

Publication

Activity of tribendimidine and praziquantel combination therapy against the liver fluke Opisthorchis viverrini in vitro and in vivo

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Opisthorchiasis, caused by the liver fluke Opisthorchis viverrini, a food-borne trematode, is an important public health problem; however, only a single drug, praziquantel is available. We investigated tribendimidine-praziquantel combinations against O. viverrini in vitro and in vivo. The IC50 values of 0.16 μ g/ml and 0.05 μ g/ml were determined for praziquantel and tribendimidine, respectively, against adult O. viverrini in vitro. When O. viverrini was exposed to both drugs simultaneously (using a drug ratio based on the IC50 (1:3.2)) a synergistic effect was calculated (combination index (CI) at the IC50=0.7). A similar result was observed when drug addition in vitro was spaced by the respective half-lives of the drugs (a CI of 0.78 at the IC50 for tribendimidine followed by praziquantel and a CI of 0.47 at the IC50 for praziquantel followed by tribendimidine). In vivo median-effect dose (ED50) values of 191 mg/kg and 147 mg/kg were calculated for praziquantel and tribendimidine, respectively. Low to moderate worm burden reductions (38-62%) were observed in O. viverrini infected hamsters when both drugs were administered simultaneously or on subsequent days, pointing to antagonistic effects in vivo. Further studies are necessary to understand the striking differences between the in vitro and in vivo observations using combinations of praziquantel and tribendimidine on O. viverrini.

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