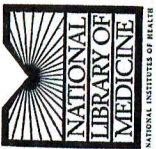


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Anti-Infectives

Recent progress on the topical therapy of onychomycosis

Michael RK Alley, Stephen J Baker, Karl R Beutner & Jacob Plattner[†]

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Onychomycosis is a fungal infection of the fingernails and toenails that results in thickening, discoloration, splitting of the nails and lifting of the nail from the nail bed. The disease is caused by dermatophytes and has a high incidence within the general population, especially among older individuals. Present treatment options include both oral and topical drugs, with oral therapies giving better outcomes; however, neither of these treatment options provides high cure rates that are durable. The difficulty in treating onychomycosis results from the deep-seated nature of the infection within the nail unit (nail plate, nail bed and surrounding tissue) and the inability of drugs to effectively reach all sites. Ongoing drug development activities have focused on novel delivery technologies to facilitate penetration of existing antifungal drugs through the nail plate and on the discovery of inherently penetrable antifungals. AN-2690 represents an oxaborole antifungal that is designed to penetrate the nail plate and is showing promising results in clinical trials.

Keywords: antifungal agent, dermatophyte, fungal infection, leucyl-tRNA synthetase, nail penetration, onychomycosis, oxaborole, tinea unguium

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1. Introduction

Onychomycosis is a progressive fungal infection of the nail unit that leads to the destruction and deformity of toenails and (less frequently) fingernails. This condition is common and represents ~ 50% of all nail disorders. Onychomycosis has a high occurrence throughout the world, with recent epidemiological data indicating a prevalence of 6.5 – 13.8% in North America [1]. The infection shows an increasing incidence in older individuals and 1 study reported that 48% of people aged 70 years are infected with onychomycosis [2]. The susceptibility to onychomycosis is higher in men than in women, although women seek medical treatment more frequently.

The infection is caused by fungi that infect the nail unit (the nail bed, the nail plate and surrounding tissue) and these include yeasts, dermatophytes and other molds. By far the most common fungi that cause onychomycosis are the dermatophytes, which account for ~ 90% of all cases. Dermatophytes are also the cause of skin fungal infections [3] and many patients with a nail infection also have a co-existing skin infection. The *Trichophyton* spp., *Microsporum* spp. and *Epidermophyton* spp. are the main causative dermatophytes, with *Trichophyton rubrum* and *T. mentagrophytes* representing the two most common isolates [3-5].

2. Description of onychomycosis

Tinea unguium is the medical term that is used to describe a nail infection caused by a dermatophyte, whereas onychomycosis is used more broadly to characterize all fungal nail infections. Distal subungual onychomycosis represents the most

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