Antifungal activity of *Piper arboreum* extracts

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Introduction: Piperaceae species have been extensively investigated as a source of new natural products with potential antitumoral, antimicrobial, antifungal, and insecticidal activities (Regasini, L.O. AFr. J. Biotechnol., v. 8, p. 2866, 2009). The broad biological potential is due to the accumulation of different classes of metabolites among which stand out amides, benzoic acid derivatives, chromenes, lignans, neolignans, and a few alkaloids (Silva, R. V. Phytochemistry, v. 59, p. 521, 2002). It is known that the synthetic antifungal drugs have showed toxicity in the treatment of mycoses in general as well as low tolerance to certain drugs, which increase the demand for new alternatives therapy. The search for new antifungal agents from plants could facilitate the treatment of major mycoses by reducing the adverse reactions. Systemic mycoses caused by yeasts are a worldwide problem. In Brazil, cryptococcosis and systemic candidiasis are the major opportunistic fungal diseases of immunocompromised patients, especially those with AIDS. The objectives of this study were to evaluate the antifungal activity of the crude extracts obtained from *Piper arboreum* against four species of the genus *Candida* and *Cryptococcus neoformans*.

Experimental Part: Plant material (fruits, leaves and branches) of *P. arboreum* were dried, at room temperature, and powdered. The extract was prepared by exhaustive maceration in ethanol at room temperature, filtered and concentrated under vaccum. The strains of human pathogen fungal used in this study were: *Candida albicans* ATCC 90028, *Candida krusei* ATCC 6258, *Candida parapsilosis* ATCC 22019, *C. glabrata* ATCC 90180 and *Cryptococcus neoformans* ATCC 90012. The microorganisms were originally obtained from the Clinical Mycology Laboratory of the Faculty of Pharmaceutical Science at UNESP/Araraquara. The yeast strains were cultured in Sabouraud dextrose agar overnight at room temperature. The minimal inhibitory concentration (MIC) of the crude extracts of *P. arboreum* was determined by the broth microdilution method following the European Committee on Antimicrobial Susceptibility Testing document EDef 7.1 (2008) with modifications (EUCAST, Clin Microbiol Infect, 15, 2009). The used drugs as for control were fluconazole and amphoteracin B.

Results and discussion: All samples tested were able to inhibit the growth of fungi, with minimum inhibitory concentration values ranging from 31 to 125 µg/mL. Crude extracts of the leaves had the most fungicidal activity for *C. albicans*, *C. krusei*, *C. parapsilosis* and *Cryptococcus neoformans*, with values of 31.2, 62.5, 31.2 and 62.5µg/mL respectively. The extract of the fruits showed potent activity against *C. krusei*, *C. glabrata* and *Cryptococcus neoformans*, with values of 62.5, 62.5 and 31.2 µg/mL, respectively. Extract of fruit showed higher activity against *Cryptococcus neoformans* when compared to the leaves extract with values of 31.2 and 62.5 µg/mL, respectively.

Conclusions: According to our results the *P. arboreum* extracts showed to be a promising source for search new bioactive metabolites, especially against some opportunistic fungi.

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