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BIOGUIDED STUDY OF *Miconia willdenowii* LED THE IDENTIFICATION OF TWO ACTIVE COMPOUNDS AGAINST *Trypanossoma cruzi* EPIMASTIGOTE FORM

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Abstract: Neglected diseases are endemic pathologies that plague many areas of the world, especially the poorest and most vulnerable regions on the planet. A disease which affects a large number of our country's population is the Chagas' disease, caused by the protozoan *Trypanosoma cruzi* species. In Brazil, the great diversity of plant species allows a tireless for active compounds against various diseases, especially neglected diseases. In this sense, it is important to study extracts, fractions and isolated substances from plant materials submitting them to biological assays, generating progress and developing bioprospection, showing the real value of the biodiversity. In this work, crude extract from *Miconia willdenowii* was studied about anti-Chagas activity with epimastigote form of *Trypanosoma cruzi* parasites. This plant species has not been reported in phytochemicals studies and the genus *Miconia* has over 1,000 species described, most with several biological e pharmaceutical activity related. Anti-epimastigote bioassay was conducted using colorimetric method with resazurin solution [1]. The crude extract was subjected to partitioning by liquid-liquid extraction with hexane, ethyl acetate and ethanol:water mixture, allowing the separation of compounds in groups by difference in polarity. The fractions obtained were submitted to bioguided assay in order to determine the most active. The ethyl acetate fraction displaying the higher potential against epimastigote form of Chagas' disease parasites was extensively purified under CC conditions. In the end, this process provided a total of 12 subfractions. All subfractions were subjected to bioguided assay, determining those with the greatest potential against epimastigote. Overall, three subfractions showed trypanocidal activity (A2, A3 and A4), which were analyzed by HPLC-UV-DAD, and two substances previously reported for other species *Miconia*: miconidin and primin, could be isolated. Both compounds had their structures identified by NMR spectroscopy, mass spectrometry and confirmed by database comparison in the literature. The quantification of these two compounds was made for each sample of *M. willdenowii* (crude extract, acetate fraction and subfractions), which allowed deducing that their presence or absence is related to trypanocidal activity. The anti-*T. cruzi* bioassay, when performed to the isolated compounds, allowed observing higher trypanocidal potential than the reference drug (benznidazole). The *in vitro* cytotoxicity assay for miconidin and primin, using normal human skin-derived fibroblasts, showed that they only present cytotoxicity over 50 μg/mL, in which is higher than the EC50 presented by these compounds in the tripanocidal assay, suggesting high potential for effective use of these compounds as therapeutical alternative for Chagas' disease after further studies.

References:

[1] RÓLON, M. et al. Development of resazurina microtiter assay for drug sensibility testing of *Trypanosoma Cruzi* epimastigotes. Parasitology Research., v. 99, p. 103-107, 2006.