Malaria is a major and constant public health problem in the world, especially in developing countries. In Kenya, more than half of the population is exposed to malaria with minimal opportunities for treatment. This is increased by emergence of resistant vectors (female *Anopheles spp.*.) and multidrug-resistant strains of malaria causing parasite, thereby calling for alternatives. Plants contain secondary metabolites that are a probable source of natural compounds which could have antimalarial activity. In this study, the antimalarial activities of aqueous and organic plant extracts were determined, acute toxicity evaluated using the mouse model and major phytochemical compounds in the extracts investigated. Crude extracts were prepared from four plant species; *Commiphora schimperi* (Berg.) Engl. (Burseraceae), *Ricinus communis* L. (Euphorbiaceae), *Grewia hexamita* Burret. (Tiliaceae) and *Securidaca longependuculata* Fres. (Polygalaceae) collected from Msambweni district, Kenyan. Adult healthy Swiss mice (*Mus musculus* L.) were infected intraperitoneally with *Plasmodium berghei* (ANKA) to induce malaria and then treated orally at 100 mg/kg of each crude plant extracts according to the Peter’s 4-day suppressive test. The negative control was treated with distilled water and the positive with chloroquine (CQ). Healthy Swiss female mice were used for acute toxicity testing as per Organisation for Economic Co-operation and Development (OECD) guidelines. To determine the presence of secondary metabolites in all extracts, Thin Layer Chromatography (TLC) was used. The means obtained from the 4-day suppressive test were analyzed using student’s t-test and Analysis of Variance (ANOVA). Among the four plants, *S. longependuculata* had the highest chemosuppression level of 91.03%. Extracts from *C. schimperi*, *R. communis* and *G. hexaminta* were safe at 2000 mg/kg and were considered non toxic to mice while *S. longependuculata* was considered non toxic at 300 mg/kg during a 24 hour period. Alkaloids and flavonoids were present in all extracts while Sesquiterpene lactones were absent in all the extracts. Saponins were present in both extracts of *S. longependuculata* and organic extracts of *G. hexamita* only. The current study provides insights into in vivo antimalarial activity and acute toxicity of organic and aqueous crude extracts from the four plants. These results support a rational rather than random approach to the selection of antimalarial screening candidates, and have identified a number of promising species for further investigation as plant based antimalarial agents.

**Key words:** In vivo Antimalarial activity, Acute toxicity, Phytochemical analysis, *Mus musculus*, *Plasmodium berghei*, *Commiphora schimperi*, *Ricinus communis*, *Grewia hexaminta* and *Securidaca longependuculata*. 