N-BENZYL-SUBSTITUTED IMIDAZOLIUM SALTS AS POTENT ALTERNATIVES TO CONVENTIONAL ANTIFUNGAL AGAINST NON- ALBICANS CANDIDA SP.

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INTRODUCTION: Infections caused by non-albicans *Candida* sp. have become an important clinical challenge due to their increasing prevalence and reduced susceptibility to conventional antifungal therapy. Among these pathogens *Candida glabrata*, *Candida krusei*, and *Candida parapsilosis* are frequently associated with oral, systemic, and healthcare-related infections, particularly in immunocompromised patients. These species exhibit distinct virulence factors, including biofilm formation, reduced susceptibility to azole antifungals, and adaptive stress response mechanisms, which contribute to therapeutic failure and infection persistence. In this context, *N*-benzyl-substituted imidazolium salts have gained attention as promising candidates due to their structural properties, which enhance interactions with fungal cell membranes and potentially disrupt key cellular processes. Therefore, investigating the antifungal activity of these compounds against clinically relevant non-albicans *Candida* sp. is essential for the development of new therapeutic strategies aimed at overcoming current limitations in antifungal therapy. OBJECTIVE: To evaluate the antifungal activity of *N*-benzyl-substituted imidazolium salts against non-albicans *Candida* spp. METHODS: Isolates of *Candida glabrata* (ATCC 2001), *Candida krusei* (ATCC 34135), and *Candida parapsilosis* (CFP 00893) from the MUMIC/UFRGS mycology collection were evaluated. Minimum Inhibitory Concentration (MIC) and Minimum Fungicidal Concentration (MFC) assays were performed according to CLSI protocols, with adaptations. The compounds C16BnImCl and C18BnImCl) were tested at concentrations ranging from 0.0019 to 1.0 µg/mL. Miconazole, ketoconazole, fluconazole, and amphotericin B were used as reference antifungal agents. Results were assessed after 24 and 48 hours of incubation at 37 °C. RESULTS: C16BnImCl exhibited MIC and MFC values of 0.125 µg/mL against *Candida glabrata* (ATCC 2001), whereas C18BnImCl showed values of 0.0625 µg/mL. Against *Candida krusei* C16BnImCl presented MIC and MFC values of 0.125 µg/mL, while C18BnImCl showed values of 0.0625 µg/mL. For *Candida parapsilosis*. C16BnImCl exhibited MIC and MFC values of 0.250 µg/mL, whereas C18BnImCl showed values of 0.125 µg/mL. In contrast, miconazole, ketoconazole, fluconazole, and amphotericin B displayed MIC and MFC values ranging from 1.0 to 2.0 µg/mL across all tested species. Overall, both imidazolium salts demonstrated markedly superior antifungal potency compared with all commercial references drugs. CONCLUSION: *N*-benzyl-substituted imidazolium salts displayed potent fungicidal activity against clinically relevant non-albicans *Candida species* at concentrations substantially lower than those required for conventional antifungal drugs. These findings position C16BnImCl and C18BnImCl as highly promising candidates for next-generation strategies targeting difficult- to-treat candidiasis, particularly infections involving intrinsically resistant species.

Further studies on toxicity, biofilm eradication, and translational pharmaceutical formulations are warranted. Moreover, these compounds may serve as candidates for future medical formu

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