NOVEL INDOLE-BASED MARINOQUINOLINES AS PROMISING CANDIDATES AGAINST *TOXOPLASMA GONDII*

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Toxoplasma gondii, an obligate intracellular parasite, is widely distributed globally, with higher prevalence in warm and humid regions. This protozoan, the causative agent of toxoplasmosis, infects approximately 30% of the population, representing a significant public health challenge. The main drugs used to treat the disease, such as pyrimethamine and sulfadiazine, have notable limitations, acting only during the acute phase of infection and often causing allergic reactions and severe side effects. Marinoquinolines (MQs), a class of compounds originally isolated from marine microorganisms, have demonstrated significant pharmacological potential, including anti-*T. gondii* activity in both *in vitro* and *in vivo* studies. Given the limited therapeutic options for toxoplasmosis, this study aimed to explore new derivatives with inhibitory activity against the parasite. Sixteen novel synthetic MQs were evaluated, distinguished from previously reported compounds by the incorporation of indole derivatives linked to the marinoquinoline scaffold. The effective concentration (EC50) against intracellular *T. gondii* tachyzoites (RH strain) and cytotoxic concentration (CC50) against human foreskin fibroblasts (HFF) were determined for all derivatives. Selectivity indexes (SI) were calculated as the CC50/EC50 ratio. Among the compounds, one derivative stood out with an SI value of 170. Additionally, two derivatives (MQ-262 and MQ-263) exhibited SI values greater than 60, along with favorable ADMET predictions, including high gastrointestinal absorption, blood-brain barrier permeability, and no predicted toxicity. These findings highlight indole-based MQs as promising candidates for further evaluation in experimental models of toxoplasmosis, suggesting their potential as an effective treatment for this significant parasitic disease.

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