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Antitrypanosomal acetylene fatty acid derivatives from seeds of *Porcelia macrocarpa* (Annonaceae)

Luciana de Á. Santos[1,*] (PQ), Alberto J. Cavalheiro[1] (PQ), Andre G. Tempone[2] (PQ), Daniela S. Correa[2] (PQ), Tatiana R. Alexandre[2] (PG), Natalia F. Quintiliano[3] (PG) André F. Rodrigues-Oliveira[3] (PG), Diogo Oliveira-Silva[3] (PQ), Roberto Carlos C. Martins[4] (PQ), João Henrique G. Lago[3] (PQ)

[1]*NuBBE - Núcleo de Bioensaios, Biossíntese e Ecofisiologia de Produtos Naturais, Instituto de Química, Universidade Estadual Paulista, 14800-060, Araraquara, SP, Brazil.*
[2]*Centro de Parasitologia e Micologia, Instituto Adolfo Lutz, 01246-902, São Paulo, SP, Brazil.*
[3]*Instituto de Ciências Ambientais, Químicas e Farmacêuticas, Universidade Federal de São Paulo, 09972-270, Diadema, SP, Brazil.*
[4]*Instituto de Pesquisa em Produtos Naturais, Universidade Federal do Rio de Janeiro, 21941-902, Rio de Janeiro, RJ, Brazil.*

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Introduction

Chagas' disease affects 6 million people in America (WHO). Considering the single and highly toxic available drug in Brazil, benznidazole, the study of alternative therapies is essential. Previous chemical studies on *Porcelia macrocarpa* (Warming) R. E. Fries (Annonaceae) were carried out and leads to the isolation of several compounds, including acetylene acetogenins from seeds [1]. As a part of our ongoing studies devoted to the investigation of the antiparasitic compounds from Brazilian plants [2,3], the hexane extract from seeds of *P. macrocarpa* displayed *in vitro* antitrypanosomal activity and was subjected to several chromatographic steps to give three acetylene fatty acids derivatives (**1 – 3**).

Results and Discussion

Crude hexane extract from seeds of *P. macrocarpa* displayed antitrypanosomal activity (IC_{50} = 65.44 μg/mL) and was subjected to several chromatographic fractionation procedures to afford one active fraction III (IC_{50} = 5.32 μg/mL) with no toxicity against NCTC mammalian cells (CC_{50} > 100 μg/mL). Compound **1** was isolated as main derivative after continuous chromatographic steps of this fraction and killed 100% of trypomastigote forms of *T. cruzi* at the highest tested concentration, resulting in IC_{50} value of 10.70 μg/mL. Despite the toxicity to NCTC cells (CC_{50} = 44.27 μg/mL), compound **1**, named macrocarpic acid, was approximately ten times more effective than the standard drug benznidazole (IC_{50} = 139.0 μg/mL). Additionally, fraction II was chromatographed over SiO_2 and gave new acetylene di/triacylglycerol derivatives **2** and **3.** These two compounds were also evaluated against *T. cruzi*, but did not display activity (IC_{50} > 200 μg/mL). The structures of compounds **1 – 3** (figure 1) were elucidated by analysis of NMR and HRESIMS spectra.

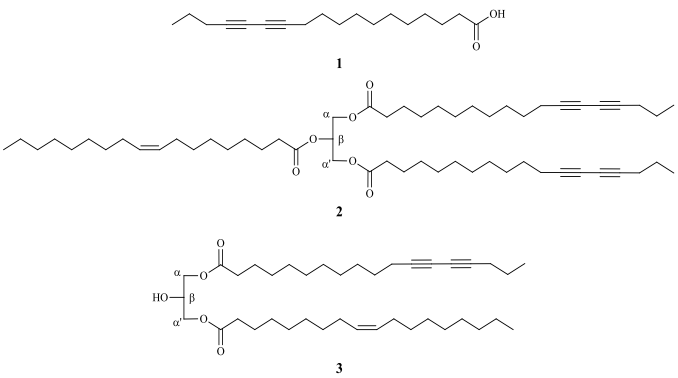

Figure 1. Structures of acetylene compounds **1 – 3**.

Conclusion

New acetylene derivatives **1** - **3** from the seeds of *P. macrocarpa* were evaluated for their antitrypanosomal activity. Compound **1** exhibited potential (IC_{50} = 10.70 μg/mL) and toxicity against NCTC cells (CC_{50} = 44.27 μg/mL) while **2** and **3** were inactives. Comparatively, compound **1** was ten times more effective than the standard drug (benznidazole) suggesting the use of macrocarpic acid as a promising prototype to development of new derivatives to the treatment of Chagas Disease.

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