

Geopropolis Enhances Neutrophil Activity and Exhibits Fungicidal Effects Against *Paracoccidioides* spp.

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Introduction: Paracoccidioidomycosis-PCM is a systemic mycosis caused by fungi of the *Paracoccidioides* spp. complex. In Brazil, the most prevalent species associated with PCM are *Paracoccidioides brasiliensis*-Pb and *Paracoccidioides lutzii*-Pl. PCM is a challenging fungal disease that requires prolonged treatment with currently available antifungal agents. The use of propolis and its various compounds and types may represent a promising alternative in the treatment of fungal diseases, as it exhibits fungicidal activity and potential to modulate the immune response at the site of infection. In this context, geopropolis is a natural product produced by mandaçaia bees (*Melipona quadrifasciata* and *Melipona fasciculata*) with antimicrobial and immunomodulatory properties has potential for investigation in the treatment of PCM. **Furthermore, its complex chemical composition, rich in bioactive compounds.**

Objectives: The aim of this study was to evaluate the activity of neutrophils-PMNs collected from the air pouch infection model using Pb and Pl, treated with geopropolis at different concentrations (200, 500, and 1000mg/mL). **Methods:** The fungicidal capacity was assessed by counting viable fungi and colony-forming units-(CFU). Additionally, the effect of geopropolis at a concentration of 500mg/mL on the production of oxygen metabolites (catalase and nitric oxide-[NO] and total protein levels was evaluated. **Results:** Treatment with different concentrations of geopropolis demonstrated fungicidal activity at all tested concentrations. Geopropolis at 500mg/mL was further evaluated for its immunomodulatory potential, particularly regarding the production of oxygen metabolites and proteins. However, only the results for Pb, and not for Pl, showed a reduction in the production of reactive oxygen species-(ROS) and total proteins. **Conclusion:** Geopropolis exhibits direct fungicidal activity against both Pb and Pl and may represent a potential therapeutic candidate for the treatment of PCM.

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