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Effects of canthin-6-one alkaloids from *Zanthoxylum chiloperone* on *Trypanosoma cruzi*-infected mice

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Abstract

Canthin-6-one (**1**), isolated from *Zanthoxylum chiloperone* (*Rutaceae*), possesses a broad spectrum of antifungal and leishmanicidal activities. In this study, we have examined the antiparasitic effects of canthin-6-one (**1**), 5-methoxycanthin-6-one (**2**), canthin-6-one *N*-oxide (**3**), as well as that of the total alkaloids of *Zanthoxylum chiloperone* stem bark, in Balb/c mice infected either acutely or chronically with *Trypanosoma cruzi*. The compounds were administered orally or subcutaneously at 50 mg/kg/day for 2 weeks, whereas the alkaloidal extract was given at 500 mg/kg/day for 2 weeks. The antiparasitic activity was compared with that of benznidazole given at 500 mg/kg/day for 2 weeks. In the case of acute infection, parasitemia was significantly reduced following oral treatment with canthin-6-one (**1**). Moreover, the total alkaloids of *Zanthoxylum chiloperone* stem bark led to high levels of parasitological clearance

Zanthoxylum chiloperone stem bark led to high levels of parasitological clearance. Seventy days post-infection, the serological response in the acute model was significantly different between oral canthin-6-one (**1**) and benznidazole-treated mice. Chronic model of the disease showed that both canthin-6-one (**1**) and the alkaloidal extract at the above dosage induced 80–100% animal survival compared to untreated controls. These results indicate that canthin-6-one (**1**) exhibits trypanocidal activity in vivo in the mouse model of acute or chronic infection. This is the first demonstration of anti-*Trypanosoma cruzi* activity for a member of this chemical group (canthinones). Considering the very low toxicity of canthin-6-one (**1**), our results suggest that long-term oral treatment with this natural product could prove advantageous compared to the current chemotherapy of Chagas disease.



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Keywords

Zanthoxylum chiloperone; Rutaceae; Paraguay; Canthin-6-one; Chagas disease; Experimental treatment

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