Abstract:

The CH2Cl2-MeOH (1:1) extract of the aerial parts of Sphaeranthus bullatus, an annual herb native to tropical East Africa, showed activity against chloroquine sensitive D6 (IC50 9.7 microg/mL) and chloroquine resistant W2 (IC50 15.0 microg/mL) strains of Plasmodium falciparum. Seventeen secondary metabolites were isolated from the extract through conventional chromatographic techniques and identified using various spectroscopic methods. The compounds were evaluated for their in vitro antiplasmodial, antileishmanial and anticancer activities revealing activity of four carvotacetone derivatives, namely 3-acetoxy-7-hydroxy-5-tigloyloxycarvotacetone (1), 3,7-dihydroxy-5-tigloyloxycarvotacetone (2), 3-acetoxy-5,7-dihydroxycarvotacetone (3) and 3,5,7-trihydroxy-carvotacetone (4); with antiplasmodial IC50 values of 1.40, 0.79, 0.60 and 3.40 microg/mL, respectively, against chloroquine sensitive D6 strains of P. falciparum; antiplasmodial activity of IC50 2.00, 0.90, 0.68 and 2.80 microg/mL, respectively, against chloroquine resistant W2 strains of P. falciparum; antileishmanial IC50 values of 0.70, 3.00, 0.70 and 17.00 microg/mL, respectively, against the parasite L. donovanii promastigotes, and anticancer activity against human SK-MEL, KB, BT-549 and SK-OV-3 tumor cells, with IC50 values between <1.1 - 5.3 microg/mL for 1-3. In addition, cytotoxic effects of the active compounds were evaluated against monkey kidney fibroblasts (VERO) and pig kidney epithelial cells (LLC-PK11). The structures of carvotacetone derivatives were determined by 1D and 2D NMR spectroscopy; the absolute stereochemical configuration of 3-acetoxy-7-hydroxy-5-tigloyloxycarvotacetone (1) was determined as 3R, 4R, 5S by circular dichroism, specific rotation, 1H NMR and 2D NMR ROESY and NOESY experiments