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ANTIPLASMODIAL ACTIVITY OF COMPOUNDS FROM *Drypetes gerrardii*

Margaret Mwihaki Ng′ang′a,[1] Hidayat Hussain,[2,3*] Sumesh Chhabra,[1] Caroline Langat-Thoruwa,[1] Beatrice N. Irungu,[4] Ahmed Al-Harrasi,[3] Muhammad Riaz,[5] and Karsten Krohn[2]

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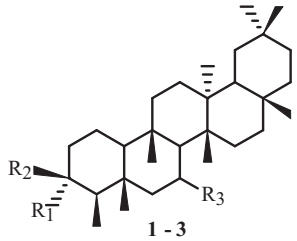
Drypetes gerrardii J. Hutch (Manyenyee Kikuyu; Ol-durdiene Maasai) is a large tree and one of the many species of the *Drypetes* genus found in Kenya. Other species that are widely distributed in Kenya include *Drypetes natalensis* J. Hutch and Drypetes aromacia Pax & Hoffm [1].

The leaves of *D. gerrardii* were collected in Kilifi District, Coast Province, Kenya, in July 2004 and authenticated by Simon Mathenge of Nairobi University, Kenya. A voucher specimen (MM/07/04) is deposited in the Nairobi University herbarium, Chiromo Campus.

The $CHCl_3$ extract of the stem of *D. gerrardii* was subjected to column chromatography on silica gel using petroleum ether, petroleum ether–EtOAc, EtOAc–MeOH, and finally pure MeOH as the mobile phase to yield compounds **1–8**. These compounds consists of four friedelane-type triterpenoids, namely friedelin (**1**) [2], epifriedelanol (**2**) [3], friedelanol methyl ether (**3**) [4], and 5β,24-cyclofriedelan-3-one (**4**) [5] together with 3-epimoretenol (**5**) (hopane-type triterpenoid) [6], resinone (**6**) (lupane-type triterpenoid) [7], β-sitosterol glucopyranoside (**7**) [8], and amentoflavone (**8**) [9].

Eight compounds **1–8** isolated from *D. gerrardii*, were tested for *in vitro* antiplasmodial activity against a K1 multidrug-resistant strain of *P. falciparum.* The IC_{50} values are tabulated in Table 1. The antiplasmodial activity for the pure compounds **1–8** was considered high when $IC_{50} < 1$ μg/mL, moderate when between 1 and 5, and low when between 5 and 10 μg/mL. Compounds with IC_{50} exceeding 10 μg/mL were considered to be inactive [10].



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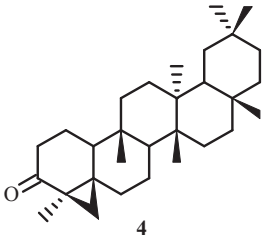

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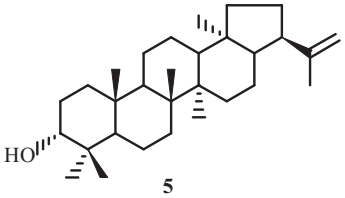
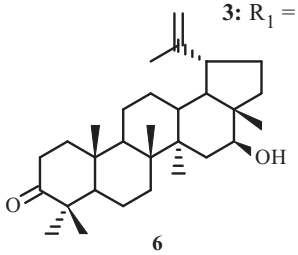


5

1: $R_1R_2 = O$, $R_3 = H$
2: $R_1 = R_3 = H$, $R_2 = OH$
3: $R_1 = OCH_3$, $R_2 = R_3 = H$



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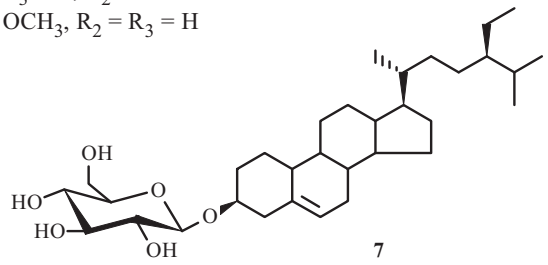

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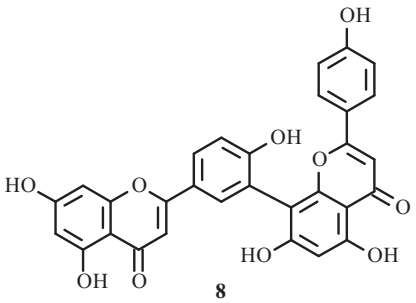

8

1) Department of Chemistry, Kenyatta University, P.O. Box 43844-00100, Nairobi, Kenya; 2) Department of Chemistry, Universitat Paderborn, Warburger Street 100, 33098 Paderborn, Germany, e-mail: Hidayat110@gmail.com; 3) Department of Biological Sciences and Chemistry, College of Arts and Sciences University of Nizwa, Birkat Al-Mouz, PC 616, Oman; 4) Centre for Traditional Medicine and Drug Research, Kenya Medical Research Institute, P. O. Box 54840-00200, Nairobi, Kenya; 5) NUST Center of Virology and Immunology, National University of Science and Technology, H-12, Islamabad, Pakistan. Published in *Khimiya Prirodnykh Soedinenii*, No. 2, March–April, 2012, pp. 304–305. Original article submitted January 4, 2011.

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TABLE 1. Antiplasmodial and Cytotoxicity Activity of Compounds **1–8** of *D. gerrardii**

Compound	IC_{50}, μg/mL	CC_{50} ± S.E, μg/mL	SI	Compound	IC_{50}, μg/mL	CC_{50} ± S.E, μg/mL	SI
1	4.8 ± 0.11	> 90	18.75	**5**	> 10	7.9 ± 0.05	> 0.79
2	>10	90.0 ± 1.30	> 9.00	**6**	0.09 ± 0.01	84.8 ± 2.34	942.2
3	>10	32.8 ± 0.90	3.28	**7**	5.4 ± 0.02	14.3 ± 0.03	1.46
4	2.2 ± 0.02	21.2 ± 0.01	9.64	**8**	2.6 + 0.01	0.34 ± 0.00	0.13

**P. falciparum* – K1 strain, L-6 – rat skeletal myoblast cells, IC_{50} – inhibitory concentration for 50% of tested parasites, CC_{50} – cytotoxic concentration for 50% of tested cells, chloroquine IC_{50} 0.063 + 0.03, artemisinin IC_{50} 0.002 + 0.000, Pdx – podophyllotoxin CC_{50} 0.009 + 0.000.

Resinone (**6**) exhibited high antiplasmodial activity against K1 strain of *P. falciparum* with an IC_{50} value of 0.09 ± 0.01 μg/mL as well as a satisfactory selectivity index. Amentoflavone (**8**) and 5*β*,24-cyclofriedelan-3-one (**4**) also exhibited moderate antiplasmodial activity, with IC_{50} 2.6 + 0.01 μg/mL and 2.2 ± 0.02 μg/mL respectively. Interestingly, amentoflavone (**8**) had high toxicity, with CC_{50} 0.34 ± 0.00 μg/mL, as compared to 5*β*,24-cyclofriedelan-3-one (**4**) that displayed mild toxicity. This clearly indicated that the high antiplasmodial activity observed for amentoflavone (**8**) was probably due to cytotoxicity rather than activity against the parasites The other compounds (**1–3**, **5–7**) had antiplasmodial activity ranging from 4.8 ± 0.11 μg/mL to >10 μg/mL. In addition, 5*β*,24-cyclofriedelan-3-one (**4**), which exhibited good antiplasmodial activity, did not demonstrate sufficient selectivity to kill the parasites without damaging mammalian cells. The selectivity index observed suggested that the antiplasmodial activity might be due to general toxicity.

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