Antischistosomal activities of mefloquine-related arylmethanols

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Interesting antischistosomal properties have been documented for the antimalarial mefloquine, a 4-quinolinemethanol. We evaluated the antischistosomal activities of nine mefloquine related compounds, belonging to the 4-pyridinemethanols, 4-phenanthrenmethanols and related 4-quinolinemethanols. Eight compounds revealed high activities against Schistosoma mansoni in vitro, with two drugs (4-quinolinemethanols WR7573 and WR7930) characterized by significantly lower IC(50)s (2.7 and 3.5 muM, respectively) when compared to mefloquine (11.4 muM). Mefloquine and WR7930 showed significantly decreased IC(50) values when incubated in the presence of hemoglobin. High worm burden reductions (WBR) were obtained with enpiroline (WBR: 82.7%, dosage 200 mg/kg), its threo-isomers ((+)-threo WBR: 100%, (-)-threo WBR: 89%) and WR7930 (WBR: 87%, dosage 100 mg/kg) against adult S. mansoni in mice. Furthermore excellent in vitro and in vivo antischistosomal activity was observed for two WR7930 related structures (WR29252, WR7524). In addition, mefloquine (WBR: 81 %), enpiroline (WBR: 77 %) and WR7930 (WBR: 100 %) showed high activities on S. haematobium harbored in mice following single oral doses of 200 mg/kg. These results provide a deeper insight into the structural features of the aminoalcohols that rule antischistosomal activity. Further studies should be launched with enpiroline and WR7930
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