

INTERACTION BETWEEN AGROCHEMICAL AND CLINICAL ANTIFUNGALS  
AGAINST *Cryptococcus gattii*

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The species *Cryptococcus gattii* is an encapsulated leaven which causes Cryptococcosis and commonly attacks immunocompetent hosts. The conventional treatment for Cryptococcosis is determined by prolonged antifungal therapy, usually using Fluconazole (FCZ) and Amphotericin B (AMB). However, this therapy is distinguished by its high toxicity and can be involved with the emergence of resistant lineages. This emergence, in turn, can be provoked by the use of pesticides in eucalyptus cultures where the microorganism is found. Among the several chemical compounds used on a large scale as protectors of these cultures, the insecticide Fipronil (FIP) was selected for the tests carried out in the present work. For this study, the agrochemical was tested in combination with the antifungals Fluconazole and Amphotericin B to determine the interactions' types (synergism, antagonism or no interaction/indifferent). The tests were performed against thirteen isolates: eleven of clinical origin and two environmental; and two reference strains of *Cryptococcus gattii*. The tests of combination were made with the checkerboard method. The interaction between the antifungals and agrochemical was quantitatively evaluated by determining the fractional inhibitory concentration (FIC). The interaction between these drugs was classified as synergism if  $FIC \leq 0.5$ , indifferent if  $0.5 < FIC < 4.0$ , and antagonism for  $FIC > 4.0$ . The interactions between this agrochemical and the FCZ antifungal were considered indifferents, but it was observed a synergism pattern for the interactions between the agrochemical and the AMB antifungal when it was analysed for each lineage and dependent of concentration. The results of the fipronil suggest use as an aid compound in the treatment of cryptococcosis. However, already was reported the fipronil's neurotoxicity in murine model. Nevertheless, further tests should be performed to better understand the patterns of interaction, selectivity and susceptibility of *C. gattii* to agrochemical.

Key-words: *Cryptococcus gattii*, agrochemicals, combination, synergism, antagonism, no interaction.

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