Effectiveness of new aliphatic diamines against causative fungi of dermatomycoses

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Dermatomycoses are superficial infections caused by dermatophytes that affect keratinized tissues, such as skin, hair and nails. Its incidence is related to socioeconomic factors, individual habits and customs, geographical region and professional activities. Drug treatment against this pathology has limited effectiveness, provides large number of relapses and toxicity to the patient. Therefore, the aim of this study was the preparation of three lipophilic diamines and the evaluation of their antifungal activity. The compounds were synthesized by treatment of commercial diamines with alkyl chlorides in ethanol at reflux for 48 hours and then subjected to antifungal activity (7.80 µg mL⁻¹ and 1,000 µg mL⁻¹) in accordance with the M38-A2 protocol against ATCC strains: Trichophyton mentagrophytes ATCC 11481, Tricophyton rubrum CCT 5507 URM 1666 and Epidermophyton floccosum CCF-IOC-3757. The minimum inhibitory concentration (MIC) was established as the lowest concentration able to inhibit fungal growth and minimum fungicidal concentration (MFC) as the lowest concentration capable of causing the microorganism death. Ketoconazole and terbinafine were used as reference drugs. The three synthesized diamine compounds were generically identified as A (C₁₃H₂₉N₂); B (C₁₅H₃₅N₂) and C (C₁₆H₃₅N₂) and were effective across the three mentioned fungal strains. The MIC and MFC values to compound A were 500 µg mL⁻¹; to compound B, 1.95 µg mL⁻¹ and 250 µg mL⁻¹, respectively and to compound C, 31.25 µg mL⁻¹ and 500 µg mL⁻¹ on the strains analyzed. The MIC values of drugs ketoconazole and terbinafine were in the range from 0.03 to 4 µg mL⁻¹ and MFC between 0.03 and 16 µg mL⁻¹ for the fungi T. mentagrophytes and T. rubrum, and the MIC value to the fungus E. floccosum was greater than 640 µg mL⁻¹. According to our findings, these antifungal activities are directly related to the presence of diamine group, the lipophilicity and with the number of carbon atom of its alkyl chain, as compound B, having 15 carbon atoms, was more active. Although there are MIC and MFC values higher than reference drugs, our results are promising since structural changes could increase the pharmacological potency. Should note that the molecules were more effective against the E. floccosum when compared to reference drugs. Thus, all three lipophilic diamines molecules were effective front of the three strains evaluated, being a possible alternative for the treatment of dermatomycoses.

Keywords: dermatomycoses, organic synthesis, diamine.

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