

TITLE: ACTIVITY OF ETHANOLIC AND SUPERCRITICAL EXTRACTS OF BRAZILIAN RED PROPOLIS ON FLUCONAZOLE-RESISTENT *Malassezia pachydermatis* ISOLATES

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ABSTRACT:

Malassezia pachydermatis is a non-lipophilic, non-mycelial and unipolar yeast. This commensal yeast may become pathogenic under the influence of predisposing factors, causing otitis and different clinical forms of dermatitis in domestic animals and humans. *M. pachydermatis* is one of most frequent etiological agents of skin disorders in dogs and humans. The disease requires long treatments and/or high doses of antifungal agents. Commercial antifungal drugs have many disadvantages, such as high cost, side effects, low biological safety and induction of fungal resistance. *In vitro* resistance of selected genotypes of *M. pachydermatis* to azoles has emerged recently, and the resistance to fluconazole is more commonly reported. New therapeutic alternatives for the control of these mycoses, presenting a broad spectrum of activity, fungicidal rather than fungistatic action, being safe and cost-effective are needed. Propolis, with recognized therapeutic and prophylactic functions on diverse microorganisms, has a high potential as a new fungicidal compound. In the present study, the susceptibility of fluconazole-resistant *M. pachydermatis* strains to ethanolic and supercritical extracts of Brazilian red propolis was evaluated *in vitro* using CLSI reference broth microdilution method (CLSI M27-A2 2002). A total of 12 *M. pachydermatis* strains obtained from dogs with skin lesions (6), from dogs with otitis (3) and from an asymptomatic free-living *Didelphis* (3) were tested. The red propolis extracts were obtained by conventional ethanolic extraction and by extraction with CO₂ as a supercritical fluid on a specific equipment. All *M. pachydermatis* strains were resistant to fluconazole. Both ethanolic and supercritical extracts of red propolis were able to kill all *M. pachydermatis* isolates at the concentration range of 4 to 16 mg/mL and 8 to 16 mg/mL, respectively. The ethanolic extract showed a lower MIC than the MIC value obtained with supercritical extract. In conclusion, the red propolis presented a significant antifungal activity against fluconazole-resistant *M. pachydermatis* strains and the ethanolic extract showed lowest MIC values on all the tested strains. This extract can be tested in further studies on the control and treatment of dermatomycosis.

Keywords: antifungal activity, dermatitis, otitis.