Lactic acid increases the susceptibility of *Candida albicans* to fluconazole [O6/05]

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Candida spp. often inhabit niches that are glucose-limited but rich in alternative carbon sources, such as lactate or acetate, an ability that contributes to cells' virulence. In glucose-poor niches, *Candida albicans* cells express *JEN1* and *JEN2* genes encoding the carboxylic acids transporters Jen1 and Jen2, respectively, which have been reported to be important in the early stages of infection. In this work, we aimed at analysing biofilm formation and antifungal drug resistance of *C. albicans* cells grown either in the presence of glucose or lactic acid. Additionally, we tested the involvement of Jen1 and Jen2 on these processes. Our results show that biofilm formation and susceptibility to fluconazole depend on the carbon source used. Wild-type and jen1jen2 lactic acid-grown cells formed more biofilm biomass, with predominance of yeast cells, than the ones grown in glucose. In the presence of this sugar a hyphae network is observed only for wild-type cells. In the presence of lactic acid, a jen1jen2 mutant strain exhibited a more compact biofilm with higher resistance to fluconazole when compared to the wild type. In the case of planktonic cells, the phenotype was exactly the opposite; the double mutant strain was more susceptible to fluconazole in lactic acid containing media. These findings show that carboxylic acids transporters have an important role in biofilm formation and in the acquisition of resistance to antifungal drugs, supporting the view that adaptation of *Candida* cells to the carbon source present in host niches affects their pathogenicity.

Keywords: Candida albicans, lactic acid, biofilms, antifungal drug resistance

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