Miltefosine Induces Apoptosis In *Leishmania amazonensis*

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Leishmaniasis remains a major health problem of the tropical and subtropical world. The pathology is manifested in cutaneous, mucocutaneous or visceral forms. Dramatic increases in the rates of infection and drug resistance and the non availability of safe vaccines have highlighted the need for identification of novel anti-leishmanial agents and their modes of action. Miltefosine has proved to be a potent oral treatment for human visceral leishmaniasis, as observed in *Leishmania donovani.* In the present study, we have demonstrated that in promastigotes of *Leishmania amazonensis,* the etiological agent of cutaneous leishmaniasis, miltefosine exerts its leishmanicidal effect by triggering a programmed cell death. At the concentration of 30 µM, this compound promoted the loss of plasma membrane integrity as detected by binding of annexin V and propidium iodide, the arrest of cell-cycle at the sub G_0/G_1 phase, the fragmentation of genomic DNA into oligonucleosomal fragments and the DNA nicking shown by deoxynucleotidyltransferase-mediated dUTP end labeling (TUNEL). These data suggest that miltefosine was able to induce programmed cell death in *Leishmania amazonensis* promastigotes. The identification of the death-signaling pathways activated in miltefosine-treated parasites appears to be essential for a better understanding of the molecular mechanisms of action in these parasites.

Key Words: Miltefosine, *Leishmania amazonensis*, apoptosis.

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