An optimized nanoparticle delivery system based on chitosan and chondroitin sulphate molecules reduces the toxicity of amphotericin B and is effective in treating tegumentary leishmaniasis

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Amphotericin B (AmpB) is active against leishmaniasis, but its use is hampered due to its high toxicity observed in the patients. In this study, a nanoparticle delivery system for AmpB (NQC-AmpB) containing chitosan (Cs) and chondroitin sulphate (ChS) was evaluated in BALB/c mice against *Leishmania amazonensis*. An *in vivo* biodistribution study, including biochemical and toxicological evaluations, was performed to evaluate the toxicity of AmpB. Nanoparticles were radiolabeled with technetium-99m and injected in mice. The products presented a similar biodistribution in the liver, spleen, and kidneys of the animals. Free AmpB induced alterations in the body weight of the mice, which, in the biochemical analysis, indicated hepatic and renal injury, as well as morphological damage to the kidneys of the animals. In general, no significant organic alteration was observed in the animals treated with NQC-AmpB. Mice were infected with *L. amazonensis* and treated with the nanoparticles or free AmpB; when parasitological and immunological analyses were performed. The NQC-AmpB group, as compared to the control groups, presented significant reductions in the lesion size and in the parasite burden in all evaluated organs. These animals presented significantly higher levels of IFN- and IL-12, and low levels of IL-4 and IL-10, when compared to the control groups. The NQC-AmpB system was effective in reducing the infection in the animals, and proved to be effective in reducing in significant levels the toxicity evoked by AmpB, which was observed when it was administered alone. In conclusion, the NQC-AmpB could be considered a viable possibility for future studies in the treatment of leishmaniasis.

Keywords: Amphotericin B; nanoparticles; treatment; leishmaniasis; toxicity; *Leishmania amazonensis.*

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