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PHENYLPROPANOIDS AND OTHER SECONDARY METABOLITES FROM FRESH FRUITS OF *PICRASMA QUASSIOIDES*

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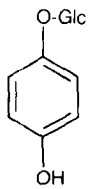
Key Word Index—*Picrasma quassioides*; Simaroubaceae; benzofuran; neolignan; phloroglucinol; picraquassiosides A, B, C and D.

Abstract—Four new constituents; two benzofuran glucosides (picraquassiosides A and B), a neolignan (picraquassioside C) and a phenol (picraquassioside D) were isolated from fresh fruits of *Picrasma quassioides*, together with seven known compounds. The structures of the new compounds were elucidated as 6-hydroxy-4-methoxy-5-benzofuranpropionic acid 6-*O*-β-D-glucopyranoside, 6-hydroxy-4,7-dimethoxy-5-benzofuranpropionic acid 6-*O*-β-D-glucopyranoside, 1-(4′-*O*-glucopyranosyl-4′-hydroxy-3′,5′-dimethoxyphenyl)-2{2″,6″-dimethoxy-4″-[1-(E) propen-3-ol]-phenoxy}-propan-1,3-diol(threo), and methylphloroglucinol β-D-glucopyranoside by spectroscopic means.

INTRODUCTION

Picrasma quassioides Benn. is distributed in India, Taiwan, China, Korea and Japan. Its bark has long been used in traditional medicine as a gastrointestinal, insecticidal or vermifuge agent [1]. The constituents of the bark have been investigated intensively because of these pharmacological properties and various compounds have been isolated: quasinoids [2–6], tirucallanes [7], ionone [8] and β-carbolin alkaloids [9–13]. However, no chemical studies have been carried out on the fruits. This paper reports on the isolation of 11 compounds from the fresh fruits of *P. quassioides* and their characterization as the known compounds arbutin (**1**), phlorin (**2**) [14], koaburaside (**3**) [15], syringin (**4**) [16], citrusin B (**5**) [16], cnidioside B (**6**) [17] and flavaprenin 7,4′-diglucoside (**7**) [18], three novel phenyl propanoids (**8–10**) and one phenolic compound (**11**).



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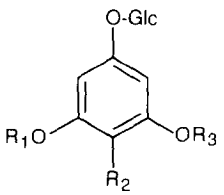
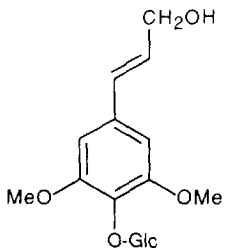


	R_1	R_2	R_3
2	-H	-H	-H
3	-Me	-OH	-Me
11	-H	-H	-Me



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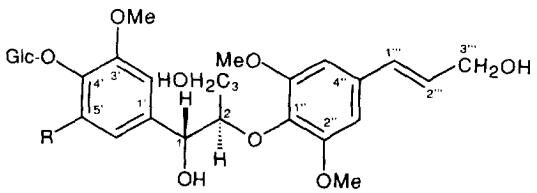
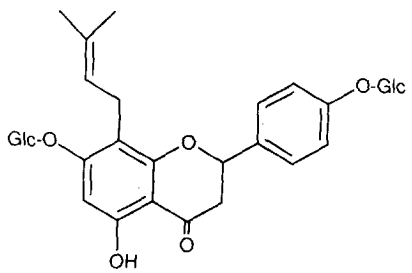


R	
5	-H
10	-OMe



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RESULTS AND DISCUSSION

Careful separation of the polar fraction of the fresh fruits of *P. quassioides* afforded 11 polar compounds. The seven known compounds were identified as **1–7** by comparison with published data [14–18].

Picraquassioside A (**8**), $[\alpha]_D^{20}$ −32.0° (MeOH), had the same molecular formula, $C_{18}H_{22}O_{10}$ (negative FAB-MS: *m/z* 397 $[M-H]^-$) as cnidioside B (**6**) [17]. Its IR spectrum contained absorptions for hydroxy groups

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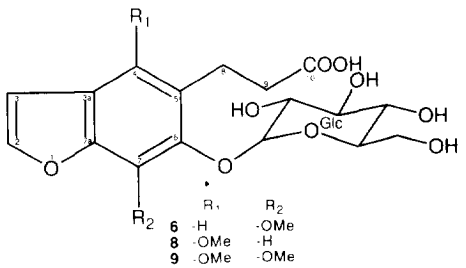

(3400 cm^{-1}), an aromatic ring (1600 and 1515 cm^{-1}) and a carboxy group (2650–3300 and 1715 cm^{-1}). The presence of the latter was supported by the ^{13}C NMR data (δ176.8). Acid hydrolysis of **8** afforded D-glucose; confirmed by specific rotation using chiral detection HPLC. The ^{1}H and ^{13}C NMR spectra (Table 1) revealed two methylene groups connected to each other (δ_H3.61, 3.66 each 1H, *dt*, J = 14.0, 7.5 Hz; δ_C20.5 *t* and δ_H3.01, 317 each 1H, *dt*, J = 16.0, 7.5 Hz; δ_C35.5*t*), two methine groups coupled to each other (δ_H6.95, 7.64 each 1H, *d*, J = 1.5 Hz; δ_C105.2 *d*, 143.7 *d*), an isolated methine (δ_H7.63 *s*; δ_C94.5 *d*) in a benzene ring and a methoxyl group (δ_H3.97, *s*; δ_C60.1 *q*) together with one glucosyl moiety and six quaternary carbons. These spectral data resembled those of **6**, except for the chemical shifts due to the benzene ring, indicating that **8** might be the regioisomer of the methoxyl group on the benzene ring. This assumption was supported by an HMBC experiment (Table 2). The NOE between H-3 and the methoxyl group indicated the site of the methoxyl group as C-4. The β-configuration of the anomeric centre of D-glucopyranosyl was suggested by the large $^{3}J_{H1,H2}$ coupling constant (J = 7.0 Hz). Hence **8** was formulated as 6-hydroxy-4-methoxy-5-benzofuranpropionic acid 6-*O*-β-D-glucopyranoside.

Picraquassioside B (**9**), $[\alpha]_D^{20}$ −10.3° (MeOH), was assigned the molecular formula $C_{19}H_{24}O_{11}$ (negative FAB-MS, *m/z* 427 $[M-H]^-$), CH_2O more than that of **8**. Acid hydrolysis of **9** afforded D-glucose. The coupling patterns of each proton in the ^{1}H NMR spectrum of **9** were very similar to those of **8**, except for the presence of an additional methoxy group in place of a hydrogen, indicating that **9** was a tetra-substituted benzofuran containing one more methoxy group than the trisubstituted furan **8**. The ^{13}C NMR data of **9** were very similar to those of **8**, except for the carbons in **9** due to the benzene ring showing the presence of an extra methoxy group (C-7) and the disappearance of H (C-7). This was verified by an HMBC experiment (Table 2) and by the observa-

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **8–10** (600/150 MHz, C_5D_5N)

	8		**9**		**10**		
C/H	^{13}C	^{1}H	^{13}C	^{1}H	C/H	^{13}C	^{1}H
1	–	–	–	–	1	73.6	5.66 *d* (5.5)
2	143.7	7.64 *d* (1.5)	145.3	7.77 *d* (1.5)	2	87.6	4.82 *ddd* (5.5, 4.5, 3.5)
3	105.2	6.95 *d* (1.5)	105.8	6.95 *d* (1.5)	3	61.2	4.60 *dd* (12.0, 3.5, 4.20 *dd* (12.0, 4.5)
3a	113.0	–	117.3	–	1′	139.7	–
4	151.6	–	147.9	–	2′	106.0	7.20 *d* (1.5)
5	116.8	–	122.3	–	3′	153.4	–
6	155.6	–	145.5	–	4′	135.2	–
7	94.5	7.63*s*	134.6	–	5′	153.4	–
7a	156.0	–	146.9	–	6′	106.0	7.20 *d* (1.5)
8	20.5	3.66 *dt* (14.0, 7.5)	21.7	3.67 *dt* (14.0, 7.5)	*O*-Me	56.5(×2)	3.72(×2) *s*
		3.61 *dt* (14.0, 7.5)		3.61 *dt* (14.0, 7.5)	1″	136.2	–
9	35.5	3.17 *dt* (16.0, 7.5)	35.9	3.15 *dd* (16.0, 7.5)	2″	153.9	–
		3.01 *dt* (16.0, 7.5)		3.12 *dd* (16.0, 7.5)	3″	104.4	6.87 *br d* (1.5)
10	176.8	–	176.9	–	4″	133.8	–
O-Me	60.1	3.97 *s*	61.9	4.20 *s*	5″	104.4	6.87 *br d* (1.5)
			60.9	3.93 *s*	6″	153.9	–
					1‴	129.3	6.89 *br d* (15.5)
					2‴	131.2	6.62 *dt* (15.5, 5.0)
					3‴	62.7	4.59 *d* (5.0), 4.59 *d* (5.0)
					O-Me	56.2(×2)	3.75(×2) *s*
Glc					Glc		
1″	103.5	5.59 *d* (7.0)	105.8	5.83, 6.5		105.3	5.73 *d* (7.0)
2″	75.0	4.34 *dd* (8.5, 7.0)	76.0	ca. 4.36 *m*		76.1	ca. 4.33 *m*
3″	78.8	4.32 *dd* (9.5, 8.5)	78.6	ca. 4.36 *m*		78.4	ca. 4.33 *m*
4″	71.2	4.29 *dd* (9.5, 9.5)	71.6	ca. 4.36 *m*		71.6	ca. 4.33 *m*
5″	79.0	4.10 *ddd* (9.5, 5.5, 2.5)	78.9	3.91 *m*		78.6	3.93 *m*
6″	62.4	4.52 *dd* (12.0, 2.5)	62.6	4.41 *dd* (12.0, 2.5)		62.6	4.38 *dd* (12.0, 2.5)
		4.37 *dd* (12.0, 5.5)		ca. 4.36 *m*			ca. 4.33 *m*

Table 2. ^{13}C-^{1}H long-range correlations in the HMBC of **8**–**10**

C	**8**	**9**	C	**10**	C	**10**
2	H-3	H-3	1	H-2′ (6′)	1″	H-2, H-2″ (6″)
3	H-2	H-2	2	H-1	2″	H-3″, CH_3-O-$C_{3''}$
3a	H-2, H-3, H-7	H-2, H-3	3	H-1	3″	H-1‴
4	H-8, CH_3-O-C_4	H-8, CH_3-O-C_4	1′	H-2′ (6′), H-1	4″	H-2″ (6″), H-2‴
5	H-7, H-8, H-9	H-8, H-9	2′	H-1	5″	H-1‴
6	H-7, H-8, H-1 of Glc	H-8, H-1 of Glc	3′	H-2′, CH_3-O-$C_{3'}$	6″	H-5″, CH_3-O-$C_{6''}$
7	–	CH_3-O-C_7	4′	H-2′ (6′), H-1 of Glc	1‴	H-2″ (6″)
7a	H-2, H-3, H-7	H-2, H-3	5′	H-6′, CH_3-O-C_5	2‴	H-1‴
8	H-9	H-9	6′	H-1	3‴	H-1‴, H-2‴
9	H-8	H-8				
10	H-8, H-9	H-8, H-9				

tion of the NOEs between H-3 and H_3C-O-C_4, and between H_3C-O-C_7 and H-1 of Glc. Thus the structure of **9** was shown to be 6-hydroxy-4,7-dimethoxy-5-benzofuranpropionic acid 6-*O*-*β*-D-glucopyranoside.

Picraquassioside C (**10**), $[\alpha]_D^{20}$ −9.7° (MeOH), had the molecular formula $C_{28}H_{38}O_{14}$ (negative FAB-MS, *m/z* 597 $[M-H]^-$), CH_2O more than that of citrusin B (**5**) [16]. Acid hydrolysis of **10** afforded D-glucose. The ^1H and ^{13}C NMR spectra of **10** resembled those of **5** except for an additional methoxyl group and the absence of the doublet protons from the benzene ring, indicating that the hydrogen at C-5′ of **5** was replaced by a methoxyl group in **10**. The presence of the symmetrical proton signal at *δ* 7.20 (2H, *d*, *J* = 1.5 Hz) on a benzene ring and one singlet signal of two methoxyl groups in the ^1H NMR spectrum and the signals of three sp^2 due to the benzene ring of the guaiacylglycerol part in the ^{13}C NMR spectrum (Table 1) suggested that **10** was 5′-methoxycitrusin B. The relative configuration for C-1 and C-2 were established as threo on the basis of the chemical shift values (*δ* 73.6 and 87.6) of C-1 and C-2 [19]. Hence **10** was formulated as 1-(4′-*O*-glucopyranosyl-4′-hydroxy-3′,5′-dimethoxyphenyl)-2{2″, 6″-dimethoxy-4″-[1-(E) propen-3-ol]-phenoxy}-propan-1,3-diol (threo).

Picraquassioside C (**11**), $[\alpha]_D^{20}$ −55.7° (MeOH), showed a quasi-molecular ion peak $[M-H]^-$ at *m/z* 301 corresponding to $C_{13}H_{18}O_8$, with one CH_2 more than **2** in the negative FAB mass spectrum. Acid hydrolysis of **11** afforded D-glucose. All the spectral data indicated that **11** was a substituted phloroglucinol. The ^1H NMR spectrum of **11** contained *meta*-coupled aromatic proton signals at *δ* 6.20 (*d*, *J* = 2.0 Hz), 6.17 (*d*, *J* = 2.0 Hz) and 6.04 (*d*, *J* = 2.0 Hz) attributable to a 1,3,5-trisubstituted benzene ring as well as a methoxy group signal at *δ* 3.71 (3H, *s*) and anomeric proton signal at *δ* 4.84 (*d*, *J* = 7.5 Hz). Hence, **11** was formulated as methyl phloroglucinol *β*-D-glucopyranoside (methylphlorin).

EXPERIMENTAL

General. Mp: uncorr.; NMR: 600 (^1H) and 150 (^{13}C) MHz, TMS as standard. NMR experiments included ^1H-^1H COSY, ^1H-^{13}C COSY, DEPT, TOCSY, ROESY and HMBC (512 × 1024 data matrix size, 128 scans, recycle delay = 1.16s). Coupling constants (J values) are given in Hz. EIMS: 1Qev, direct inlet; FABMS: (Xe gun, 10 kV, *m*-nitrobenzyl alcohol as matrix. CC: silica gel 60 (40–63 *μ*m, Merck); TLC: silica gel 60F-254 (Merck).

Plant material. Fruits were collected in the garden of the Faculty of Pharmaceutical Sciences, Tokushima Bunri University, in September 1993 and identified by Professor Y. Nishimoto. The voucher specimen is deposited at the Institute of Pharmacognosy.

Extraction and isolation of compounds **1**–**11**. Fresh fruits (10 kg) were extracted with MeOH at room temp. for 3 months. The MeOH soln was evaporated to dryness *in vacuo*. The residue (370 g) was suspended in H_2O, extracted successively with EtOAc and *n*-BuOH. The solvents were evaporated *in vacuo* to give the EtOAc-soluble (120 g), *n*-BuOH soluble (90 g) and water soluble fractions (150 g). The *n*-BuOH-soluble fraction was subjected to CC on silica gel, eluting with CH_2Cl_2–MeOH–H_2O (25:5:0.1–65:35:4) to afford frs 1–5. Fr. 5 (1.0 g) was subjected to CC on silica gel, eluting with CH_2Cl_2–MeOH–H_2O (25:2:0.1) to afford flavaprenin 7,4′-diglucoside (**7**, 35 mg). Fr. 3 (15 g) was further subjected to CC on silica gel, eluted with CH_2Cl_2–MeOH–EtOAc–H_2O (4:2:4:1, lower layer) to give frs.I (4.5 g), II (3.5 g), III (0.5 g) and IV (1.5 g). Fr. II was further purified by prep. HPLC (ODS, H_2O) to afford arbutin (**1**, 380 mg), phlorin (**2**, 30 mg), picraquassioside D (**11**, 170 mg), coaburaside (**3**, 20 mg) and syringin (**4**, 50 mg). Fr. III was purified by prep. HPLC (ODS, 10–12% MeCN) to give picraquassioside C (**10**, 10 mg) and citrusin B (**5**, 20 mg). Fr. IV was purified by prep. HPLC (ODS, 12% MeCN) to give picraquassioside A (**8**, 20 mg), picraquassioside B (**9**, 50 mg) and cnidioside B (**6**, 170 mg).

Picraquassioside A (**8**). Amorphous powder, $[\alpha]_D^{20}$ −32.0° (MeOH; 1.0). FABMS *m/z* 397$[M-H]^-$ 235 $[M-Glc-H]^-$; EIMS *m/z*: 236 (100), 218 (98), 176 (56), 147 (11), 133 (5.5); IR ν_{max} (film) cm^{-1}: 3470, 1700, 1600, 1520, 1100; UV λ_{max}^{MeOH} nm (log *ε*): 213 (4.32), 251 (3.88); ^1H and ^{13}C NMR Table 1.

Picraquassioside B (**9**). Amorphous powder, $[\alpha]_D^{20}$ −10.3° (50% MeOH; 0.4). FABMS *m/z*: 427 $[M-H]^-$, 265 $[M-Glc-H]^-$; EIMS *m/z* 428 (0.4), 410 (1), 378 (1), 280

(1.5), 266 (100), 248 (82), 233 (24), 218 (6), 206 (63), 191 (46), 177 (12), 163 (19); IR ν_{max} (film) cm^{-1}: 3450, 1710, 1600, 1520, 1110; UV λ_{max}^{MeOH} nm (log ε): 215 (4.51), 251 (4.00) ^1H and ^{13}C NMR: Table 1.

Picraquassioside C (**10**). Amorphous powder, $[\alpha]_D^{20}$ −9.7° (MeOH; 1.1). FABMS *m/z*: 597 $[M-H]^-$; IR ν_{max} (film) cm^{-1}: 3420, 1600, 1515, 1220, 1075; UV λ_{max}^{MeOH} nm (log ε): 207 (4.34), 269 (3.74); ^1H and ^{13}C NMR: Table 1.

Picraquassioside D (**11**). Amorphous powder, $[\alpha]_D^{20}$ −55.7° (MeOH; 3.6). FABMS *m/z*: 301 $[M-H]^-$; CIMS *m/z*: 303 $[M+H]^+$; IR ν_{max} (film) cm^{-1}: 3600-3100, 1600, 1500, 1200, 1175, 1075; UV λ_{max}^{MeOH} nm (log ε): 212 (3.90), 226 (3.85), 269 (2.88); ^1H NMR (200 MHz, CD_3OD) δ: 6.20 (1H, *t*, $J = 2.0$ Hz), 6.17 (1H, *t*, $J = 2.0$ Hz), 6.04 (1H, *t*, $J = 2.0$ Hz), 4.84 (1H, *d*, $J = 7.5$ Hz, H-1 of Glc), 3.90 (1H, *dd*, $J = 12.0$, 2.0 Hz, H-6 of Glc), 3.71 (3H, *s*), 3.4–3.45 (5H, *m*, H-2, 3, 4, 5, and 6); ^{13}C NMR (50 MHz, CD_3OD) δ: 162.7 (C-3), 160.6 (C-1), 159.8 (C-5), 101.9 (C-1 of Glc), 97.7 (C-4), 96.7 (C-6), 95.5 (C-2), 77.7 (C-3 and C-5 of Glc), 74.6 (C-2 of Glc), 71.1 (C-4 of Glc), 62.3 (C-6 of Glc), 55.7 (CH_3–O).

Acid hydrolysis of picraquassiosides A (**8**), *B* (**9**), *C* (**10**) *and D* (**11**). A soln of **8**–**11** (each 3 mg) in 5% H_2SO_4 in 5% EtOH was heated at 100° for 3 hr. The reaction mixture was extracted with Et_2O. The aq. layer was neutralized with Amberlite IR-45 and evaporated to dryness *in vacuo*. The sugar was determined by HPLC using (Shodex RSpal CD-613, 75% MeCN, 1 ml/min, 70°) RI detection (Waters 410) and chiral detection (Shodex OR-1), respectively, and comparing with authentic sugars (10 mM each of D-glc). The sugar part gave a peak indicating a positive optical rotation at 7.38 min (D-glc, 7.36 min).

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