TITLE: ANTI-DERMATOPHYTE AND CYTOTOXIC ACTIVITY OF A NEW SYNTHETIC CHALCONE DERIVATIVE.

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ABSTRACT:

In the last few decades there has been an increase in the number of fungal infections worldwide. Meanwhile, the current arsenal of antifungal drugs is exceedingly short and its efficacy is limited because of toxicity issues, problems of selectivity and, more recently, the emergence of resistance. Thus, there is an urgent need for the development of safe and effective new antifungal agents. In the present study we have synthesized a series of seven chalcones with the aim to evaluate their antifungal activity against reference strains of *Candida albicans* and *Trichophyton rubrum* by broth microdilution test, establishing their minimum inhibitory concentrations (MIC) and minimum fungicidal concentrations (MFC). Among the tested compounds, only one (identified as B6) showed promising activity, with some selectivity towards *T. rubrum* (MIC 7.81 µg/mL and MFC 15.62 µg/mL), since this compound did not present activity against either the bacteria *Staphylococcus aureus* or the yeast *Candida albicans* (MICs > 250 µg/mL). Thus, B6 was further evaluated towards a panel of 16 clinical isolates of dermatophytes, revealing activity profiles similar to that against *T. rubrum* reference strain. Microscopic examination of fungal structures was carried out by confocal microscopy and revealed a drastic decrease in hyphal density of *T. rubrum* under B6 treatment when compared to control. B6 was also evaluated for its cytotoxicity in human cell lines (MRC-5), using the MTT assay, and showed IC50 (inhibitory concentration for 50% of the cells) value of 152.35 µg/mL, which was considerably greater than its MIC (7.81 µg/mL). Therefore, B6 had a high selectivity index (rate between IC50 and MIC) value (19.5) for *T. rubrum*. In conclusion, the data set indicates that B6 has potential to be developed as a novel antifungal agent directed to the treatment of human mycoses caused by dermatophytes.

Keywords: synthetic compounds, chalcones, antifungal activity, dermatophytes, cytotoxicity.

Development Agencies: FAPEMIG