

## **Title: NEW ANTIFUNGAL STRATEGY USING HYDROETHANOLIC EXTRACTS OF *Astronium graveolens* IN COMBINATION WITH A NANOSTRUCTURED SYSTEM**

**Authors:** Bonifácio, B.V.<sup>1</sup>, Silva, P.B.<sup>1</sup>; Negri, K.M.S.<sup>1</sup>; Ramos, M.A.S.<sup>1</sup>; Souza, L.P.<sup>2</sup>; Vilegas, W.<sup>3</sup>; Chorilli, M.<sup>1</sup>; Bauab, T.M.<sup>1</sup>

**Institutions:** <sup>1</sup>School of Pharmaceutical Sciences, São Paulo State University, Araraquara, São Paulo, Brazil; <sup>2</sup>Chemistry Institute, São Paulo State University, Araraquara, São Paulo, Brazil; <sup>3</sup>Coastal Campus of São Vicente, São Paulo State University, São Vicente, São Paulo, Brazil.

### **Abstract:**

Because the incidence rates and estimated number of infections caused by several *Candida* sp strains are increasing, concerns have been raised about the potential spread of this microorganism both in community and hospital environments. In addition, strains with the ability to resist most conventional antimicrobials have stimulated the search for new natural sources of antimicrobial agents, such as medicinal plants. *Astronium graveolens* Jacq. (Anacardiaceae), an arboreal species widely distributed in the Brazil's Atlantic Forest, contains antimicrobial properties and was tested in this study in order to control fungal diseases. The antifungal activity of the hydroethanolic extract of the stalk and leaves of *A. graveolens* (concentrations from 1000 to 7.81 µg/mL) was evaluated by microdilution method against *Candida albicans* (ATCC 18804, 10231 and 5314) and *Candida glabrata* (ATCC 2001), including one clinical strain for each species (CAV3 and CGV3, respectively); amphotericin B and fluconazole were used as positive controls. Since some studies have shown that nanostructured systems are able to optimize the properties of plants, the extracts were loaded into a microemulsion comprised of 10% oil phase, 10% surfactant and 80% aqueous phase, prepared by sonication. Of the extracts not loaded into the system, the stalk of *A. graveolens* had shown activity only against *C. albicans* ATCC 10231 (MIC 1000 µg/mL), *C. glabrata* ATCC 2001 (MIC 15.62 µg/mL) and CGV3 (MIC 500 µg/mL) while the leaves showed activity against *C. albicans* ATCC 10231, CAV3 and CGV3 (MIC's 62.5 µg/mL) and *C. glabrata* ATCC 2001 (MIC 15.62 µg/mL). After loading the extracts into the system, the activity of some stalk and leaves extracts was enhanced when retested: the stalk against *C. albicans* ATCC 18804 (MIC from >1000 µg/mL) and 10231 (MIC from 1000 µg/mL) started presenting MICs of 62.5µg/mL; CAV3 (MIC from >1000 to 500 µg/mL), *C. albicans* ATCC 5314 (MIC from > 1000 to 500 µg/mL) and CGV3 (MIC from 500 to 31.25 µg/mL); highlighted results for the leaves include *C. albicans* ATCC 18804 (MIC from >1000 to 125 µg/mL), *C. albicans* ATCC 10231 (MIC from 62.5 to 31.25 µg/mL), *C. albicans* ATCC 5314 (MIC from >1000 to 31.25 µg/mL) and *C. glabrata* ATCC 2001 (MIC from 15.62 to 7.81 µg/mL). These results proved that *A. fraxinifolium* loaded into the nanosystem can improve antifungal activity against some strains of *Candida* sp and can be further used to improve other biological properties.

**Keywords:** *Astronium graveolens*, microemulsion, *Candida* sp

**Financial support:** grant#2009/52237-9, grant#2013/25432-0 and grant#2013/25121-5, São Paulo Research Foundation (FAPESP) and Brazilian National Council for Scientific and Technological Development – CNPq (process number 133916/2012-0)