

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 ($7.80 \mu\text{g mL}^{-1}$ and $1,000 \mu\text{g mL}^{-1}$) in accordance with the M38-A2 protocol against ATCC strains: *Trichophyton mentagrophytes* ATCC 11481, *Trichophyton 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 ($\text{C}_{13}\text{H}_{29}\text{N}_2$); B ($\text{C}_{15}\text{H}_{33}\text{N}_2$) and C ($\text{C}_{16}\text{H}_{35}\text{N}_2$) and were effective across the three mentioned fungal strains. The MIC and MFC values to compound A were $500 \mu\text{g mL}^{-1}$; to compound B, $1,95 \mu\text{g mL}^{-1}$ and $250 \mu\text{g mL}^{-1}$, respectively and to compound C, $31,25 \mu\text{g mL}^{-1}$ and $500 \mu\text{g mL}^{-1}$ on the strains analyzed. The MIC values of drugs ketoconazole and terbinafine were in the range from 0.03 to $4 \mu\text{g mL}^{-1}$ and MFC between 0.03 and $16 \mu\text{g mL}^{-1}$ for the fungi *T. mentagrophytes* and *T. rubrum*, and the MIC value to the fungus *E. floccosum* was greater than $640 \mu\text{g mL}^{-1}$. 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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