A Trypanosomiasis, a protozoan disease causes morbidity and death to humans and severely limits livestock production in endemic areas. It occurs predominantly in Africa, South America and Asia. Although Chemotherapy has been used to control the disease, cases of resistance have been reported and prospects of short-term vaccine development are remote. To address these challenges, herbal medicines have increasingly been used to control the disease in endemic areas. This study evaluated efficacy of selected indigenous plant extracts on T evansi. Test extracts included Azadirachta indica (neem), Prunus africana, Bidens pilosa, Physalis peruviana, Senna didymobotrya and Croton megalocarpus. 96 well micro titer plates were used and trypanocidal activities evaluated in vitro by calculating minimum inhibitory concentrations (MIC) of respective extracts. Safety of extracts was tested in mice (Swiss white) by evaluating parasitemia, clinical presentations and histological analysis of liver, Kidney, heart, lungs, muscle and brain tissue. Of the 27 extracts evaluated, chloroform extracts of Azadirachta indica leaves had the highest activity (minimum inhibitory concentration of 18.75 ug/ml). This extract was toxic to host cells in vivo at doses exceeding 500 mg/kilogram body weight and was associated with dyspnoea and lethargy. Histopathology showed damage to kidneys, lungs and liver. Because chloroform extracts of Azadirachta indica leaves performed better both in vitro and in vivo than suramin, a commercial trypanocide, future studies should address purification, structure elucidation and biochemical characteristic of active components of Azadirachta indica leaves. This study has confirmed the hypothesis that some Kenyan plants have trypanocidal potential.