

TITLE: NEW PERSPECTIVES OF PHOTODYNAMIC THERAPY WITH HYPERICIN ON *Candida albicans* infections

AUTHORS: SAKITA, K. M.; CONRADO, P. C. V.; FARIA, D. R.; ARITA, G. S.; PIERALISI, N.; CESAR, G. B.; GONÇALVES, R. S.; CAETANO, W.; BONFIM-MENDONÇA, P. S.; SVIDZINSKI, T. I. E.

INSTITUTION: UNIVERSIDADE ESTADUAL DE MARINGÁ, MARINGÁ, PR (AVENIDA COLOMBO, 5790, CEP 87020-900, MARINGÁ-PR, BRAZIL)

ABSTRACT:

Candida albicans is the main causative agent of oropharyngeal candidiasis (OC), one of the most common infections in immunocompromised patients. The ideal therapy consists of fewer side effects and better efficacy. Photodynamic therapy (PDT) can be applied locally avoiding systemic side effects, because is based in a interaction between a photosensitizer (PS) and a light source (L) with specific wavelength that promote the production of reactive oxygen species (ROS) causing local damage to the cells. Hypericin is a natural PS extracted from plants of the genus *Hypericum*, especially *Hypericum perforatum* L., which presented great activity in PDT. As Hypericin belong to the family of polycyclic aromatic naphthodianthrone, is known that in aqueous solutions form nonfluorescent high molecular weight aggregates. This study aimed to show the effect of Hypericin, encapsulated in Pluronic P123, as PS in PDT against reference strain *C. albicans* ATCC 90028 and clinical isolates of *C. albicans*. Starting from a inoculum of 10^6 CFU.mL⁻¹ were tested 8 concentrations of Hypericin, ranging from 0.25 to 32 $\mu\text{mol.L}^{-1}$. The plate was incubated in a orbital shaker for 120 min at 37 °C. After this period of dark incubation, the 96-well plate was irradiated by the LED device in a fluence of 10.8 J.cm⁻². After, aliquots were placed in SDA and incubated at 37 °C for 24 h for evaluation of minimum fungicidal concentration (MFC). Positive control (PS-L-), light control (PS-L+) and dark control (PS+L-) was carried out together to guarantee the efficacy of the treatment was due to PS+L+. The MFC was determined as the concentration in which no colony growth was observed. No significant difference between the controls was found (data not shown). The reference strain and 50 % of clinical isolates (n=3) showed MFC of 1.0 $\mu\text{mol.L}^{-1}$ and 17 % (n=1) showed MFC of 2.0 $\mu\text{mol.L}^{-1}$. However, in 33 % of the isolates (n=2) was not possible to determine the MFC until the highest concentration tested (32 $\mu\text{mol.L}^{-1}$). Hypericin as PS for PDT use showed to be a promising alternative to treat oropharyngeal candidiasis as can be applied locally and is fungicidal for *C. albicans*. It is necessary to highlight that LED power used in this study was lower than those already reported in the literature, suggesting lower toxicity to healthy tissue. Other studies with high concentrations of Hypericin and high light doses are needed to test in strains that showed no reduction in lighter conditions.

Keywords: *Candida albicans*, Hypericin, Photodynamic therapy.

Development Agencies: CAPES, CNPQ.