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RECENT ADVANCEMENTS IN THE TREATMENT OF ONYCHOMYCOSIS: A COMPREHENSIVE REVIEW

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ABSTRACT: The most prevalent condition affecting the nails is onychomycosis. It is a typical nail fungal infection that causes millions of individuals globally. Yeasts, non-dermatophyte moulds, and dermatophytes can all be the cause. It's not only results in physical discomfort but also has a major negative effect on the affected person's quality of life. This infection affects the nails of the toes and fingers, causing discoloration, thickness, and brittleness of the nails. While the condition is not life threating, but it can be uncomfortable and unsightly, leading many patients to seek treatment. Previously these treatments ranged from oral medication to topical ointments and laser therapy, each with its benefits and drawbacks Fortunately, recent improvements in onychomycosis diagnosis and treatment have provided new hope for patients. It will deal with the recent treatment available and the novel treatment which can be developed. In this comprehensive review, we will explore the latest research and developments in the field, discussing novel treatment modalities, diagnostic techniques, and safety considerations. Additionally, new techniques include photodynamic treatment and laser therapy are discussed, emphasizing their potential in overcoming the limitations of traditional treatments. Furthermore, we examine the importance of early diagnosis and patient education in improving treatment outcomes.

INTRODUCTION: Nail fungus, or onychomycosis, is characterised by thickness, discoloration, and detachment of the nail from the nail bed. Dermatophytes, like *Trichophyton rubrum* and mentagrophytes, are the main culprits; they cause about 90% of nail infections in toenails and 75% of nail infections in fingers. Onychomycosis can also be caused by other organisms, such as yeasts and non-dermatophyte Moulds [1-5].

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Onychomycosis affects 10% of the general population, 20% of people over 60, and a startling 50% of people over 70. The prevalence of the disease varies with age. The chance of developing onychomycosis is increased by a number of risk factors, including diabetes mellitus, immunologic diseases, peripheral vascular disease, and HIV infection [6-11].

Accurate Diagnosis for Effective Treatment: Accurate diagnosis is crucial for the effective management of onychomycosis. Clinical examination alone has shown limited sensitivity and specificity, leading to the potential for misdiagnosis and inappropriate treatment. Therefore, various diagnostic techniques have been

employed to confirm the presence of onychomycosis and identify the causative organism [12-16].

Mycologic Testing: Mycologic testing involves direct microscopic examination, fungal culture, histopathology, and polymerase chain reaction (PCR) assays. These techniques allow for the identification of fungal elements and the detection of specific DNA sequences, providing a definitive diagnosis. PCR, in particular, has shown excellent sensitivity and specificity and has become increasingly accessible [17-21].

Artificial Intelligence: Recent studies have explored the purpose of artificial intelligence (AI) for the investigation of onychomycosis. Deep neural networks have shown comparable sensitivity and specificity to clinical examination by dermatologists, making AI a potential supplement to clinical evaluation. However, mycologic confirmation is still necessary before initiating treatment [22-26].

Advancements in Oral Treatments: Oral Treatment offer a non-invasive and convenient approach to treating onychomycosis, particularly for mild to moderate cases and when systemic Antifungal medications are either intolerable or contraindicated. Current advancements in topical treatments have focused on improving efficacy and safety profiles [27-35].

Terbinafine: For onychomycosis, oral terbinafine tablets have been used extensively as a first-line treatment; meta-analyses have demonstrated 76% mycotic cure rates. Although rare occurrences of hepatotoxicity have been recorded, it is generally well tolerated. It is advised to closely monitor liver function while receiving therapy.

Indication: Recommended for dermatophytes-induced onychomycosis of the fingernail or toenail (tinea unguium 250 mg/1 tablet) taken orally once daily for 6 weeks for the fingernail and 12 weeks for the toenail) [36].

Itraconazole: Another oral antifungal agent, itraconazole capsule, has also demonstrated efficacy in the treatment of onychomycosis. It can be administered in both pulse dosing and continuous dosing regimens. However, itraconazole has a higher risk of drug interactions and requires monitoring of liver function and cardiac health.

Indication: To treat toenail infections, use 200 mg once daily continuously for 12 weeks cycle, and treat fingernail infections for 6 weeks [37].

Griseofulvin: Although less commonly used due to the availability of more effective alternatives, griseofulvin may still be considered in certain cases. It is generally well-tolerated but requires long-term treatment and monitoring.

Indication: 500mg (Grifulvin V).

Duration of treatment: Depending on the location of the infection: Tinea corporis: two to four weeks Tinea capitis: 4-6 weeks, with a potential 8–12-week period For 4–8 weeks, tinea pedis Unguium tinea: 4-6 months [38].

Metoconazole Serious fungal or yeast infections such as histoplasmosis (Darling's disease), blastomycosis (Gilchrist's disease), coccidio-idomycosis (Valley fever, San Joaquin Valley fever), paracoccidioidomycosis (South American blastomycosis, Lutz-Splendore-Almeida disease), or candidiasis (thrush, oral thrush) can all be treated with ketoconazole. This medication functions by either eliminating the yeast or fungus or stopping its growth**.**

Indication: The recommended starting dose of ketoconazole tablets is a single daily administration of 200 mg (one tablet). For the duration of 6 months [39].

Voriconazole: Voriconazole is a new broad spectrum systemic antifungal that has demonstrated excellent activity against a variety of dermatophytes, including Trichophyton and Microsporum species, in two *in-vivo* trials of resistant dermatophytosis and numerous in vitro studies.

Significance: 100 mg used orally every 12 hours if less than 40 kg. For a minimum of 40 kg: 200 mg taken orally every 12 hours for a period of time (between 2 and 232 days) [40].

Advancements in Topical Treatments: Although there are topical therapies for onychomycosis, a fungal infection of the nails, oral drugs may work

better in this situation. Onychomycosis cases that are mild to severe are typically better treated with topical medications. It's crucial to remember that nail fungus can be difficult to treat and frequently needs constant, ongoing care. These are a few typical topical choices.

EConazole Nitrate Cream: Econazole is used to treat a range of fungal skin infections, including ringworm, jock itch, onychomycosis, and athlete's foot. In addition, pityriasis (tinea versicolor), a fungal infection resulting in a lightening or darkening of the skin on the arms, legs, neck, and chest, is treated with this medicine. An azole antifungal called econazole inhibits the growth of fungus [40].

Usage: This drug should only be applied topically. The treated area should be properly cleaned and dried. As prescribed by your physician, apply this medication once or twice daily to the afflicted area and surrounding areas.

Butenfine HCl: An antifungal drug called butenafine hydrochloride is frequently included in topical formulations to treat fungal infections of the skin, like ringworm and athlete's foot. It is not typically the first line of treatment for nail fungal infections, even though it possesses fungicidal qualities and works well against dermatophytes, one of the main causes of nail fungal infections (onychomycosis).

Significance: For fungus-related skin infections: Individuals and minors aged 12 years and above for two weeks, apply once daily to the skin's affected region or areas. Children under 12 years old: Your doctor must determine the use and dosage [41].

Clotrimazole Solution: A drug called clotrimazole is used to treat and manage fungal infections. It belongs to the imidazole drug class. The usefulness of clotrimazole as a treatment for fungal infections is discussed in this activity, along with its indications, mode of action, and contraindications [41].

Significance: Application of Cream Topically Gently massage a lotion or solution into the soiled area of skin. Topical medicines shouldn't be applied intravaginally or in the eyes.

Miconazole Solution: Miconazole is used to treat fungal skin infections (candidiasis), including ringworm, jock itch, athlete's foot, and others. In addition, pityriasis (tinea versicolor), a fungal infection resulting in a lightening or darkening of the skin on the arms, legs, neck, and chest, is treated with this medicine. An azole antifungal called miconazole functions by stopping the growth of fungus.

Indication: Only apply this medication topically. The treated area should be properly cleaned and dried. Usually twice a day, or as prescribed by your physician, apply this medication to the affected area of skin. Before applying, thoroughly shake the bottle if you're using the spray version. The type of infection being treated determines the dosage and duration of treatment. Don't use this more frequently than advised.

Sulfacetamide Sodium 15%/Sulphur 5% Topical Cream: Bay view Pharmacy's Sulfacetamide Sodium 15%/Sulphur 5% Topical Cream is a semisolid preparation dispensed in a pump mechanism. This formulation is designed for convenient and controlled application on the skin, providing localized treatment for conditions such as Onychomycosis, Folliculitis, and Tinea Versicolor [42].

Indication: To use this medication, apply a thin layer of the cream to the affected area of skin twice daily, or as directed by your healthcare provider. The cream should be gently massaged into the skin until it is fully absorbed. It is important to wash your hands after applying the cream.

Amorol Cream: Amoral cream is composed with Amorolfine is a medication that is used to treat fungal infections of the nails. It is categorised as an antifungal [43].

Indication: Always take this medication exactly as prescribed by your physician or pharmacist. Apply it to the affected finger or toenails as instructed by your physician. Clean your nails and file down the affected area before using this medication. Use the included swabs to clean the nail's surface and remove any grease. Use one of the reusable spatulas to apply the varnish.

Efinaconazole Solution: This drug is used to treat fungal infections of the toenails. It functions by inhibiting the development of specific fungi. Efinaconazole is a member of the azole antifungals medication class. This drug exclusively addresses fungal infections. Other forms of infections, such those brought on by bacteria, will not be treated by it. Any medication used to treat infection may become less effective if it is used excessively or unnecessarily.

Indication: The infected toenail(s) should be cleaned and dried before using this medication. After bathing, showering, or washing, give yourself at least ten minutes before applying. Only apply this medication to the infected toenail(s) as prescribed by your physician; this is often once a day for 48 weeks. An adult should administer this drug to children if they are to be used on them [44].

Additional Drug under Trial:

Tavaborole Solution: For the treatment of toenail onychomycosis, tavaborole is a topical nail solution that is water soluble, lightweight, and the first member of a new class of boron-containing antifungals. Tavaborole exhibits a distinct mode of action against fungi and keeps its antifungal characteristics when keratin is present. Tavaborole 5.0% nail solution is presently being considered for US Food and Drug Administration licencing after demonstrating a good safety and efficacy profile in Phase II/III clinical trials.

Albaconazole: The oral medication albaconazole has shown strong antifungal action and excellent levels of bioavailability. It was being developed to treat vulvovaginal candidiasis and onychomycosis. It was being developed to treat vulvovaginal candidiasis and onychomycosis. Additionally, patients with tinea pedis participated in phase I of a randomised, placebo-controlled clinical trial where albaconazole was assessed. There were no significant side effects reported in the albaconazole investigations. Nevertheless, the drug's study was stopped [45].

Combination Therapies for Enhanced Efficacy: Combining different treatment modalities has shown promise in improving the efficacy of onychomycosis treatment. By targeting the infection from multiple angles, combination therapies can increase cure rates and reduce the risk of recurrence.

Urea 40% and Bifonazole 1%: By chemically avulsing the nail with urea and bifonazole, fungal-infected debris is removed, improving the penetration and effectiveness of antifungal treatments. Patients who used their urea and -bifonazole ointment less frequently were able to remove their nails earlier, according to prior clinical observations.

Significance: Applying ointment once a week for a week together with sealing is linked to a one-week reduction in the time it takes for the chemical avulsion of the nail to be completed [46].

Nail Debridement: Concomitant nail debridement, which involves the physical removal of infected nail material, is often recommended to enhance the penetration of topical and systemic antifungal agents. Nail debridement is a procedure that reduces the thickness and length of a toenail. The goal is to allow the patient to walk without pain. Nail Debridement can be done with an electric grinder or manually with an instrument. If medication is not effective in treating the infection, then it might be required. A sick toenail bed or a viable nail plate must be removed during nail debridement. This can be done using an electric grinder or by hand using an instrument. Patients diagnosed with nail debridement are typically treated by podiatrists When a medical professional performs debridement of mycotic nails, they remove your fingernail or toenail surgically. If medication is not effective in treating the infection, then it might be required. A nail might take up to a year to grow back [47].

Nail Debridement can be used to: Extract a diseased toenail that is bed or viable nail plate Reduce pain Allow a topical treatment to penetrate more effectively Surgically remove a toenail or fingernail Nail debridement can be painful if it's mechanical or sharp.

Basics of professional toenail debridement include: Antiseptic pads/ cleansers Bleeding control/ haemostasis. Bacitracin ointment Instrument disinfection/care Safety glasses Foot care services are considered medically necessary once in 60

days. This mechanical approach can help reduce the fungal burden and improve treatment outcomes.

Laser and Photodynamic Therapies: Physical treatments, such as laser therapy and photodynamic therapy, have been utilized in combination with topical or systemic antifungal agents. Laser therapy and photodynamic therapy (PDT) are those medical treatments that use light to treat various medical conditions, including cancer, skin disorders, and eye problems. Both therapies harness the power of light for therapeutic purposes, but they differ in their mechanisms and applications [48]. These therapies aim to immediately attack the fungal infection by penetrating the tough nail plate. Although the matter is still being investigated, initial research has yielded encouraging findings. PDT and laser therapy are both extremely specialised procedures that call for the knowledge and skills of qualified medical specialists. The patient's general health, the severity of the ailment, and the condition being treated all influence which option is best. It's crucial to speak with a healthcare professional to figure out the best course of action [49].

Trans Ungual Drug Delivery System:

Ciclopirox Nail Lacquer: The nail lacquer Ciclopirox Topical Solution, 8%, contains ciclopirox, a synthetic antifungal medication. It is meant to be applied topically to the skin very next to fingernails and toenails.

Indication: Ciclopirox Topical Solution, 8% (Nail Lacquer) may be used safely and effectively if used daily for a period of time longer than 48 weeks.

Loceryl Nail Lacquer: This nail lacquer contains an antifungal agent. It is applied to treat nail fungal infections. It aids in the treatment of the infection and eradicates the fungus.

Indication: Utilise it according to your doctor's recommended dosage and duration. Before using, read the directions on the label. Cut your nails. After using an applicator brush to apply the medication to the nail and its underside, wait 30 seconds for it to dry [50].

Novel Drug Delivery System: Nano sponge Technology: One notable advancement in topical treatments is the use of Nano sponge technology. Nano sponges are microscopic particles that can encapsulate antifungal agents, enhancing their penetration into the nail plate. This targeted drug delivery system has shown promising results in improving the efficacy of topical treatments for onychomycosis. These "nano sponges" are typically composed of nanomaterials, such as nanoparticles or nanofibers, and can be used to absorb, store, or deliver substances at the nanoscale. Nano sponge technology has found applications in a wide range of fields, including environmental remediation, drug delivery, and material science. Nano sponge technology has shown promise in various medical applications, including cancer treatment, drug delivery for infectious diseases, and even as a means of detoxification for certain toxins. However, it's essential to conduct more further research and human trials to validate its safety and effectiveness for specific medical conditions. The field of nanomedicine continues to advance, and nano sponge technology represents one innovative approach to improving drug delivery and therapeutic outcomes [51].

Novel Antifungal Agents: Researchers have also been exploring the potential of new antifungal agents for topical use. It refers to the use of advanced nanotechnology approaches to develop and deliver novel and improved antifungal drugs for the management of fungal infections. Fungal infections can be challenging to treat due to the similarity between fungal and human cells, which can lead to limited drug options and potential side effects.

Nanotechnology-based drug delivery systems can address some of these challenges by enhancing drug efficacy, targeting specific infection sites, and reducing adverse effects. These agents may exhibit enhanced antifungal activity and improved nail penetration, addressing the limitations of traditional topical treatments. Clinical trials are underway to evaluate the safety and efficacy of these novel formulations. In recent years, researchers have been exploring various nanotechnological approaches to develop novel antifungal agents and drug delivery systems. These innovations aim to address the limitations of current antifungal therapies and improve the management of fungal infections, especially in cases of drug-resistant fungi or severe

systemic infections. As research in this field advances, it may lead to the development of more safe and less toxic dose for a wide range of fungal diseases [52].

Safety Considerations and Adverse Effects: The safety of antifungal therapies is a critical consideration in the management of onychomycosis. While these medications can effectively treat the fungal infection, which may also be related with adverse effects and potential drug pharmacokinetics.

Pregnancy and Immunosuppressed Patients: Recent studies have provided reassuring data on the effectiveness of oral terbinafine in pregnant women and immunosuppressed patients. No increased risk of adverse pregnancy outcomes or significant drug interactions were observed. However, caution should still be exercised, and individual patient factors should be considered.

Monitoring Liver Function: Oral antifungal agents, especially terbinafine and itraconazole, may have hepatotoxic effects. Regular monitoring of liver function tests is recommended during treatment to detect any potential liver abnormalities. Patients with pre-existing liver conditions should be closely monitored [53].

Quality of Life Considerations: In addition to having an adverse effect on physical health, onychomycosis also significantly lowers a person's quality of life. Nail fungus symptoms that are apparent can be embarrassing, self-conscious, and socially stigmatising. Thus, one of the most important aspects of treating onychomycosis is improving quality-of-life outcomes.

Results as reported by Patients: The quality of life has been evaluated in relation to onychomycosis and treatment using patient-reported outcome measures. Research has demonstrated that onychomycosis has a substantial impact on quality of life, and that therapy improves a person's physical, mental, and social well-being, among other aspects of their life.

Psychosocial Support: In addition to medical treatment, psychosocial support can play a crucial role in addressing the psychological and emotional impact of onychomycosis. Patient education, counselling, and support groups can help individuals cope with the challenges associated with the condition [54].

Future Directions: Emerging Therapies and Nail lacquer:

Medicated Nail Lacquer: Topical antifungal nail lacquers, like ciclopirox, offer a convenient and effective treatment option for onychomycosis. Ciclopirox nail lacquer is applied directly to the infected nails and surrounding skin. It is typically used daily for a specified period, such as 48 weeks. The lacquer helps eradicate the fungal infection and promotes the growth of healthy nails. Although it may take up to a year to see significant improvement, ciclopirox nail lacquer has demonstrated positive results in clinical studies [55].

Medicated Nail Cream: Another topical treatment option is antifungal nail cream, such as Eficonazole along with Tavaborole. These preparation are applied to the infected nails after soaking and, in some cases, thinning the nails. The creams penetrate the hard nail surface to reach the underlying fungus and inhibit its growth. Urea-containing creams can be used to soften and thin thick nails before applying the antifungal cream. It is important to follow the prescribed treatment regimen and consult a healthcare provider if any adverse reactions occur [56].

CONCLUSION: In conclusion, there have been recent developments in a number of fields related to the treatment of onychomycosis, a common fungal infection of the nail. Thanks to advancements in microscopic examination, histopathologic examination, fungal culture, and polymerase chain reaction assays, onychomycosis evaluation and diagnosis have improved. The most successful treatments are still oral antifungal medications like terbinafine and itraconazole, but these medications have serious side effects. Topical treatments may be considered for mild to moderate instances, despite their lower effectiveness owing to inadequate nail penetration. In addition, newer advancements have concentrated on investigating innovative experimental strategies and enhancing the efficacy of topical treatments. Topicals are being utilised in conjunction with physical and laser therapies to pierce the thick nail plate. Long-term research is still required to evaluate the

effectiveness of different treatments, and safer and more efficient treatment alternatives are also required. Enhancing medication delivery to the nail bed and making sure patients follow their prescribed courses of action and preventive measures are essential. Overall, this thorough analysis emphasises the intricacy of onychomycosis and the significance of future research in this area to completely comprehend its possible effects and create more effective treatment plans. Patients with onychomycosis, a common nail disorder, now have new hope because to recent breakthroughs in diagnosis and therapy. Researchers and doctors are always working to improve treatment outcomes, safety profiles, and quality of life for people with onychomycosis. This includes anything from new medicines and enhanced diagnostic procedures to nano sponge technology. It's critical to stay current with new developments in the industry and give patients the most efficient, individualised care possible as it continues to change.

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REFERENCES:

1. Gupta AK & Stec N: Recent advances in therapies for onychomycosis and its management. F1000 Research 2019; 8.
2. Vlahovic TC: Onychomycosis: Evaluation, Treatment Options, Managing Recurrence, and Patient Outcomes. Clin Podiatr Med Surg 2016; 33(3): 305–18
3. Lipner SR and Scher RK: Onychomycosis: Treatment and prevention of recurrence. J Am Acad Dermatol 2019; 80(4): 853–67.
4. Leung AK, Lam JM, Leong KF, Hon KL, Barankin B, Leung AA & Wong AH: Onychomycosis: an updated review. Recent Patents on Inflammation & Allergy Drug Discovery 2020; 14(1): 32-45.
5. Gupta AK, Versteeg SG and Shear NH: A practical guide to curing onychomycosis: how to maximize cure at the patient, organism, treatment, and environmental level. Am J Clin Dermatol 2019; 20(1): 123–33.
6. Kaul S, Yadav S & Dogra S: Treatment of dermatophytosis in elderly, children, and pregnant women. Indian Dermatology Online Journal 2017; 8(5): 310.
7. Havlickova B, Czaika VA and Friedrich M: Epidemiological trends in skin mycoses worldwide. Mycoses 2008; 51: 2-15.
8. Weitzman I and Summerbell RC: The dermatophytes. Clin Microbiol Rev 1995; 8: 240-59.
9. Nenoff P, Krüger C, Ginter-Hanselmayer G and Tietz HJ: Mycology - an update. Part 1: Dermatomycoses: Causative agents, epidemiology and pathogenesis. J Dtsch Dermatol Ges 2014; 12: 188-209.
10. Hay RL and Ashbee RH: Fungal Infections. In: Griffiths CEM, editor. Rook's Textbook of Dermatology, 9th ed. New Delhi: Wiley-Blackwell 2016; 32.1-55.
11. Sahoo AK and Mahajan R: Management of tineacorporis, tineacruris, and tineapedis: A comprehensive review. Indian Dermatol Online J 2016; 7: 77-86.
12. Scher RK and Baran R: Onychomycosis in clinical practice: factors contributing to recurrence. Br J Dermatol 2003; 149: 5-9.
13. Scher RK: Onychomycosis is more than a cosmetic problem. Br J Dermatol 1994; 130(43): 15.
14. Sigurgeirsson B and Steingrimsson O: Risk factors associated with onychomycosis. J Eur Acad Dermatol Venereol 2004; 18(1): 48-51.
15. Svejgaard EL and Nilsson J: Onychomycosis in Denmark: prevalence of fungal nail infection in general practice. Mycoses 2004; 47(3-4): 131-5.
16. Lipner SR and Scher RK: Prognostic factors in onychomycosis treatment. Infect Dis Ther 2015; 3(1): 1-6.
17. Ghannoum MA, Hajjeh RA, Scher R, Konnikov N, Gupta AK and Summerbell R: A large-scale North American study of fungal isolates from nails: The frequency of onychomycosis, fungal distribution, and antifungal susceptibility patterns. J Am Acad Dermatol 2000; 43: 641-8.
18. Weinberg JM, Koestenblatt EK, Tutrone W, Tishler HR and Najarian L: Comparison of diagnostic methods in the evaluation of onychomycosis. J Am Acad Dermatol 2003; 49: 193-7.
19. Gianni C, Morelli V, Cerri A, Greco C, Rossini P and Guiducci A: Usefulness of histological examination for the diagnosis of onychomycosis. Dermatology 2001; 202: 283-8.
20. Andrés TS & Alexandro B: Candida onychomycosis: an old problem in modern times. Current Fungal Infection Reports 2020; 14: 209-216.
21. Gupta AK, Venkataraman M & Quinlan EM: Onychomycosis in the Twenty-First Century: An Update on Epidemiology and Diagnosis. In Dermatophytes and Dermatophytoses Cham: Springer International Publishing 2021; 41-64.
22. Hogarty DT, Mackey DA and Hewitt AW: Current state and future prospects of artificial intelligence in ophthalmology: a review. Clin Exp Ophthalmol. 2019; 47(1): 128–39. Https://doi. Org/10.1111/ceo.13381.
23. Dembskey N & Abrahamse H: The efficacy of phototherapy for the treatment of Onychomycosis: an observational study. In Photonics MDPI 2021; 8(9): 350.
24. Rawson TM, Ahmad R, Toumazou C, Georgiou P and Holmes AH: Artificial intelligence can improve decision-making in infection management. Nat Hum Behav 2019; 3: 543–5.
25. Filice R: Deep-learning language-modeling approach for automated, personalized, and iterative radiology-pathology correlation. J Am Coll Radiol 2019 Https://doi.org/10.1016/j. Jacr.2019.05.007.
26. Forlenza GP: Use of artificial intelligence to improve diabetes outcomes in patients using multiple daily injections therapy. Diabetes Technol Ther 2019; 21: 24–8.
27. Falotico JM & Lipner SR: Updated perspectives on the diagnosis and management of onychomycosis. Clinical, Cosmetic and Investigational Dermatology 2022; 1933-1957.

28. Machado DR: Comparação da eficácia dos lasers Erbium-Doped Yttrium Aluminium Garnet (Er: YAG) e Neodymium-Doped Yttrium Aluminum Garnet (ND-YAG) em monoterapia e/ou terapia combinada com antifúngicos tópicos, em relação à monoterapia com antifúngicos tópicos no tratamento da onicomicose: uma revisão sistemática 2021.
29. Leeyaphan C, Suiwongsa B, Komesmuneeborirak P, Kiratiwongwan R, Wongdama S, Prasong W & Bunyaratavej S: Effectiveness and safety of topical amphotericin B in 30% dimethyl sulfoxide cream versus 30% dimethyl sulfoxide cream for nondermatophyte onychomycosis treatment: A pilot study. Indian Journal of Dermatology, Venereology and Leprology 2022; 88(4): 494-499.
30. Giri Y, Behera A, Mohanty B, Pattnaik G & Habibullah SK: Transungual Drug Delivery System for the Topical Treatment of Onychomycosis: A Review. Drug Delivery Letters 2022; 12(1): 2-18.
31. Anandam S & Sateesh K: Dual Dermatophyte Infections in a Young Patient with Onychomycosis from Coastal Karnataka: A Rare Experience. Journal of Medical Sciences and Health 2020; 6(2): 59-62.
32. Garoufalis MG: Total Dystrophic Onychomycosis Successfully Treated with Efinaconazole Topical Solution in Times of Coronavirus Disease of 2019: A Case Study. Journal of the American Podiatric Medical Association 2022; 112(2).
33. Wikanto JR, Wijaya L, Astiarani Y & Regina R: Journal of General-Procedural Dermatology & Venereology Indonesia.
34. Sumbali G & Sharma A: Understanding onychomycosis-a neglected form of cutaneous mycosis.
35. Higham R: Update on Diagnosis, Treatment, and Management of Onychomycosis. Culture 2016; 31(59): 83-100.
36. Amin N, Shenoy MM & Pai V: Clinical and mycological characterization of chronic and recurrent dermatophytes using various staining and microscopic methods. Journal of Pure & Applied Microbiology 2023; 17(4).
37. Hogarty DT, Su JC, Phan K, Attia M, Hossny M, Nahavandi S & Yazdabadi A: Artificial intelligence in dermatology—where we are and the way to the future: a review. American J of Clin Dermatology 2020; 21: 41-47.
38. Gupta AK & Stec N: Recent advances in therapies for onychomycosis and its management. F1000 Research, 2019; 8.
39. Huang T, Zhao Y, He J, Cheng H & Martyniuk CJ: Endocrine disruption by azole fungicides in fish: A review of the evidence. Scie of the Total Envi 2022; 822: 153412.
40. Li X, Lai F, Jiang Z, Li M, Chen Z, Cheng J & Wen F: Effects of inflammation on voriconazole levels: A systematic review. British Journal of Clinical Pharmacology 2022; 88(12): 5166-5182.
41. Mendling W, Atef El Shazly M & Zhang L: Clotrimazole for vulvovaginal candidosis: more than 45 years of clinical experience. Pharmaceuticals 2020; 13(10): 274.
42. Yuen MV, Gianturco SL, Pavlech LL, Storm KD & Mattingly AN: Sulfacetamide sodium monohydrate: Summary Report 2021.
43. Nofal A, Fawzy MM & El-Hawary EE: Successful treatment of resistant onychomycosis with voriconazole in a liver transplant patient. Dermatologic Therapy 2020; 33(6): 14014.
44. Naeimifar A, Samadi A, Ahmad Nasrollahi S, Fattahi A, Ghasemi Z, Azizzadeh-Roodpishi S & Dowlatiy Y: Efinaconazole topical solution 10%: Formulation and efficacy assessment in the treatment of toenail onychomycosis. Mycoses 2020; 63(5): 517-524.
45. Fávero ML, Bonetti AF, Domingos EL, Tonin FS & Pontarolo R: Oral antifungal therapies for toenail onychomycosis: a systematic review with network meta-analysis toenail mycosis: network meta-analysis. Journal of Dermatological Treatment 2022; 33(1): 121-130.
46. Shemer A, Eshel Y, Gupta AK, Farhi R, Haneke E, Daniel, CR & Quinlan EM: Once weekly application of urea 40% and bifonazole 1% leads to earlier nail removal in onychomycosis. Skin Appendage Disorders 2020; 6(5): 304-308.
47. Prakash P, Kunjal KK & Shabaraya A: Dendrimer architecture: A comprehensive review. World Journal of Pharmaceutical Research 2021.
48. Fernández J, del Valle Fernández I, Villar CJ & Lombó F: Combined laser and ozone therapy for onychomycosis in an *in-vitro* and *ex-vivo* model. Plos one 2021; 16(6): e0253979.
49. Morton CA, Szeimies RM, Basset-Séguin N, Calzavara-Pinton PG, Gilaberte Y, Haedersdal M & Braathen LR: European Dermatology Forum guidelines on topical photodynamic therapy 2019 Part 2: emerging indications–field cancerization, photorejuvenation and inflammatory/infective dermatoses. Journal of the European Academy of Dermatology and Venereology 2020; 34(1): 17-29.
50. Piraccini BM, Iorizzo M, Lencastre A, Nenoff P & Rigopoulos D: Ciclopirox hydroxypropyl chitosan (HPCH) nail lacquer: a review of its use in onychomycosis. Dermatology and Therapy 2020; 10: 917-929.
51. Garg A, Sharma GS, Goyal AK, Ghosh G, Si SC & Rath G: Recent advances in topical carriers of anti-fungal agents. Heliyon 2020; 6(8).
52. Jacobs SE, Zagaliotis P & Walsh TJ: Novel antifungal agents in clinical trials. F1000 Research 2021; 10.
53. Deng J, Wei W, Chen Z, Lin B, Zhao W, Luo Y & Zhang X: Engineered liver-on-a-chip platform to mimic liver functions and its biomedical applications: A review. Micromachines 2019; 10(10): 676.
54. Mehrandish S & Mirzaeei S: A review on ocular novel drug delivery systems of antifungal drugs: functional evaluation and comparison of conventional and novel dosage forms. Adv Pharmaceut Bulletin 2021; 11(1): 28.
55. Thatai P & Sapra B: Terbinafine hydrochloride nail lacquer for the management of onychomycosis: Formulation, characterization and *in-vitro* evaluation. Therapeutic Delivery 2018; 9(2): 99-119.
56. Plotino G, Grande NM & Mercade M: Photodynamic therapy in endodontics. International Endodontic Journal 2019; 52(6): 760-774.

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