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Natural sesquiterpene lactones as potential Trypanocidal and Leishmanicidal agents

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Chagas disease and Leishmaniasis are life-threatening illnesses that affect mainly the poorest and the most marginalized communities. The scarcity of effective chemotherapy, due to the low investment in the Research and development (R&D) of new drugs, together with a high incidence of side effects, and the emergence of drug resistance phenomena emphasizes the urgent need for new therapeutic agents. Sesquiterpene lactones (STLs) are a large group of naturally occurring terpenoids derived from plants which display a broad spectrum of biological activities including antiprotozoal activity. In this context, this work focuses on the potential of the STLs uvedalin, enhydrin and polymatin B, isolated from *Smilax sonchifolius*, as potential Trypanocidal and Leishmanicidal agents. The three STLs were isolated from *S. sonchifolius* by bioassay guided-fractionation and their inhibitory effect on the growth of the infective and non-infective forms of *Leishmania mexicana* and *Trypanosoma cruzi* was evaluated *in vitro*. The changes produced by the compounds on the ultrastructure of parasites were examined by Transmission electron microscopy (TEM). Enhydrin and uvedalin were also studied in a murine model of acute *T. cruzi* infection. The cytotoxicity of the compounds was evaluated in Vero cells and the selectivity index was calculated. Serum activities of the hepatic enzymes were used as biochemical markers of hepatotoxicity. The three compounds exhibited significant *in vitro* Leishmanicidal and Trypanocidal activity. The TEM evaluation showed marked ultrastructural alterations, such as an intense vacuolization and mitochondrial swelling in both *L. mexicana* promastigotes and *T. cruzi* epimastigotes exposed to the STLs. In the *in vivo* study, enhydrin and uvedalin displayed a significant decrease in circulating parasites and no signs of hepatotoxicity were detected. Uvedalin, enhydrin and polymatin B may provide valuable leads for the development of new drugs against Chagas disease and Leishmaniasis.

Biography

Liliana V Muschietti is a Professor in the Department of Pharmacognosy, Faculty of Pharmacy and Biochemistry, University of Buenos Aires (UBA), Argentina and received her PhD from the same university. She has worked in multiple research projects funded by UBA, National Scientific and Technical Research Council (CONICET) and Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT). She has her expertise in Phytochemistry and Biodiscovery. She is also involved in the isolation and structure elucidation of bioactive natural compounds, from Argentine medicinal species, with special emphasis on drug candidates for Chagas disease, leishmaniasis, cancer and viral infections.

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