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Activity and pharmacokinetics of a praziquantel crystalline polymorph in the Schistosoma mansoni mouse model

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Author(s) Lombardo, Flavio C.; Perissutti, Beatrice; Keiser, Jennifer
Author(s) at UniBasel Lombardo, Flavio ; Keiser, Jennifer ;
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Schistosomiasis is a global disease of significant public health relevance. Only one racemic drug, praziquantel, characterized by low bioavailability, low water solubility and extensive first pass metabolism, is currently available. We studied a new praziquantel formulation (polymorph B), which is based on a racemic praziquantel crystalline polymorph (TELCEU01). Its in vitro activity was tested on newly transformed schistosomula (NTS) and adult Schistosoma mansoni. In vivo studies were conducted in mice harboring chronic S. mansoni infections. Pharmacokinetic (PK) profiles of R- and S-praziquantel and R- and S- polymorph B following oral administration with both formulations were generated by sampling mice at 30, 60, 240/min and 24/h post-treatment, followed by LC-MS/MS analysis. PK parameters were calculated using a non-compartmental analysis with a linear trapezoidal model. In vitro, commercial praziquantel and the polymorph B performed similarly on both NTS (IC; 50; =/2.58 and 2.40/ţg/mL at 72/h) and adults (IC; 50; =/0.05 and 0.07/ţg/mL at 72/h). Praziquantel showed higher in vivo efficacy with an ED; 50; of 58.75/mg/kg compared to an ED; 50; of 122.61/mg/kg for the polymorph B. The PK profiles of the two drugs exhibited differences: R-praziquantel showed an overall 40% higher area under the plasma drug concentration-time curve (AUC; 024;) (R-praziquantel/=/3.42; R-polymorph B/=/2.05/h*ţg/mL) and an overall 30% lower apparent clearance (Cl/F) (R-praziquantel/=/70.68 and R-polymorph B/=/97.63 (mg)/(ţg/mL)/h). Despite the lack of improved activity and PK properties of polymorph B against S. mansoni, here presented; research on pharmaceutical polymorphism remains a valid and cost-effective option for the development of new praziquantel formulations with enhanced properties such as increased solubility and/or dissolution.
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