Antileishmanial activities of 8-hydroxyquinoline-containing polymeric micelle system against murine tegumentary leishmaniasis.

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The current treatment of leishmaniasis has been hampered due to the high toxicity of the available drugs and long duration protocols, which often lead to its abandonment. In the present study, a poloxamer 407-based delivery system was developed, and a molecule, 8-hydroxyquinoline (8-HQN), was incorporated with it, leading to an 8-HQN/micelle (8-HQN/M) composition. Assays were performed to evaluate the in vitro antileishmanial activity of 8-HQN/M against Leishmania amazonensis stationary promastigotes. The cytotoxicity in murine macrophages and in human red cells, as well as the efficacy of the treatment in macrophages infected by parasites, was also assessed. This product was also evaluated for the treatment of murine tegumentary leishmaniasis, using L. amazonensis-infected BALB/c mice. To evaluate the in vivo efficacy of the treatment, the average lesion diameter (area) in the infected tissue, as well as the parasite load at the site of infection (skin), spleen, liver and draining lymph nodes were examined. Non-incorporated micelle (B-8-HQN/M) and the free molecule (8-HQN) were used as controls, besides animals that received only saline. The parasite burden was evaluated by limiting dilution and quantitative real-time PCR (qPCR) techniques, and immunological parameters associated with the treatments were also investigated. In the results, the 8-HQN/M group, when compared to the others, presented more significant reductions in the average lesion diameter and in the parasite burden in the skin and all evaluated organs. These animals also showed significantly higher levels of parasite-specific IFN-γ, IL-12, and GM-CSF, associated with low levels of IL-4 and IL-10, when compared to the saline, 8-HQN/M, and B-8-HQN groups. A predominant IL-12-driven IFN-γ production, against parasite proteins, mainly produced by $CD4^+$ T cells, was observed in the treated animals, post-infection. In conclusion, 8-HQN/M was highly effective in treating L. amazonensis-infected BALB/c mice and can be considered alone, or combined with other drugs, as an alternative treatment for tegumentary leishmaniasis. Graphical Abstract Therapeutic scheme and immunological and parasitological parameters developed in the present study.