Poloxamer 407 (Pluronic® F127)-based polymeric micelles for amphotericin B: *in vitro* activity, toxicity and *in vivo* therapeutic efficacy against murine tegumentary leishmaniasis

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ABSTRACT

Amphotericin B (AmpB) has shown an effective *in vitro* antileishmanial activity against different *Leishmania* species, although its *in vivo* use has been hampered due to its high toxicity. In the present study, a Poloxamer 407 (P407, Pluronic® F127)-based polymeric micelles system was used as a delivery for AmpB (AmpB/M), and this formulation was employed to treat BALB/c mice experimentally infected with *Leishmania amazonensis* stationary promastigotes. Clinical, parasitological and immunological evaluations were performed in the infected animals, which either received saline or were treated with free AmpB, AmpB/M or B-AmpB/M (non-incorporated micelles). In the results, free AmpB-treated and infected mice presented alterations in their body weight, which were associated with hepatic and renal damage. On the other hand, no organic alteration was observed in the AmpB/M-treated and infected animals. When parasitological parameters were evaluated, AmpB/M group mice, when compared to the others, showed significant reductions in their lesion average size and in the parasite burden in all evaluated tissue and organs. These animals also showed significantly higher levels of parasite-specific IFN-γ, IL-12, GM-CSF, as well as a higher nitrite production in their *in vitro* cultured spleen cells, which were associated with low levels of IL-4, IL-10 and anti-*Leishmania* IgG1 isotype antibodies, when compared to the control groups. In conclusion, this non-toxic AmpB-containing polymeric micelles system could be considered as a viable alternative for future studies in the treatment of the disease caused by *L. amazonensis*.

Keywords: Amphotericin B; poloxamer 407; toxicity; tegumentary leishmaniasis; treatment; *Leishmania amazonensis.*

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53