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The Sensitivity Modifying Activity of Nerolidol and α-Bisabolol Against *Trichophyton* spp

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Abstract

Trichophyton spp. is one of the main causative agents of dermatophytosis such as *tinea ungium* and *tinea pedis*. Resistance to antifungal drugs is a significant clinical problem in dermatophytosis. The main molecular mechanism of antifungal resistance to conventional therapy in dermatophytes is the expression of efflux pumps. Efforts aimed at improving the efficacy of current antifungals such as griseofulvin are relevant. Given this, sesquiterpenes such as α-bisabolol and nerolidol found in essential oils represent promissing alternatives. Griseofulvin sensitivity modulation activity in *T. rubrum, T. interdigitale* H6, and *T. interdigitale Δmdr2* (mutant strain of *T. interdigitale*) promoted by α-bisabolol and nerolidol were investigated. The minimum inhibitory concentration (MIC) of the test drugs were determined by microdilution. Subsequently, the effect of the drugs tested on plasma membrane functionality (K^+ release) was analyzed. The MIC of griseofulvin was determined at sub-inhibitory sesquiterpene concentrations (modulation assay). An association study was performed with griseofulvin and sesquiterpenes (checkerboard). α-bisabolol was more potent than nerolidol; presenting lower MIC values. All of the fungi were sensitive to griseofulvin, starting at 8 µg/mL. With the exception of griseofulvin, all of the test drugs increased K^+ release ($p < 0.05$). Nerolidol modulated the sensitivity of all strains to griseofulvin; α-bisabolol sensitivity modulation was limited to *T. interdigitale* H6 and

interdigitale Δmdr2. In association with griseofulvin: nerolidol and α-bisabolol respectively presented synergism and additivity. Finally, the results of our study suggest using α-bisabolol and nerolidol compounds as potential antifungal agents and griseofulvin sensitivity modulators for *Trichophyton* spp.

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