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ARISTOLACTAMS FROM *Piper truncatum* VELL. WITH ANTI-*Trypanosoma cruzi* ACTIVITY

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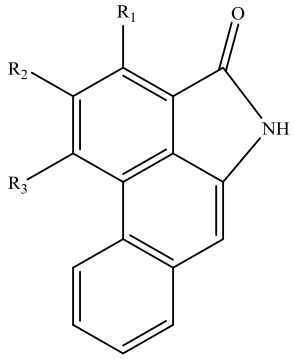

1 R_1 = H; R_2 = R_3 = OCH_3
2 R_1 = H; R_2 = OCH_3; R_3 = OH
3 R_1 = OCH_3; R_2 + R_3 = OCH_2O

In continuation of our studies on the isolation of antiprotozoal metabolites from *Piper* species[1], the present study aims to detect anti-*Trypanosoma cruzi* metabolites from *P. truncatum*. Initially, the branches were defatted with hexane, then extracted with MeOH. Evaluation of the anti-*T. cruzi* potential revealed potent activity to MeOH extract, with 100% of trypomastigote forms killed at 300 µg/mL. After partitioning with hexane, CH_2Cl_2, and EtOAc, we observed that the bioactivity was concentrated in the CH_2Cl_2 phase. Thus, 1 g of this material was chromatographed over silica gel, yielding 26 fractions (A–Z). Groups M, Q, and V exhibited potent activity against *T. cruzi* and were purified by HPLC, which afforded three aristolactams (**1–3**). The ^{1}H NMR spectra of compounds **1** and **2** showed aromatic hydrogen signals between δ 9.1–7.1 and singlets corresponding to methoxyl groups between δ 4.1–4.0. The spectra also showed signals attributed to the amide N–H hydrogen at δ 10.8 (s). The respective ^{13}C NMR spectra showed signals of the amide carbonyl group at δ 168, methoxyl carbons at δ 60–57 and sp² carbons of a phenanthrenic system at δ 154–105. These signals allowed for the identification of aristolactam BII (**1**) and piperolactam A (**2**).[2] The ^{1}H NMR spectrum of compound **3** showed characteristics of the phenanthrene moiety observed in **1** and **2**, as well as a singlet at δ 6.47 attributed to methylenedioxy hydrogens and another singlet at δ 3.87 corresponding to an additional methoxy group.[3] These results indicated the structure of **3**, a previously unreported aristolactam, as shown in Figure 1. Finally, the molecular formulas of compounds **1–3** were confirmed by ESI-HRMS analysis. Among the isolated aristolactams, compound **1** exhibited significant activity against amastigotes, with an EC_{50} of 8.6 µM and reduced toxicity (CC_{50} >200 µM), a comparable to the results for the positive control, benznidazole, which has an EC_{50} of 5.5 µM and a CC_{50} >200 µM.

Keywords*: Chagas disease, aristolactams.* **References:** [1]Gonçalvez M.M. et al., *Chem. Biodivers*. **2024**, 21, e202400547. [2]Qu,W. et al., Nat. Med. **2011** 9, 425-8., [3]Holzbach, J.C. et al., *Molecules* **2010**, 15, 9462-72. **Acknowledgements:** CAPES/FAPESP/CNPq