HIV Aspartyl Peptidase Inhibitors Interfere with Cellular Proliferation, Ultrastructure and Macrophage Infection of *Leishmania amazonensis*

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Leishmania is a protozoan etiologic agent of leishmaniasis. Current therapy for leishmaniasis is suboptimal due to toxicity of the available therapeutic agents and the emergence of drug resistance. Compounding these problems is the increase in the number of cases of *Leishmania*-HIV coinfection, due to the overlap between the AIDS epidemic and leishmaniasis. In the present report, we have investigated the effect of HIV aspartyl peptidase inhibitors (PIs) on the *Leishmania amazonensis* proliferation, ultrastructure, interaction with macrophage cells and expression of classical peptidases which are directly involved in the *Leishmania* pathogenesis. All the HIV PIs impaired parasite growth in a dose-dependent fashion. PIs treatment caused profound changes in the *Leishmania* ultrastructure, including cytoplasm shrinking, increase in the number of lipid inclusions and some cells presenting the nucleus closely wrapped by endoplasmic reticulum, as well as chromatin condensation, which is suggestive of apoptotic death. The treatment of promastigote forms with PIs drastically reduced the association indexes during the interaction with murine macrophage cells and intracellular development of *Leishmania*. Despite all these beneficial effects, the PIs induced an increase in the expression of cpb and gp63, two well-known virulence factors expressed by *Leishmania* spp. The results presented herein add new in vitro insight into the wide spectrum efficacy of HIV PIs and suggest additional studies about the synergistic effects of classical antileishmanial compounds and HIV PIs in *Leishmania*-HIV-1 macrophages coinfection.

Key-words: HIV Aspartyl Peptidase Inhibitors, *Leishmania amazonensis*
Suppoted by: CNPq, Faperj and Fiocruz