TITLE: ANTIFUNGAL ACTIVITY OF CURCUMIN ANALOGUES AGAINST *Candida albicans* AND *Cryptococcus neoformans*

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ABSTRACT:
Fungal infections have increased in the last decades, whilst the classes of antifungal agents available remain the same. These infections have become a serious clinically problem because of their high incidence and mortality. Thus, the search for new therapeutic strategies is urgent. The literature has demonstrated the antimicrobial activity of several natural products. Among these, curcumin from *Curcuma longa* rizomes, exhibited effect on $\Delta^{5,6}$ desaturase (ERG3), leading reduction in the ergosterol of fungal cell. Reduction in production of ergosterol results in cell death via generation of reactive oxygen species (ROS). The present study aimed the synthesis of **31** analogues of curcumin, and their evaluation against reference strains of *Candida albicans* (ATCC 90028) and *Cryptococcus neoformans* (ATCC 22019). The antifungal evaluation was performed of the broth microdilution test in concentrations ranging from 250.00 to 0.48 μg/mL, determining their minimum inhibitory concentrations (MIC). Compounds **30** and **31** displayed activity against *C. albicans* with MIC values of 62.50 to 31.25 μg/mL, respectively, and against *C. neoformans* with MIC values of 3.90 μg/mL. Curcumin had MIC of 250.00 μg/mL for *C. albicans* and 3.90 μg/mL for *C. neoformans*. Fluconazole was used as antifungal reference, displaying MIC values of 8.0 and 4.0 μg/mL against *C. albicans* and *C. neoformans*, respectively. Thus, hydroxylated curcumin analogus **30** and **31** presented potent activity against *C. albicans* strains and a similar antifungal action against strains of *C. neoformans*, in relation to curcumin. These data indicated compounds **30** and **31** have potential for the development of new antifungal prototypes.

Keywords: Curcumin**,** Antifungal, *Candida albicans*, *Cryptococcus neoformans*. **Development Agency**: FAPESP