

In vitro and in vivo Potential Effect of the N-Acylsulfonamide Bis-oxazolidin-2-ones on Toxoplasma gondii

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Abstract : Toxoplasmosis is a cosmopolitan infection due to *Toxoplasma gondii* (T.gondii). It is a significant cause of congenital disease and an important opportunistic pathogen which has become a worldwide increasing problem due to the AIDS epidemic. Current available drugs do not give satisfactory results and often have only a static and several adverse side effects as it is the case of pyrimethamine. So, the need to develop and evaluate new drugs is critical. The purpose of this study is to investigate the in vitro and in vivo effects of the new chiral N-acylsulfonamide bis-oxazolidin-2-ones on T.gondii. In this study, anti-T.gondii RH strain activities, of two new chiral N-acylsulfonamide bis-oxazolidin-2-ones were evaluated in vitro, using a MRC-5 fibroblast tissue cultures to determine the concentration that inhibit parasite multiplication by 50% (IC50) of each drug and in vivo, by PCR detection of the tachyzoites in mice ascites after new molecules treatment, using the 35-fold repetitive B1 gene of T.gondii. The in vitro results demonstrated that the treatment with the tested molecules decreased the amount of tachyzoites in cell culture in a dose-dependent manner. The inhibition was complete for concentrations over 4 mg/ml. The IC50 of Mol 1 and Mol 2 were 1.5 and 3 mg/ml, respectively, and were quite similar to the control one (2 mg/ml). The Mol 1 was highly active against T.gondii in cell cultures than Mol 2; these results were similar to those of sulfadiazine-treated group ($p < 0.05$). Toxoplasma-specific DNA was demonstrated in all ascites samples from infected mice of the different tested groups. Mol 1 showed better effect than Mol 2, but it did not completely inhibit the parasite proliferation. The intensity of amplification products increased when the treatment started late after infection. These findings suggest continuous parasite replication despite the treatment. In conclusion, our results showed a promising treatment effect of the tested molecules and suggest that in vitro, the Mol 1, and Mol 2 have a dose-dependent effect and a high cytotoxicity on the studied cells. The present study revealed that concentration and duration of tested molecules treatment are major factors that influence the course of Toxoplasma infection in infected mice.

Keywords : cytotoxicity, PCR, sulfonamide, *Toxoplasma gondii*

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