

**TITLE:** ANTIFUNGAL ACTIVITY EVALUATION OF IMIDAZOLE ALKALOIDS FROM JABORANDI LEAVES AND THE SYNERGISTIC EFFECT OF THE ASSOCIATION OF TERBINAFINE WITH PILOCARPINE CHLORYDRATE

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**ABSTRACT:**

Fungal infections affect millions of individuals worldwide and contribute for the human morbimortality. For the control of mycosis, the search for new molecules is needed, as well as pharmacotherapy optimization. *Pilocarpus microphyllus*, popularly known as jaborandi, is a plant native of Brazil, from whom several alkaloids have been isolated. Among them, only pilocarpine is available for use in the glaucoma and xerostomia treatment. Even so, these alkaloids lack in studies referring to their antifungal potential. In this study it was evaluated the antifungal activity of five alkaloids (pilocarpine, isopilocarpine, epiisopilosine, isopilosine and pilosine) in their different salts. Considering that pilocarpine is the most abundant compound on the jaborandi leaves, its effect when combined with terbinafine were also evaluated. For the study were used nine fungal isolates, comprehending representatives of chromoblastomycosis, sporotrichosis, dermatophytosis, aspergillosis, candidiasis and cryptococcosis. The fungal susceptibility assay was performed in accordance with the protocols M27-A3 and M38-A2 by CLSI. Interaction evaluation of pilocarpine/terbinafine was carried out using chessboard technique. From the tested alkaloids, pilocarpine chlorydrate and pilosine showed activity against *Fonsecaea pedrosoi* and *Trichophyton interdigitale*, respectively. Pilocarpine/terbinafine interaction was synergic for all the tested isolates, including the ones where the alkaloids had no activity when they were tested alone. FICI values ranged from 0.031 to 0.5, being the best synergic effect obtained for *Aspergillus fumigatus*. This synergic interaction indicates the potential of this alkaloids as a new agent to be used on combination antifungal therapy and encourages us to explore ways for research in this area.

**Keywords:** *In vitro* fungal susceptibility, mycosis, *Pilocarpus microphyllus*

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