

## **A Novel Bioactive Extract from Spirulina with Multi-Functional Properties Shows Clinical Efficacy against Onychomycosis and Tinea Infections; And Its Implications for Other Dermatological Conditions**

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### **Extended Abstract**

#### **Abstract**

AMYCOT® is a bioactive extract derived from a strain of Spirulina (*Arthrospira maxima*), a cyanobacterium, which is commonly used as food supplement and has been consumed for centuries by the Aztecs in Mexico and tribes in Africa. AMYCOT® is produced through a proprietary process which enriches for the bioactive(s). The complex mixture contains a variety of molecules known to have anti-fungal activity as well as a unique activity targeting chitin, a cell wall component present in a broad range of fungi including yeasts. The fungicidal property of AMYCOT® is supported by electron microscopic studies showing rupture of test fungi after a few days as well as in vitro zone inhibition studies against a variety of dermatophytes and yeasts. Preclinical in vitro studies including use of an in vitro 3D human epidermis model have shown that AMYCOT® is non-toxic and non-allergenic with stimulation of skin cell growth properties. Furthermore, the bioactive extract demonstrates anti-inflammatory activity by reducing secretion of IL-1 alpha, a cytokine central to skin inflammation (unpublished results). Previous open-label studies by independent investigators demonstrated efficacy of AMYCOT® against a variety of dermatological fungal infections such as tinea and onychomycosis (2; unpublished results). To further confirm these studies, a single-center, randomised, double-blind, placebo-controlled clinical study was conducted in India. AMYCOT® was formulated as a lotion (8% AMYCOT®) to treat onychomycosis and as a cream (12% AMYCOT®) against tinea infections. The study's sample size was determined from a previous study on a cream and lotion that observed an 81% cure rate for the experimental drugs and an assigned 10% IGA response of 'cleared' or 'excellent' for the placebo group using a two-group Fisher's-exact test of equal proportions. Based on these assumptions, there is over 95% power to detect a significant difference between the treatment and placebo groups with 14 subjects per group (28 subjects overall) at 5% level of significance, and assuming a 20% dropout rate. From screening 50 potential patients, a total of 28 patients, 18 with tinea and 10 with onychomycosis were randomized in a ratio of 1:1 to treatment or placebo group. All were positive for all three parameters constituting mycological cure, which was assessed, was assessed by potassium hydroxide (KOH) smear, fungal culture and live spore count. Clinical cure was defined as Investigator global assessment (IGA) response of 'cleared' (100% improvement) or 'excellent' (>90% improvement). At the end of treatment, all three parameters were negative in the treatment arm, while KOH smear was positive in all subjects, and culture and live spore count were positive in six of them in the placebo arm. The treatments showed a significant improvement in all three parameters.

#### **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. 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.

#### **Chemical-based anti-fungal and their limitations**

Anti-fungal drugs involve varied mechanisms of action. They interfere with or affect the synthesis of membrane/cellwall components (echinocandins), membrane permeability (amphoterecin-B, azoles, allylamines), synthesis of nucleic acids (flucytosine), and/or microtubule/mitotic spindle function (griseofulvin). Generally, agents who 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. Although the previous study was tested with *Candida albicans*, similar observations were seen with other dermatophytes.

### **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.

### **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 and have been formulated into a cream ointment and a dermatological 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

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. Thus, the application of a *Spirulina* extract as a topical agent may be considered harmless.

### **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 antifungals 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 antifungal 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.