

Leish119- *In vitro* activity of antimalarial drugs against *Leishmania amazonensis*

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Introduction: Leishmaniasis comprises a broad spectrum of diseases caused by *Leishmania* parasites. Treatment with the first-line drugs for leishmaniasis, the pentavalent antimonials, can be complicated by side effects, less sensitivity or resistance of some *Leishmania* species, variations in pharmacokinetics, drug-host immune response interaction and high cost. Therefore, it is pivotal the development of safer, cheaper and more effective treatments for leishmaniasis. Drug repositioning is a strategy to identify and develop new uses for existing drugs, reducing expenditures and research time. In this context, the aim of this work was to evaluate the antileishmanial activity of antimalarial drugs. **Methods:** Promastigotes of *Leishmania amazonensis* were incubated in the presence of increased concentrations of artesunate, chloroquine, hidroxichloroquine, mefloquine or primaquine, ranging from 0.6 to 50 μ M, in order to determine the concentration that inhibits in 50% the parasite growth (IC₅₀). The cell cycle was assessed in drug-treated promastigotes using propidium iodide incorporation in flow cytometry analysis. Cytotoxicity to mammalian cells was evaluated in BALB/c mice splenocytes by incorporation of [*methyl*-³H]-thymidine, allowing the calculation of lethal concentrations for 50% of cells (LC₅₀). Peritoneal macrophages from CBA mice were infected with promastigotes of *L. amazonensis* and treated with antimalarial drugs in various concentrations to determine the IC₅₀ against amastigotes. Infected and treated macrophages were analyzed by transmission electron microscopy. **Results:** Chloroquine and hidroxichloroquine did not significantly affect promastigote growth at 50 μ M. At this concentration artesunate and primaquine significantly inhibited parasite growth, although less than 50%. Mefloquine at 50 μ M inhibited completely the growth of *L. amazonensis*, compared to controls, with an IC₅₀ of $8.4 \pm 0.7 \mu$ M. Incubation with mefloquine at the IC₅₀ concentration for 48 h caused a G2/M cell cycle arrest. Only chloroquine, hidroxichloroquine and mefloquine were active against amastigotes at a maximum tested concentration of 5 μ M and presented an IC₅₀ of $0.78 \pm 0.08 \mu$ M, 0.67 ± 0.12 and $1.56 \pm 0.18 \mu$ M, respectively. There was no cytotoxicity effect of these drugs at the concentrations tested. The ultrastructural analyses by transmission electron microscopy showed that, after treatment with chloroquine parasites, showed a Golgi complex damage and increased in vacuolization in the cytoplasm, while membrane blebbing was observed after mefloquine treatment of infected cells. **Conclusion:** Chloroquine, hidroxichloroquine and mefloquine showed a promising antileishmanial activity, low toxicity and may constitute an alternative therapy to conventional treatment of cutaneous leishmaniasis. *In vivo* assays will be performed to validate the effect against *L. amazonensis* of these antimalarial drugs. **E-mail:** vinicius@aluno.bahia.fiocruz.br