

Title: In vitro evaluation of the leishmanicidal activity of the essential oil derivative R (-) carvone in promastigotes and amastigotes of *Leishmania amazonensis*

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RESUMO

According to the World Health Organization Leishmaniasis is endemic in 98 countries and is among the seven main tropical diseases, being considered a public health problem responsible for 20 to 40 thousand deaths annually. Due to the diversity of agents, vectors and reservoirs, the control of this disease is a challenge for the competent authorities. The available therapeutic alternatives have limitations that make it difficult for patients to adhere to treatment, such as high toxicity and the need for prolonged parenteral administration, in addition to the possible selection of resistant strains. Thus, the objective of this work was to evaluate the effect of the essential oil R (-) carvone in the experimental model of leishmaniasis. Through the colorimetric test with Resazurin, the leishmanicidal activity of R (-) carvone was evaluated in cultures of promastigotes (10^6 parasites/ml) of *Leishmania amazonensis*. Then, the toxicity of R (-) carvone in murine peritoneal macrophages (10^5 cells /ml). Finally, the test of infection of peritoneal macrophages with amastigotes of *L. amazonensis* (infection ratio 3 parasites/cell) was carried out for 24 h at 37°C and 5% CO₂ in different concentrations of the essential oil R (-) carvone. The viability test in promastigotes cultures showed that at concentrations 6.5 µM and 3.125 µM cell viability was high, approximately 90%. However, at higher concentrations of 25 µM and 50 µM Carvone, approximately 50% of treated promastigotes died (IC₅₀=15.75). The treatment of parasitic macrophages with amastigotes of *L. amazonensis* showed modulatory potential, as there was a decrease in the percentage of parasitized cells in all concentrations tested with a dose-dependent effect. Our data also suggest that treatment with Carvone at different concentrations did not change the average number of amastigotes per macrophage, demonstrating stability in the number of intracellular parasites in all groups, which suggests that the infection rate decreased due to the reduction of infected cells and not by the reduction of intracellular parasites. Thus, these results indicate, for the first time, the therapeutic potential of the essential oil derivative R (-) carvone in the experimental model of leishmaniasis.

Keywords: Leishmaniasis, Essential Oils, R (-) carvone, *L. amazonensis*.