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IN VITRO *ANTILEISHMANIAL ACTIVITY OF DICENTRINE FROM BRANCHES OF Ocotea langsdorffii (LAURACEAE)*

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Leishmaniasis is a neglected tropical disease caused by protozoan parasites of the genus *Leishmania*. Current chemotherapeutic options, such as pentavalent antimonials, pentamidine, amphotericin B, and miltefosine, have several limitations including high toxicity. Continuing our studies on the discovery of new antileishmanial compounds from Brazilian plant biodiversity, this study evaluated the antileishmanial activity of alkaloid dicentrine from *Ocotea langsdorffii*, a chemically unknown lauraceous species. To this end, the branches of *O. langsdorffii* (250 g) were defatted with hexane and subject to chemically active extraction to afford an alkaloidal phase (113 mg). A portion of this material (100 mg) underwent CC over silica gel, yielding a fraction (55 mg), which was then purified by CC over silica gel, producing pure dicentrine (8.2 mg). Dicentrine exhibited antileishmanial activity against the promastigote forms of *L. infantum*, *L. amazonensis*, and *L. braziliensis*, with EC_{50} values of 1.64, 0.95, and 0.86 µg/mL, respectively. This potency is similar to that of the positive control, AmpB. Cytotoxicity was evaluated against murine macrophages and afforded CC_{50} values of 162.5 and 0.79 µg/mL for dicentrine and AmpB, respectively. The selectivity index (SI) of dicentrine against the tested parasites was determined to be 99.1, 171.7, and 188.3, respectively; the SIs for AmpB were 6.1, 3.2, and 4.0, respectively. When tested against intracellular amastigotes of *L. braziliensis*, dicentrine caused a concentration-dependent reduction in infection. At concentrations of 1, 2, and 4 µg/mL, dicentrine led to reductions in the degree of infection of 11.3%, 23.9%, and 26.3%, respectively. Additionally, the percentage of recovered amastigotes decreased by 74.2%, 81.1%, and 84.0%, respectively, after treatment. The mechanism of action revealed that dicentrine induces mitochondrial disruption and ROS accumulation in parasite promastigotes. Dicentrine also showed potential to reduce the percentages of infected macrophages and amastigotes against the three *Leishmania* species. These findings improve our understanding of the antileishmanial effects of dicentrine and support its potential as a promising candidate for the development of future drugs against leishmaniasis.

Keywords: Ocotea langsdorffii, *alkaloids, dicentrine, leishmaniasis,* L. infantum, L. braziliensis, L. amazonensis.