ANTIFUNGAL ACTIVITY OF CHLORIDE IMIDAZOLIUM SALTS AGAINST NON-ALBICANS CANDIDA SPECIES IN CANCER SETTINGS: POTENTIAL APPLICATIONS IN BIOMATERIALS AS API-ILs

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INTRODUCTION: The oncologic microenvironment creates a permissive niche for opportunistic infections due to immune dysregulation, epithelial barrier disruption, and microbiota imbalance. In this context, non-*albicans Candida* species have emerged as clinically relevant pathogens associated with persistent oral, systemic, and device-related infections in cancer patients. These species often exhibit intrinsic or acquired resistance to azoles, strong biofilm-forming capacity, and high adaptability to adverse conditions, particularly on medical devices such as catheters and stents. Imidazolium chloride salts have emerged as promising antifungal agents with additional potential as active pharmaceutical ingredient ionic liquids (API-ILs). Their incorporation into biomaterials represents an innovative strategy for antifungal coatings aimed at reducing *Candida* colonization and biofilm-associated infections. **OBJECTIVE:** To evaluate the antifungal activity of imidazolium chloride salts against clinically relevant non-*albicans Candida* species, with emphasis on their potential application as API-ILs in pharmaceutical formulations and antifungal biomaterials. **METHODS:** Isolates of *Candida glabrata* (ATCC 2001), *Candida krusei* (ATCC 34135), and *Candida parapsilosis* (CFP 00893) were investigated. Minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) assays were performed according to adapted CLSI guidelines. Imidazolium chloride salts (C_{12}MImCl, C_{14}MImCl, C_{16}MImCl, and C_{18}MImCl) 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 recorded after 24 and 48 h of incubation at 37 °C. **RESULTS:** C_{12}MImCl exhibited MIC and MFC values of 0.5 µg/mL against *Candida glabrata* and *Candida krusei*, and 0.25 µg/mL against *Candida parapsilosis*. C_{14}MImCl showed values of 0.0625 µg/mL against *Candida glabrata*, 0.5 µg/mL against *Candida krusei*, and 0.125 µg/mL against *Candida parapsilosis*. C_{16}MImCl displayed values of 0.5 µg/mL against *Candida glabrata*, 0.03125 µg/mL against *Candida krusei*, and 0.25 µg/mL against *Candida parapsilosis*. C_{18}MImCl exhibited values of 0.25 µg/mL against *Candida glabrata* and 0.125 µg/mL against *Candida parapsilosis*, with strong activity also observed against *Candida krusei*. In contrast, conventional antifungals showed MIC and MFC values ranging from 1.0 to 2.0 µg/mL. Overall, compounds bearing longer alkyl chains demonstrated enhanced antifungal potency, with C_{18}MImCl showing the best overall performance, followed by C_{16}MImCl and C_{14}MImCl. **CONCLUSION:** Imidazolium chloride salts demonstrated potent antifungal activity against clinically relevant non-*albicans Candida* species at concentrations substantially lower than those required for conventional antifungal drugs. These findings highlight their potential as innovative API-IL platforms for next-generation pharmaceutical formulations and antifungal biomaterials, particularly coatings for medical devices aimed at preventing

Candida colonization and biofilm-related infections in vulnerable cancer patients.

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