Biofilm formation by *Candida albicans* and *Candida glabrata* under acidic conditions: Implications on vulvovaginal candidiasis

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Vulvovaginal candidiasis (VVC) affects millions of women every year and is considered an important public health problem. VVC is mainly caused by *Candida albicans*, but *Candida glabrata*, which is a species with intrinsically high resistance to common antifungals, has been increasingly identified in women with VVC. The high incidence of VVC and difficulty in its treatment, make it crucial to increase the knowledge on *Candida* vaginal virulence. Contrary to most other pathogens the vaginal acidity does not prevent *Candida* infections, to which *Candida* biofilm formation, on mucosa or intrauterine devices, may contribute. Thus, the aim of this study was to analyse the biofilm formation and matrix composition of *C. albicans* and *C. glabrata* vaginal isolates at pH 4, promoted by lactic acid, comparatively to a neutral environment. *Candida glabrata* strains presented increased ability to produce biofilms at acidic conditions suggesting high adaptability to the vaginal environment. In contrast, *C. albicans* strains presented lower biofilm quantity and filamentation at acidic conditions, what may suggest an acidic-induced biofilm dispersion that may contribute to the dissemination of an infection. Additionally, the biofilm matrix composition was significantly affected in both species, in general presenting lower quantity of components at acidic conditions. A high-throughput mass spectroscopy analysis of *C. glabrata* biofilm matrix proteins, which were not investigated before in this species, revealed 397 different proteins at acidic conditions and 606 at pH 7. Importantly, the acidic conditions were found to induce and block the secretion of 71 and 280 proteins, respectively, to the matrix. This study shows that acidic conditions have a specific and relevant modulation of virulence features of *Candida* species. As such, the identification of species-specific virulence determinants that may settle the ability of *Candida* species to survive in the vaginal environment may contribute to the disclosure of new targets to treat VVC.

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