



## Article

# In Vitro Activity of Essential Oils from *Piper* Species (Piperaceae) against Tachyzoites of *Toxoplasma gondii*

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**Abstract:** Toxoplasmosis is a tropical and neglected disease caused by the parasitic protozoa *Toxoplasma gondii*. Conventional treatment with sulfadiazine and pyrimethamine plus folinic acid, has some drawbacks, such as inefficacy in the chronic phase, toxic side effects, and potential cases of resistance have been observed. In this study, the activity of essential oils (EOs) from three *Piper* species and their main constituents, including  $\alpha$ -Pinene (*Piper lindbergii* and *P. cernuum*),  $\beta$ -Pinene (*P. cernuum*), and dillapiolene (*P. aduncum*), were evaluated against tachyzoites of *T. gondii*.  $\alpha$ -Pinene was more active [IC<sub>50</sub> 0.3265 (0.2958 to 0.3604)  $\mu$ g/mL] against tachyzoites than *P. lindbergii* EO [0.8387 (0.6492 to 1.084)  $\mu$ g/mL]. Both  $\alpha$ -Pinene and *P. lindbergii* EO exhibited low cytotoxicity against NHDF cells, with CC<sub>50</sub> 41.37 (37.64 to 45.09)  $\mu$ g/mL and 83.80 (75.42 to 91.34)  $\mu$ g/mL, respectively, suggesting they could be of potential use against toxoplasmosis.

**Keywords:** toxoplasmosis; essential oils; *Piper*



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## 1. Introduction

*Toxoplasma gondii* (Nicolle and Manceaux, 1909) is an apicomplexan parasite present in approximately one-third of the human population worldwide. In addition to humans, it can infect practically all warm-blooded vertebrates. This zoonotic infection represents an important public health problem in human and veterinary medicine [1]. Transmission occurs mainly by ingestion of oocysts in the environment and of tissue cysts in raw or undercooked meat. Although most people affected are asymptomatic, serious cases can occur in congenitally infected newborns and in immunocompromised patients [2,3].

Toxoplasmosis treatment usually consists of a combination of sulfadiazine and pyrimethamine plus folinic acid. This combination has a synergic action and traditionally shows good results in the acute stage of infection [4,5]. However, these and the other currently recommended drugs for toxoplasmosis treatment have limitations. A notable limitation is that one of the mechanisms of action involves the reduction of nucleic acid synthesis, which makes a teratogenic drug. Adverse effects, resistance, and intolerance against these and other known treatments are commonly reported in the literature. In addition, all drugs are inefficient against the chronic phase of infection. These limitations affect the success of the treatments, mainly in immunocompromised patients and in ocular and congenital cases, which raises the need for new treatment options [6–11].

In the search for alternatives to the treatment of toxoplasmosis, essential oils (EOs) can represent an excellent source of mixtures of biologically active natural products. In this context, the genus *Piper* L. (Piperaceae) is one of the most diverse and widely distributed plant groups in pantropical regions, with approximately 1000 species worldwide and

biological activity. In addition, it highlights  $\alpha$ -Pinene as a promising compound for in vivo testing and against *T. gondii* bradyzoites.

## 5. Conclusions

The EO from *P. lindbergii* and its major monoterpene  $\alpha$ -Pinene showed excellent anti-*T. gondii* activity, displaying a negative influence on the invasion of the parasite in the studied model, with a good selectivity index. These findings support future studies with these compounds using in vivo models of activity against *T. gondii* to search for new compounds and targets for the development of alternatives for the treatment of toxoplasmosis.

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