Activity profile of an FDA-approved compound library against Schistosoma mansoni

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As plans to expand mass drug treatment campaigns to fight schistosomiasis form, worries about reliance on praziquantel as the sole available treatment motivate the investigation for novel antischistosomal compounds. Drug repurposing might be an inexpensive and effective source of novel antischistosomal leads.; 1600 FDA approved compounds were first assayed against Schistosoma mansoni schistosomula at a concentration of 10 ţM. Active compounds identified from this screen were advanced to the adult worm screen at 33.33 ţM, followed by hit characterization. Leads with complementary pharmacokinetic and toxicity profiles were then selected for in vivo studies.; The in vitro screen identified 121 and 36 compounds active against the schistosomula and adult stage, respectively. Further, in vitro characterization and comparison with already available pharmacokinetic and toxicity data identified 11 in vivo candidates. Doramectin (10 mg/kg) and clofazimine (400 mg/kg) were found to be active in vivo with worm burden reductions of 60.1% and 82.7%, respectively.; The work presented here expands the knowledge of antischistosomal properties of already approved compounds and underscores variations observed between target-based and phenotypic approaches and among laboratories. The two in vivo-active drugs identified in this study, doramectin and clofazimine are widely available and present as novel drug classes as starting points for further investigation.

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