Indonesian Medicinal Plants. XIV.[1] Characterization of 3′-*O*-Caffeoylsweroside, a New Secoiridoid Glucoside, and Kelampayosides A and B, Two New Phenolic Apioglucosides, from the Bark of *Anthocephalus chinensis* (Rubiaceae)

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A new secoiridoid glucoside named 3′-*O*-caffeoylsweroside (1), and two new phenolic apioglucosides, named kelampayoside A (4) and kelampayoside B (6), together with eleven known compounds (five iridoids and six alkaloids), were isolated from the bark of *Anthocephalus chinensis* (Rubiaceae), an Indonesian medicinal plant from Sumatra Island, Indonesia. The chemical structures of 1, 4 and 6 have been elucidated respectively as 3′-*O*-caffeoylsweroside (1), antiarol 1-*O*-β-D-apiofuranosyl(1→6)-β-D-glucopyranoside (4), and antiarol 1-*O*-β-D-5″-*O*-caffeoylapiofuranosyl(1→6)-β-D-glucopyranoside (6) on the bases of their chemical and physicochemical properties. Among fourteen constituents characterized, cadambine (13), one of the major indole alkaloidal constituents of *A. chinensis*, was shown to exhibit moderate growth-inhibitory activity against the malarial parasite *Plasmodium falciparum* (a chloroquine-resistant K1 strain) cultured in human erythrocytes.

Key words Indonesian medicinal plant; *Anthocephalus chinensis*; Rubiaceae; phenolic apioglucoside; secoiridoid glucoside; anti-malaria

Anthocephalus chinensis is a medium-sized tree with a typical capitulum type of inflorescence in the family Rubiaceae, being widely distributed in southeast tropical Asia and India. In Ayurvedic medicine, the bark has been used to treat uterine complaints, blood disease, leprosy, and dysentery.[3] The chemical constituents of *A. chinensis* of various origins have been extensively investigated and so far, terpenoids such as oleanolic acid,[4] cadambagenic acid,[4] and several alkaloids such as cadambine,[4–6] 3α-dihydrocadambine,[4–6] 3β-dihydrocadambine,[4,5,7] 3α-isodihydrocadambine,[5,8] 3β-isodihydrocadambine,[4,5,7] cadamine,[5,9] isocadamine,[5,9] cinchonine,[10] and dihydrocinchonine,[10] have been identified, though the active constituents have not yet been identified. The plant, *A. chinensis*, is called "kelampayan" in the Indragiri Hulu area, Riau Province of Sumatra Island, Indonesia. The powdered bark, leaves and roots are locally used as internal medicines for malaria.[11] As a part of our pharmacochemical investigations of Indonesian medicinal plants,[1,11] we have been engaged in the chemical analysis of the bark of *A. chinensis*, searching for the anti-malarial constituent. The details are presented here.

The methanol extract of the bark was partitioned into a chloroform–methanol–water (4:4:3) mixture. Separation and purification of the chloroform-soluble portion (chloroform extract) by repeated silica gel and Sephadex LH-20 column chromatographies and semi-preparative reversed-phase (ODS) high-performance liquid chromatography (HPLC) provided loganol (**8**),[12] the aglycone of loganin (**7**),[12] and two known non-glycosidic indole alkaloids, vallesiachotamine (**9**)[13] and isovallesiachotamine (**10**).[13] The water-soluble portion (aqueous phase) was further partitioned with a mixture of *n*-butanol and water. Separation and purification of the *n*-butanol-soluble portion (*n*-BuOH ext.) by silica gel column chromatography, centrifugal partition chromatography (CPC) and semi-preparative reversed-phase (ODS) column chromatography, gave four known iridoid (or secoiridoid) glucosides identified as loganin (**7**),[12] 8-epikingiside (**11**),[14] loganic acid (**12**),[15] and sweroside (**2**),[16] and four known indole alkaloid glucosides, cadambine (**13**),[4–6] strictosidine lactam (**14**),[17] desoxycordifoline (**15**),[18] and 5α-carboxystrictosidine (**16**),[19] as well as a novel secoiridoid caffeoylglucoside **1** and two new phenolic apioglucosides named kelampayoside A (**4**) and kelampayoside B (**6**) (Figs. 1—3). A full account of the structure elucidation of these new compounds (**1**, **4** and **6**) is given below.

3′-*O*-Caffeoylsweroside (1) The glucoside **1** was obtained as a white amorphous solid. The fast atom bombardment mass spectrum (FAB-MS) of **1** gave a *quasi*-molecular ion peak at *m/z* 543 $[(M+Na)^+]$, whose molecular formula was defined as $C_{25}H_{28}O_{12}$ from the high-resolution (HR) FAB-MS. The infrared (IR) spectrum of **1** showed absorption bands due to hydroxyl (3360 cm^{-1}) and α,β-unsaturated ester (1693, 1610 cm^{-1}) groups, while the ultraviolet (UV) spectrum showed absorption maxima at 219 ($\varepsilon=13500$), 240 ($\varepsilon=13000$), 297 ($\varepsilon=10000$) and 328 ($\varepsilon=12300$) nm.

The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of the glucoside **1** showed the presence of two *trans* olefinic protons [δ 6.28 (d, $J=15.9$ Hz) and δ 7.54 (d, $J=15.9$ Hz)], and three 1,2,4-trisubstituted benzene ring protons [δ 6.73 (d, $J=8.2$ Hz), δ 6.90 (dd, $J=8.2$, 2.0 Hz), δ 7.00 (d, $J=2.0$ Hz)]. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **1** was closely

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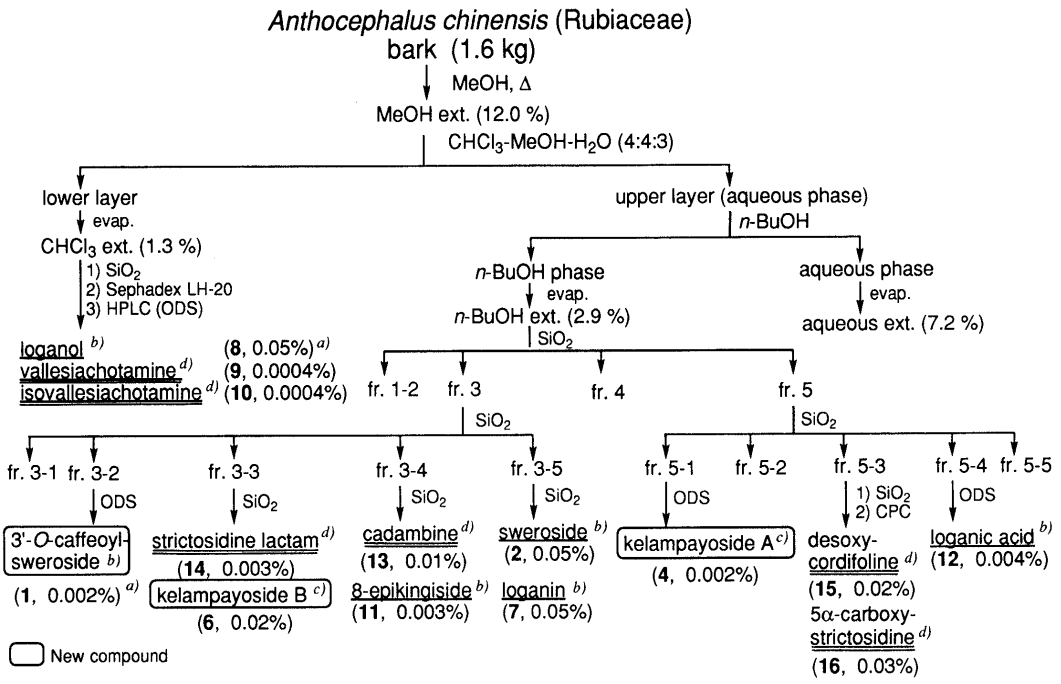

Fig. 1. Isolation Procedure for the Constituents

a) The yield from air-dried bark. *b*) Iridoid or iridoid glucoside. *c*) Phenolic glycoside. *d*) Indole alkaloid.

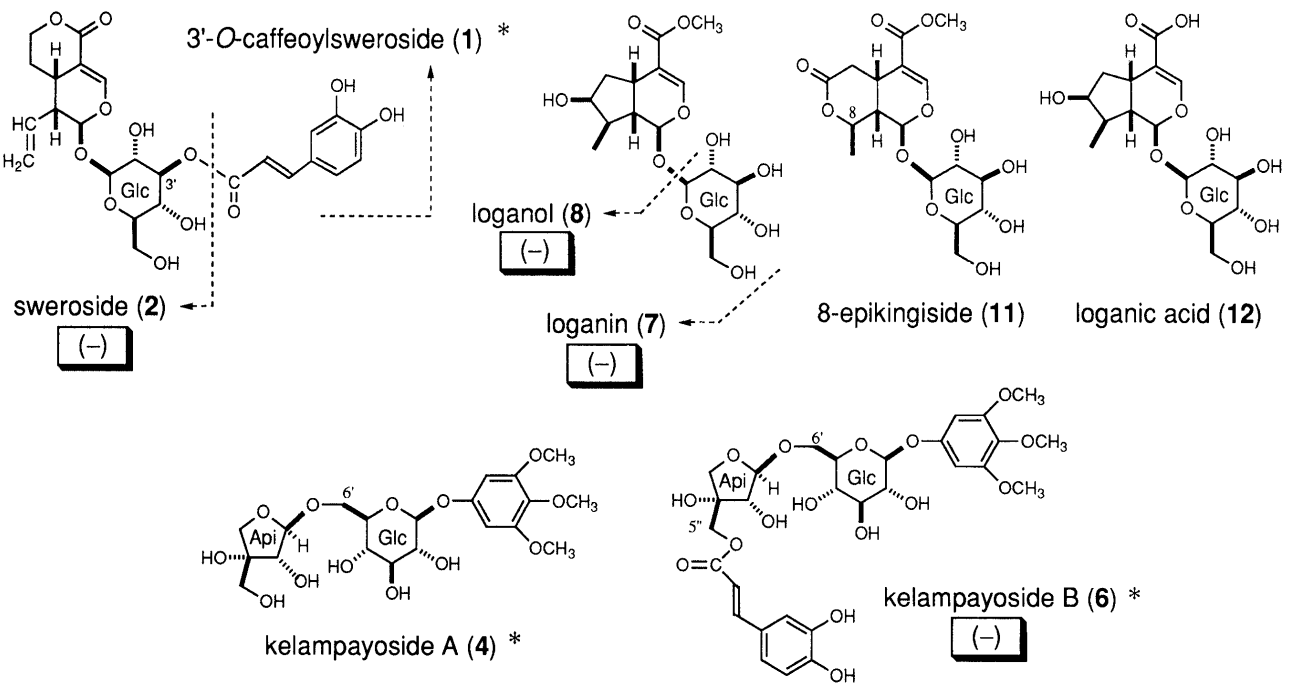

Fig. 2. Various Glycosides Isolated from the Bark of *Anthocephalus chinensis*

* new compound; (-), no anti-malarial activity at 100 μM.

similar to that of sweroside (**2**), except that additional olefinic carbon signals due to a caffeoyl moiety were observed in **1**. Treatment of **1** with sodium carbonate in methanol liberated sweroside (**2**) and caffeic acid methyl ester (**3**) (Fig. 4). These findings have led us to presume that the glucoside **1** is a caffeoyl derivative of sweroside (**2**). In the ^{13}C-NMR spectrum of **1** (Table 1), the signals due to C-1′ (δ_C 100.5) and C-3′ (δ_C 79.5) were observed at lower field (C-1′, +0.1 ppm; C-3′, +1.0 ppm) as compared with those of **2**, while the signals due to C-2′ (δ_C 74.0) and C-4′ (δ_C 70.6) were observed at higher field (C-2′, −1.3 ppm; C-4′, −1.6 ppm), thus demonstrating that the caffeoyl moiety in **1** is attached to the C-3′ hydroxyl group in the sugar moiety of **1**.[20] Furthermore, in the ^{1}H-NMR spectrum of **1**, the signal of 3′-H was observed at lower field (δ 5.01). Based on the accumulated evidence, the chemical structure of **1** has been determined as 3′-*O*-caffeoylsweroside.

Kelampayoside A (4) The FAB-MS of kelampayoside A (**4**) gave a *quasi*-molecular ion peak at *m/z* 501, the

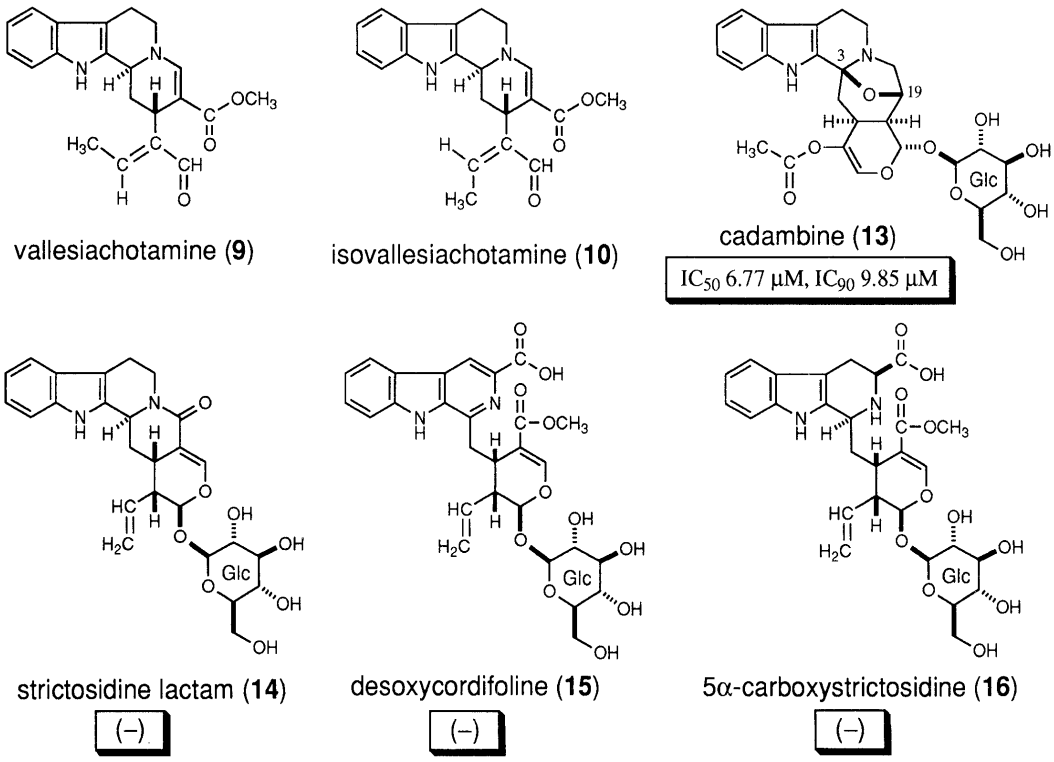

Fig. 3. Indole Alkaloids Isolated from the Bark of *Anthocephalus chinensis*
□, *in vitro* anti-malarial activity; (−), no activity at 100 μM.

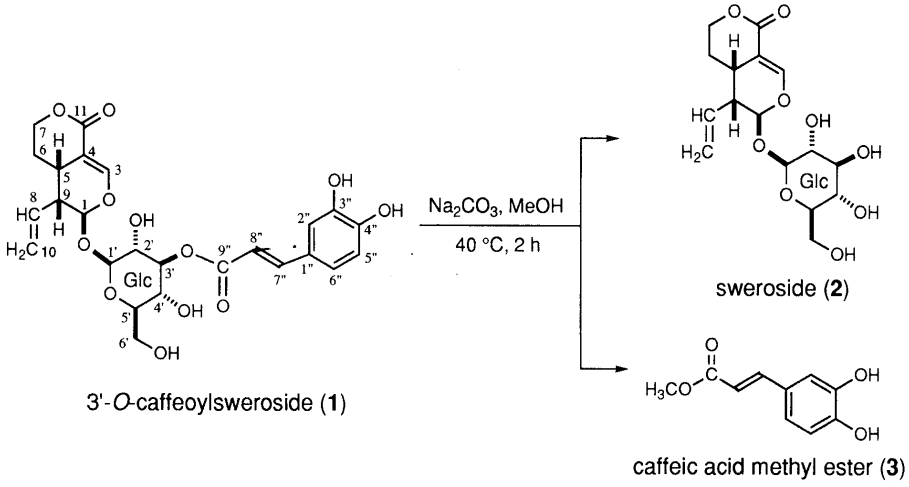

Fig. 4

composition being defined as $C_{20}H_{30}O_{13}Na$ $(M+Na)^+$ from the HR FAB-MS analysis. The IR spectrum of **4** showed absorption bands due to hydroxyl groups (3394 cm^{-1}) and an aromatic ring (1601, 1506 cm^{-1}), while the UV spectrum showed absorption maxima at 223 ($\varepsilon=5400$) and 275 ($\varepsilon=700$) nm, suggesting the presence of an aromatic ring in its structure.

The ^{1}H-NMR spectrum of kelampayoside A (**4**) showed signals assignable to two benzene-ring protons (δ 6.38 ppm, 2H, s), three methoxyl groups on the benzene ring [δ 3.60 (3H, s), δ 3.74 (6H, s)], and two anomeric protons [δ 4.83 (d, $J=7.3$ Hz), δ 4.92 (d, $J=2.0$ Hz)], suggesting that **4** is a disaccharide possessing a symmetrically substituted benzenoid aglycone.

In the correlation spectroscopy *via* long-range coupling (COLOC) NMR experiment on kelampayoside A (**4**), the following ^{1}H–^{13}C long-range correlations were observed: i) between the 4-methoxyl protons at δ 3.60 and the C-4 carbon signal at δ_C 133.5, ii) between the 3- and 5-methoxyl protons at δ 3.74 (6H, s) and the C-3 and C-5 carbons at δ_C 153.4 respectively, and iii) between the anomeric proton at δ 4.83 ppm (d, $J=7.3$ Hz) and the C-1 carbon at δ_C 154.2 (Fig. 5). Upon acidic hydrolysis, **4** liberated D-apiose, D-glucose, and antiarol (**5**)[21] (Fig. 5).

In the ^{13}C-NMR spectrum of kelampayoside A (**4**), the signal due to C-6′ was observed at lower field (δ_C 67.2) which suggested that the sequence in the sugar moiety of **4** is D-apiofuranosyl(1→6)-D-glucopyranose (Table 2). Furthermore, the coupling constant ($J=7.3$ Hz) of the anomeric proton signal of the D-glucosyl moiety (1′-H) as

Table 1. ^{13}C-NMR Data for 3-*O*-Caffeoylsweroside (**1**) and Sweroside (**2**) (67.8 MHz, MeOH-d_4, δ_C)

	Carbon	1	2		Carbon	1	2
Secoiridoid moiety	C-1	98.9	98.7	1-*O*-β-D-Glucopyranosyl moiety	C-1′	100.5	100.4
	C-3	154.8	154.7		C-2′	74.0	75.3
	C-4	106.7	106.7		C-3′	79.5	78.5
	C-5	29.2	29.1		C-4′	70.6	72.2
	C-6	26.7	26.6		C-5′	79.0	79.0
	C-7	70.5	70.4		C-6′	63.2	63.3
	C-8	134.0	134.0	3′-*O*-Caffeoyl moiety	C-1″	128.6	
	C-9	44.6	44.4		C-2″	115.9	
	C-10	121.7	121.7		C-3″	147.6	
	C-11	169.2	169.2		C-4″	150.3	
					C-5″	117.3	
					C-6″	123.7	
					C-7″	147.8	
					C-8″	116.1	
					C-9″	169.8	

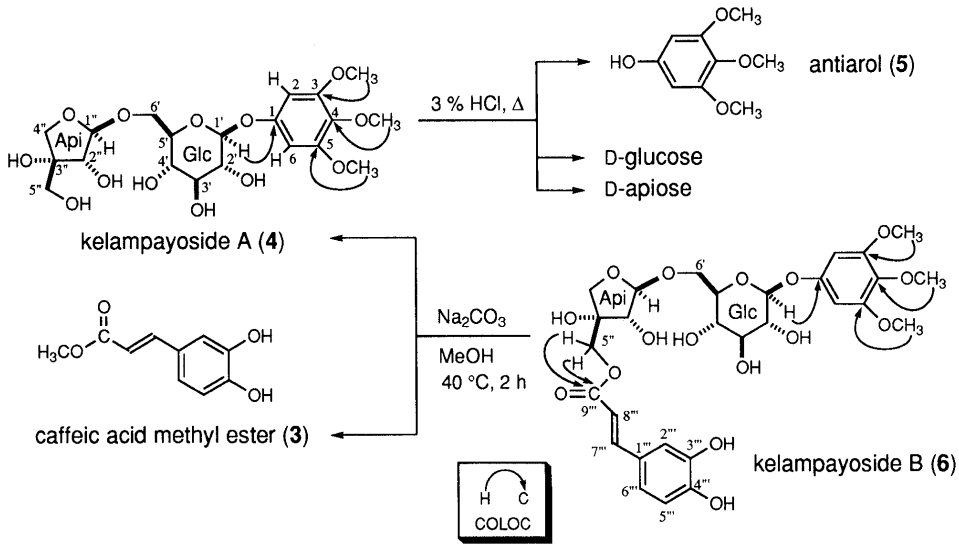

Fig. 5

Table 2. ^{13}C-NMR Data for Kelampayoside A (**4**) and Kelampayoside B (**6**) (67.8 MHz, in Acetone-d_6, δ_C)

	Carbon(s)	4	6		Carbon	6
Aglycone moiety	C-1	154.2	154.1	5″-*O*-Caffeoyl moiety	C-1‴	126.9
	C-2, C-6	94.8	95.2		C-2‴	114.2
	C-3, C-5	153.4	153.4		C-3‴	145.1
	C-4	133.5	133.6		C-4‴	147.7
	3-O$\underline{C}$H$_3$, 5-O$\underline{C}$H$_3$	55.4	55.5		C-5‴	115.3
	4-O$\underline{C}$H$_3$	59.5	59.7		C-6‴	121.6
1-*O*-β-D-Glucosyl moiety	C-1′	101.4	101.4		C-7‴	145.2
	C-2′	73.4	73.4		C-8‴	114.0
	C-3′	76.8	76.7		C-9‴	166.5
	C-4′	70.2	70.2			
	C-5′	75.4	75.4			
	C-6′	67.2	67.2			
6′-*O*-β-D-Apiosyl moiety	C-1″	109.3	109.0			
	C-2″	76.5	77.2			
	C-3″	78.9	77.4			
	C-4″	73.5	73.5			
	C-5″	64.3	66.0			

well as the chemical shift (δ_C 110.7 in pyridine-d_5) of the anomeric carbon of the D-apiosyl moiety (C-1″),[22] demonstrated that both sugar moieties have β-anomeric configurations.

Based on the aforementioned evidence, the structure of kelampayoside A has been elucidated to be antiarol 1-*O*-β-D-apiofuranosyl(1→6)-β-D-glucopyranoside (**4**).

Kelampayoside B (6) The HR FAB-MS of kelampayo-

side B (**6**) showed a *quasi*-molecular ion peak $[M+Na]^+$ at *m/z* 663.1890 which corresponded to the composition $C_{29}H_{36}O_{16}Na$, so that the molecular formula of **6** was determined as $C_{29}H_{36}O_{16}$. The IR spectrum showed absorption bands of hydroxyl groups (3383 cm^{-1}) and an ester-carbonyl group (1695 cm^{-1}), whereas the UV spectrum showed absorption maxima at 296 ($\varepsilon=15500$) and 327 ($\varepsilon=16200$) nm with a shoulder around 238 nm. The ^{1}H-NMR spectrum of kelampayoside B (**6**) was similar to that of kelampayoside A (**4**), except that the former showed additional proton signals assignable to a caffeoyl moiety [δ 7.53 (d, $J=16.1$ Hz), δ 6.26 (d, $J=16.1$ Hz), δ 7.00 (dd, $J=8.2$, 2.0 Hz), δ 7.13 (d, $J=2.0$ Hz), and δ 6.80 (d, $J=8.2$ Hz)]. Treatment of **6** with sodium carbonate in methanol afforded **4** and caffeic acid methyl ester (**3**). These results led us to presume that kelampayoside B (**6**) is a caffeoyl ester of kelampayoside A (**4**) (Fig. 5).

In the COLOC experiments on kelampayoside B (**6**) (Fig. 5), significant correlations between apiosyl 5″-H protons [observed at δ 4.17 (d, $J=15.5$ Hz) and δ 4.19 (d, $J=15.5$ Hz)] and the caffeoyl carbonyl carbon at C-9‴ (δ_C 166.5) were observed. Furthermore, acylation shifts[20] for the carbon signals due to the apiosyl C-5″ (+1.7 ppm) and C-3″ (−1.5 ppm) in **6** were observed as compared to those signals in **4** (Table 2).

Based on these findings, the chemical structure of kelampayoside B has been determined to be antiarol 1-*O*-β-D-5″-*O*-caffeoylapiofuranosyl(1→6)-β-D-glucopyranoside (**6**).

As mentioned above, the air-dried powder of "kelampayan" bark has been locally prescribed for treatment of malaria. Among fourteen compounds isolated by us from the bark, we have so far tested eight compounds (**2**, **6**, **7**, **8**, **13**, **14**, **15**, and **16**) for *in vitro* anti-malarial activity against the cultured malarial parasite *Plasmodium falciparum* K1 of a chloroquine-resistant strain.[23] The results obtained in the primary screening (100 μM each) test are shown in Figs. 2 and 3. As can be seen, cadambine (**13**), one of the major alkaloidal constituents, showed moderate inhibitory activity (IC_{50} 6.77 μM, IC_{90} 9.85 μM), which may provide some scientific basis for the medicinal use of the bark.

Experimental

The instruments used to obtain physical data and the experimental conditions for chromatography were the same as in our previous paper.[1] A CPC Chromatograph Model LLB (Sanki Engineering Limited) was used for centrifugal partition chromatography (CPC) and Cosmosil $75C_{18}$-OPN (Nacalai Tesque) for reversed-phase column chromatography.

Isolation of 3′-*O*-Caffeoylsweroside (1), Kelampayoside A (4), Kelampayoside B (6), and Other Known Constituents The air-dried bark (1.6 kg) of *Anthocephalus chinensis* (Rubiaceae), collected in the Indragiri Hulu area of Sumatra Island, Indonesia in July 1990 (our third expedition), was extracted with MeOH under reflux and the solvent was evaporated off under reduced pressure to give the MeOH extract (196 g, 12.0% from the bark). The MeOH extract was partitioned into $CHCl_3$–MeOH–water (4:4:3, 2 l). The lower layer ($CHCl_3$ phase) was taken and concentrated under reduced pressure to give the $CHCl_3$ extract (20 g, 1.3%), while the upper layer (aqueous phase) was further partitioned with *n*-butanol (BuOH) (1 l each, twice). The *n*-BuOH phase and the aqueous phase were each concentrated under reduced pressure to afford the *n*-BuOH extract (46 g, 2.9%) and the aqueous extract (115 g, 7.2%) (Fig. 1). The $CHCl_3$ extract was subjected to column chromatography (SiO_2 1 kg, gradient elution with *n*-hexane : ethyl acetate = 15 : 1 → 1 : 2, ethyl acetate, and MeOH) to give fr. C-1 (0.9 g), fr. C-2 (0.9 g), fr. C-3 (2.5 g), fr. C-4 (1.1 g), fr. C-5 (3.6 g), and fr. C-6 (8.8 g). Fraction C-5 (eluted with *n*-hexane : ethyl acetate = 1 : 2, 3.5 g) was again chromatographed on Sephadex LH-20 (Sephadex LH-20 100 g, developed with $CHCl_3$: MeOH = 1 : 2) to afford fr. C5-1 (0.7 g), fr. C5-2 (0.7 g), fr. C5-3 (1.2 g), and fr. C5-4 (0.9 g). Fr. C5-4 (0.9 g) was then subjected to column chromatography (SiO_2 30 g, $CHCl_3$: MeOH = 100 : 3) to give loganol (**8**)[12] in 0.05% yield from the bark, and a mixture of alkaloids (20 mg). The mixture (20 mg) was further purified by HPLC [YMC-Pack, AM-323 (ODS), 10 mm (i.d.) × 30 cm (l.), MeOH : water = 3 : 2] to afford vallesiachotamine (**9**)[13] (0.0004%) and isovallesiachotamine (**10**)[13] (0.0004%).

The *n*-BuOH extract (30 g) was subjected to column chromatography (SiO_2 1.2 kg, gradient elution with $CHCl_3$: MeOH = 10 : 1 → 1 : 1 and MeOH) to give fr. 1 (1.1 g), fr. 2 (1.1 g), fr. 3 (5.2 g), fr. 4 (3.2 g), and fr. 5 (9.8 g). Fraction 3 (eluted with $CHCl_3$: MeOH = 2 : 1, 5.0 g) was again chromatographed on an SiO_2 column (SiO_2 100 g, ethyl acetate : MeOH : water = 4 : 1 : 1) to give fr. 3-1 (0.1 g), fr. 3-2 (0.1 g), fr. 3-3 (0.9 g), fr. 3-4 (0.7 g), and fr. 3-5 (2.1 g). Fraction 3-2 (0.1 g) was further purified by ODS column chromatography (Cosmosil $75C_{18}$-OPN 30 g, MeOH : water = 1 : 1) to provide 3′-*O*-caffeoylsweroside (**1**, 0.002% from the bark). Fraction 3-3 (0.9 g) was again chromatographed on an SiO_2 column (SiO_2 50 g, $CHCl_3$: MeOH : water = 7 : 3 : 1, lower phase) to provide strictosidine lactam[17] (**14**, 0.003%) and kelampayoside B (**6**, 0.02%). Fraction 3-4 (0.7 g) was separated by silica gel column chromatography (SiO_2 25 g, $CHCl_3$: MeOH : water = 7 : 3 : 1, lower phase) to afford cadambine[4-6] (**13**, 0.01%) and 8-epikingiside (**11**)[14] (0.003%). Fraction 3-5 (2.1 g) was further separated by silica gel column chromatography (SiO_2 80 g, $CHCl_3$: MeOH : water = 7 : 3 : 1, lower phase) to afford sweroside[16] (**2**, 0.05%) and loganin[12] (**7**, 0.05%). Fraction 5 (eluted with MeOH, 9.0 g) was subjected to column chromatography (SiO_2 120 g, ethyl acetate : MeOH : water = 4 : 1 : 1) to give fr. 5-1 (0.3 g), fr. 5-2 (1.5 g), fr. 5-3 (2.4 g), fr. 5-4 (3.7 g), and fr. 5-5 (0.7 g). Purification of fr. 5-1 (0.3 g) by ODS column chromatography (Cosmosil $75C_{18}$-OPN 30 g, MeOH : water = 1 : 3) afforded kelampayoside A (**4**, 0.002% from the bark). Fraction 5-3 (2.4 g) was subjected to column chromatography (SiO_2 80 g, $CHCl_3$: MeOH : water = 7 : 3 : 1, lower phase) and then to CPC (ascending method, $CHCl_3$: MeOH : water = 4 : 4 : 3, the upper phase was used as the mobile phase and the lower phase as the stationary phase) to give desoxycordifoline[18] (**15**, 0.02%) and 5α-carboxystrictosidine[19] (**16**, 0.03%). Fraction 5-4 (3.7 g) was subjected to ODS column chromatography (Cosmosil $75C_{18}$-OPN 150 g, MeOH : water = 1 : 4) to afford loganic acid[15] (**12**, 0.004%). Loganol (**8**),[12] vallesiachotamine (**9**),[13] isovallesiachotamine (**10**),[13] strictosidine lactam (**14**),[17] cadambine (**13**),[4-6] 8-epikingiside (**11**),[14] sweroside (**2**),[16] loganin (**7**),[12] desoxycordifoline (**15**),[18] 5α-carboxystrictosidine (**16**),[19] and loganic acid (**12**)[15] were identified by comparisons of melting point, optical rotation, IR, UV, ^{1}H-NMR, and ^{13}C-NMR data with reported values.

3′-*O*-Caffeoylsweroside (**1**): A white amorphous solid, $[\alpha]_D$ −134° ($c=0.10$, in MeOH at 21 °C). IR ν_{max}^{KBr} cm^{-1}: 3360, 2930, 1693, 1610, 1520, 1445, 1408, 1280, 1070. UV λ_{max}^{MeOH} nm (log ε): 219 (4.13), 240 (4.12), 297 (3.99), 328 (4.09). ^{1}H-NMR (270 MHz, CD_3OD) δ: 1.63—1.70 (2H, m, 6-H_2), 2.63—2.68 (1H, m, 9-H), 3.03—3.10 (1H, m, 5-H), 3.38—3.42 (2H, m, 2′-H, 5′-H), 3.49 (1H, t, $J=8.9$ Hz, 4′-H), 3.65 (1H, m, 6′-H_a), 3.86 (1H, dd, $J=11.9$, 2.0 Hz, 6′-H_b), 4.25—4.42 (2H, m, 7-H_2), 4.76 (1H, d, $J=7.3$ Hz, 1′-H), 5.01 (1H, t, $J=8.9$ Hz, 3′-H), 5.23 (1H, dd, $J=9.9$, 2.0 Hz, 10-H_a), 5.26 (1H, dd, $J=17.5$, 2.0 Hz, 10-H_b), 5.48 (1H, m, 8-H), 5.56 (1H, d, $J=1.7$ Hz, 1-H), 6.28 (1H, d, $J=15.9$ Hz, 8″-H), 6.73 (1H, d, $J=8.2$ Hz, 5″-H), 6.90 (1H, dd, $J=8.2$, 2.0 Hz, 6″-H), 7.00 (1H, d, $J=2.0$ Hz, 2″-H), 7.54 (1H, d, $J=15.9$ Hz, 7″-H), 7.55 (1H, d, $J=2.3$ Hz, 3-H). ^{13}C-NMR: as given in Table 1. FAB-MS (positive) *m/z*: 543 $(M+Na)^+$, 521 $(M+H)^+$. HR FAB-MS *m/z*: Calcd for $C_{25}H_{28}O_{12}Na$ $(M+Na)^+$: 543.1478. Found: 543.1462.

Kelampayoside A (**4**): A white amorphous solid, $[\alpha]_D$ −81.7° ($c=0.90$, in MeOH at 21 °C). IR ν_{max}^{KBr} cm^{-1}: 3394, 2938, 1601, 1506, 1464, 1128, 1060. UV λ_{max}^{MeOH} nm (log ε): 223 (3.73), 275 (2.80). ^{1}H-NMR (270 MHz, acetone-d_6, δ): 3.31—3.61 (5H, m, other glucosyl protons), 3.53 (2H, s, 5″-H_2), 3.60 (3H, s, 4-OCH_3), 3.68 (1H, d, $J=9.6$ Hz, 4″-H_b), 3.74 (6H, s, 3-OCH_3, 5-OCH_3), 3.87 (1H, d, $J=2.0$ Hz, 2″-H), 3.88 (1H, d, $J=9.6$ Hz, 4″-H_a), 4.00 (1H, dd, $J=9.5$, 2.0 Hz, 6′-H_a), 4.83 (1H, d, $J=7.3$ Hz, 1′-H), 4.92 (1H, d, $J=2.0$ Hz, 1″-H), 6.38 (2H, s, 2-H, 6-H). ^{13}C-NMR: as given in Table 2 (in acetone-d_6); chemical shifts of sugar moiety carbons (67.8 MHz, in pyridine-d_5, δ_C): glucosyl: 103.0 (C-1′),

74.2 (C-2′), 78.2 (C-3′), 71.4 (C-4′), 77.0 (C-5′), 68.7 (C-6′), apiosyl: 110.7 (C-1″), 77.4 (C-2″), 80.0 (C-3″), 74.7 (C-4″), 65.0 (C-5″). FAB-MS (positive) *m/z*: 501 $(M+Na)^+$, 478 (M^+), 460 $(M-H_2O)^+$. *Anal.* Calcd for $C_{20}H_{30}O_{13}$: C, 50.21; H, 6.32. Found: C, 50.66; H, 6.35. HR FAB-MS *m/z*: Calcd for $C_{20}H_{30}O_{13}Na$ $(M+Na)^+$: 501.1584. Found: 501.1576.

Kelampayoside B (**6**): A white amorphous solid, $[\alpha]_D$ −70.3° (*c* = 0.80, in MeOH at 26 °C). IR ν_{max}^{KBr} cm^{-1}: 3383, 2943, 1695, 1601, 1506, 1450, 1422, 1125, 1065. UV λ_{max}^{MeOH} nm (log ε): 238 sh, 296 (4.09), 327 (4.21). ^{1}H-NMR (270 MHz, acetone-d_6, δ): 3.26—3.51 (5H, m, other glucosyl protons), 3.59 (3H, s, 4-OCH_3), 3.74 (6H, s, 3-OCH_3, 5-OCH_3), 3.78 (1H, d, *J* = 9.8 Hz, 4″-H_b), 3.91 (1H, d, *J* = 2.1 Hz, 2″-H), 3.97 (1H, d, *J* = 9.8 Hz, 4″-H_a), 4.04 (1H, dd, *J* = 10.5, 1.3 Hz, 6′-H_a), 4.17 (1H, d, *J* = 15.5 Hz, 5″-H_b), 4.19 (1H, d, *J* = 15.5 Hz, 5″-H_a), 4.82 (1H, d, *J* = 7.3 Hz, 1′-H), 4.95 (1H, d, *J* = 2.1 Hz, 1″-H), 6.26 (1H, d, *J* = 16.1 Hz, 8‴-H), 6.37 (2H, s, 2-H, 6-H), 6.80 (1H, d, *J* = 8.2 Hz, 5‴-H), 7.00 (1H, dd, *J* = 8.2, 2.0 Hz, 6‴-H), 7.13 (1H, d, *J* = 2.0 Hz, 2‴-H), 7.53 (1H, d, *J* = 16.1 Hz, 7‴-H). ^{13}C-NMR: as given in Table 2 (in acetone-d_6); chemical shifts of sugar moiety carbons (67.8 MHz, in pyridine-d_5, δ_C): glucosyl: 103.3 (C-1′), 74.8 (C-2′), 78.3* (C-3′), 71.6 (C-4′), 77.3 (C-5′), 68.9 (C-6′), apiosyl: 110.5 (C-1″), 78.4* (C-2″), 78.4 (C-3″), 74.9 (C-4″), 67.2 (C-5″) [* These assignments may be interchanged]. FAB-MS (positive) *m/z*: 663 $(M+Na)^+$, 640 (M^+). *Anal.* Calcd for $C_{29}H_{36}O_{16}\cdot H_2O$: C, 52.89; H, 5.81. Found: C, 53.27; H, 5.70. HR FAB-MS *m/z*: Calcd for $C_{29}H_{36}O_{16}Na$ $(M+Na)^+$: 663.1901. Found: 663.1890.

Methanolysis of 3′-*O*-Caffeoylsweroside (1) Giving Sweroside (2) and Caffeic Acid Methyl Ester (3) A methanolic solution (5 ml) of 3′-*O*-caffeoylsweroside (**1**, 3 mg) was treated with Na_2CO_3 (2 mg) at 40 °C for 2 h. The reaction mixture was neutralized with Dowex 50w × 8 (H^+ form) and the resin was removed by filtration. The filtrate was evaporated under reduced pressure to give a crude product. Purification of the product by silica gel column chromatography (SiO_2 1.5 g, $CHCl_3$: MeOH : water = 10 : 3 : 1, lower phase) afforded sweroside (**2**, 1.6 mg) and caffeic acid methyl ester (**3**, 0.8 mg), which were shown to be identical with authentic samples by SiO_2 TLC comparisons [**2**: developed with 1) $CHCl_3$: MeOH : water = 6 : 4 : 1 and 2) saturated aqueous *n*-butanol; **3**: developed with 1) *n*-hexane : ethyl acetate = 1 : 2 and 2) $CHCl_3$: MeOH = 10 : 1], and by comparing ^{1}H-NMR (in acetone-d_6 for **2**; in $CDCl_3$ for **3**) and IR (KBr) data.

Acidic Hydrolysis of Kelampayoside A (4) Giving D-Apiose, D-Glucose, and Antiarol (5) A solution of kelampayoside A (**4**, 30 mg) in 3% aqueous HCl (3 ml) was heated under reflux for 5 h. After cooling, the reaction mixture was neutralized with Na_2CO_3 and the solvent was evaporated off under reduced pressure. Separation and purification of the residue by column chromatography (SiO_2 5 g, $CHCl_3$: MeOH : water = 6 : 4 : 1) provided D-apiose (6 mg, $[\alpha]_D$ +8.2°, *c* = 0.06, 24 h after dissolution in H_2O at 22 °C), D-glucose (10 mg, $[\alpha]_D$ +46.9°, *c* = 0.10, 24 h after dissolution in H_2O at 22 °C), and antiarol (**5**, 5 mg) [^{1}H-NMR (acetone-d_6) δ: 6.08 (2H, s), 3.69 (6H, s), 3.57 (3H, s); and direct IR (KBr) comparison with an authentic sample].

Methanolysis of Kelampayoside B (6) Giving Kelampayoside A (4) and Caffeic Acid Methyl Ester (3) Kelampayoside B (**6**, 70 mg) was treated with Na_2CO_3 in MeOH according to the same procedure as described for methanolysis of **1**. Separation and purification of the reaction mixture yielded kelampayoside A (**4**, 40 mg, 75%) and caffeic acid methyl ester (**3**, 12 mg) which were identified by SiO_2 TLC comparisons [**4**: developed with 1) $CHCl_3$: MeOH : water = 6 : 4 : 1 and 2) saturated aqueous *n*-BuOH, **3**: as described above] and by comparing ^{1}H-NMR, ^{13}C-NMR (in acetone-d_6 for **4**, in $CDCl_3$ for **3**) and IR (KBr) data.

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