Abstract

The choice of drugs for the treatment of sleeping sickness is extremely limited. To redress this situation, the recently synthesised diamidine, 2,5-bis(4-amidinophenyl)-furan (DB75, furamidine) and its methamidoxime prodrug, 2,5-bis(4-amidinophenyl)-furan-bis-O-methylamidoxime (DB289, pafuramidine) were, together with pentamidine, evaluated for efficacy in acute rodent models. The activity was compared in three common mouse models that mimic the first stage of human African trypanosomiasis. The mice were infected with the pleomorphic T .b. rhodesiense strains KETRI2537 and STIB900 or with the monomorphic T. b. brucei strain STIB795. Importantly, DB75 showed activity superior to that of pentamidine at comparable doses in all three mouse models. Complete cures were achieved with oral dosing of the prodrug DB289 in all three models without any overt toxicity. This shows that the prodrug strategy was successful in terms of reducing toxicity and increasing efficacy and oral bioavailability.