New Quassinoid Glucosides, Javanicinosides I, J, K, and L, from Picrasma javanica

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NEW QUASSINOID GLUCOSIDES, JAVANICINOSIDES I, J, K, AND L, FROM *PICRASMA JAVANICA*

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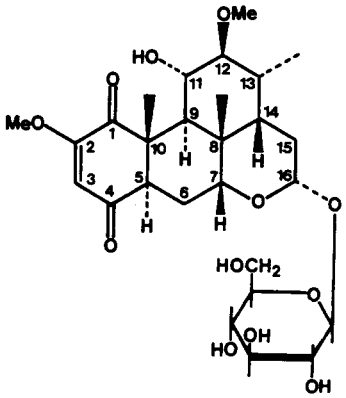
ABSTRACT.—Four new quassinoid glucosides, javanicinosides I [**1**], J [**2**], K [**3**], and L [**4**], have been isolated from the stem of *Picrasma javanica*. Their structures were elucidated by spectral and chemical evidence.

Picrasma javanica Bl. (Simaroubaceae) is used as a traditional antimalarial medicine in Indonesia. In previous phytochemical studies of the plant, we isolated eight new quassinoid glucosides, javanicinosides A–H (1–3). In our continuing studies of this same plant, we have now isolated four new quassinoid glucosides, javanicinosides I [**1**], J [**2**], K [**3**], and L [**4**].

RESULTS AND DISCUSSION

Javanicinoside I [**1**], $C_{27}H_{40}O_{12}$, was obtained as colorless needles, mp 165–167°. Its ir and uv spectra showed absorption bands due to hydroxyl [ν max 3400 (br) cm^{-1}] and α,β-unsaturated ketone (ν max 1700 and 1640 cm^{-1} and λ max 258 nm) groups. The ^1H-^1H COSY suggested the presence of two isolated structural units, -C(5)H-C(6)H_2-C(7)H- and -C(9)H-C(11)H-C(12)H-C(13)H(Me)-C(14)H-C(15)H_2-C(16)H-, in **1**. The presence of two carbonyl carbons was indicated by ^{13}C-nmr signals at δ 195.23 and 200.53. The conjugated 1,4-diketone moiety was located in the A ring by a COLOC experiment, which indicated coupling between a carbonyl carbon (C-1, δ 200.53) and both the methyl protons (Me-10, δ 1.45) and the olefinic proton (H-3, δ 6.19), and between carbonyl carbon (C-4, δ 195.23) and both the olefinic proton (H-3) and the methine proton (H-5, δ 2.42). The ^1H- and ^{13}C-nmr spectra of **1** (Tables 1 and 2), except for that associated with the A ring, showed close correspondence with those of javanicinoside A [**5**] (1). The ^1H downfield shifts observed for H-3 ($\Delta\delta$ 0.74), H-6 ($\Delta\delta$ 0.58 and 1.45) in **1**, compared with those of **5**. These downfield shifts are due to



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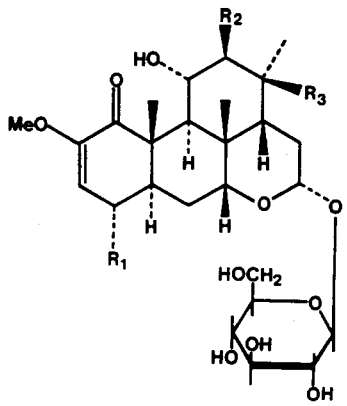

2 R_1=Me, R_2=OAc, R_3=OH
3 R_1=H, R_2=OAc, R_3=OH
4 R_1=Me, R_2=R_3=OH
5 R_1=R_3=H, R_2=OMe
6 R_1=Me, R_2=OMe, R_3=OH

TABLE 1. ^{1}H-nmr Spectral Data of Javanicinosides I [**1**], J [**2**], K [**3**], and L [**4**].[a]

Proton	Compound			
	1	**2**	**3**	**4**
H-3	6.19 s	5.28 d (2)	5.41 dd (6,2)	5.29 d (2)
H-4	—	2.28 m	1.78 m 2.10 m	2.28 m
H-5	2.42 brd (6)	2.19 m	2.57 m	2.16 m
H-6	2.06 m 3.03 m	1.75 m 1.84 m	1.51 m 1.97 m	1.75 m 1.82 m
H-7	3.23 brt (2)	3.23 brt (2)	3.15 brt (2)	3.23 brt (2)
H-9	3.47 d (11)	3.03 d (11)	2.96 d (11)	2.88 d (11)
H-11	3.93 q (11)	4.54 q (11)	4.53 q (11)	4.27 m
H-12	3.05 t (11)	5.39 d (11)	5.35 d (11)	3.75 d (10)
H-13	2.01 m	—	—	—
H-14	1.20 ddd (13,4,4)	1.73 dd (12,4)	1.68 dd (12,4)	N.A.
H-15	1.67 m 1.75 m	1.62 m 1.80 m	1.53 m 1.72 m	1.71 m 1.88 m
H-16	5.03 dd (9,2)	5.21 dd (9,2)	5.21 dd (9,2)	5.22 dd (9,2)
Me-4	—	0.81 d (7)	—	0.84 d (7)
Me-8	0.96 s	1.57 d	1.54 s	1.53 s
Me-10	1.45 s	1.52 s	1.43 s	1.50 s
Me-13	0.92 d (7)	1.23 s	1.20 s	1.38 s
2-OMe	3.45 s	3.44 s	3.41 s	3.46 s
12-OMe	3.67 s	—	—	—
12-OAc	—	2.03 s	2.03 s	—
11-OH	—	4.10 d (11)	4.31 d (11)	4.38 d (11)
Glc-1	5.43 d (8)	5.42 d (8)	5.44 d (8)	5.42 d (8)
Glc-2	4.12 t (8)	4.14 m	4.15 m	4.12 m
Glc-3	4.38 m	4.30 m	4.30 m	4.30 m
Glc-4	4.30 m	4.30 m	4.30 m	4.30 m
Glc-5	4.02 m	4.04 m	4.06 m	4.05 m
Glc-6	4.40 dd (12,6) 4.59 dd (12,2)	4.42 dd (12,6) 4.64 dd (12,2)	4.47 dd (12,6) 4.64 dd (12,2)	4.42 dd (12,6) 4.64 dd (12,2)

[a]Coupling constants (J in Hz) are given in parentheses. Spectra were measured in C_5D_5N.

influence of the ketone group at C-4. Acid hydrolysis of **1** with 1.5 M H_2SO_4 in aqueous MeOH afforded D-glucose, which was identified as its TMSi derivative by glc. The ^{1}H-nmr spectrum of **1** showed glucopyranosyl signals and a J value of 8 Hz for the doublet associated with the anomeric proton indicating the β configuration of the glucosyl moiety. The orientation of the D-glucosyl unit was determined to be α by the J values (9 and 2 Hz) between the H-16 methine proton and the H-15 methylene protons in the ^{1}H-nmr spectrum of **1**. Thus, structure **1** is proposed for javanicinoside I.

Javanicinoside J [**2**], $C_{29}H_{44}O_{13}$, was obtained as colorless needles, mp 202°. The ir and uv spectra of **2** indicated the presence of hydroxyl [ν max 3400 (br) cm^{-1}] and α,β-unsaturated carbonyl (ν max 1700, 1630 cm^{-1} and λ max 267 nm) groups. The ^{1}H nmr of **2** showed signals due to acetyl protons at δ 2.03 (3H, s), methoxy protons at δ 3.44 (3H, s), the anomeric proton of glucosyl at δ 5.42 (1H, d, J = 8 Hz), and an olefinic proton at δ 5.28 (1H, d, J = 2 Hz, H-3). The ^{1}H-nmr spectrum of **2** was very similar to that of picrasinoside G [**6**] (4), except that the methoxyl group in **6** was replaced by an acetyl group in **2**. Comparing the ^{1}H-nmr chemical shifts of **2** with those of **6** revealed a clear downfield shift for H-12 (Δδ = 2.3). The acetyl group of **2** was located by a COLOC experiment, which showed a coupling between the carbonyl carbon

TABLE 2. ^{13}C-nmr Spectral Data of Javanicinosides I [**1**], J [**2**], K [**3**], and L [**4**].[a]

Carbon	Compound			
	1	**2**	**3**	**4**
C-1	200.53	206.46	205.94	206.58
C-2	166.57	148.46	149.35	148.60
C-3	109.20	118.47	112.35	118.50
C-4	195.23	32.20	29.44	32.21
C-5	51.80	44.70	37.67	44.59
C-6	24.47	25.59	28.24	25.61
C-7	77.49	77.78	77.95	78.21
C-8	36.96	38.57	39.67	38.73
C-9	42.32	40.03	40.37	39.29
C-10	49.64	48.83	48.84	49.65
C-11	71.62	69.29	69.17	70.77
C-12	88.92	81.43	81.53	80.32
C-13	34.00	75.35	75.41	75.76
C-14	48.85	53.21	53.32	52.29
C-15	27.78	31.51	29.44	31.92
C-16	98.83	98.63	98.40	99.60
Me-4	—	19.07	—	19.21
Me-8	21.99	23.96	24.02	24.08
Me-10	16.63	12.86	11.62	12.96
Me-13	15.31	26.01	26.07	26.85
2-OMe	55.95	54.98	54.94	54.81
12-OMe	60.89	—	—	—
12-OAc	—	171.28	171.35	—
	—	20.97	21.05	—
Glc-1	100.04	100.39	100.15	100.10
Glc-2	75.34	75.21	75.24	75.18
Glc-3	78.41	78.13	78.22	78.33
Glc-4	71.49	71.61	71.68	71.59
Glc-5	78.64	78.28	78.90	78.86
Glc-6	62.70	62.89	62.95	62.86

[a]Spectra were measured in C_5D_5N.

of the acetyl group and H-12. Furthermore, in an nOe experiment, irradiation of the methoxyl proton at δ 3.44 induced 8% nOe enhancement of H-3, suggesting the location of the methoxyl and the acetoxyl groups to be at C-2 and C-12, respectively. Thus, structure **2** is proposed for javanicinoside J.

The stereochemistry of javanicinosides I [**1**] and J [**2**] was determined by phase-sensitive NOESY experiments (Table 3) and coupling constants between H-9 and H-11 (J = 11 Hz) and between H-11 and H-12 (J = 11 Hz). From these observations, all the angular chiral centers (C-5, C-7, C-8, C-9, C-10, and C-14) and other chiral centers [C-4 (of **2**), and C-13] were compatible with the usual picrasane skeleton (5,6), and H-9, H-11, and H-12 were deduced to be α-, β-, and α-axials, respectively.

Javanicinoside K [**3**], $C_{28}H_{42}O_{13}$, was obtained as an amorphous powder. The ^{1}H nmr spectrum of **3** showed signals due to three tertiary methyls at δ 1.20 (Me-13), 1.43 (Me-10), and 1.54 (Me-8), one acetyl at δ 2.03 (12-OAc), one methoxyl at δ 3.41 (2-OMe), an anomeric proton (1H, d, J = 8 Hz), and an olefinic proton at δ 5.41 (1H, dd, J = 6 and 2 Hz, H-3). Comparison of the ^{1}H- and ^{13}C-nmr spectra of **3** with those of javanicinoside J [**2**] suggested that the main difference between **2** and **3** was the lack of the methyl signal at C-4 in **3**. On the basis of the above results, the structure of javanicinoside K is proposed to be **3**.

TABLE 3. NOe's of Javanicinosides I [1] and J [2] from NOESY.

Observed proton	Compound	
	1 (show nOe to H)	**2** (show nOe to H)
H-3	2-OMe	2-OMe
H-4	—	Me-4, Me-10
H-5	H-9	Me-4, H-9
H-7	Me-8, H-14, H-16	Me-8, H-14, H-16
H-9	H-5	H-5
H-11	Me-8, Me-10, 12-OMe, H-13	Me-8, Me-10, 12-OAc
H-12	Me-13	Me-13
H-13	12-OMe, H-11	—
H-14	Me-8, H-7	Me-8, H-7
H-16	H-7, Glc-H-1	H-7, Glc-H-1
Me-4	—	H-4, H-5
Me-8	Me-10, H-7, H-11, H-14	H-7, H-11, H-14
Me-10	Me-8, H-11	H-5, H-11
Me-13	H-12	H-12
2-OMe	H-3	H-3

Javanicinoside L [**4**] was obtained as amorphous powder. Its molecular formula, $C_{27}H_{42}O_{12}$, was found to be 42 mass units less than that of javanicinoside J [**2**]. The spectral characteristics of **2** and **4** are very similar except for the disappearance of an acetyl signal in the latter. Thus, javanicinoside L [**4**] was identified as the free C-12 hydroxyl derivative of **2**, as the natural product **4** had an hplc retention time and ^{1}H-nmr spectrum identical to those of the deacetyl derivative of **2**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were measured with a Yanagimoto micro-melting point apparatus (hot-stage type) and are uncorrected. Uv spectra were recorded on a Hitachi 340 Uv-Vis spectrometer and ir spectra on a Hitachi 260-30 ir spectrometer. Optical rotations were measured on a JASCO DIP-4 polarimeter. Eims and hrms were determined on JEOL D-300 and DX-303 mass spectrometers. ^{1}H-nmr (400 MHz) and ^{13}C-nmr (100 MHz) spectra were recorded on JEOL GX-400 and JEOL EX-400 FTNMR spectrometers in C_5D_5N, using TMS as an internal standard. Results are given in Tables 1 and 2.

ISOLATION OF JAVANICINOSIDES I [**1**], J [**2**], K [**3**], AND L [**4**].—The dried stems (3.7 kg) of *P. javanica* were collected in Indonesia in July 1986. A voucher specimen has been deposited in the Department of Pharmacognosy, Toho University. The stems were extracted with MeOH (49 liters). The extract was concentrated under reduced pressure, and an equal volume of H_2O was added to the residue. The aqueous solution was extracted with $CHCl_3$ (12 liters) followed by *n*-BuOH (3.6 liters). The *n*-BuOH-soluble fraction (70 g) was subjected to repeated cc on Si gel and Diaion HP-20 (Mitsubishi Kasei) and further purified by preparative medium-pressure lc [column LiChroprep Rp-18 Merck, 25 mm i.d. × 310 mm, solvent system MeOH-H_2O (2:3), uv detector 254 nm] and hplc [column Shiseido Capcell Pak C18 SG-120, 10 mm i.d. × 250 mm, solvent system MeOH-H_2O (2:3), uv detector 254 nm] to afford javanicinosides I [**1**] (60 mg), J [**2**] (11 mg), K [**3**] (4 mg), and L [**4**] (2 mg).

Javanicinoside I [**1**].—Colorless needles (MeOH): mp 165–167°; $[\alpha]^{22}D$ −3.4° (c = 2.7, MeOH); uv λ max (MeOH) 252 (4.34) nm; ir ν max (KBr) 3400 (br), 2930, 1700, 1640, 1605, 1445, 1365, 1210, 1170 cm^{-1}; hrms *m/z* $[M]^+$ 556.2482 (calcd for $C_{27}H_{40}O_{12}$, 556.2508); eims (70 eV) (rel. int.) *m/z* $[M]^+$ 556 (1), 395 (6), 377 (100), 359 (64), 345 (39), 327 (34), 299 (18), 269 (19).

ACID HYDROLYSIS OF **1**.—A mixture of javanicinoside I [**1**] (2 mg), 1.5 M H_2SO_4 (2 ml), and MeOH (3 ml) was stirred at 80° for 5 h. After cooling the reaction mixture, H_2O (10 ml) was added and the product was extracted with $CHCl_3$. The H_2O layer was neutralized with an ion-exchange resin (Amberlite MB-3) and evaporated to give a residue which was trimethylsilylated with *N*-trimethylsilylimidazole and subjected to glc (column SE-30, 2%, 3 mm i.d. × 1.5 m; carrier gas N_2 at 50 ml; column temperature 150°; detection fid). The chromatogram showed two peaks (Rt 30.6 and 17.2 min) that were identical with those from D-glucose.

Javanicinoside J [**2**].—Colorless prisms (MeOH): mp 202°; $[\alpha]^{26}D$ −2.1° (*c* = 1.0, MeOH); uv λ max (MeOH) 262 (3.49) nm; ir ν max (KBr) 3400 (br), 2900, 1700, 1670, 1630, 1440, 1365, 1085, 1230, 1030 cm^{-1}; hrms *m/z* $[M]^+$ 600.2797 (calcd for $C_{29}H_{44}O_{13}$, 600.2769); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 600 (1), 582 (1), 378 (26), 360 (68), 317 (35), 270 (20), 239 (10), 43 (100).

Javanicinoside K [**3**].—Colorless needles (MeOH): mp 254–255°; $[\alpha]^{22}D$ +14.5° (*c* = 0.4, MeOH); hrms *m/z* $[M]^+$ 586.2563 (calcd for $C_{28}H_{42}O_{13}$, 586.2613); eims (70 eV) (rel. int.) *m/z* $[M]^+$ 586 (100), 361 (11), 344 (46), 331 (24), 313 (27), 289 (62), 269 (6), 255 (9), 205 (9), 195 (13).

Javanicinoside L [**4**].—Amorphous powder: $[\alpha]D$ −12.0° (*c* = 0.1, MeOH); eims (70 eV) *m/z* (rel. int.) $[M]^+$ 558 (32), 374 (12), 360 (73), 344 (54), 329 (93), 311 (11), 301 (27), 285 (13), 269 (12), 253 (18), 232 (17), 217 (72).

ALKALINE HYDROLYSIS OF **2**.—A solution of javanicinoside J [**2**] (4 mg) in 1 N KOH (2 ml) was reacted at 50° for 3 h. After cooling, the reaction mixture was neutralized with an ion-exchange resin (Amberlite MB-3) and evaporated to give a residue subjected to analytical hplc [column Shiseido Capcell Pak C18 SG-120 4.6 mm i.d. × 250 mm; solvent system MeOH-H_2O (2:3); detection, uv 254 nm]. The chromatogram showed one peak (Rt 24.2 min) identical with that of javanicinoside L [**4**]. The ^1H-nmr spectrum of **4** was superimposable on that of the deacetyl derivative of **2**.

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LITERATURE CITED

1. T. Ohmoto, K. Koike, K. Mitsunaga, H. Fukuda, K. Kagei, T. Kawai, and T. Sato, *Chem. Pharm. Bull.*, **37**, 993 (1989).
2. K. Koike and T. Ohmoto, *Phytochemistry*, **29**, 2617 (1990).
3. K. Ishii, K. Koike, and T. Ohmoto, *Phytochemistry*, **30**, 4099 (1991).
4. T. Matsuzaki, N. Fukamiya, M. Okano, T. Fujita, K. Tagahara, and K.-H. Lee, *J. Nat. Prod.*, **54**, 844 (1991).
5. J. Polonsky, *Fortschr. Chem. Org. Naturst.*, **30**, 101 (1973).
6. J. Polonsky, *Fortschr. Chem. Org. Naturst.*, **43**, 221 (1986).

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