CHLORIDE IMIDAZOLIUM SALTS AS PROMISING API-ILS FOR CANCER- ASSOCIATED CANDIDIASIS: INFLUENCE OF ALKYL CHAIN LENGTH ON ANTIFUNGAL ACTIVITY

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INTRODUCTION: Candidiasis associated with cancer is an important clinical complication affecting oral, cutaneous, and systemic sites, particularly in patients undergoing immunosuppressive therapies. Disruption of epithelial barriers, microbiota imbalance, and impaired host immunity favor the overgrowth of *Candida* spp., increasing morbidity and negatively impacting quality of life. In oncologic settings, recurrent infections frequently involve strains with reduced susceptibility to conventional antifungal agents. In this context, chloride imidazolium salts have attracted attention as active pharmaceutical ingredient ionic liquids (API-ILs) due to their tunable physicochemical properties, enhanced solubility, and potential to improve drug delivery and bioavailability. OBJECTIVE: To evaluate the antifungal activity of chloride imidazolium salts against *Candida albicans* and *Candida tropicalis*, with emphasis on the influence of alkyl chain length and their potential application as API-ILs in pharmaceutical formulations. METHODS: Five *Candida albicans* strains (CFP00107, CFP00283, CFP00292, CFP00895, and ATCC 44858) and two *Candida tropicalis* strains (CFP00319 and ATCC 13803) from the MUMIC/UFRGS mycology collection were investigated. Minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) assays were performed according to adapted CLSI guidelines. Chloride imidazolium salts (C12MImCl, C14MImCl, C16MImCl, and C18MImCl) 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: C12MImCl exhibited MIC and MFC values against *Candida albicans* ranging from 0.125 to 1.0 µg/mL and against *Candida tropicalis* from 0.5 to 1.0 µg/mL. C14MImCl showed values ranging from 0.0625 to 0.250 µg/mL for *Candida albicans* and from 0.0625 to 0.125 µg/mL for *Candida tropicalis*. C16MImCl displayed enhanced potency, with MIC and MFC values ranging from 0.0039 to 0.250 µg/mL for *Candida albicans* and from 0.0625 to 0.125 µg/mL for *Candida tropicalis*. Similarly, C18MImCl showed values ranging from 0.0039 to 0.250 µg/mL for *Candida albicans* and 0.125 µg/mL for *Candida tropicalis*. In contrast, miconazole, ketoconazole, fluconazole, and amphotericin B exhibited MIC and MFC values of 2.0 µg/mL and 1.0 µg/mL, respectively, for both species. Overall, compounds bearing longer alkyl chains demonstrated markedly superior antifungal activity, with C16MImCl and C18MImCl emerging as the most potent derivatives. CONCLUSION: Chloride imidazolium salts exhibited potent antifungal activity against *Candida albicans* and *Candida tropicalis* at concentrations

substantially lower than those required for conventional antifungal drugs. The clear structure–activity relationship observed indicates that increasing alkyl chain length enhances antifungal efficacy, highlighting C16MImCl and C18MImCl as lead candidates. These findings support the development of chloride imidazolium salts as innovative API-IL platforms for next-generation pharmaceutical formulations targeting cancer-associated candidiasis.

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