**Leishmania major**: activity of tamoxifen against experimental cutaneous leishmaniasis

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Leishmaniasis is a family of diseases caused by protozoan parasites of the genus *Leishmania*. Various *Leishmania* species can cause human infection, producing a spectrum of clinical manifestations. The current treatments are unsatisfactory, and in absence of a vaccine, there is an urgent need for effective drugs to replace/supplement those currently in use. Recent studies have shown that the antineoplastic drug, tamoxifen, had direct leishmanicidal effect on several *Leishmania* species *in vitro*. Moreover, *in vivo* testing was carried out on some of the species and showed promising results. The authors have carried out the present work to complement previous published studies by investigating *in vivo* activity of tamoxifen in an experimental model of cutaneous leishmaniasis (CL) caused by *Leishmania major*. Groups of infected mice were given tamoxifen, orally, at a dose of 20 mg/kg/day for 15 days. Efficacy was assessed clinically, parasitologically, histopathologically by light and Transmission Electron Microscope (TEM). Results showed that untreated infected mice suffered from autoamputation of the inoculated foot pad. However, those which received tamoxifen showed marked improvement of the cutaneous lesions and reduction of parasite burden. TEM of the cutaneous lesions from infected mice revealed the fine structure of normal *Leishmania* amastigotes, whereas those from infected mice treated with tamoxifen showed considerable changes. All male mice that received tamoxifen showed scrotal swelling with evident histopathological changes in the testes that could seriously compromise fertility of male mice. In conclusion, although tamoxifen causes significant side effects to the male reproductive system in the mouse model, it could provide an alternative to current agents. Results of this study demonstrated *in vivo* activity of tamoxifen against *Leishmania major*, thus, suggesting that tamoxifen is a suitable lead for the synthesis of more effective and less toxic antileishmanial derivatives.

**Keywords**: *Leishmania major*; tamoxifen, *in vivo*; experimental; testis; cutaneous leishmaniasis.