

TITLE: ANTIFUNGAL AND ANTIBIOFILM ACTIVITY OF *Plantago major* EXTRACT AGAINST *Candida auris*

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ABSTRACT:

Candida auris was first identified in Japan in 2009 and since then, it has been identified in more than 40 countries on all continents and has become a global threat due to its rapid emergence, multi-resistance to antifungals and high mortality rates. In hospital settings, *C. auris* is often associated with bloodstream infections, resulting in mortality rates ranging between 30 and 60%. Microbial resistance to available drugs has become a serious public health problem. So, the development of new antimicrobials is necessary. Natural products, including medicinal plants, molecules that can be used in the development of antimicrobials have been widely studied for searching of new compounds with therapeutic purposes. *Plantago major*, is a plant used to treat infections caused by bacteria, diarrhea, cancer and has anti-inflammatory, antioxidant and healing activities. The aim of this study was to evaluate the activity of the methanol extract of *P. major* leaves against *C. auris* ATCC 11903 and a clinical isolate obtained from the first outbreak occurred in Bahia, Brazil.. To determine the MIC, microdilution tests were carried out in 96-well microplates. Using concentrations ranged between 10 mg/ml and 50 mg/ml. Subcultures were performed on Sabouraud agar with to determine the CFM. The synergistic effect was evaluated through the combination of subinhibitory concentrations of extract and amphotericin B. The results were read in a spectrophotometer at 600 nm. To determine the antibiofilm activity, the yeasts were cultivated in Yeast Nitrogen Base containing 0.9% glucose, with different extract concentrations. The adhered biofilm was fixed with 95% ethanol and stained with 0.4% crystal violet. The results were read in a spectrophotometer at 540 nm. The MIC for *C. auris* ATCC 11903 and clinical isolate was 10 mg/mL. At the concentrations tested, the extract did not show fungicidal activity. Therefore, it is concluded that its activity is fungistatic. For both strains, there was a synergistic fungistatic interaction with amphotericin B. The biofilm reduction was up to 69.3% for *C. auris* ATCC 11903 and up to 90.78% for clinically isolated. The results show that the extract from the leaves of *P. major* has inhibitory activity against *C. auris* and may represent a new natural compound to be studied aiming therapeutic purposes.

Keywords: Antifungal resistance, Biofilm, *C. auris*, *P. major*

Development Agency: FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo, grant number 2020/04211-0)