

## **Determination of antifungal activity and isolation of chalcone resistant mutant of *Trichophyton rubrum* by ultraviolet light radiation**

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**Introduction:** The dermatophyte *Trichophyton rubrum* (*T. rubrum*) is the most frequent causative agent of superficial dermatomycoses in Brazil and worldwide. Despite the importance of dermatophytosis, there are a limited number of antifungals on the market due to lack of specific targets, because of the similarity between fungal and mammalian cells. The cell wall of fungi is essential for development of fungi and plays a critical role in host infection. Thus, the cell wall has become an important target for the development of antifungals with new mechanisms of action and low toxicity to humans. The chalcones are precursors of flavonoids biosynthesis that occur in plants as defensive molecules exhibiting significant antifungal activity. The mode of action for the most number of chalcones with antifungal activity has been related to the inhibition of the enzymes  $\beta$  (1,3)-glucan and chitin synthase of fungal cell wall. **Objective:** The aim of this study was to determine the survival curve of *T. rubrum* after the exposition to ultraviolet light (5% of survival) in order to obtain mutants resistant to chalcones. Another objective was to determine the minimum inhibitory concentration (MIC) of six chalcones (metoxychalcone, transchalcone, Hesperidine, 4-Nitrochalcone, 2,4 dimethyl-4(dimethylamino) chalcone, 4-cloro-4(dimethylamino) chalcone) against the wild type strain (H6), sensitive mutant ( $\Delta TruMDR2$ ) and resistant mutant to chalcone, and to select the most effective. **Methods:** The susceptibility assay was carried out through broth microdilution. The survival curve was obtained after the exposition of conidia to ultraviolet light and was settled the time necessary to obtain 5 % of survivors of U.V. This time was used to obtain resistant mutants resistant to chalcones. **Results:** Transchalcone and methoxychalcone were the most effective among the chalcones tested, both with MIC of 7.8  $\mu\text{g/ml}$  for H6 strain, and 3.9  $\mu\text{g/mL}$  and 1.95  $\mu\text{g/mL}$  for sensitive mutant, respectively. The survival curve showed the irradiation time necessary to obtain 5% of survival was 30 seconds. The MIC of chalcone resistant mutants were 31.2  $\mu\text{g/mL}$ . **Conclusion:** The antifungal activity presented of chalcones are attractive for production of new antifungal agents and the resistant mutants of chalcones might be an interesting tool to studies of mechanism of action for these compounds.

**Keywords:** Dermatophyte; Chalcones; resistant mutants.

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