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Mini Review

Ringworm Disease- Causes, Diagnosis and Treatment: AMYCOT®, a Novel Natural Treatment for Ringworm and other Tinea Infections

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Abstract

Ringworm is a frequently encountered infection commonly known as tinea. Most topical treatments are chemical-based and typically work against mild tinea infections, but are not effective in treating severe cases. There are a few potent oral chemical drugs against severe tinea including nail fungal (onychomycosis) infections, but they have serious toxic side effects like liver damage which have been known to result in deaths. Chemical-based anti-fungals are contraindicated for pregnant and breast-feeding women. Topical treatments based on natural products exist and are preferred but they are generally not supported by sufficient clinical evidence on efficacy and safety. An exception is AMYCOT®, a novel extract derived from Spirulina, a cyanobacterium or blue-green algae used as a food supplement for centuries. It has shown positive outcomes in a randomized double-blind, placebo-controlled clinical trial, as a natural alternative for the treatment of ringworm and onychomycosis.

ABBREVIATIONS

MIC: Minimum Inhibitory Concentration; USFDA: United States Food and Drug Administration

INTRODUCTION

Ringworm or dermatophytosis is a superficial fungal infection of the hair, skin, or nails caused by dermatophytes that typically belong to the genera *Tricophyton, Microsporum or Epidermophyton*. The common manifestations of dermatophytoses are *Tinea capitis*, *Tinea pedis*, and *Tinea unguium* or onychomycosis [1]. Ringworm is the most common type of fungal infection, adversely affecting the quality of life of individuals across all age groups, estimated to affect 20-25% of the global population [2-4].

Chemical-based anti-fungals and their limitations

Anti-fungal drugs involve varied mechanisms of action. They interfere with or affect the synthesis of membrane/cell-wall components (echinocandins), membrane permeability (amphoterecin-B, azoles, allylamines), synthesis of nucleic acids (flucytosine), and/or microtubule/mitotic spindle function (griseofulvin) [5,6]. Generally, agents which disrupt the cell wall/membrane are fungicidal and therefore lethal while inhibitors of fungal cell division are fungistatic or simply keep fungal growth on hold. The fungicidal property of anti-fungals also apparently depends on MIC. Of the eleven (11) agents tested, only amphotericin B, mulundocandin and aculeacin showed fungicidal activity at concentrations close to the MIC; the rest comprising the majority were fungicidal only at concentrations much higher than the MIC [7]. Although the previous study was tested with *Candida albicans*, similar observations were seen with other dermatophytes [8,9].

Dermatophytosis requires long-term therapy usually with allylamines (e.g., terbinafine) and azoles (e.g. ketoconazole, miconazole) [2]. Early stage dermatophytosis is often successfully treated with topical fungistatic agents based on the aforementioned chemical –based antifungal agents. However, if not immediately and properly treated, these infections may become chronic, requiring oral fungicidal drugs, which are often associated with hepatotoxicity [10]. Furthermore, complications like bacterial super infection, lichenification and maceration can occur. Therefore, dermatophytosis should be treated promptly and effectively [11]. Of all the types of dermatophytoses, onychomycosis remains resistant to most anti-fungal therapies. Onychomycosis can develop from untreated tinea whereby infection spreads to the nail from the infected feet or hands. A number of currently available topical therapies are not effective not only because of poor penetrability into the nail but also because they are only fungistatic. Tavaborole and efinaconazole have been approved for topical use in onychomycosis by the USFDA in 2014 [12,13]. Since onychomycosis often does not respond well to topical therapies, toxic oral therapy is often used as a last resort. For chronic tinea infections, a further complication is the incidence of inflammation. This has led to the inclusion of

steroids in some anti-fungal formulations, which can be harmful to certain patient populations by increasing susceptibility to infections.

Need for natural treatment alternatives

Considering the challenges in the management of dermatophytosis, there is a need for novel, effective therapies which can cure the infection in a relatively short period with fewer adverse events. However, a significant segment of the population who are susceptible to tinea infections such as pregnant women, the elderly, infants and diabetics are recommended not to or are averse to use chemical-based treatments because of the associated side effects including toxicity. This is coincident with the growing trend towards preference for natural - over chemical-based treatments for skin-related conditions.

Several natural treatments have been shown to work anecdotally or heavily promoted in mass media. They have manifested anti-fungal activity *in vitro* but have limited clinical testing to substantiate efficacy. These include tea tree oil [14-16], apple cider vinegar [17], coconut oil, garlic and extracts from the Golden Seal plant (*Hydrastis canadensis*).

AMYCOT, a novel natural bioactive agent against ringworm

AMYCOT® is derived from *Arthospira maxima*, a filamentous, undifferentiated, non-toxigenic cyanobacterium used as food for centuries. Its extracts have demonstrated broad antimicrobial activities [18], and have been formulated into a cream ointment and a dermaceutical lotion. The formulated AMYCOT® has shown positive results in preclinical studies and medically supervised non-randomised human trials against a wide range of tinea infections including onychomycosis.

AMYCOT®'s unique fungicidal property works by enzymatically digesting chitin, the structural component of the fungal cell wall. Since AMYCOT® is composed of a complex variety of proteins, lipids and carbohydrates that have been known to collectively exhibit anti-fungal properties, it is possible that all of these molecules act synergistically to manifest efficacy. Efforts are underway to deconvolute the therapeutic activities of the components in AMYCOT®. *In vitro* studies have shown that AMYCOT® is effective against fungi such as *Trichophyton mentagrophytes, Trichophyton rubrum, Candida albicans, Epidermophytonfloccosum*, and *Malassezia furfur*. Additional clinical studies confirmed that AMYCOT® was effective in *Tinea cruris*, *Tinea corporis*, *Tinea pedis*, *Tinea capitis* and onychomycosis [19]. AMYCOT® has no skin irritating side effects, and in fact stimulates the growth and protein synthesis of skin cells such as keratinocytes, and has anti-inflammatory properties (unpublished results, Australian Provisional Patent filed). These multi-functional properties of AMYCOT® can therefore address severe tinea infections compounded with inflammation.

Further validation of AMYCOT's clinical efficacy was confirmed in a randomized double-blind, placebo-controlled trial of subjects with severe to very severe tinea and onychomycosis infections, who were treated with different AMYCOT® formulations. The results showed significantly greater than 90% mycological cure and 100% clinical cure rates in the treated patients compared with subjects treated with placebo. No adverse events associated with the treatment were reported [20].

Although reproductive toxicology studies have not yet been conducted for AMYCOT®, it should be noted that Spirulina, the source of AMYCOT®, has been ingested orally as human food for centuries. There has been no reported toxicity even with up to 8 grams consumed per day [21]. Thus, the application of a Spirulina extract as a topical agent may be considered harmless.

DISCUSSION AND CONCLUSION

Ringworm infections will continue to rise as the elderly and diabetic populations increase due to their susceptibility to fungal infections. Moreover, there is an unmet need for anti-fungals suitable for treating ringworm among pregnant and breast-feeding women as well as infants since chemical-based treatments are not recommended for these patients. In addition to the need for more efficacious and safer anti-fungals against severe ringworm infections, one of the greater challenges is the growing customer preference towards natural treatments for skin-related conditions such as ringworm. However, most natural treatments in the market lack well controlled clinical studies and have been promoted based on anecdotal evidence or *in vitro* studies. On the other hand, AMYCOT® is a natural anti-fungal derived from an extract of a particular Spirulina strain that has been clinically tested to show excellent efficacy and safety profiles. AMYCOT® serves as an example to demonstrate the potential of developing natural botanical-based treatments to address the underserved patient population especially pregnant and breast-feeding women and an alternative option for infants, diabetics, the elderly and the immuno-compromised.

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CONFLICT OF INTEREST

LLI owns stock of Xerion Limited, which owns Biovite Australia Pty Ltd, the developer of AMYCOT®

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