Abstract

Human African trypanosomiasis (HAT) is a tropical disease caused by two subspecies of Trypanosoma brucei, the East African variant T. b. rhodesiense and the West African variant T. b. gambiense. Melarsoprol, an organic arsenical, is the only drug used to treat late stage T. b. rhodesiense infection. Unfortunately, this drug induces an extremely severe post treatment reactive encephalopathy (PTRE) in up to 10% of treated patients, half of whom die from this complication. A highly reproducible mouse model was adapted to assess the use of Kenyan purple tea anthocyanins and/or coenzyme-Q10 in blocking the occurrence of PTRE. Female Swiss white mice were inoculated intraperitoneally with approximately 10(4) trypanosome isolate T. b. rhodesiense KETRI 2537 and treated sub-curatively 21days post infection with 5mg/kg diminazene aceturate (DA) daily for 3days to induce severe late CNS infection that closely mirrors PTRE in human subjects. Thereafter mice were monitored for relapse of parasitemia after which they were treated with melarsoprol at a dosage of 3.6mg/kg body weight for 4days and sacrificed 24h post the last dosage to obtain brain samples. Brain sections from mice with PTRE that did not receive any antioxidant treatment showed a more marked presence of inflammatory cells, microglial activation and disruption of the brain parenchyma when compared to PTRE mice supplemented with either coenzyme-Q10, purple tea anthocyanins or a combination of the two. The mice group that was treated with coenzyme-Q10 or purple tea anthocyanins had higher levels of GSH and aconitase-1 in the brain compared to untreated groups, implying a boost in brain antioxidant capacity. Overall, coenzyme-Q10 treatment produced more beneficial effects compared to anthocyanin treatment. These findings demonstrate that therapeutic intervention with coenzyme-Q10 and/or purple tea anthocyanins can be used in an experimental mouse model to ameliorate PTRE associated with cerebral HAT.