

TITLE: ANTIMICROBIAL ACTIVITY AND TOXICITY OF A NOVEL NITRO-CHALCONE AGAINST *Candida* BIOFILMS UNDER DIFFERENT OXYGEN CONDITIONS.

AUTHORS: SARDI, J.C.O.; FREIRES, I.A.; PAGANINI, E.R.; MENDES-GIANNINI, M.J.S.; LOPEZ-RIBOT, J.L.; REGASINI, L.O.; ROSALEN, P.L.

INSTITUTION: DEPARTMENT OF PHYSIOLOGICAL SCIENCES, PIRACICABA DENTAL SCHOOL, UNICAMP–SP. (AV. LIMEIRA, 901).

ABSTRACT:

Candida spp. are opportunistic pathogens with great capacity to cause superficial and systemic mycoses. Broadly recognized as important causative agents of nosocomial infections, yeasts can easily adapt to extreme oxygen conditions, which may shift their susceptibility to antimicrobial drugs. In our study, we determined the antimicrobial activity and toxicity of a novel nitro-chalcone, NC-E23, against *Candida* biofilms grown under different oxygen conditions (normoxia, hypoxia and anoxia). The Minimal Inhibitory Concentration (MIC) of NC-E23 and its effects on *Candida* spp. biofilm formation and morphology (SEM) were further determined. The data were analyzed by one-way ANOVA with Tukey post-hoc test ($P < 0.05$). Our findings revealed that yeast cells were able to form biofilm regardless of the oxygen tension (normoxia, hypoxia and anoxia) ($p > 0.05$). The MIC of NC-E23, fluconazole and amphotericin B (used as standard drugs) on *Candida* spp. ranged from 15.39 to 123.39 mM; 6.5 to 208.6 mM; and 0.13 to 0.54 mM, respectively. Treatment with NC-E23 at 10xMIC significantly reduced by 6 Log_{10} the amount of *C. albicans* and *C. krusei* biofilms, and by 5 Log_{10} the amount of *C. tropicalis* and *C. glabrata* biofilms grown under different oxygen conditions ($P < 0.05$). Under all oxygen conditions analyzed, NC-E23 significantly affected the architecture and integrity of mature biofilms ($P < 0.001$). At 10xMIC, NC-E23 did not show significant toxicity on macrophages and *Galleria mellonella* larvae ($P < 0.05$). Survival rates of *G. mellonella* larvae injected with NC-E23, amphotericin B and fluconazole at 10xMIC were found to be 80%, 60% and 40%, respectively, after 48 h. In summary, the nitro-chalcone NC-E23 demonstrated excellent antifungal activity on *Candida* spp. while presenting low toxicity *in vivo*. When compared to conventional antifungals, NC-E23 had a promising anti-biofilm effect. This compound could be considered a promising candidate for the treatment of hospital-acquired *Candida* infections.

Keywords: Biofilm, Nitro-chalcone, *Candida* spp., *Galleria mellonella*.

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