

ANTIPLASMODIAL ACTIVITY OF COMPOUNDS FROM *Drypetes gerrardii*

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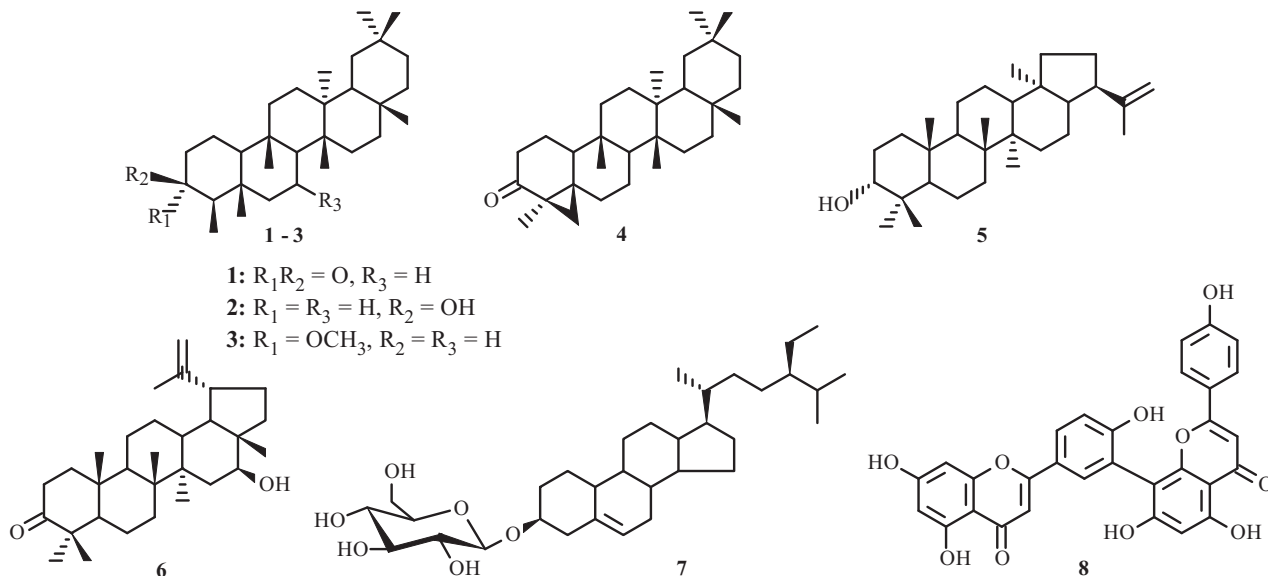
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Drypetes gerrardii J. Hutch (Manyenyee Kikuyu; Ol-durdiene Maasai) is a large tree and one of the many species of the *Drypetes* genus found in Kenya. Other species that are widely distributed in Kenya include *Drypetes natalensis* J. Hutch and *Drypetes 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 CHCl₃ 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 5 β ,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 IC₅₀ values are tabulated in Table 1. The antiplasmodial activity for the pure compounds **1–8** was considered high when IC₅₀ < 1 μ g/mL, moderate when between 1 and 5, and low when between 5 and 10 μ g/mL. Compounds with IC₅₀ exceeding 10 μ g/mL were considered to be inactive [10].



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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, IC₅₀ – inhibitory concentration for 50% of tested parasites, CC₅₀ – cytotoxic concentration for 50% of tested cells, chloroquine IC₅₀ 0.063 ± 0.03, artemisinin IC₅₀ 0.002 ± 0.000, Pdx – podophyllotoxin CC₅₀ 0.009 ± 0.000.

Resinone (**6**) exhibited high antiplasmodial activity against K1 strain of *P. falciparum* with an IC₅₀ value of 0.09 ± 0.01 µg/mL as well as a satisfactory selectivity index. Amentoflavone (**8**) and 5β,24-cyclofriedelan-3-one (**4**) also exhibited moderate antiplasmodial activity, with IC₅₀ 2.6 ± 0.01 µg/mL and 2.2 ± 0.02 µg/mL respectively. Interestingly, amentoflavone (**8**) had high toxicity, with CC₅₀ 0.34 ± 0.00 µg/mL, as compared to 5β,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, 5β,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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