent solution and Efinaconazole 10 percent solution, are currently being used to treat onychomycosis that is brought by dermatophytes. The FDA approved Efinaconazole 10% nail solution in June 2014 for the area that has mild to moderate DLSO without nail debridement. This triazole antifungal is dosed once daily and does not require the daily removal of the nail and has the same efficacy as oral itraconazole. One study conducted recently showed that Efinaconazole was more effective in various degrees of early stages of onychomycosis (25–27).

Tavaborole is an oleic for water soluble, topical nail lacquer to cure the toe nail onychomycosis. It has first international certification in this regard from the USA. While efficacy was demonstrated in Phase II studies, all patients need Phase III studies as markers for its safety and efficiency(28–30). These treatment modalities of the future are terbinafine nail solution and spray, TDT 067, MOB-015, and TMI-358, which are in phase 2 trials only.
Liconazole belongs to the imidazole class of antifungals with fungicidal and fungistatic effects and has entered phase 1 and 2a, specifically for moderate to severe distal subungual onychomycosis the phase 2b/3 is ongoing and liconazole exhibit good tolerability

The treatment by means of photodynamic therapy (PDT) is based on the laser system and photo sensitizers with the purpose of elimination of nail fungi. PDT forms ROSs, which are chemically inactivated by light. It has been seen to be effective against several fungal species for instance T. rubrum. Phenothiazine dyes, porphyries, ALA and MAL form a list of photo sensitizers that can be used to generate singlet oxygen. There are six on PDT in onychomycosis in vivo; however, we could identify only two reports of clinical trials(31,32). From this study, it is observed that photosensitizer treatment needs nail abrasion or maceration and PDT possesses certain drawbacks due to the session of many sessions. It is important to note that increasing irradiation may lead to shorter duration of sessions whilst posing additional risks of burning and temporary discomfort among the patients. More studies must be carried out to determine the appropriate light source and the frequency of the treatments.
Laser therapy like carbon dioxide laser, ND: YAG laser and diode with 870nm and 930nm wavelengths are preferred for onychomycosis treatment because it is painless and requires only a few sittings. The oldest of the five-laser type is carbon dioxide laser which is rarely used today. ND: YAG laser has been reported to have high mycological cure rates with some small-scale trials producing a mycological cure rate of 87.5%. Secondly, it's been established that longer pulse duration of ND: YAG at 1064 nm has been more effective on the damaged toenails as compared to the fingernails.

After reviewing 12 papers published in the English language, researchers determined that diode lasers maintained a mycological cure of 38% at a nine months' follow-up. Once again, in the majority of cases (10/12) the 1064-nm neodymium laser was studied with few to no side effects. Laser therapy in onychomycosis has been found to be less invasive with no significant side effects.

The author also pointed out that treatment of onychomycosis with lasers has yielded mixed results given that no comparison has been made with routine treatments and additional research must be conducted to better ascertain the effectiveness of this type of therapy.

2] SYSTEMIC TREATMENT:

Terbinafine is given as pulse dose at the dosage of 500 mg for one week followed by 4 weeks of no treatment or at the dosage of 250 mg per day for 12 consecutive weeks. Itraconazole, pulse treatment is given daily for one week every month for a total of three months for toenails or two months for fingernails(24,33).
Potassium iodide and itraconazole pulse therapy is effective and safe for the treating of dermatophyte toenail onychomycosis in diabetic patients. Some of these regimens may be associated with topical nail lacquers. Nevertheless, there is lack of literature on cure rates of combination therapy using systemic and topical

antifungals (34). One has to bear in mind that the routine nail plate removal or using urea ointment may enhance the improvement. The recurrence rate may reach up to 20% of the healed patients and the reinfections rates may also be high.

The management of dermatophyte onychomycosis is done with fluconazole at 150-300 mg weekly for more than six months. Terbinafine, itraconazole, and fluconazole are relatively safe drugs but have been associated with rare side effects which include hepatotoxicity and renal toxicity.

Two drugs to be considered as an alternative are Albaconazole and Posaconazole. Topical treatment and periodic nail plate excision is the recommended treatment for non-dermatophyte moulds that cannot be treated with systemic antifungal agents. Terbinafine will not be effective against Candida sp. Onychomycosis; this is so because yeast does not respond positively to it. Nail isolation should be done in the presence of Candida onychomycosis associated with diabetes or immune depression.

However, in dermatophytosis, dystrophic onychomycosis, or involving the lateral nail plate, avulsing surgery or chemical might be required accompanied with itraconazole and terbinafine topical or systemic treatment. The treatment required is several months because nails grow slowly, especially in the elderly. This is because factors such as the type and severity of onychomycosis and the patient's medical conditions determine the drug to be used. Topical antifungal is useful and may require nail plates removal on certain occasions with persistent fungal infections.

II. CONCLUSION:

Onychomycosis is a fungus, thus requires special attention once it affects the nails due to long time that it took to develop, especially affecting the older people. It may last for a few months and depends on the stage and complications that may be associated with the patient. Dermatophytes tend to affect one or the other or both of the great toenails in the development of DLSO. Topical therapy is the management of choice, while systemic therapy requires fluconazole, itraconazole, or terbinafine for DLSO, PSO, and distal PWNWO. There is a requirement for more studies on laser and photodynamic treatment for standardization.

Onychomycosis is a frequent and chronic disease involving the nails that mostly affects elderly people and shows the aspect of drug resistance. This is why early intervention and constant care are important in managing it because it has a slow progress. Some common versions include; Distal Lateral Subungual Onychomycosis (DLSO) which is the most common and this is caused by the dermatophytes. There are other subtypes of the fungus which manifest differently, and they include; White Superficial Onychomycosis (WSO) and Proximal Subungual Onychomycosis (PSO).

The management of onychomycosis therefore depends on correct diagnosis and treatment options to be taken. Topical antifungals are thus the best approach of treatment that treats mild to moderate infections with less invasion. However, the results are also long lasting as one is only required to be patient because the nails grow slowly. The topical antifungal agents are clotrimazole, tinea and miconazole which are comparatively less aggressive than the systemic ones, including fluconazole, itraconazole and terbinafine but they can only be administered with a doctor's prescription because they have systemic side effects.

Laser and photodynamic treatments are among the improving method of facial and skin infection treatment especially in cycles or difficult to heal ones. However, there is still the need to conduct clinical trials to determine safety as well as efficacy of such contraceptives. More efforts are being made in the development of these techniques and their incorporation into complex operative treatments to make them more efficient and less invasive.

Onychomycosis prevention there are some measures, which can be taken in order to treat fungal infection and prevent new cases of the same. Thus, one should not wear shoes that are airtight and should not let his or her feet come into contact with water, although its nails should be clean. Although treatment of this condition is still undergoing research, many attempts are in the research process as the medical field explores the possibilities of natural antibiotics and topical and systemic treatments. Advances in material science endeavor to improve the topical formulations' delivery into the target site, across the barrier, to respond to stubborn infections.

Onychomycosis is a difficult to treat fungal disease that may require description of molecular targeted treatment depending on the type of the fungal invader, nail thickness and general health status. Better diagnosis equipment maybe applied to check signs at an early stage, and this will enhance the results as distinguished from the early intervention. The original one invariably cures onychomycosis but despite the relative difficulty in affording this cure, further studies and advancements indicates that onychomycosis is curable. A holistic

approach of prevention, early diagnosis, as well as the correct application of treatment, can lead to a reduction of the impact of this common nail condition.

REFERENCES:

[1]. Heikkila H, Stubb S. The prevalence of onychomycosis in Finland. Br J Dermatol. 1995;133(5):699–703.
[2]. Roseeuw D. Achilles foot screening project: preliminary results of patients screened by dermatologists. J Eur Acad Dermatology Venereol. 1999;12(s1).
[3]. Scher RK, Rich P, Pariser D, Elewski B. The epidemiology, etiology, and pathophysiology of onychomycosis. Semin Cutan Med Surg. 2013;32:S2–4.
[4]. Nouripour-Sisakht S, Mirhendi H, Shidfar MR, Ahmadi B, Rezaei-Matehkolaei A, Geramishoar M, et al. Aspergillus species as emerging causative agents of onychomycosis. J Mycol Med. 2015;25(2):101–7.
[5]. Gupta AK, Drummond-Main C, Cooper EA, Brintnell W, Piraccini BM, Tosti A. Systematic review of nondermatophyte mold onychomycosis: Diagnosis, clinical types, epidemiology, and treatment. Vol. 66, Journal of the American Academy of Dermatology. 2012. p. 494–502.
[6]. Jayatilake JAMS, Tilakaratne WM, Panagoda GJ. Candidal onychomycosis: A mini-review. Mycopathologia. 2009;168(4):165–73.
[7]. Pichardo-Geisinger R, Mora DC, Newman JC, Arcury TA, Feldman SR, Quandt SA. Comorbidity of tinea pedis and onychomycosis and evaluation of risk factors in latino immigrant poultry processing and other manual laborers. South Med J. 2014;107(6):374–9.
[8]. Wulkan AJ, Tosti A. Pediatric nail conditions. Vol. 31, Clinics in Dermatology. 2013. p. 564–72.
[9]. Ghannoum MA, Mukherjee PK, Warshaw EM, Evans S, Korman NJ, Tavakkol A. Molecular analysis of dermatophytes suggests spread of infection among household members. Cutis. 2013;91(5):237–45.
[10]. Piraccini BM, Starace M, Bruni F. Onychomycosis in children. Vol. 7, Expert Review of Dermatology. 2012. p. 569–78.
[11]. Finch J, Arenas R, Baran R. Fungal melanonychia. Vol. 66, Journal of the American Academy of Dermatology. 2012. p. 830–41.
[12]. Piraccini BM, Tosti A. White superficial onychomycosis: Epidemiological, clinical, and pathological study of 79 patients. Arch Dermatol. 2004;140(6):696–701.
[13]. Piraccini BM, Lorenzi S, Tosti A. "Deep" white superficial onychomycosis due to molds [1]. Vol. 16, Journal of the European Academy of Dermatology and Venereology. 2002. p. 532–3.
[14]. Tosti A, Baran R, Piraccini BM, Fanti PA. Endonyx onychomycosis: A new modality of nail invasion by dermatophytes. Acta Derm Venereol. 1999;79(1):52–3.
[15]. Piraccini BM, Balestri R, Starace M, Rech G. Nail digital dermoscopy (Onychoscopy) in the diagnosis of onychomycosis. J Eur Acad Dermatology Venereol. 2013;27(4):509–13.
[16]. Salaheldin TA, Husseiny SM, Al-Enizi AM, Elzatahry A, Cowley AH. Evaluation of the cytotoxic behavior of fungal extracellular synthesized Ag nanoparticles using confocal laser scanning microscope. Int J Mol Sci. 2016;17(3).
[17]. Arrese JE, Quatresooz P, Pi?rard-Franchimont C, Pi?rard GE. Nail histomycology. Protean aspects of a human fungal bed | Histomycologie ungu?ale. Ann Dermatol Venereol. 2003;130(12 II).
[18]. Tsunemi Y, Takehara K, Miura Y, Nakagami G, Sanada H, Kawashima M. Screening for tinea unguium by Dermatophyte Test Strip. Br J Dermatol. 2014;170(2):328–31.
[19]. Idriss MH, Khalil A, Elston D. The diagnostic value of fungal fluorescence in onychomycosis. J Cutan Pathol. 2013;40(4):385–90.
[20]. Smijs TG, Jachtenberg JW, Pavel S, Bakker-Schut TC, Willemse-Erix D, de Haas ERM, et al. Detection and differentiation of causative organisms of onychomycosis in an ex vivo nail model by means of Raman spectroscopy. J Eur Acad Dermatology Venereol. 2014;28(11):1492–9.
[21]. Del Rosso JQ. The role of topical antifungal therapy for onychomycosis and the emergence of newer agents. J Clin Aesthet Dermatol. 2014;7(7):10–8.
[22]. Friedman-Birnbaum R, Cohen A, Shemer A, Bitterman O, Bergman R, Stettendorf S. Treatment of onychomycosis: A randomized, double-blind comparison study with topical bifonazole-urea ointment alone and in combination with short-duration oral griseofulvin. Int J Dermatol. 1997;36(1):67–9.
[23]. Hay RJ, Baran R. Onychomycosis: A proposed revision of the clinical classification. Vol. 65, Journal of the American Academy of Dermatology. 2011. p. 1219–27.
[24]. Gupta AK, Daigle D, Foley KA. Topical Therapy for Toenail Onychomycosis: An Evidence-Based Review. Vol. 15, American Journal of Clinical Dermatology. 2014. p. 489–502.
[25]. Elewski BE, Rich P, Pollak R, Pariser DM, Watanabe S, Senda H, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter, randomized, double-blind studies. J Am Acad Dermatol. 2013;68(4):600–8.
[26]. Lipner SR, Scher RK. Efinaconazole 10% topical solution for the topical treatment of onychomycosis of the toenail. Vol. 8, Expert Review of Clinical Pharmacology. 2015. p. 719–31.
[27]. Rich P. Efinaconazole topical Solution, 10%: The benefits of treating onychomycosis early. J Drugs Dermatology. 2015;14(1):58–62.
[28]. Jinna S, Finch J. Spotlight on tavaborole for the treatment of onychomycosis. Vol. 9, Drug Design, Development and Therapy. 2015. p. 6185–90.
[29]. Markham A. Tavaborole: first global approval. Drugs. 2014;74(13):1555–8.
[30]. Toledo-Bahena ME, Bucko A, Ocampo-Candiani J, Herz-Ruelas ME, Jones TM, Jarratt MT, et al. The efficacy and safety of tavaborole, a novel, boron-based pharmaceutical agent: Phase 2 studies conducted for the topical treatment of toenail onychomycosis. J Drugs Dermatology. 2014;13(9):1124–32.
[31]. Elewski BE, Ghannoum MA, Mayser P, Gupta AK, Korting HC, Shouey RJ, et al. Efficacy, safety and tolerability of topical terbinafine nail solution in patients with mild-to-moderate toenail onychomycosis: Results from three randomized studies using double-blind vehicle-controlled and open-label active-controlled designs. J Eur Acad Dermatology Venereol. 2013;27(3):287–94.
[32]. Dominicus R, Weidner C, Tate H, Kroon HA. Open-label study of the efficacy and safety of topical treatment with TDT 067 (terbinafine in Transfersome®) in patients with onychomycosis. Vol. 166, British Journal of Dermatology. 2012. p. 1360–2.
[33]. Gupta AK, Paquet M, Simpson F, Tavakkol A. Terbinafine in the treatment of dermatophyte toenail onychomycosis: A meta-analysis of efficacy for continuous and intermittent regimens. Vol. 27, Journal of the European Academy of Dermatology and Venereology. 2013. p. 267–72.
[34]. Gupta AK, Gover MD, Lynde CW. Pulse itraconazole vs. continuous terbinafine for the treatment of dermatophyte toenail onychomycosis in patients with diabetes mellitus. J Eur Acad Dermatology Venereol. 2006;20(10):1188–93.