TITLE: LMM6 AS NEW POTENTIAL ANTIFUNGAL AGAINST *Paracoccidioides* spp.

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ABSTRACT:
Paracoccidioidomycosis (PCM) is important invasive fungal infection in Latin America. Due to long periods of treatments, the conventional antifungals present problems related to toxicity. Therefore, *in silico* methods have been used to the development of new specific drugs against the fungus. In this work the antifungal potential of the LMM6 compound, selected by virtual screening, against clinical isolates of *Paracoccidioides* spp. was evaluated, as well as the evaluation of the micromorphological alterations. The minimal inhibitory concentrations (MIC) of LMM6 against 5 isolates were evaluated by the microdilution method (CLSI - M27-A3) with modifications. The compound was prepared in a range of concentrations from 0.06 to 32.0 ug/mL and incubated with yeast at 35°C for 7 days. The MIC values was determined by color change visual after 24h of incubation with resazurin solution (0.02%). The minimal fungicidal concentrations (MFC) were determined by subculture from MIC in plate BHI-agar at 35°C for 7 day. For scanning electron microscopy (SEM) the Pb18 yeast cells were incubated with 4 μg/mL for 5 days at 35°C. After treatment, yeasts were observed with Shimazu SS-550 Super scan (magnifications of 10000x). The MICs values ranging between 0.25 - 2 μg/mL for all isolates of *Paracoccidioides* spp. Otherwise, the MFCs values ranging between 0.5 - 4 μg/mL. The morphological alterations were observed in the yeast from *P. brasiliensis* after treatment with LMM6 2 μg/mL (4xMIC). The electron micrographs revealed deformations, as rough surface. The typical morphology of *P. brasiliensis* yeast cells were detected only in the control no treated. Therefore, the antifungal activity was observed at low concentrations of LMM6 compound. The capacity of cell changes, showing a promising candidate a novel antifungal against PCM.

KEYWORDS: paracoccidioidomycosis, antifungal agents, specific drugs, scanning electron microscopy, minimal inhibitory concentrations