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Smallanthus sonchifolius ETHANOLIC EXTRACT: POTENTIAL ANTI-*Trypanosoma cruzi* HERBAL MEDICINE?

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INTRODUCTION

Chagas disease is a neglected endemic tropical disease caused by the protozoan parasite *Trypanosoma cruzi* and recognized by the World Health Organization as one of the biggest public health problems. The only two therapeutic options are benznidazole and nifurtimox. However, these can cause systemic toxicity and adverse effects. Consequently, innovative, and cost-effective approaches to drug discovery and development are urgently needed. *Smallanthus sonchifolius* (Poepp.) H. Rob., commonly known as "yacón", is an herbaceous perennial species native to South America. In previous studies we have reported the in vitro trypanocidal activity of an ethanol extract of yacon (EE-SS) against *T. cruzi* epimastigotes and trypomastigotes. This study aimed at determining the in vitro activity against intracellular amastigotes, the in vivo activity, and the chemical profile of EE-SS.

MATERIAL AND METHODS

S. sonchifolius leaves (clone LIEY 97–2) were collected in Vicente López, Buenos Aires, Argentina in March 2019. EE-SS was obtained from dried powdered leaves extracted with 96% ethanol. Chemical composition of EE-SS was determined by TLC, FT-IR and HPLC/MS-MS. To evaluate the ability of EE-SS to inhibit the intracellular amastigote forms of *T. cruzi*, transgenic parasites of the Tulahuen β-galactosidase strain were incubated in presence of the extract (0-100 µg/mL). For the in vivo assay Balb-C mice were infected with *T. cruzi* trypomastigotes by intraperitoneal injection. Mice were orally administered with: 100 µL of sterile PBS, 1 or 10 mg/Kg/day of EE-SS for 7 days. Protocols were approved by the Comité Institutional para el Cuidado y Uso de Animales de Laboratorio from the Universidad de Buenos Aires (Res CD 2540/2019).

RESULTS

The main compounds identified in EE-SS, were the sesquiterpene lactones: smallanthin, uvedalin aldehyde, polymatin B, enhydrin, the dimers enhydrofolin and uvedafolin and two acyclic diterpenes: smaditerpenic acids E and F. Against *T. cruzi* amastigotes EE-SS produced a concentration dependent inhibition of parasite growth with an IC_{50} value of 30.2 µg/mL. In the in vivo assay, a significant reduction in the number of circulating parasites was found in *T. cruzi*-infected mice treated with EE-SS. Until day 7 post-infection, mice treated with 10 mg/Kg/day had lower parasitemia and a better survival rate than the control group. Moreover, EE-SS prevents mortality respect to the control group ($p<0,05$).

CONCLUSIONS

Considering the urgent need for new, safe and cost-effective treatments against Chagas disease we suggest that EE-SS may be considered as a starting point to develop an herbal medicine for Chagas disease.

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