## Oral Administration of Azithromycin Ameliorates Trypanosomosis in Trypanosoma congolense and T. Brucei Brucei Infected Mice

Authors: Nthatisi I. Molefe-Nyembe, Keisuke Suganuma, Oriel M. M. Thekisoe, Xuan Xuenan, Noboru Inoue

Abstract: African trypanosomosis is a devastating disease of animals caused by parasites of the genus Trypanosoma negatively affecting the economic status of more than 36 African countries. Few available drugs for the treatment of trypanosomosis remain inaccessible in remote areas, are associated with severe toxicity and most importantly, resistance has widely developed against their usage. Therefore, safe, effective and easily administrable drugs are urgently in need. The objective of the current study was to determine efficacy of azithromycin (AZM), on T. congolense, T. brucei brucei in vitro and in vivo. A 96 well luciferase assay was conducted to determine the trypanocidal effect of AZM on T. congolense, T. b. brucei and T. evansi as well as the cytotoxicity effect on the MDBK and NIH 3T3 cells. Additionally, TEM analysis was conducted to determine the morphological alteration on the AZM treated samples. Mice were infected with T. congolense and T. b. brucei and orally treated with AZM for 7 and 28 days referred to as the short and the long-term treatment. The in vitro IC50 values of AZM on T. congolense, T. b. brucei and T. evansi was  $0.19 \pm 0.17$ ;  $3.69 \pm 2.26$  and  $1.81 \pm 1.82$  µg/mL, respectively, while the cytotoxicity effects values were greater than 25 µg/mL. A vacuole-like structure was observed in the TEM imaging of AZM treated T. congolense, while the presence of glycosomes and acidocalcisome-like structured were detected in T. b. brucei samples. In vivo, AZM was more effective against T. congolense infected mice than T. b. brucei. In conclusion, AZM exhibited the trypanocidal effects on T. congolense and T. b. brucei infected mice. However, further studies are necessary to determine the metabolic pathway responsible for the observed efficacy.

Keywords: animal trypanosomosis, azithromycin, oral administration, trypanosoma congolense

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