Plasma membrane disruption of *Trypanosoma cruzi* induced by a metabolite from the Brazilian plant *Baccharis retusa* (Asteraceae)

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Baccharis retusa, a medicinal Brazilian plant from Asteraceae, has been in folk medicine to treatment of several diseases, including an antiparasitic potential. Phytochemical investigation resulted in the isolation and characterization of two active compounds: 15β-senecioloxy-*ent*-kaurenoic acid (**1**) and *trans*-hexan-18-enyl coumarate (**2**). The antitrypanosomal activity of the compounds was performed against cell-derived trypomastigotes using the colorimetric resazurin assay. To study the plasma membrane integrity of trypomastigotes in the presence of the active compound, a fluorimetric assay was developed using the vital dye Sytox Green. Finally, the mammalian cytotoxicity was investigated using L929 cells by the colorimetric MTT assay. Our results demonstrated that compound **2** induced no mammalian cytotoxicity to the highest tested concentration of 200 µM, while compound **1** displayed a CC_{50} value of 189.7 µM. Compound **1** was the only effective against the trypomastigote forms of *T. cruzi*, with an IC_{50} value of 3.8 µM. The selectivity index, given by ratio between the mammalian toxicity and the activity against the parasites, resulted in a value of 49 for compound **1**. The effect of compound **1** in the plasma membrane of T. cruzi was investigated after 120 minutes incubation. Compound **1** induced a considerable interference in the plasma membrane permeability (57%) of the parasite when compared to the untreated trypomastigotes. The positive control with 0.5% Triton X-100, indicated maximal permeabilization (100%). This data demonstrate for the first time the antitrypanosomal activity of 15β -senecioloxy-*ent*-kaurenoic acid, a metabolite isolated from a Brazilian plant. Support: FAPESP 2013/50228-8, 2015/11936-2 and CAPES.