Advances with the Chinese anthelminthic drug tribendimidine in clinical trials and laboratory investigations

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The anthelminthic drug tribendimidine has been approved by Chinese authorities for human use in 2004, and a first comprehensive review was published in Acta Tropica in 2005. Here, we summarise further advances made through additional clinical trials and laboratory investigations. Two phase IV trials have been conducted in the People's Republic of China, the first one enrolling 1292 adolescents and adults aged 15-70 years and the second one conducted with 899 children aged 4-14 years who were infected with one or multiple species of soil-transmitted helminths. Oral tribendimidine (single 400mg enteric-coated tablet given to adolescents/adults and 200mg to children) showed high cure rates against Ascaris lumbricoides (90.1-95.0%) and moderate-to-high cure rates against hookworm (82.0-88.4%). Another trial done in school-aged children using a rigorous diagnostic approach found a cure rate against hookworm of 76.5%. A single oral dose of tribendimidine showed only low cure rates against Trichuris trichiura (23.9-36.8%) confirming previous results. Tribendimidine administered to children infected with Enterobius vermicularis (two doses of 200mg each on consecutive days) resulted in a high cure rate (97.1%). Importantly, a series of randomised, exploratory trials revealed that tribendimidine shows interesting activity against the liver flukes Opisthorchis viverrini and Clonorchis sinensis, the tapeworm Taenia spp. and the threadworm Strongyloides stercoralis with respective cure rates of 70.0%, 40.0%, 53.3% and 36.4%. Pharmacokinetic studies in healthy Chinese volunteers indicated that after oral administration of tribendimidine, no parent drug was detected in plasma, but its primary metabolite, p-(1-dimethylamino ethylimino) aniline (aminoamidine, deacylated amidantel) (dADT), was found in plasma. dADT is then further metabolised to acetylated dADT (AdADT). dADT exhibits activity against several species of hookworm and C. sinensis in experimental studies, similar that of tribendimidine. First studies elucidating the mechanism of action suggested that tribendimidine is an L-type nicotinic acetylcholine receptor agonist. Additional experimental studies revealed that the anti-parasite spectrum of tribendimidine is very broad. Indeed, to date, activity has been documented against 20 different nematode, trematode and cestode species. Taken together, tribendimidine warrants further scientific inquiry, including more comprehensive toxicity appraisals, mechanism of action studies and clinical investigation as it holds promise as a broad spectrum anthelminthics.
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