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XANTHONOLIGNOIDS FROM *HYPERICUM SUBALATUM*

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Abstract --- The isolation and characterization of three xanthonolignoids, kielcorin, cadensin D, and a new compound named as subalatin, from the whole plant of *Hypericum subalatum* Hayata are described.

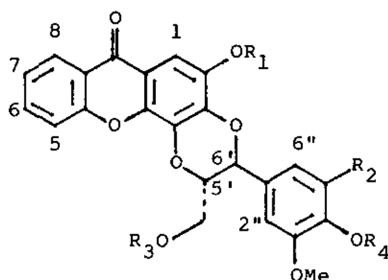
In the series of research on the constituents of *Hypericum* genus, a subfamily Hypericoideae of the family Guttiferae,[1] xanthone derivatives from *H. sampsonii* Hance[2] and flavonoids from *H. nagasawai* Hayata[3] have been reported previously. There is no report on the constituents of *H. subalatum* Hayata, a plant indigenous to Taiwan, though several xanthonolignoids have been isolated from some *Hypericum* species.[4-7] The present investigation on the whole plant of *H. subalatum* has led to the isolation of three xanthonolignoids. Among these compounds, subalatin (IV) is described here for the first time.

Fractionation of the ethanol extracts of the whole herb of *H. subalatum* on a charcoal column gave three groups of eluates. Repeated chromatographic separation of the EtOH/$CHCl_3$(7/3) fraction on silica gel resulted in the isolation of three crystalline compounds. From the available data, the first two xanthonolignoids were identified, on the basis of spectroscopic evidences, to have the structure of kielcorin (I), and cadensin D (II) respectively. Kielcorin was the first xanthonolignoid isolated from *Hypericum* species,[4-6] *Kielmeyera* species,[8-10] and *Vismia guaramirangae*,[11] respectively. Cardona and co-workers isolated cadensin D from *Hypericum canariensis*,[6] and Vishwakarma and co-workers isolated later the same compound from *Hypericum mysorense*[7] but named as hypericorin. The ^1H- and ^{13}C-nmr data of di-O-acetylcadensin D (III) have not previously been described.

The new xanthonolignoid, mp 265°C, $[\alpha]_D^{25°}$ +600° (MeOH; c 0.005), showed a molecular ion at m/z 452 in agreement with a molecular formula $C_{24}H_{20}O_9$. The uv spec-

trum in methanol (290, 317, and 363 nm) and ir spectrum in KBr (1640, 1610, and 1520 cm^{-1}) were indicative of a xanthone nucleus. The fragment ions at m/z 285 and 244 in the mass spectrum of the new compound (which appeared at m/z 299 and 258 in cadensin D) indicated that one phenolic group, instead of methoxyl group in cadensin D,[6] was present on the xanthone ring. The ^{1}H-nmr of the new compound showed a doublet doublet at relatively low field (δ 8.25, J=8.0 and 1.5 Hz), assignable to the proton peri to the carbonyl group on an unsubstituted xanthone ring,[12] and a singlet at δ 7.30, characteristic of a proton at C-1 of a 2,3,4-trioxygenated xanthone.[6] The phenolic group was situated at C-2 because the C-1 carbon resonated at relatively lower field (δ 101.2) than that of cadensin D (δ 96.5), and the C-1 proton signal was shifted downfield to δ 7.70 when triacetate (V) was prepared (which appeared at δ 7.38 in cadensin D diacetate (III)). The presence of a trans-substituted 1,4-dioxane ring between the xanthone framework and the C_6-C_3 ring was deduced from the doublet at δ 5.18(J=7.7 Hz). The regiochemistry of the dioxane ring was ascertained by opening the ring with NaOMe[4] to create a phenolic group at C-3, as indicated by a bathochromic shift in the uv spectrum,[13] by addition of NaOAc. From a comparison with cadensin D, the characteristic fragment ions at m/z 210, 208, 182, 181, 167, and 154 indicated that one phenolic and two methoxyl groups were present on the phenyl ring.[6] The two-proton singlet at δ 6.90 and the six-proton singlet at δ 3.87 indicated a 4-hydroxy-3,5-dimethoxyphenyl ring. The mass fragmentation pattern of the triacetate (V), M^+ 578, was similar to those reported for O-acetylxanthonolignoid.[11] All of the spectroscopic evidences, with respect to those of cadensin D, led to the proposition of the structure of the new xanthonolignoid as IV. This compound is described here for the first time, and the name of subalatin is proposed.

	R_1	R_2	R_3	R_4
I.	Me	H	H	H
II.	Me	OMe	H	H
III.	Me	OMe	Ac	Ac
IV.	H	OMe	H	H
V.	Ac	OMe	Ac	Ac



Xanthonolignoids are of great interest chemotaxonomically. The isolations of them from the natural sources have been reported from the family Guttiferae only.

Table 1. ^{1}H-Nmr Chemical Shifts of Xanthonolignoids[a]

Compound	I	II	III	IV	V
Solvent	DMSO-d_6	DMSO-d_6	$CDCl_3$	Acetone-d_6	$CDCl_3$
H-1	7.19(s)	7.18(s)	7.38(s)	7.30(s)	7.70(s)
H-5	7.66(d) J=8.0	7.65(d) J=8.5	7.59(dd) J=1.6, 8.4	7.67(d) J=8.2	7.59(dd) J=1.6, 8.4
H-6	7.84(t) J=8.0	7.83(t) J=7.7	7.70(ddd) J=1.2, 6.6, 8.4	7.85(dt) J=1.1, 7.0	7.75(ddd) J=1.7, 6.6, 8.4
H-7	7.47(t) J=7.6	7.47(t) J=7.4	7.38(ddd) J=1.6, 6.6, 8.0	7.47(t) J=7.9	7.40(ddd) J=1.6, 6.6, 8.0
H-8	8.18(d) J=8.0	8.18(dd) J=1.4, 8.0	8.34(dd) J=1.2, 8.0	8.25(dd) J=1.5, 8.0	8.34(dd) J=1.7, 8.0
H-5	4.4(m)	4.43(m)	4.42(m)	4.4(m)	4.34(m)
CH_2-5'	3.7(m)	3.6(m)	4.50(dd) J=3.3, 12.3	3.61(dd) J=4.2, 12.5	4.58(d) J=9.3
	3.4(m)	3.44(dd) J=4.3, 12.6	4.18(dd) J=4.4, 12.3	3.49(m)	4.19(dd) J=4.0, 12.3
H-6'	5.04(d) J=7.8	5.03(d) J=7.6	5.05(d) J=7.6	5.18(d) J=7.7	5.14(d) J=7.9
H-2"	7.01(s)	6.75(s)	6.65(s)	6.90(s)	6.64(s)
H-5"	6.82(d) J=8.0	----	----	----	----
H-6"	6.89(d) J=8.0	6.75(s)	6.65(s)	6.90(s)	6.64(s)
OMe	3.87(3H) 3.79(3H)	3.85(3H) 3.75(6H)	3.96(3H) 3.82(6H)	3.87(6H)	3.84(6H)
OH	8.35 5.57	8.18 4.89	----	9.6 4.9	----
OAc	----	----	2.32(3H) 2.09(3H)	----	2.35(3H) 2.29(3H) 2.13(3H)

[a]All chemical shift values are given in δ (ppm) relative to TMS, and coupling constants in Hz.

EXPERIMENTAL

Melting points were determined with Yanaco micro-melting point apparatus and are uncorrected. Ir and uv spectra were measured on Hitachi 270-30 infrared spectro-

photometer and Hitachi U-3200 spectrophotometer respectively. Mass spectra were recorded on JEOL JMS-D100 spectrometer. ^{1}H- and ^{13}C-Nmr spectra were recorded on either Bruker WP-100sy or AM-400 spectrometer using tetramethylsilane as an internal standard. Optical rotations were taken on a JASCO DIP-360 polarimeter.

Isolation

The dried whole herbs of Hypericum subalatum Hayata (2.5 Kg), Guttiferae, collected from Hsintien (Taipei county, Taiwan) were powdered and extracted with hot ethanol. The combined extracts were subjected to a charcoal column eluting succesively with EtOH, EtOH/$CHCl_3$(7/3), and $CHCl_3$. Repeated column chromatography of the EtOH/$CHCl_3$(7/3) fraction (36.5 g) on silica gel resulted in the isolation of kielcorin (2 mg), cadensin D (94 mg), and a new xanthonolignoid subalatin (6 mg).

Kielcorin (I)

Pale yellow needles from $CHCl_3$-MeOH, mp 251-252°C (lit.[10], mp 250-251°C).

Cadensin D (II)

Pale yellow needles from $CHCl_3$-MeOH, mp 242-243°C (lit.[6], mp 243-245°C), $[\alpha]_D^{25°}$ 0° (DMSO; c 0.015); uv λ_{max} nm(log ϵ) in MeOH: 244(3.73), 315(3.29); ir ν(KBr) cm^{-1}: 3600-3100, 1610, 1480, 1460, 1400, 1360, 1320, 1290, 1220, 1140, 1110, 1090; ms m/z(rel. int.): 466(M^+, 10), 448(2), 436(9), 299(3), 274(3), 258(100), 243(21), 229(4), 228(3), 210(87), 208(8), 182(15), 181(10), 180(10), 177(4), 167(23), 154 (11), 149(8); ^{13}C-nmr in DMSO-d_6: δ 174.6, 155.2, 148.0(2C), 145.8, 141.2, 139.5, 136.4, 134.7, 132.5, 125.8, 125.6, 124.2, 120.7, 118.0, 113.9, 105.8(2C), 96.5, 77.7, 76.6, 59.5, 56.2(2C), 55.7.

Cadensin D diacetate (III)

Cadensin D (27 mg) in 2 ml of Ac_2O/pyridine(1:1) was heated on steam bath for 0.5 hr to give diacetate (III), colorless needles from MeOH, mp 226-229°C; ir ν (KBr) cm^{-1}: 1745, 1735, 1630, 1600, 1480, 1450, 1435, 1420, 1395, 1360, 1345, 1325, 1240, 1215, 1140; ms m/z(rel. int.): 550(M^+, 27), 520(5), 508(30), 478(2), 448 (10), 420(4), 418(2), 407(4), 341(4), 269(4), 258(5), 257(4), 252(100), 243(3), 229(2), 228(2), 222(11), 209(17), 192(8), 191(6), 181(6), 179(7), 177(4), 167(4),

161(7), 157(4), 149(9), 133(4), 131(3), 121(3), 118(3), 111(3), 105(4); ^{13}C-nmr in $CDCl_3$: δ 176.2, 170.4, 168.4, 156.1, 152.9(2C), 146.2, 141.9, 139.2, 134.2, 133.1, 132.2, 129.9, 126.6, 124.0, 121.5, 118.2, 115.3, 104.4(2C), 97.9, 77.3, 75.3, 62.5, 56.4(3C), 20.6, 20.3.

Subalatin (IV)

Pale yellow needles from $CHCl_3$-MeOH, mp 265°C(dec.), $[\alpha]_D^{25°C}$+600° (MeOH; c 0.005); uv λ_{max} nm(log ϵ): in MeOH 290(3.85), 317(4.05), 363(3.78); in MeOH+NaOMe 297, 339, 413; in MeOH+NaOAc 297, 331, 415; ir ν (KBr) cm^{-1}: 3600-2600, 1640, 1610, 1520, 1485, 1470, 1430, 1320, 1220, 1145, 1115, 1100, 1080; ms m/z(rel. int.): 452(M^+, 4), 434(4), 285(2), 269(3), 244(100), 226(7), 216(3), 215(3), 210(22), 208(7), 193(3), 187(5), 182(9), 181(5), 180(5), 170(9), 167(19), 154(9), 149(9), 142(8), 121(7), 114(12), 113(9), 108(6), 105(6), 103(6), 102(6); ^{13}C-nmr in acetone-d_6: δ 175.9, 156.5, 148.8(2C), 144.6, 141.2, 140.1, 137.3, 135.2, 133.6, 126.9, 126.7, 124.6, 121.8, 118.7, 115.5, 106.3(2C), 101.2, 79.1, 77.5, 60.9, 56.7(2C).

Subalatin triacetate (V)

Subalatin (3 mg) was treated as described above to give triacetate (V), colorless needles from MeOH, mp 221-223°C; ms m/z(rel. int.): 578(M^+, 8), 536(38), 494(25), 434(11), 290(10), 275(20), 252(100), 247(4), 209(12), 192(5), 191(5), 190(7), 181 (4), 167(3), 161(7), 149(10), 111(5), 109(4), 105(4).

Methanolysis of subalatin

Subalatin (2 mg) in 2 ml of NaOMe/MeOH(1.2 N) was heated at reflux for 0.5 hr, then acidified with dil. HCl, extracted with $CHCl_3$, and separated by preparative tlc ($CHCl_3$-EtOAc, 7:3, two elutions) on silaca gel. Uv λ_{max} nm: in MeOH 258, 283, 338sh; in MeOH+NaOAc 285, 327, 389sh.

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