

TITLE: A NANOSTRUCTURED LIPID SYSTEM AS A STRATEGY TO IMPROVE THE ACTIVITY OF NITROCHALCONE AGAINST *Candida* BIOFILM.

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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. Research suggests that most of the infections produced by this pathogen are associated with growth as a biofilm. The great concern with drug resistance shows the need to search for new alternatives and associations of molecules with antimicrobial potential, aiming at new molecular targets. In our study, we determined the antimicrobial activity and toxicity of a novel nitrochalcone, NC-E23 associated a nanostructured lipid system, 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. 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 and NC-E23 associated a nanostructured lipid system on *Candida* spp. ranged from 3.90 to 15.62 $\mu\text{g/ml}$ and 0.48 to 1.95 $\mu\text{g/ml}$, respectively. Treatment with NC-E23 associated a nanostructured lipid system at 10xMIC significantly reduced by 8 Log_{10} the amount of *C. albicans*, *C. parapsilosis* and *C. glabrata* biofilms, and by 6 Log_{10} the amount of *C. tropicalis* and *C. krusei* biofilms grown under different oxygen conditions ($P < 0.05$). At 10xMIC, NC-E23 associated a nanostructured lipid system did not show significant toxicity on *Galleria mellonella* larvae ($P < 0.05$). In summary, the nitrochalcone 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, Nitrochalcone, *Candida* spp., *Galleria mellonella*.

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