

THE EFFECTS OF THE CALPAIN INHIBITOR MDL28170 AGAINST
LEISHMANIA AMAZONENSIS

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Leishmaniasis is a group of diseases with large spectrum of clinical manifestations caused by protozoans of the genus *Leishmania*. Here, we demonstrate that MDL28170, a potent calpain inhibitor, causes leishmanial death. *L. amazonensis* possesses calpain homologues that may be the site of action of this proteolytic inhibitor. MDL28170 caused several ultrastructural alterations in vitro in *L. amazonensis*. Electron microscopy analysis of promastigotes incubated for 48 h with the IC₅₀ of the drug showed that this compound induced condensation and breaking up of nuclear chromatin. These phenomena are suggestive of apoptosis-like death. Additionally, the inhibitor caused vacuolization in the cytoplasm. Calpain is upregulated in *Leishmania* isolated from patients of post kala-azar dermal leishmaniasis, and may contribute to the persistence of parasites after clinical cure of visceral leishmaniasis. Understanding of MDL28170-mediated death will facilitate the design of new therapeutic strategies against *Leishmania* parasites.

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