ABSTRACT

Malaria is one of the top three killers among communicable diseases, particularly in sub-Saharan Africa. As the parasite continuously develops resistance to drugs, the search for effective and alternative antimalarial drugs especially from medicinal plants with recorded therapeutic uses is of utmost importance. Formulation control and treatment. The interest in traditional medicine stems from the recognition that three major antimalarial drugs: quinine, atovaquone and artemisinin, trace their origin to traditional medicine. In this context, the present study aimed to investigate antimalarial potential of traditionally used medicinal plants A. lebbeck, R. cordifolia, P. hieracioides and T. alexandrium against in vitro and in vivo P. berghei (NK-65) infection in BALB/c mice.

Ethanolic extracts of A. lebbeck (bark), R. cordifolia (leaf), P. hieracioides (leaf) and T. alexandrium (whole plant), EBEAL, ELERC, ELEPH and EWETA, respectively, were subjected to phytochemical analysis. EBEAL contained phenols, alkaloids, saponins, cardiac glycosides, flavonoids, diterpenes and phytosterols. Phenols, saponins, anthraquinones and phytosterols were detected in ELERC, whereas, in ELEPH, phenols, alkaloids and triterpenes were present. EWETA revealed the presence of phenols, cardenolides, diterpenes and phytosterols. WHO schizont maturation inhibition assay was employed to examine the effect of extracts on the maturation of parasite from ring to schizont stage. EBEAL and ELERC showed IC50 < 5 µg/ml, whereas, the value was observed to be 5 µg/ml for ELEPH and EWETA, proving antimalarial potential of these extracts against P. berghei in vitro.

Acute oral toxicity assessed the safety of plant extracts in female BALB/c mice. LD50 of all the extracts was revealed to be >5 g/kg. In Peter’s 4-day test, ED50 of EBEAL, ELEPH and EWETA was revealed to be <100 mg/kg, and that of ELERC was <750 mg/kg. All plant extracts displayed chemosuppression in a dose-dependent fashion on day 5. MST of mice administered EBEAL (750 mg/kg), ELERC (100-750 mg/kg) and ELEPH (100 mg/kg) was greater than that of positive control mice (CQ, 5 mg/kg). Low parasitaemia of 1-9%, on day 28, was observed in 2-4 surviving mice treated with EBEAL (100 mg/kg), ELERC (750 mg/kg), ELEPH (250 mg/kg) and EWETA (750 mg/kg), respectively. In prophylactic assay, EBEAL (100-750 mg/kg), ELERC (100-500 mg/kg) and ELEPH (500 and 750 mg/kg) showed chemosuppression greater than 50% on day 7. All the concentrations of administered extracts showed significantly low (p<0.05) parasitaemia than infected control on day 7. When suppressive activity of extracts in established P. berghei infection was checked, 750 mg/kg concentration of all extracts showed higher chemosuppression than CQ (5 mg/kg) on day 7.
MST of 500 mg/kg (EBEAL), 100, 250 and 750 mg/kg (ELERC), 250 and 500 mg/kg (ELEPH) and 500 mg/kg (EWETA) treated mice was also found to be greater than CQ treated mice (17.8±6.9 days) and was significant (p<0.05) than that of negative control mice as well.

Biochemical functioning of liver and kidney of normal, *P. berghei*-infected and SSV treated mice was assessed on day 7 and of drug/extract treated groups on days 7 and 28, respectively. SGOT, SGPT, ALP activities and bilirubin, urea and creatinine levels in infected mice were significantly (p<0.05) increased than in normal mice on day 7. Extract concentrations in surviving mice of EBEAL (100 mg/kg), ELEPH (250 mg/kg) and EWETA (750 mg/kg) showed activities of SGOT and ALP activities less or comparable than G3 mice on day 28. Raised bilirubin levels in mice of ELERC and EWETA (750 mg/kg) on day 7 decreased on day 28 and were comparable to values in CQ treated mice. Urea levels in all extract treated concentrations, whereas, creatinine levels in EBEAL (100-500 mg/kg), ELERC (100-750 mg/kg), ELEPH (100-750 mg/kg) and EWETA (100 and 750 mg/kg) treated mice were low than G1 mice on day 7. Urea levels were less than in CQ treated mice, in surviving mice of EBEAL (100 mg/kg), ELERC (750 mg/kg), ELEPH (250 mg/kg) and EWETA (750 mg/kg) on day 28. Histological studies also revealed that infected and CQ treated liver represented distorted hepatocytes, haemozoin deposition and blocked sinusoids with Kupffer cells. EBEAL (100 mg/kg) treated liver showed morphology comparable to CQ, whereas, in case of ELERC (750 mg/kg) treated liver, endothelial cell proliferation, haemozoin deposition and sinusoidal infiltration were seen. Liver sections in ELEPH (250 mg/kg) treated mice revealed haemozoin pigmentation and sinusoidal dilations but that of EWETA (750 mg/kg) showed almost regular liver morphology. Infected spleen revealed indistinguishable marginal zone and infiltration of white pulp. CQ treated spleen showed indistinct marginal zone and deposition of haemozoin pigment. EBEAL (100 mg/kg), ELEPH (250 mg/kg) and EWETA (750 mg/kg) treated spleen sections were comparable to CQ treated ones. ELERC (750 mg/kg) treated mice spleen showed enlarged white pulp area and sinusoidal dilations. *P. berghei*-infected and CQ (5 mg/kg) treated mice kidney sections revealed distorted tubular epithelium and narrowed lumen of PCTs and DCTs. Kidney of ELERC (750 mg/kg) and ELEPH (250 mg/kg) treated mice revealed glomerular constriction and mesangial cell proliferation. Kidney of EWETA (750 mg/kg) treated mice showed regular architecture with slight mesangial cell proliferation which was also evident in EBEAL (100 mg/kg) treated mice kidney.