A new alkamide with an endoperoxide structure from acmella ciliata (asteraceae) and its in vitro antiplasmodial activity

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From the aerial parts of Acmella ciliata (H.B.K.) Cassini (basionym Spilanthes ciliata Kunth; Asteraceae), three alkamides were isolated and identified by mass- and NMR spectroscopic methods as (2E,6E,8E)-N-isobutyl-2,6,8-decatrienamide (spilanthol, (1)), N-(2-phenethyl)-2E-en-6,8-nonadiynamide (2) and (2E,7Z)-6,9-endoperoxy-N-isobutyl-2,7-decadienamide (3). While 1 and 2 are known alkamides, compound 3 has not been described until now. It was found that the unusual cyclic peroxide 3 exists as a racemate of both enantiomers of each alkamide; the 6,9-cis- as well as the 6,9-trans-configured diastereomers, the former represents the major, the latter the minor constituent of the mixture. In vitro tests for activity against the human pathogenic parasites Trypanosoma brucei rhodesiense and Plasmodium falciparum revealed that 1 and 3 possess activity against the NF54 strain of the latter (IC50 values of 4.5 and 5.1 ţM, respectively) while 2 was almost inactive. Compound 3 was also tested against multiresistant P. falciparum K1 and was found to be even more active against this parasite strain (IC50 = 2.1 ţM) with considerable selectivity (IC50 against L6 rat skeletal myoblasts = 168 ţM).
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