TITLE: NEW COMPOUND INDUCES MORPHOLOGICAL ALTERATIONS IN *Paracoccidioides brasiliensis*

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Paracoccidioides brasiliensis is the main etiological agent of Paracoccidioidomycosis (PCM) in Latin America. PCM is considered the 8th largest cause of mortality among predominantly chronic diseases and the highest mortality rate among systemic mycoses. Therapies have several limitations, such as drug interactions, infusion-related events and nephrotoxicity. Therefore, the drug development that act selectively in target pathogenic fungi without producing collateral damage are necessary. A new compound targeted to enzyme chorismato synthase was selected by virtual screening with focus in new antifungal agent more selective and specific. Therefore, the aim of this study was to evaluate the micromorphological alterations of *Paracoccidioides brasiliensis* (Pb18) after interaction with new compound, named CP1. For scanning electron microscopy (SEM) the Pb18 yeast cells were incubated with two concentration of CP1 (64 or 128mg/L) for 72h at 35°C. The cells were dehydrated and fixed using Poly-L-lysine (Sigma). The samples were metallized and observed with Shimazu SS-550 Super scan at magnifications of 1000x and 3000x. The CP1 compound (128mg/L and 64mg/L) was able to cause the morphological alterations in the yeast cells from *Paracoccidioides* sp. The electron micrographs revealed deformations, including depression and rough surface and some cells presented extravasation of intracellular fluid. Furthermore, fungal cells showed irregular-shaped and multi-budding yeast was not well preserved. The agglomeration of yeast cells were, also, detected. These hallmark changes were observed in approximately 80% of treated cells with CP1, while the typical morphology of *P. brasiliensis* yeast cells were detected in the control. CP1 is a promising new inhibitor of the shikimate pathway, its action may result in partial or total loss of amino acids essential for fungal viability and deficiency of important metabolites that could lead to morphological alterations.

Keywords: Antifungal, paracoccidoidomycosis, scanning electron microscopy, chorismate synthase.