

# IN VIVO TRYPANOCIDAL ACTIVITY OF (-)-HINOKININ, A LIGNAN DERIVATIVE, AGAINST TRYPOMASTIGOTE FORMS OF *TRYPANOSOMA CRUZI*

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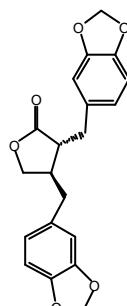
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## Introduction

In the search of new and effective trypanocidal compounds, many plants extracts were evaluated, leading to the identification of several classes of active plant metabolites, from which lignans stand out<sup>[1-3]</sup>. The trypanocidal and anti-inflammatory activities of tetrahydrofuran and dibenzylbutyrolactone lignans were previously report by our group<sup>[1,4,5]</sup>. Recently, Souza et al. (2005) reported the *in vitro* trypanocidal activity of five lignans derivatives against amastigote forms of *T. cruzi*, particularly for (-)-hinokinin (**1**), making this class a promising one to be fully investigated against Chagas disease. Therefore, the aim of this work was to evaluate the *in vivo* trypanocidal activity of (-)- hinokinin.



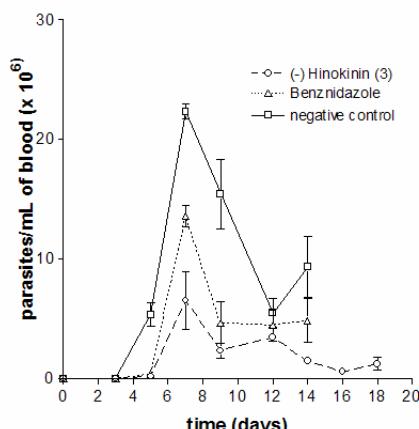
### 1. Chemical structure of (-)-hinokinin

## Results and Discusion

The results of the therapeutic effect of (-)-hinokinin are displayed in figure 1, which shows the data of the experimental infection by *T. cruzi* in comparison with both benznidazole and negative control. It may be observed that (-)-hinokinin possess *in vivo* activity, reducing the number of trypomastigote forms of *T. cruzi* in infected mice. (-)-hinokinin displayed better therapeutic activity in comparison with the negative control, since it was able to reduce the number of parasites not only in the parasitaemic peak, but also in the course of infection. (-)-Hinokinin displayed 70.8% reduction of the infection at the parasitaemic peak in comparison with negative control group, while benznidazole displayed approximately 29.0% of

parasites reduction.

Moreover, it was observed that hinokinin displayed better survival rates, once it survived until the 22<sup>nd</sup> day after the beginning of the infection, than the group treated with benznidazole, which survived until 16<sup>th</sup> day.



**Figure 1.** Parasitaemic curve of the treated mice infected with  $4 \times 10^4$  trypomastigote forms of the Y strain of *Trypanosoma cruzi* by oral rout with (-) hinokinin and benznidazole (40 mg/Kg/day) during 20 days.

## Acknowledgement

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- 1) Bastos, J. K.; Albuquerque, S.; Silva, M. L. A. *Planta Med.* **1999**, 65, 541.
- 2) Da Silva Filho, A. A.; Albuquerque, S.; Silva, M. L. A., Eberlin, M. N.; Tomazela, D. M.; Bastos, J. K. *J. Nat. Prod.* **2004b**, 67, 42.
- 3) Cunha, W. R.; Martins, C.; Ferreira, D.S.; Crottí, A. E. M.; Lopes, N. P.; Albuquerque, S. In vitro trypanocidal activity of triterpenes from *Miconia* species. *Planta Medica* **2003**, 69, 470.
- 4) Da Silva Filho, A. A.; Bueno, P.C.P.; Gregório, L.E.; Silva, M. L. A.; Albuquerque, S.; Bastos, J. K. *J. Pharm. & Pharmacol.* **2004a**, 56, 1195.
- 5) Da Silva Filho, A. A.; Silva, M. L. A.; Carvalho, J.C.T.; Bastos, J. K. *J. Pharm. and Pharmacol.*, **2004c**, 56, 1179.

- 6) Souza, V. A.; Silva, R.; Pereira, A. C.; Royo, V. A.; Saraiva, J.; Montanheiro, M.; Souza, G. H. B.; Da Silva Filho, A. A.; Grando, M. D.; Donate, P. M.; Bastos, J. K.; Albuquerque, S.; Silva, M. L. A. *Bioorg. & Med. Chem. Let.* **2005**, 15, 303.