Allylimines: antifungal activity alone and in combination with amphotericin B against *Cryptococcus gattii* strains

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Introduction: Cryptococcosis is an invasive mycosis of global occurrence, mainly caused by *Cryptococcus neoformans* and *Cryptococcus gattii* and affects patients, both immunocompromised as immunocompetent. The treatment of the disease is very difficult, may be complicated by the toxicity of the drugs used and the emergence of resistant strains. The discovery of new antifungal compounds and the combination therapy are important tools for the effective treatment of fungal infections. The allylimines exhibit similar structures to the antifungal group of allylamines, containing one double bond next to the nitrogen atom present in the molecule. Material and methods: In the present work we evaluated the *in vitro* antifungal activity of three allylimines (A1, A2, A3) alone and in combination with amphotericin B (AMB) against 12 *Cryptococcus gattii* strains. The compounds were evaluated for minimum inhibitory concentration (MIC), minimal fungicidal concentration (MFC) and the checkerboard assay was used to determinate the fractional inhibitory concentration index (FIC). Discussion of the Results: All strains were susceptible to the tested compounds with MIC values between 2.3 and 7.5 µg/mL and MFC values between 4.8 and 65.8 µg/mL. For most of the tested strains the interaction of A1 and A2 with amphotericin B was indifferent ($0.5 > FIC \leq 4$). The compound A3, however, was able to interact synergistically with AMB ($FIC \leq 0,5$) for one third of the *C. gattii* strains tested. Although the allylimines A1 and A2 had the best MIC and MFC values, A3 showed better interaction with AMB against the strains tested. Conclusions: Considering the results obtained in this study these allylimines may be considered promising antifungal agents for the treatment of cryptococcosis and further studies will be done in our research group.

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