J Bioequiv Availab 2017, 9:5 (Suppl)
DOI: 10.4172/0975-0851-C1-031

Novel nitroimidazole analog as a potent anti-tuberculosis agent

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New compounds against tuberculosis are urgently needed to combat the crisis of drug resistance in tuberculosis (TB). We have identified a novel nitro-dihydro-imidazooxazole (NHIO) analog, as a new anti-tubercular agent with a MIC of 0.21 μM against H37Rv. Physicochemical properties, drug metabolism and pharmacokinetics (DMPK) were studied for the compound. Physicochemical parameters were determined in silico. Lipophilicity was determined experimentally as octanol-PBS partition coefficient (log P). Passive and active permeability of the compound was determined by PAMPA and Caco-2 cell permeability analysis, respectively. Plasma protein binding was found by rapid equilibrium dialysis. The compound was found to be stable *in vitro* in liver microsomes with very low intrinsic clearance. The compound exhibited very good lipophilicity (log P) which makes it optimal for oral administration. The compound showed a low solubility and permeability and high plasma protein binding. However, it was highly stable in rat liver microsomes with very low intrinsic clearance. It was found to be non-hepatotoxic and did not induce any significant DNA damage at high concentrations up to 50 μM. The compound did not have any inhibitory effects on human CYPs 1A2, 2C9, 2D6, 3A4 and 2C19 up to concentrations of 50μM, which is an important attribute for a TB-drug. The compound showed satisfactory *in-vivo* pharmacokinetic properties and a good oral bioavailability of 46.5%. The results insinuate that the novel NHIO analog should undergo further development as a potential treatment for tuberculosis.

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