LEISHMANICIDAL POTENTIAL DIARYLPENTANOIDS: *In vitro* EVALUATION AGAINST *Leishmania amazonensis* AND *Leishmania infantum*

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Leishmaniasis is a disease caused by protozoa of the genus Leishmania spp. Current treatments are limited due to significant side effects and the emergence of resistant strains. Curcumin has shown promising activity against these parasites in in vitro studies; however, its low bioavailability in biological systems compromises its in vivo efficacy. Consequently, the development of analogues has become a major focus of research. In this context, this study evaluated the in vitro leishmanicidal activity of diarylheptanoids (DH) and diarylpentanoids (DP) against Leishmania amazonensis and Leishmania infantum. Initial screening was conducted using 14 compounds against promastigote forms of L. amazonensis. The compounds that exhibited more than 60% lysis were further tested to determine the effective concentrations (EC50) against both promastigote and axenic amastigotes forms. Cytotoxicity was assessed by the XTT method in J774A murine macrophages and by hemolysis assays using defibrinated sheep blood. Among the compounds evaluated, DP6 showed potent leishmanicidal activity against promastigote forms of *L. amazonensis* and *L. infantum*, with EC50 values lower than 10 μM. Compound DP5 demonstrated efficacy against amastigote forms of both species, with EC50 values ranging from 5.01 to 38.43 μM. In addition, both compounds exhibited low cytotoxicity, with cell viability rates above 90% in concentrations up to 100 μM, and with no hemolytic effects in tested concentrations. These results indicate that diarylpentanoids are promising candidates for the in vivo studies against leishmaniasis, contributing to the advancement of more effective, safe and accessible therapeutic alternatives.

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