

## abstract

Nefang, a polyherbal product composed of *Mangifera indica* (bark and leaf), *Psidium guajava*, *Carica papaya*, *Cymbopogon citratus*, *Citrus sinensis*, and *Ocimum gratissimum* (leaves), is a potential therapy against *P. falciparum* malaria. In vitro antiplasmodial activities of its constituent solvent extracts were analyzed on CQ-sensitive (3D7) and multidrug resistant (Dd2) *P. falciparum* strains. The interactions involving the differential solvent extracts were further analyzed using a variable potency ratio drug combination approach. Effective concentration 50 (EC50) values were determined by nonlinear regression curve-fitting of the dose-response data and used in calculating the fractional inhibitory concentration 50 (FIC50) and combination indices (CI) for each pair. The derived EC50 values (3D7/Dd2,  $\mu\text{g/mL}$ ) are Nefang-96.96/55.08, MiB-65.33/34.58, MiL-82.56/40.04, Pg-47.02/25.79, Cp-1188/317.5, Cc-723.3/141, Cs-184.4/105.1, and Og-778.5/118.9. Synergism was obtained with MiB/Pg (CI = 0.351), MiL/Pg (0.358), MiB/Cs (0.366), MiL/Cs (0.482), Pg/Cs (0.483), and Cs/Og (0.414) when analyzed at equipotency ratios. Cytotoxicity testing of Nefang and the solvent extracts on two human cell lines (Hep G2 and U2OS) revealed no significant toxicity relative to their antiplasmodial activities (SI > 20). Taken together, our data confirm the antimalarial activities of Nefang and its constituent plant extracts and identified extract pairs with promising synergistic interactions for exploitation towards a rational phytotherapeutic and evidence-based antimalarial drug discovery.