**In vitro** schistosomicidal activity of the crude extract, fractions and Primin, the major active benzoquinone constituent from the leaves of *Miconia willdenowii* (Melastomaceae)

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**ABSTRACT**

Eight native plant extracts from the Brazilian Atlantic Forest, *Acacia polyphylla*, *Allophylus racemosus*, *Casearia arborea*, *Duguetia lanceolata*, *Metrosideros stipularis*, *Trichilia emarginata*, *Miconia willdenowii*, *Mollinedia widgrenii*, were screened for potential schistosomicidal activity. The crude ethanolic extract of *Miconia willdenowii* (at a concentration of 200 μg/mL) showed the most promising results, killing approximately 65% of the *Schistosoma mansoni* worms, in comparison to praziquantel. This extract was then submitted to a bioguided-phytochemical study. After liquid-liquid partition was performed, the hexane subfraction disclosed the most significant schistosomicidal activity of 80% against the adult worms at a concentration of 75 μg/mL and 25% at 50 μg/mL. Purification of this active subfraction led to the isolation of 2-methoxy-6-pentyl-benzoquinone (1, also known as Primin) as the active metabolite responsible for the observed schistosomicidal effect (IC50 = 7.08 μg/mL). The schistosomicidal effect of *M. willdenowii* and Primin is the first time in which such a result has been reported.

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1. Introduction

Neglected tropical diseases (NTDs) are a group of infectious diseases that are the main causes of mortality in poor communities worldwide, despite the available treatment and relative facility control (Njoroge et al., 2014). Among these tropical diseases, Chagas' disease, dengue, schistosomiasis, sleeping sickness, lymphatic filariasis and leishmaniasis are characteristic of poor communities living in tropical and subtropical developing countries, with deficiencies in sanitary policies and public healthcare. These parasitic pathologies are known as neglected diseases due to the absence of efficient public politics focused on prevention, with higher incidences in poverty, and the consequent low market interest and investments of the pharmaceutical industry (Pereira et al., 2012).

*Schistosoma* are parasitic worms responsible for infections that are collectively known as schistosomiasis, bilharziasis or snail fever (Njoroge et al., 2014). This infection affects approximately 78 countries located in Sub-Saharan Africa, the Middle East, the Caribbean and South America but almost 90% of the patients live in African continent (Colley et al., 2014). In 2014, approximately 258 million people required preventive treatment; however, only 61.6 million received effective treatment (World Health Organization, 2016). Among NTDs, schistosomiasis is responsible for the majority of annual deaths ranging from 200 million people worldwide (Njoroge et al., 2014), once malaria, tuberculosis and AIDS are no longer considered as neglected diseases (Canuto et al., 2015). The larvae forms of *Schistosoma* are released from the Biomphalaria species (freshwater snails) when penetrating a human’s skin. After contamination, adult worms stay inside the mesenteric veins of the human host, where they reproduce and release their eggs. Some authors supported the idea that parasite eggs are in fact responsible for schistosomiasis morbidity and not only the adult worms. In addition, the eggs cannot be completely excreted while they are located in the host liver and intestine (*S. mansoni*, *Schistosoma japonicum*) or in the bladder and urogenital system (*Schistosoma haematobium*). As a consequence, the eggs stimulate an inflammatory process with the appearance symptoms which are characteristic of the disease, including anemia, diarrhea, malnutrition, abdominal pain, and rectal bleeding (Colley et al., 2014).

Since there is no effective vaccine available, the primary treatment of schistosomiasis is praziquantel (PZ), which has been widely used since...