TITLE: ANTI-*Candida albicans* ACTIVITY OF UNLOADED AND LOADED ESSENTIAL OIL OF *Cymbopogon nardus* IN THE NANOSTRUCTURED LIPID SYSTEM

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ABSTRACT

The ability of *Candida albicans* to colonize and proliferate in humans is related to its pathogenicity. The main pathogenicity mechanisms of *C. albicans* are hyphae and biofilm formation. The biofilm eradication is difficult due to low drug penetration, cell proliferation and emergence of resistant strains. This work aimed to evaluate the activity of unloaded and loaded essential oil (EO) of *Cymbopogon nardus* (L.) Rendle in the nanostructured lipid system (microemulsion) against *C. albicans*, in order to determine the minimal inhibitory concentration and inhibition of mature biofilm of *C. albicans.* The microemulsion developed consisted of grape seed oil as the oil phase (10% w/w), Brij 35® (20% w/w) and phosphate buffered saline (70% w/w) as aqueous phase prepared by sonication. The EO was loaded in the microemulsion (LEO) by sonication. The minimal inhibitory concentration (MIC) of EO and LEO against *C. albicans* (ATCC 10231 and a clinical isolate) was determined by microdilution assay according to the protocol described by CLSI, with modifications. Biofilm assay was performed using *C. albicans* suspension ($1{,}0x10^8$ cells/mL), which was added to microplate and incubated at 37 °C for 2h. After the pre-adhesion period, the supernatant was removed and 100µL RPMI medium were added to each microplate well for 48h, with RPMI renewed after 24h. The EO and LEO was added after 48h. The microplates were re-incubated for 24h at 37 °C, and XTT® reduction assay was performed. EO showed MIC values of 500 µg/mL (ATCC) and >500 µg/mL (clinical isolate). Moreover, LEO improved the action of the EO, with decreasing of MIC to 31.2 µg/mL and 62.5 µg/mL against ATCC and clinical isolate, respectively. Thus, the use of the nanotechnology enhanced the action of EO. A concentration of 10xMIC of EO exhibited high inhibition against mature biofilm of *C. albicans* with inhibition percentage of 87% (ATCC) and 89% (clinical isolate). LEO (10xCIM) inhibited *C. albicans* mature biofilm with percentage of inhibition of 73% (ATCC) and 52 % (clinical isolate). EO showed better anti-biofilm activity than LEO, in the concentration of 10xMIC, against ATCC strain, however, lower concentrations of LEO showed better activity than EO. The EO of *C. nardus* shows antifungal activity against *C. albicans* strains. In addition, the use of the nanotechnology (microemulsion) in order to improve the activity of EO can be a promising antifungal agent in the control of candidiasis caused by *C. albicans.*

Key-words: *Candida albicans*; *Cymbopogon nardus*; essential oil; nanostructured lipid system; antifungal activity

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