HIV ASPARTYL PEPTIDASE INHIBITORS INTERFERE WITH ULTRASTRUCTURE OF *Phialophora verrucosa*

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Phialophora verrucosa is one of the major dematiaceous fungi causing phaeohyphomycosis, and other infections such as mycetoma and endophthalmitis, but mainly chromoblastomycosis (CBM). CBM is extremely difficult to treat and often refractory to various therapeutic approaches. The pathogenesis of CBM is not fully understood. Several studies have shown that secreted peptidases are associated with important biological processes and fungal virulence. In this context, our research group has focused on the identification, biochemical characterization and investigation of biological function of secreted proteases in black fungi. In the previous study, we showed that HIV aspartic protease inhibitors (HIV PIs) such as ritonavir and lopinavir inhibited *P. verrucosa* extracellular aspartic protease activity at about 80%. Besides that, we demonstrated that among the HIV PIs tested, ritonavir and lopinavir were also able to inhibit the fungal growth in a dose-dependent manner. Therefore, the aim of the present study was to evaluate the effect of HIV PIs on *P. verrucosa* ultrastructure. For this assay, *P. verrucosa* conidia were incubated for 20 h in RPMI medium in the absence (control) or presence of HIV PIs and processed by scanning electron microscopy (SEM) as described by Sangetha et al., Micron 40:439-43. SEM analyses demonstrated that HIV PIs treatment induced different cellular alterations such as increased the size of cells, surface invaginations, cell disruption, surface deposits and filamentous formation. Collectively, our finding corroborate the supposition that aspartic peptidase could be potential targets for future alternative therapeutic intervention in infections caused by *P. verrucosa*.

Keywords: *Phialophora verrucosa*, aspartic peptidase and proteolytic inhibitors.

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