

In vitro study of anti-*Leishmania infantum* and immunomodulatory activity of *Ximenia americana* L. (Olacaceae) in human peripheral blood mononuclear cells

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Visceral leishmaniasis is a neglected tropical disease that can have high mortality in humans when not treated correctly. This disease is transmitted through the bite of the vector insect, the sandfly that infects the host with the parasite of the genus *Leishmania*. The immune response to *Leishmania infantum* infection involves the formation of a Th1 response that contributes to the anti-inflammatory process, and the Th2 response that is responsible for activating the humoral immune response, resulting from the production of antibodies. The objective of this study was to evaluate the leishmanicidal and immunomodulatory activity of secondary metabolites of the aqueous extract of the bark of *Ximenia americana* L. For this purpose, the secondary metabolites present in the aqueous extract of the bark of *X. americana* L. were evaluated for their immunomodulatory and cytotoxic capacity (CC₅₀), through the measurement of cytokines of the cellular immune response, which were carried out in peripheral blood mononuclear cells (PBMCs). The leishmanicidal capacity of promastigotes of *L. infantum* was verified by establishing its IC₅₀ and its Selectivity Index (SI). A phytochemical analysis was also performed using Thin Layer Chromatography (TLC), in addition an ultrastructural analysis of the promastigotes forms of *L. infantum* was performed with the aid of transmission and scanning electron microscopy. The evaluation of the biological activity in promastigotes forms of *L. infantum* showed an IC₅₀ of 223.2µg/mL and it was not possible to establish the CC₅₀ of the extract in peripheral blood mononuclear cells because the extract was not cytotoxic at the tested concentrations, however it influenced the increase in the production of immunomodulatory cytokines. The phytochemical profile performed on the aqueous extract of the bark on TLC was positive for hydrolysable tannins, condensed tannins, xanthines, phenolic compounds, lignins and terpenes. The

changes caused by secondary metabolites in the ultrastructure of promastigotes of *L. infantum*, such as disruption of the cell membrane and mitochondrial swelling, suggest that the mechanism of action of this compound is the cell membranes. The leishmanicidal and immunomodulating effect observed in this study may come from the presence of secondary metabolites present in the plant, some authors have already made a correlation between secondary metabolites and the effects observed in the parasites. When these components encounter the parasite, they can induce changes in its metabolism that can lead to cell death through the process of autophagy or apoptosis, thus degrading its structures. In addition, the increase or decrease in the viability of mononuclear cells is directly associated with the oxidative stress suffered by the cell, which can induce its immunomodulation, thus substances from plant sources are an excellent source of antioxidant substances that consequently reduce the toxicity caused by free radicals that are produced by these cells, with that the classes of molecules found in the CCD, corroborate for this because such classes as phenols present antioxidant activity already described. The data obtained *in vitro* with *Ximenia americana* L on *L. infantum* encouraged us to initiate complementary studies to observe the effects of these secondary metabolites *in vivo*.