Title: NANOTECHNOLOGY-BASED MUCOADHESIVE LIQUID CRYSTAL FOR INCORPORATION OF *GOLDEN GRASS* EXTRACT: A STUDY OF THE ANTI-*Candida glabrata* POTENTIAL.

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Abstract:

Scientific studies of *Syngonanthus nitens* (Bong.) Ruhland show the use of the extract in antimicrobial activity, which is interesting to treat infections caused by *Candida glabrata*. Nanostructured systems with mucoadhesive properties are often used to improve antimicrobial activity of active constituents, such as liquid crystal precursor system (LCPS). This study evaluated the antifungal potential of the methanolic extract of scapes of *S. nitens* loaded (SNEL) or not (SNE) in LCPS against *C. glabrata* (ATCC 2001 and 3 clinical strains [CGV1,2 and 3]). The LCPS was synthesized with oleic acid (50% - oil phase), PEG-5-Ceteth-20 (40% - surfactant) and a polymer dispersion of Carbophol™ + Policarbophyl 974P™ (10% - aqueous phase). The determination of minimal inhibitory concentration (MIC) was performed by dilution in microplates (microdilution) which the SNE and SNEL were evaluated in concentrations from 1000 to 7.8 µg/mL. After the results of MIC, was developed the *Time kill assay* with the standard and more sensitive clinical strain, with the fungal (9 mL) suspensions (2.5 x 10^3 cell/mL) and SNE and SNEL (1 mL in 2x MIC value) was incubated (37º C) and aliquots of 0.5 mL were removed at different time intervals (0, 0.5, 1, 2, 4, 8, 12, 24, 36,48 hours), and resuspended in Sabouraud dextrose broth medium and 100 µL were inoculated on Sabouraud dextrose agar plates. All plates were incubated at 37°C for 48 h to count the colonies. The biofilm inhibition assay was made in microplates after 48 hours of biofilm formation and the SNE and SNEL was evaluated at concentrations from 20 to 0.6 mg/mL. amphotericin-B was used as positive control in all tests. The results showed that SNE is active against all strains (MIC values varied from 125 - 62,5 µg/mL), but their action was improved after incorporation in LPCS (MIC values varied from 15,6 – 3,9 µg/mL), this profile was noted in *Time kill* assay, which the inhibition of SNEL was higher and it was highlighted a possible fungistatic action. SNE is not active against biofilm, but SNEL was active against two strain (ATCC= 20 mg/mL and CGV2= 10 mg/mL). The lipophilic characteristic along with the mucoadhesive property of LCPS was important for the improvement of the activity, since may have promoted a direct contact of SNE with the membrane of fungal cells, which facilitated the action. These results showed the applicability of a LCPS for potentiation of SNE, which can be attractive to control of infections by *C. glabrata*.

Keywords: *Candida glabrata*, *Syngonanthus nitens*, Liquid crystal precursor system, Antifungal activity.

Acknowledgments: Brazilian National Council for Scientific and Technological Development – CNPq (Process number 140239/2015-4).