

TITLE: ANTIMICROBIAL ACTIVITY AND TOXICITY OF PENTYL CAFFEATE (C5) AGAINST MIXED BIOFILM OF *CANDIDA ALBICANS* AND *STAPHYLOCOCCUS AUREUS*.

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The oropharynx is one of the most complex niches of the human body, being colonized by several microorganisms capable of forming biofilms. These microorganisms present a symbiotic relationship with the human being, but when the individual presents the compromised immunity they can become pathogenic. Among these microorganisms we can highlight *Candida albicans* and *Staphylococcus aureus*. We investigated the antibiofilm potential of pentyl caffeate (C5) on *C. albicans* MYA 2876 and *S. aureus* ATCC 25923, and further tested its toxicity in macrophages (*in vitro*) and *Galleria mellonella* larvae (*in vivo*). The Minimal Inhibitory Concentration (CIM) of C5 and its effects on mono-species and mixed biofilm formation and morphology (SEM) of *C. albicans* and *S. aureus* were determined. The data were analyzed by ANOVA with Tukey post-test ($p < 0.05$). The MICs of C5 on *C. albicans* and *S. aureus* were 31.25 and 7.8 $\mu\text{g/ml}$, respectively. Treatment with C5 at 10xMIC reduced *C. albicans* mature biofilm survival and formation by 54% and 0%, respectively. In *S. aureus*, C5 reduced by 54% the mature biofilm survival and by 85% biofilm formation. As for mature mixed biofilms, C5 reduced *S. aureus* and *C. albicans* biofilm survival by 28% and 45%, respectively; whereas biofilm formation was reduced by 75% in *S. aureus* biofilms and totally eliminated in *C. albicans* biofilms. C5 affected the architecture / structure of biofilms under all conditions analyzed ($p < 0.001$). At the studied concentration, C5 did not show toxicity on macrophages and *G. mellonella* larvae ($p < 0.05$). In conclusion, C5 was able to affect the formation and development of *C. albicans* and *S. aureus* biofilms while presenting negligible toxicity *in vitro* and *in vivo*. This compound could be considered a promising candidate for the treatment of *S. aureus* and *C. albicans* mixed infections.

Keywords: Pentil caffeate, Biofilm, *Candida albicans*, *Galleria mellonella*, *Staphylococcus aureus*

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