

TITLE: VIRULENCE OF *Candida haemulonii* COMPLEX IN *Galleria mellonella* AND EFFICACY OF CLASSICAL ANTIFUNGAL DRUGS: A COMPARATIVE STUDY WITH OTHER CLINICALLY RELEVANT NON-*albicans* *Candida* SPECIES

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Candida haemulonii and closely related species have emerged as notorious healthcare-associated yeasts causing invasive infections with high rates of clinical treatment failures. These species have a predilection for epidemic spread and are difficult to treat, a part from being resistant to the first-line antifungals, like fluconazole, and with variable susceptibility to other azoles, amphotericin B and echinocandins. However, differences in virulence among these species have not been widely studied. Over the last few years there has been particular interest in developing non-mammalian host models to study microbial virulence to evade the huge ethical impact of the classical animal tests. In this context, *Galleria mellonella* is an invertebrate infection model which became a useful tool to study virulence of different microorganisms and drug efficacy. In this work, we firstly investigated the virulence of three Brazilian clinical isolates of *C. haemulonii* (n=1), *C. duobushaemulonii* (n=1) and *C. haemulonii* var. *vulnera* (n=1) and also three type strains of *C. tropicalis*, *C. krusei* and *C. lusitanae* on *G. mellonella* larvae and, subsequently, the efficacy of classical antifungal drugs in this infection model. When *G. mellonella* were infected with different concentrations of yeasts (1×10^6 , 3×10^6 , 6×10^6 and 9×10^6 fungi/larva), we observed a dose-dependent effect on the killing of the larva. For the further experiments, the inocula chosen for each tested fungi presented an average of 80% of larvae killing after five days of infection. Fluctuations in the hemocyte density and fungal burden were also examined. The efficacy of amphotericin B, caspofungin and fluconazole was tested with equivalent therapeutic doses, and a protective and non-protective effect was observed in a strain and antifungal dependent fashion. Fungal burden increased in infected larvae during time of infection and only caspofungin reduced the number of colony-forming units of *C. haemulonii* complex strains in the larvae. We conclude that *G. mellonella* offers a simple and feasible model to study *C. haemulonii* virulence and drug efficacy.

Keywords: Non-*albicans* *Candida*, *Candida haemulonii* complex, virulence, *Galleria mellonella*, antifungals

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