

Malaria remains a devastating scourge on the lives and livelihoods to the millions of global citizens living in the tropics. Plant-derived antimalarials have made and continue to make an immense contribution to malaria chemotherapy and novel drug entities continue to be developed through research into their constituents. The long established use of quinine and the more recent introduction of artemisinin and its derivatives as highly effective antimalarials also demonstrate that plant species are an important resource for the discovery of new antimalarial agents. In search for new antimalarial principles, three plants namely *Drypetes gerrardii*, *Euclea divinorum* and *Ozoroa insignis* normally used to treat malaria and other ailments among 'Chonyi' people in Kilifi District, Coast province were investigated. The crude extracts were screened against chloroquine (CQ) susceptible and resistant strains of *Plasmodium falciparum* (D6 and W2, respectively). Isolation and purification of bioactive principles present in the active extracts was done using chromatographic techniques (CC, TLC, Prep TLC). The *in vitro* cytotoxicity assay was carried out using VERO 199 kidney epithelial monkey cells. The structures were established conclusively by using UV, IR, MS and extensive ¹H and ¹³C NMR spectra analysis and comparison with data from the cited literature. The CH₂Cl₂ and EtOAc crude extracts obtained from the leaves of *Drypetes gerrardii* and *Euclea divinorum* as well as root bark of *Ozoroa insignis* showed high *in vitro* antiplasmodial activity in the range of IC₅₀ = 6.12 ± 0.45 - 17.29 ± 1.44 pg/ml and 8.42 ± 1.06 - 12.09 ± 0.67 gg/ml against CQ-susceptible strain, respectively. Phytochemical investigations of the petroleum ether and dichloromethane mixture and the ethyl acetate crude extracts of *Drypetes gerrardii* leaves afforded four friedelane-type triterpenoids (DGL 1 - DGL 4), one hopane-type triterpenoids (DGL 5), one lupane-type triterpenoids ((DGL 6), one steroid (DGL 7) and a biflavonoid (DGL 8) for the first time. The compounds exhibited no antiplasmodial activity (IC₅₀ > 10 pg/ml) and weak cytotoxicity (IC₅₀ > 20 pg/ml). Chemical analyses of the leaves of *Euclea divinorum* yielded three new naphthalene derivatives namely eucleanal A (EDD 5), eucleanal B (EDD 6), eucleanal C (EDD 7) among four naphthoquinones (EDD 1 - EDD 4), three lupane-type triterpenoids (EDD 8, EDD 9 and EDD 11), one ursane-type triterpenoid (EDD 10) and a sterol (EDD 12a and 12b). The 2-methylnaphthazarin (EDD2) exhibited high antiplasmodial activity against CQ-resistant strain with an IC₅₀ value of 0.50 ± 0.16 pg/ml but also displayed the highest cytotoxicity with an IC₅₀ value of 0.94 pg/ml and a selective index (SI) of 1.90. Similarly, phytochemical screening of the CH₂Cl₂ and EtOAc of the root bark of *Ozoroa insignis* yielded one oleanane-type triterpenoid (OZD 1), three lupane-type triterpenoids (OZD 2 - OZD 4), three anarcadiic acid derivatives (OZD 5-6) and a flavone (OZD 7) for the first time. 3β-Hydroxylup-12:20(29)-diene (magnificol) (OZD 3) exhibited high antiplasmodial activity (IC₅₀ = 1.81 ± 1.03 pg/ml) against CQ-resistant strain and weak cytotoxicity (IC₅₀ > 20 gg/ml) with an SI > 11.05 pg/ml indicating its selectivity for the malaria parasite. The antimalarial activity reported herein explains and verifies the therapeutic efficacy claimed for these plants in traditional medicine. In addition, the isolated compounds with appreciable activity may be chemically modified to generate leads with enhanced antiplasmodial activity, reduced cytotoxicity and improved bioavailability.