Antischistosomal Activity of Sesquiterpene Polygodial from *Drimys brasiliensis*: *In Silico*, *In Vitro* and *In Vivo* Investigations

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The World Health Organization highlights the urgent need for innovative therapeutic strategies to enhance helminthiasis control. In this context, Brazilian biodiversity represents a valuable source of bioactive molecules. This study employed bioactivity-guided fractionation of the hexane extract from *Drimys brasiliensis* (Winteraceae) branches, leading to the isolation and characterization of the sesquiterpene polygodial. The compound was then evaluated for its activity against *Schistosoma mansoni*, the causative agent of schistosomiasis. *In vitro*, polygodial exhibited significant potency against adult worms (EC_{50} = 10 µM) while showing no cytotoxicity in Vero cells (CC_{50} > 200 µM). *In silico* analyses revealed favorable pharmacokinetic properties (ADME) with no PAINS violations. *In vivo*, *S. mansoni*-infected mice treated with polygodial (400 mg/kg) showed a 44.0% reduction in worm burden, along with reductions of 71.8% in fecal egg excretion and 69.5% in intestinal egg load. These findings highlight polygodial as a promising lead compound for schistosomiasis treatment.

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