ABSTRACT

Chloroquine was the mainstay of antimalarial chemotherapy because of its safety profile, effectiveness and the relatively cheap cost. However, the emergence of chloroquine-resistant *Plasmodium falciparum* parasites has rendered this drug ineffective in most regions where malaria is endemic. Most antimalarial drugs that act through blood - stage - specific mechanism are no longer effective due to the rapid emergence of drug resistance while the costs of development of new drugs continue to rise. Ligand-mediated nanoparticulate drug delivery system can mitigate chloroquine resistance mechanisms and provide a potential cure for malaria. The objective of this study was to evaluate antiplasmodial activity of chloroquine-encapsulated heparin functionalized, solid lipid nanoparticles (SLNs). Specifically, the study determined the physicochemical properties, antiplasmodial activity of the nanoformulated SLNs against *P. falciparum in vitro* and *P.berghei* in mice. The modified double-emulsion solvent evaporation technique was used to prepare the nanoparticles. The semi-automated micro-dilution technique was adapted in assessing the *in vitro* antiplasmodial activity by use of tritium labeled hypoxanthine. The uptake of tritium labeled hypoxanthine was measured by Beta counter and recorded inform of counts per minute (CPM). The CPMs were then computed to give drug concentration capable of inhibiting 50% of the *P. falciparum* (IC_{50}), as a function of antiplasmodial efficacy. The 4-day suppressive test with modification was used to evaluate antiplasmodial activity against *P. berghei* in mice. The mean percentage parasitaemia between treatments were compared with respect to the negative control. Kruskal Wallis test was used to analyze the statistical significance at $p< 0.05$ among the treatment groups. The mean particle size, zeta potential, drug loading, and encapsulation efficiency of the SLN-CQ were 444.5 ± 6.9 nm, 9.41 ± 0.376 mV, 25%, and 90%, while for the SLN- HEP-CQ they were 374.6 ± 7.6,-4.06 ± 0.091, 21 and 78% respectively. SLN-CQ, SLN-HEP and SLN-HEP-CQ showed moderate antiplasmodial activities against chloroquine sensitive (D6) strain of *P. falciparum in vitro.* The nanoformulated drugs, SLN- HEP, SLN-CQ and SLN- HEP-CQ, showed significant antiplasmodial activity against CQ sensitive *P. berghei in vivo* in comparison to the negative control group. The *in vivo* results showed that this nanoformulated drugs worked as effective as the standard chloroquine drug and hence can be developed further to improve their efficacy.