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Antitrypanosomal derivatives from ripe fruits of *Schinus terebinthifolius* (Anacardiaceae)

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The genus *Schinus* (Anacardiaceae) includes approximately 29 species, mainly in Americas, with 11 species occurring in Brazil, being *S. terebinthifolius* and *S. molle* the most representative in South America. These species can be mainly found in the Brazilian coast, from Rio Grande do Sul to Ceará States [1,2]. Previous reports describe the characterization of antiparasitic and antitumor tirucallane triterpenoids from leaves of this species [3]. In continuation to our systematic (chemical and biological) study with *S. terebinthifolius*, the present work reports the isolation of antitrypanosomal compounds from ripe fruits. As EtOH extract from ripe fruits displayed antiparasitic activity against trypomastigotes of *Trypanossoma cruzi* (100% of parasite death at 300 μg/mL), this material was subjected to dereplication using LC-LRESIMS and NMR. Obtained data suggested the occurrence of tirucallane triterpenoids, mainly masticadienoic acid (**1**) and schinol (**2**), as well as phenolic derivatives – gallic acid (**3**), methyl gallate (**4**), ethyl gallate (**5**), *trans*-catechin (**6**), quercetin (**7**), quercitrin (**8**), and afzelin (**9**). Crude extract was subjected to a bioactivity guided fractionation over Sephadex LH-20 and prep. HPLC to afford, as active metabolites, compounds **2**, **5** and **7**. Compound **2** showed to be the most active derivative since an excellent potential against trypomastigote forms of *T. cruzi* (EC_{50} of 16.3 μg/mL) was observed in comparison to standard drug benznidazole (EC_{50} of 114.7 μg/mL). This compound displayed also reduced toxicity against NCTC cells (CC_{50} of 95.5 μg/mL). Otherwise, compounds **5** and **7** showed moderate activity, since CE_{50} were determined as 67.4 and 75.9 μg/mL, respectively. Considering the related structures of **1** and **2** associated to the absence of activity of **1** (CE_{50} > 250 μg/mL) was possible suggest that the presence of free hydroxyl at C-3 is essential to the detected activity. Therefore, the results presented herein indicate that natural tirucallane triterpenoid **2** could be used as new prototype for drug design studies against Chagas' disease.

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