Antiplasmodial activity of a new chemotype of *Croton sylvaticus* essential oils

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Abstract

Background: In the context of malaria elimination, the development of new antimalarial agents with dual activity, targeting both the asexual and sexual stages of *Plasmodium falciparum* is of paramount importance. The pivotal role of plant-derived natural products in the discovery of antimalarial drugs inspired us to investigate bioactive compounds with dual activity from *Croton sylvaticus*, a medicinal plant traditionally used to treat malaria.

Purpose: This study aims to scientifically validate the traditional medicinal use of *C. sylvaticus*, particularly for malaria treatment, by analyzing its essential oils (EOs) and evaluating their antiplasmodial activity.

Methods: EOs were extracted from the plant's leaves, roots, and trunk bark using hydrodistillation. Their chemical composition was analyzed through gas chromatography-mass spectrometry (GC-MS), and their effects were tested *in vitro* against both asexual and sexual stages of *P. falciparum*.

Results: Results showed that the major constituents identified were viridiflorene (18.13 ± 0.46%) in root EO, (E)-*β*-caryophyllene (18.40 ± 0.60%) in trunk bark EO, and farnesyl acetone (15.26 ± 0.25%) in leaf EO. Notably, the leaf EO of Cameroonian *C. sylvaticus* exhibited a distinct and newly described chemotype, characterized by high levels of farnesyl acetone, *β*-copaene-4-*α*-ol, *β*-cadinene, *α*-humulene, and *trans*-longipinocarveol. *In vitro* testing revealed significant antiplasmodial activity against both the asexual and sexual stages of *P. falciparum*, with trunk bark EO demonstrating the highest potency (IC_{50}: 9.06 ± 2.15 µg/mL for *Pf*3D7 and 0.56 µg/mL for gametocytes). Caryophyllene oxide (IC_{50} = 0.48 *µ*g/mL), (E)-*β*-caryophyllene (IC_{50} = 1.15 *µ*g/mL), and sclareol (IC_{50} = 1.30 *µ*g/mL), the major compounds in the trunk bark EO, play a crucial role in the dual antiplasmodial efficacy of the EO extracted from the trunk bark of *C. sylvaticus*.

Conclusion: These findings support the traditional antimalarial use of *C. sylvaticus* and stimulate further research in this critical field.

Keywords: *Croton sylvaticus*; Essential oils; Antiplasmodial assay.