Antifungal Potential of the Curcumin DS17 and McP40 Against Candida spp. Associated with Vulvovaginal Candidiasis

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Vulvovaginal candidiasis (VVC) is mainly caused by Candida albicans. However, other clinically significant species, such as Candida parapsilosis, may also contribute to the illness. Approximately 75% of women worldwide will experience VVC at least once in their lifetime, with recurrence (RVVC) in about 8% of cases. For Candida species that are susceptible, azole antifungals are typically the first line of treatment. In addition, amphotericin B (AmB) is primarily used to treat severe systemic fungal infections. However, due to microbial resistance, the efficacy of current treatments is declining, requiring the development of alternative therapeutic techniques. Curcumin\'s antifungal properties have led to substantial research in this field. Nonetheless, it has extremely poor water solubility, contrasting spray-dried curcumin DS17, which has improved water solubility. Thus, we aimed to investigate the effects of solid curcumin dispersions (DS17) and McP40 in the resistance and virulence of clinical isolates of C. albicans and C. parapsilosis, responsible for CVV e CVVR. Furthermore, its potential when combined with antifungals was assessed. We employed clinical isolates of C. albicans (Ca0060 and Ca0059), as well as C. parapsilosis (Cp0092 and Cp0098). Additionally, we used the reference strains C. albicans ATCC 64548 and C. parapsilosis ATCC 22019. The minimum inhibitory concentration (MIC) and fractional inhibitory concentration index (FICI) were determined using the broth microdilution method in accordance with the M27-A3 guidelines recommended by the Clinical and Laboratory Standards Institute (CLSI). The inoculum (100 µL) was added to reach a concentration of 1 × 103 CFU/mL and plates were incubated at 35 °C for 48 h. Serial dilutions of DS17 and McP40 were performed in RPMI medium. The final concentrations of DS17 and McP40 ranged between 0.24–1000 mg/L, whereas those of AmB and miconazole (MCZ) ranged between 0,007–32 mg/L. The interactions were categorized as synergism (ICIF ≤ 0.5), indifference (ICIF > 0.5 to ≤ 4.0), or antagonism (ICIF > 4.0). The metabolic activity of mature Candida spp. biofilms was quantified using MTT assay, in the presence or absence of treatments with DS17, McP40, AmB, and MCZ. Toxicity of the DS17 and McP40 was determined using Tenebrio molitor larvae, which were divided into randomized groups of 15 and monitored for 20 days. The MICs for DS17 against C. albicans ranged from 500 mg/L (Ca0059 e ATCC 64548) to 250 mg/L (Ca0060). On the other hand, C. parapsilosis isolates were

more sensitive to DS17, showing MICs of 125 mg/L (Cp0092 and Cp0098). MICs of the McP40 ranged between 500 mg/L to 250 mg/L. Only the ATCC 22019 showed a MIC of 125 mg/L. The interactions showed synergy for the majority of combinations involving DS17 and McP40 with AmB and MCZ. ICIF varied from 0.066 to 0.50. Both DS17 and McP40 markedly reduced the metabolic activity of Candida spp biofilms. The toxicity of DS17 and McP40 was low, with survival rates exceeding 80%. Our findings demonstrate that DS17 and McP40 have antifungal properties that modulate resistance and pathogenicity in Candida spp., especially when combined with therapeutically relevant antifungal agents. Thus, we established the translational potential of these formulations is a promising approach to the management of VVC and RVVC.

Agradecimentos: FAPESP 2023/02254/1.We thank the technical support of Ludmilla Tonani, Solange Bocardo, and Cristiana Gonçales.