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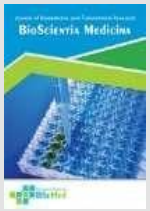

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Menthol-Camphor-Thymol-Eucalyptus Compound as a Novel Adjuvant Therapy in Fluconazole-Treated *Candida parapsilosis* Onychomycosis: A Case Report

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A B S T R A C T

Background: Onychomycosis, a fungal infection of the nail apparatus, presents a therapeutic challenge due to its recalcitrant nature and the limitations of current antifungal regimens, including potential side effects and prolonged treatment durations. *Candida parapsilosis* is an increasingly recognized, yet less commonly reported, yeast pathogen in onychomycosis, particularly in immunocompromised individuals or those with specific comorbidities. The exploration of effective, safe, and accessible adjuvant therapies is crucial to enhance treatment outcomes. This report details the use of an over-the-counter menthol-camphor-thymol-eucalyptus compound as an adjuvant to oral fluconazole. **Case presentation:** A 69-year-old male, a gold washer by occupation with a two-month history of rheumatoid arthritis (RA) treated with methotrexate, hydroxychloroquine, methylprednisolone, and celecoxib, presented with a four-month history of yellowish-brown discoloration, uneven texture, and brittleness of both thumb nails. Dermatological examination revealed onychodystrophy, subungual hyperkeratosis, and yellowish-brown discoloration of the bilateral thumb nail plates. Dermoscopy confirmed these findings. Fungal culture of nail clippings identified *Candida parapsilosis*. The patient was treated with oral fluconazole 150 mg weekly for three months and twice-daily topical application of menthol-camphor-thymol-eucalyptus compound under plastic occlusion. Significant clinical improvement in nail color and texture, with no onycholysis, was observed at the 6-week follow-up. At the 3-month evaluation, fungal culture was negative, and liver function tests remained within normal limits. **Conclusion:** This case demonstrates the successful use of a menthol-camphor-thymol-eucalyptus compound as an adjuvant to oral fluconazole in treating *Candida parapsilosis* onychomycosis in an elderly patient with RA. The combination therapy was well-tolerated and led to clinical and mycological resolution, suggesting a promising, accessible, and cost-effective adjunctive therapeutic strategy.

1. Introduction

Onychomycosis, a fungal infection affecting the nail plate, nail bed, or matrix, stands as one of the most prevalent nail disorders encountered in dermatological practice, accounting for up to 50% of all onychopathies and affecting approximately 10-14% of the general population globally, with prevalence rates varying by geographic location, age, and underlying health conditions. While dermatophytes, particularly *Trichophyton rubrum*, are the most frequently implicated pathogens, yeast species, primarily *Candida albicans* and, increasingly, non-albicans *Candida* species such as *Candida parapsilosis*, are significant contributors, especially in fingernail onychomycosis, immunocompromised individuals, and those with chronic diseases or occupational exposures involving frequent hand immersion in water. *Candida parapsilosis*, recognized for its ability to form robust biofilms and its variable susceptibility to antifungal agents, can pose unique

therapeutic challenges.[1,2]

The clinical presentation of onychomycosis is diverse, ranging from nail discoloration (white, yellow, brown, or black), subungual hyperkeratosis, onycholysis (separation of the nail plate from the nail bed), to onychodystrophy, causing not only cosmetic disfigurement but also pain, discomfort, and impaired dexterity, significantly impacting patients' quality of life. In individuals with comorbidities such as diabetes mellitus, peripheral vascular disease, or immunosuppression (due to autoimmune diseases like rheumatoid arthritis or medications such as corticosteroids and methotrexate), onychomycosis can lead to more severe complications, including secondary bacterial infections, cellulitis, and an increased risk of ulceration, particularly in the feet.[3,4]

Current therapeutic modalities for onychomycosis primarily involve oral and topical antifungal agents. Systemic therapies, including terbinafine, itraconazole, and fluconazole, generally offer higher cure rates but are associated with potential adverse effects, such as gastrointestinal disturbances, skin reactions, drug interactions, and, rarely, hepatotoxicity, necessitating careful patient selection and monitoring. Fluconazole, a triazole antifungal, inhibits fungal cytochrome P450 enzyme 14α-demethylase, which is crucial for ergosterol biosynthesis, a vital component of the fungal cell membrane. While effective against *Candida* species, its efficacy in onychomycosis, when used as monotherapy, can be variable, often requiring prolonged treatment courses of 6-9 months for fingernail infections. Topical treatments, such as ciclopirox, amorolfine, efinaconazole, and tavaborole, have a better safety profile but are often limited by poor nail plate penetration and lower efficacy, particularly in moderate to severe cases or those with matrix involvement. The long duration of therapy for both oral and topical agents contributes to issues with patient compliance and increases the overall cost of treatment.[5,6]

Given these limitations, there is a compelling need for adjunctive therapies that can enhance the efficacy of standard treatments, shorten treatment duration, reduce the risk of relapse, and improve patient safety and adherence. Complementary and alternative medicine (CAM) approaches, including the use of natural products with antifungal properties, have garnered increasing interest. Vicks VapoRub® (Procter & Gamble), an over-the-counter topical ointment traditionally used for cough and cold symptoms, contains a combination of active ingredients including camphor (4.8%), menthol (2.6%), eucalyptus oil (1.2%), and inactive ingredients such as cedarleaf oil, nutmeg oil, petrolatum, thymol, and turpentine oil. Several of these components, notably thymol, menthol, camphor, and eucalyptus oil, have been individually reported to possess antifungal properties in vitro and, in some preliminary clinical investigations, have shown promise in the treatment of onychomycosis. Thymol, a constituent of thyme oil, has demonstrated broad-spectrum antimicrobial activity, including fungicidal effects against *Candida* species, potentially by disrupting fungal cell membrane integrity and ergosterol biosynthesis. Menthol, derived from peppermint oil, also exhibits antifungal activity and has been suggested to enhance the efficacy of oral antifungals synergistically against *Candida* species, possibly by improving drug penetration or modulating fungal cell responses. Eucalyptus oil has also been explored for its antifungal effects. Pilot studies and case series have suggested that daily application of Vicks VapoRub® can lead to clinical and mycological improvement in onychomycosis, with minimal side effects reported.[7,8]

The novelty of this case report lies in presenting the successful use of Vicks VapoRub® as an adjunctive therapy to standard systemic treatment with oral fluconazole specifically for onychomycosis caused by *Candida parapsilosis*, a less commonly detailed pathogen in such adjunctive approaches, in an elderly patient with rheumatoid arthritis, a comorbidity that can complicate both the fungal infection and its management.[9,10] This study aimed to meticulously document the clinical and mycological response to this combination therapy, evaluate its safety profile in this

specific patient context, and discuss the potential rationale and implications of using this accessible menthol-camphor-thymol-eucalyptus compound as an adjuvant in the comprehensive management of challenging *Candida* onychomycosis. This report seeks to contribute to the growing body of evidence exploring integrative approaches to optimize onychomycosis treatment outcomes.

2. Case Presentation

A 69-year-old Indonesian male presented to the Dermatology and Venereology Polyclinic at Dr. Moewardi Regional General Hospital, Surakarta, with a chief complaint of progressive discoloration and changes in the texture of his right and left thumb nails over the preceding four months. The patient reported that the condition initiated with a yellowish-white discoloration at the lateral edge of the left thumbnail, which subsequently evolved into a more pronounced yellowish-brown hue and gradually spread to involve a significant portion of the nail plate. Similar changes later appeared on his right thumbnail. He also noted that the affected nails had become uneven, rough-surfaced, and increasingly brittle, causing him aesthetic concern and some discomfort during daily activities. He denied any associated pain, itching, or discharge from the affected nails or surrounding skin, and there were no symptoms such as redness or swelling in other parts of his body. The patient had not sought any prior medical consultation or attempted any specific treatment for this nail condition. The worsening appearance and spread of the discoloration prompted him to seek dermatological evaluation.

The patient's medical history was significant for rheumatoid arthritis (RA), diagnosed approximately two months prior to this presentation. His RA was being managed by the internal medicine department with a regimen consisting of oral methylprednisolone 4 mg daily, hydroxychloroquine 200 mg daily, methotrexate 10 mg once weekly, and celecoxib 200 mg daily as needed for pain. His rheumatology report indicated a rheumatoid factor of >16 IU/mL (reference range <8 IU/mL). He denied any history of hypertension, diabetes mellitus, or allergies to medications or food. The patient was a gold washer by profession, a job he had performed for many years, which involved frequent and prolonged contact of his hands with water and metallic substances, often without the use of protective gloves. He also had a 10-year history of active cigarette smoking but denied alcohol consumption. There was no family history of similar nail conditions or psoriasis.

On physical examination, the patient appeared in mild discomfort, was conscious, and oriented. His vital signs were: blood pressure 110/70 mmHg, heart rate 88 beats/minute, respiratory rate 20 breaths/minute, and temperature 36.2°C. His body weight was 60 kg and height was 170 cm, corresponding to a body mass index (BMI) of 20.8 kg/m^2 (normoweight). Dermatological examination focused on the hands revealed significant changes in the nails of both thumbs (digiti I manus bilateral). There was evident onychodystrophy, characterized by a malformed and lusterless nail plate. Subungual hyperkeratosis, presenting as a thickened accumulation of debris beneath the distal nail plate, was noted. A prominent yellowish-brown discoloration affected a substantial area of both thumb nail plates, extending from the distal and lateral edges proximally. The nail surfaces felt rough and appeared brittle. No signs of active paronychia, such as erythema, swelling, or tenderness of the periungual tissues, were observed. The remaining fingernails and toenails appeared clinically unaffected. Examination of the skin and oral mucosa did not reveal any other significant lesions. Initial laboratory investigations included a complete blood count, which was within normal limits, and liver function tests (LFTs) to establish a baseline before considering systemic antifungal therapy. Serum glutamic oxaloacetic transaminase (SGOT) was 21 U/L (reference range <35 U/L), and serum glutamic pyruvic transaminase (SGPT) was 22 U/L (reference range <45 U/L), both within the normal range.

To further evaluate the nail changes, several diagnostic procedures were performed. Dermoscopy of

the affected thumb nails revealed features suggestive of onychomycosis, including subungual hyperkeratosis and the characteristic yellowish-brown discoloration of the nail plate. Direct microscopic examination of nail scrapings prepared with 20% potassium hydroxide (KOH) solution, observed under 40x magnification, did not reveal the presence of hyphae or pseudohyphae. For fungal culture, nail clippings were collected aseptically from the affected thumb nails and inoculated onto Sabouraud Dextrose Agar (SDA) with chloramphenicol and cycloheximide. After incubation at 25–30°C for two weeks, macroscopic examination of the culture plates showed the growth of creamy, white, smooth colonies. Microscopic examination of these colonies (using lactophenol cotton blue stain, 10x magnification) revealed the presence of yeast cells and pseudohyphae, consistent with *Candida* species. The growth was identified as *Candida parapsilosis*. A nail biopsy was also performed, and the specimen was sent for histopathological examination with Periodic Acid-Schiff (PAS) staining. The PAS stain, observed under 10x magnification, did not reveal any fungal spores or hyphae.

Based on the clinical presentation, occupational history, dermoscopic findings, and positive fungal culture for *Candida parapsilosis*, a diagnosis of onychomycosis of both thumb nails due to *Candida parapsilosis* was established. The differential diagnoses considered included psoriatic nails and lichen planus of the nails, particularly given the patient's autoimmune comorbidity (RA). However, the positive fungal culture strongly favored onychomycosis. The patient's clinical and diagnostic findings are summarized in Table 1.

Table 1. Summary of patient's baseline clinical and diagnostic findings.

Parameter	**Finding**
Age / Gender	69 years / Male
Occupation	Gold washer
Relevant medical history	Rheumatoid Arthritis (RA) for 2 months. Rheumatoid factor >16 IU/mL.
RA medications	Methylprednisolone 4 mg/day, Hydroxychloroquine 200 mg/day, Methotrexate 10 mg/week, Celecoxib 200 mg/day
Presenting complaint	Yellowish-brown discoloration, uneven texture, brittleness of bilateral thumb nails for 4 months
Dermatological examination	Bilateral thumb nails: Onychodystrophy, subungual hyperkeratosis, yellowish-brown discoloration
Dermoscopy findings	Subungual hyperkeratosis, yellowish-brown discoloration of nail plate
Mycological investigations	
- KOH (20%) microscopy	Negative for hyphae/pseudohyphae (40x)
- Fungal culture (SDA)	Positive: *Candida parapsilosis* (creamy, white colonies)
- Nail biopsy (PAS Stain)	Negative for fungal elements (10x)
Baseline liver function tests	SGOT: 21 U/L (normal), SGPT: 22 U/L (normal)

Interpreting Table 1, we observe a constellation of factors that contribute to the clinical picture and inform the diagnostic process for this 69-year-old male patient. His advanced age and occupation as a gold washer are recognized predisposing elements for onychomycosis due to increased susceptibility and exposure. Critically, his recent diagnosis of rheumatoid arthritis, coupled with a treatment regimen including potent immunosuppressants like methotrexate and methylprednisolone, significantly heightened his risk for opportunistic fungal infections. The presenting complaints of nail discoloration and dystrophy localized to the thumb nails, developing over four months, are classical for onychomycosis. The

dermatological and dermoscopic examinations corroborated these symptoms, identifying key signs such as onychodystrophy, subungual hyperkeratosis, and pronounced yellowish-brown discoloration. While initial direct microscopy (KOH) and nail biopsy (PAS stain) did not yield evidence of fungal elements, a common occurrence that can be attributed to sampling variability or low fungal load in the specific sample, the fungal culture definitively identified *Candida parapsilosis* as the etiological agent. This specific pathogen is noteworthy in the context of potential immunosuppression. Importantly, baseline liver function tests were within normal limits, permitting the safe consideration of systemic antifungal therapy. Collectively, the information in Table 1 paints a comprehensive picture of an elderly, immunocompromised patient with occupationally-influenced onychomycosis caused by *Candida parapsilosis*, guiding the subsequent therapeutic decisions. The patient was commenced on a treatment regimen as detailed in Table 2.

Table 2. Summary of treatment and follow-up.

Parameter	**Details**
Diagnosis	Onychomycosis of bilateral thumb nails due to *Candida parapsilosis*
Systemic treatment	Oral Fluconazole 150 mg, single dose per week for 3 months
Topical adjuvant treatment	Vicks VapoRub® ointment applied generously twice daily (morning and evening) to affected thumb nails
- Occlusion	Plastic cling wrap over treated nails after evening application
- Duration	3 months
Non-pharmacological advice	Nail hygiene, avoid trauma, use protective gloves during work, and adhere to treatment
Follow-up	
Week 6	
- Clinical outcome	Noticeable improvement: lightened discoloration, new healthy proximal nail growth, smoother texture, no onycholysis
- Adherence & tolerability	Good adherence reported, no local or systemic side effects from Vicks VapoRub® or fluconazole
Month 3 (End of Treatment)	
- Clinical outcome	Continued significant improvement: majority of nail plates healthy, minimal distal discoloration, smooth surface, restored integrity, no subungual hyperkeratosis (Lampiran C in source)
- Mycological outcome (Repeat)	
- Fungal culture (SDA)	Negative for fungal growth
- KOH (20%) microscopy	Negative for fungal elements
- Liver function tests (Repeat)	SGOT: 24 U/L (normal), SGPT: 19 U/L (normal)
- Adverse effects reported	None throughout the 3-month treatment course

Interpreting Table 2, the therapeutic strategy for this patient diagnosed with *Candida parapsilosis* onychomycosis involved a dual approach: systemic antifungal medication supplemented by a topical adjuvant, alongside crucial non-pharmacological advice. Oral fluconazole, administered at a standard weekly dose of 150 mg for three months, targeted the infection systemically. This was innovatively combined with twice-daily topical application of Vicks VapoRub®, with overnight occlusion using plastic cling wrap to maximize penetration and efficacy over the same three-month period. The patient's adherence to lifestyle modifications, such as maintaining nail hygiene and using protective gloves, was also emphasized to support recovery and prevent recurrence. The follow-up assessments demonstrated a highly favorable response to this regimen. As early as week 6, significant clinical improvement was evident, with nails showing healthier new growth and reduced discoloration, and importantly, no adverse

effects were reported, indicating good tolerability. By the end of the three-month treatment period, the clinical outcome was marked, with nails appearing largely normal and healthy. This clinical success was strongly corroborated by mycological cure, evidenced by negative results on both repeat fungal culture and KOH microscopy. Furthermore, liver function tests remained stable and within normal limits throughout the treatment, confirming the safety of the systemic fluconazole component in this individual. The complete absence of reported adverse effects over the entire treatment duration underscores the excellent safety profile of this combined therapeutic approach in this specific case. This structured treatment and diligent follow-up led to a successful resolution of a challenging onychomycosis case.

3. Discussion

This case report details the successful management of *Candida parapsilosis* onychomycosis affecting the thumb nails of a 69-year-old male with concomitant rheumatoid arthritis, using a combination of oral fluconazole and an adjunctive topical menthol-camphor-thymol-eucalyptus compound (Vicks VapoRub®). The outcome, characterized by both clinical resolution and mycological cure after three months of therapy with no adverse effects, highlights a potentially valuable therapeutic strategy for this often challenging nail infection, particularly in a patient with underlying immunosuppressive factors.[11,12]

Onychomycosis, a persistent and often unsightly fungal infection of the nail unit, represents a significant burden to patients and a common challenge in dermatological practice. Its epidemiology is marked by a global distribution, with prevalence rates that demonstrate considerable variation influenced by climatic conditions, cultural practices, socioeconomic factors, and the demographic profile of populations. Generally, it is estimated to affect a substantial portion of the adult population, with figures often cited between 10% and 14%, and this prevalence demonstrably increases with age. This age-related increase is attributed to several factors inherent to the aging process, including reduced peripheral circulation which impairs nutrient delivery and immune surveillance in the distal extremities, slower nail growth rates which allow more time for fungal colonization and invasion, increased nail plate thickness and brittleness providing a more susceptible substrate, a higher cumulative lifetime exposure to fungal pathogens, and a greater likelihood of comorbidities such as diabetes mellitus and peripheral vascular disease that further compromise nail health and immunity. In this particular case, the patient's age of 69 years aligns perfectly with this established epidemiological trend, immediately categorizing him within a higher-risk demographic for onychomycosis development. Beyond age, his occupation as a gold washer introduced a significant environmental and behavioral risk factor. Such occupations often involve chronic exposure of the hands and nails to moisture, alkaline substances, or abrasive materials. Prolonged hydration of the nail plate can disrupt its integrity, making it more permeable to fungal elements. Microtrauma, whether overt or subclinical, from handling materials can create portals of entry for fungi. The moist environment itself is highly conducive to fungal proliferation. These occupational hazards are well-documented contributors to onychomycosis, particularly of the fingernails.[13,14]

The pathophysiology of nail invasion by fungi is a complex process involving fungal adherence to the nail surface, penetration into the keratinous structure, and subsequent proliferation within the nail plate, bed, or matrix. Fungi possess an array of virulence factors that facilitate this process. These include the production of keratinolytic enzymes (keratinases, proteases, lipases) that can degrade the dense keratin network of the nail, allowing the fungus to obtain nutrients and physically invade the tissue. Adhesins on the fungal cell surface mediate attachment to host cells and keratin. For *Candida* species, the ability to switch between yeast and hyphal or pseudohyphal forms is a key virulence factor; the yeast form may be important for dissemination, while the (pseudo)hyphal

forms are typically more invasive. Furthermore, many fungi, including *Candida parapsilosis*, are capable of forming biofilms on biotic and abiotic surfaces, including the nail plate. Biofilms are structured communities of microorganisms encased in a self-produced extracellular polymeric matrix. This matrix protects the fungi from host immune responses, antifungal agents, and desiccation, contributing significantly to the chronicity and recalcitrance of onychomycosis. *Candida parapsilosis*, the specific pathogen identified in this case, is an opportunistic yeast that has gained prominence as a cause of various human infections, including onychomycosis. It is part of the normal human skin flora but can become pathogenic under certain conditions. Its prevalence in onychomycosis varies geographically but it is often ranked as the second or third most common *Candida* species isolated, after *C. albicans*. *C. parapsilosis* exhibits several characteristics that contribute to its pathogenicity in the nail unit, including effective adherence to host tissues, the secretion of hydrolytic enzymes like aspartyl proteases and lipases, and a notable capacity for biofilm formation. These biofilms are particularly problematic as they can confer increased resistance to many standard antifungal drugs, making infections harder to eradicate. Infections with *C. parapsilosis* are frequently observed in individuals with compromised immune systems or those with indwelling medical devices, but it can also cause infections in immunocompetent individuals, especially if there is preceding trauma or chronic moisture exposure to the nails.[15,16]

A critical aspect of this case is the patient's concomitant diagnosis of rheumatoid arthritis (RA) and his ongoing treatment with immunosuppressive medications. RA is a chronic systemic autoimmune disease characterized by inflammation of the synovial joints, but it also has extra-articular manifestations and is associated with immune dysregulation that can affect the body's ability to combat infections. The immune system in RA patients is characterized by an overactive response against self-antigens, involving T cells, B cells, and pro-inflammatory cytokines. Paradoxically, this state of chronic inflammation and immune activation can be accompanied by a reduced efficacy in clearing certain pathogens. More significantly, the therapeutic agents used to manage RA are often designed to suppress these overactive immune responses, thereby increasing the risk of various infections. In this patient's regimen, methotrexate, a cornerstone in RA treatment, is a folate antagonist that inhibits DNA synthesis and has broad immunosuppressive effects, reducing lymphocyte proliferation and inflammatory cytokine production. Methylprednisolone, a corticosteroid, has potent anti-inflammatory and immunosuppressive actions, affecting the function of neutrophils, macrophages, and T lymphocytes, and decreasing the production of multiple inflammatory mediators. Hydroxychloroquine, while considered an immunomodulator with a better safety profile regarding infections compared to methotrexate or corticosteroids, can also influence immune cell function. The combined effect of these medications, particularly methotrexate and methylprednisolone, creates a state of iatrogenic immunosuppression that renders patients more vulnerable to opportunistic fungal pathogens like *Candida parapsilosis*. This context of immunosuppression is a crucial factor in both the development of his onychomycosis and the considerations for its management, as achieving a cure can be more challenging, and the risk of relapse may be higher.[17,18]

The diagnosis of onychomycosis, while often suspected clinically, ideally relies on laboratory confirmation to identify the causative pathogen and differentiate it from non-fungal nail dystrophies. In this case, while initial KOH microscopy and PAS staining were negative, fungal culture successfully identified *Candida parapsilosis*. The negativity of KOH and PAS, despite a positive culture, can occur for several reasons. KOH microscopy, though rapid and inexpensive, has variable sensitivity (often reported between 48% and 80%) depending on the quality of the sample, the experience of the microscopist, and the

specific location of viable fungi within the nail. If the fungal load in the scraped material is low or if the fungi are not actively producing easily identifiable elements like hyphae at the site of scraping, a false negative can result. PAS staining of a nail biopsy is generally more sensitive than KOH, as it can detect non-viable fungal elements and spores embedded within the nail plate keratin. However, sampling error is a significant factor; if the biopsy punch does not capture an area of active infection or sufficient fungal density, it too can yield a false negative. The presence of a positive culture, however, provides definitive evidence of viable fungal organisms and allows for species identification, which can be important for guiding therapy, as different fungal species may exhibit varying susceptibilities to antifungal agents.[19,20]

The choice of oral fluconazole (150 mg weekly) as the systemic antifungal backbone in this case was appropriate for a *Candida* species infection. Fluconazole is a bis-triazole antifungal agent that exerts its effect by inhibiting fungal cytochrome P450 enzyme 14α-demethylase. This enzyme is critical in the fungal sterol biosynthesis pathway, responsible for converting lanosterol to ergosterol. Ergosterol is the primary sterol in the fungal cell membrane, analogous to cholesterol in mammalian cells, and is essential for maintaining membrane integrity, fluidity, and the function of membrane-bound enzymes. Inhibition of 14α-demethylase leads to a depletion of ergosterol and an accumulation of toxic methylated sterol precursors, such as lanosterol. This disrupts the fungal cell membrane structure and function, leading to increased permeability, leakage of cellular contents, and ultimately, inhibition of fungal growth and replication (fungistatic effect). Fluconazole is well-absorbed orally, with bioavailability exceeding 90%, and it distributes widely into body tissues and fluids, including the skin and nails. It penetrates the nail plate primarily via the nail matrix and, to a lesser extent, the nail bed. Detectable concentrations in the nail plate persist for several weeks after discontinuation of therapy. For *Candida* onychomycosis, particularly of the fingernails, fluconazole is typically administered for 6 to 9 months, or until the affected nail has grown out completely clear. Mycological cure rates with fluconazole monotherapy for onychomycosis caused by yeasts have been reported in the range of 40-70%, depending on the specific study, patient population, and duration of treatment. While generally well-tolerated, potential side effects include gastrointestinal upset (nausea, vomiting, diarrhea, abdominal pain), headache, and skin rash. Hepatotoxicity is a rare but serious concern, necessitating baseline and periodic monitoring of liver function tests during prolonged therapy, as was prudently done in this case.

The decision to incorporate Vicks VapoRub® as an adjunctive topical therapy was an innovative aspect of this patient's management. The rationale for using adjuvant therapies in onychomycosis is multifaceted: to potentially increase the overall cure rate, accelerate the clinical response, shorten the duration of systemic therapy (thereby reducing cumulative drug exposure and risk of side effects), overcome antifungal resistance, and improve patient compliance and satisfaction. Vicks VapoRub® contains several active and inactive ingredients, with camphor, menthol, and eucalyptus oil listed as active, and thymol present as an inactive ingredient (though possessing known bioactivity). Thymol, this phenolic compound, a major constituent of thyme oil (*Thymus vulgaris*), is renowned for its potent and broad-spectrum antimicrobial properties. Its antifungal mechanism is primarily attributed to its ability to interact with and disrupt the fungal cell membrane. Thymol's lipophilic nature allows it to partition into the lipid bilayer of the fungal membrane, increasing its fluidity and permeability. This leads to the leakage of intracellular ions (such as K^+ and Ca^{2+}) and essential molecules, and impairment of membrane-bound enzymes, ultimately causing cell death. Furthermore, thymol has been shown to interfere with ergosterol biosynthesis, inhibit fungal respiration, and disrupt mitochondrial function. It can also inhibit the formation of fungal biofilms and reduce the production of fungal toxins and enzymes. Numerous *in vitro*

studies have demonstrated its efficacy against a wide range of fungi, including dermatophytes and various *Candida* species, including *C. albicans* and *C. parapsilosis*. Its activity against *Candida* biofilms is particularly relevant for infections like onychomycosis.

Menthol, A cyclic monoterpene alcohol found predominantly in peppermint oil, menthol is widely used for its cooling and analgesic effects. However, it also possesses significant intrinsic antifungal activity. Menthol's lipophilic character allows it to penetrate biological membranes. Its antifungal action is thought to involve the disruption of fungal cell membrane integrity and function, similar to other terpenes. It can alter membrane fluidity, inhibit membrane-bound enzymes (such as ATPase), and affect ion transport. Some studies suggest that menthol can also interfere with mitochondrial respiration and calcium homeostasis in fungal cells. Importantly, menthol has been reported to exhibit synergistic effects when combined with conventional antifungal drugs, such as azoles. This synergy may arise from menthol increasing the permeability of the fungal cell membrane to the co-administered antifungal, or by inhibiting fungal efflux pumps that contribute to drug resistance. Menthol might also enhance the penetration of other topical agents through the dense keratin of the nail plate due to its solvent properties. Camphor, Derived from *Cinnamomum camphora*, camphor is a cyclic ketone. Traditionally used as a topical analgesic, rubefacient, and antipruritic, its direct antifungal activity is generally considered less potent than that of thymol or menthol. However, some studies have indicated moderate antimicrobial effects. Its contribution in a topical formulation like Vicks VapoRub® might also relate to its ability to act as a penetration enhancer, facilitating the delivery of other active compounds into the nail. The sensation it produces might also improve patient perception of treatment activity. Eucalyptus Oil, The essential oil obtained from *Eucalyptus* species, primarily *Eucalyptus globulus*, contains 1,8-cineole (eucalyptol) as its main active constituent. Eucalyptus oil has a long history of use in traditional medicine for its antiseptic, anti-inflammatory, and expectorant properties. It has also demonstrated considerable antifungal activity against a variety of fungal species, including those implicated in onychomycosis. The antifungal mechanisms of eucalyptus oil and 1,8-cineole are thought to involve damage to the fungal cell wall and cell membrane, leading to increased permeability and leakage of cellular contents. It may also inhibit fungal sporulation and mycelial growth. Some research suggests it can disrupt mitochondrial function and interfere with fungal enzyme systems.

The combination of these ingredients within the petrolatum base of Vicks VapoRub® likely provides a multi-target antifungal effect. The petrolatum base itself, while inert, acts as an occlusive vehicle. Occlusion hydrates the nail plate by trapping transepidermal water loss. A hydrated nail plate is softer and more permeable than a dry one, which can significantly enhance the penetration of topically applied active substances through the dense keratin layers. The use of additional plastic cling wrap occlusion, particularly overnight as employed in this case, further maximizes this hydrating and penetration-enhancing effect. This strategy aims to increase the concentration of the antifungal components directly at the site of infection within the nail.

The clinical response observed in this patient was notably positive and relatively rapid. Significant improvement by the 6-week mark, with progression to clinical and mycological cure by 3 months, is a favorable outcome for onychomycosis, especially considering the typical timelines for systemic therapy alone. This outcome suggests that the adjunctive topical Vicks VapoRub® indeed contributed to the efficacy of oral fluconazole. The potential mechanisms for this beneficial interaction are likely several-fold: a direct antifungal effect of the VapoRub® components on *C. parapsilosis* within the nail plate, enhanced penetration of these topical components due to occlusion, and possibly even improved local bioavailability or action of the systemically administered fluconazole due to changes in nail plate

hydration or local environment. The absence of any local or systemic adverse effects throughout the treatment period further underscores the tolerability of this combined approach.

Comparing this outcome with literature, previous studies on Vicks VapoRub® as a monotherapy for onychomycosis reported cure rates that were modest but clinically significant, particularly in terms of symptomatic improvement. The use here as an *adjuvant* to a proven systemic antifungal (fluconazole) likely leverages the benefits of both modalities – the widespread systemic distribution of fluconazole targeting the infection from the matrix and nail bed, complemented by the direct, localized, multi-component antifungal assault from the topical preparation on the nail plate. The successful outcome in this patient, who had risk factors for poorer treatment response (advanced age, immunosuppressive therapy for RA, chronic moisture exposure), makes the findings even more compelling. The multi-component nature of Vicks VapoRub® may also offer an advantage by providing multiple mechanisms of action against the fungus, potentially reducing the likelihood of resistance development compared to single-agent topical therapies. The psychological benefit of an active topical application, providing a sense of direct engagement with the treatment, can also contribute to improved patient adherence, which is a critical factor in the long-term management of onychomycosis. The affordability and over-the-counter availability of Vicks VapoRub® also make it an attractive option, especially in resource-constrained settings or for patients seeking cost-effective adjunctive care. The resolution of *Candida parapsilosis* infection specifically is significant, as non-albicans *Candida* species can sometimes exhibit variable susceptibility patterns to azole antifungals. The combination approach may have provided a sufficiently robust antifungal pressure to overcome any potential reduced susceptibility. The patient's diligent adherence to non-pharmacological advice, such as wearing gloves during his work, would also have played a role by minimizing continuous exposure to moisture and potential re-inoculation with fungal elements, thereby supporting the efficacy of the pharmacological interventions.

4. Conclusion

This case report compellingly illustrates the successful clinical and mycological eradication of *Candida parapsilosis* onychomycosis affecting the thumb nails of an elderly male patient with concurrent rheumatoid arthritis managed with immunosuppressive therapy. The favorable outcome was achieved using a three-month regimen of weekly oral fluconazole 150 mg, significantly augmented by the twice-daily topical application of an over-the-counter menthol-camphor-thymol-eucalyptus compound (Vicks VapoRub®) under nocturnal occlusion. This combined therapeutic strategy not only resulted in a complete cure within a relatively short timeframe for onychomycosis but was also exceptionally well-tolerated, with no reported local or systemic adverse events and stable liver function throughout the treatment course. The findings from this case highlight the potential of this accessible and cost-effective topical preparation to serve as a powerful adjuvant to standard systemic antifungal therapy. The multi-component nature of the topical agent, with its constituents possessing known antifungal, penetration-enhancing, and possibly synergistic properties, likely contributed significantly to the observed efficacy, particularly in a patient with multiple risk factors for persistent or recurrent infection. This approach offers a practical and promising avenue for enhancing treatment outcomes in *Candida* onychomycosis, potentially shortening treatment durations, improving patient adherence, and reducing the overall burden associated with this common and often recalcitrant nail disorder. The positive experience documented herein strongly encourages further systematic investigation into this combination therapy to more definitively establish its role and benefits in the broader management of onychomycosis.

5. References

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