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HYMEXELSIN, AN APIOSE-CONTAINING SCOPOLETIN GLYCOSIDE FROM THE STEM BARK OF *HYMENODICTYON EXCELSUM*

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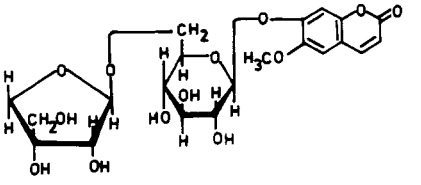
Hymenodictyon excelsum (Roxb.) Wall (Rubiaceae) is a large deciduous tree. Its intensely bitter bark is used in native medicine as an astringent and febrifuge (1) and was shown to contain scopoletin (2). Brew and Thomson (3) recorded the presence of several anthraquinones in the root bark.

The present paper records the presence and structure determination of an apioglucoside of scopoletin, now named hymexelsin, in the stem bark of this tree. Among the coumarin apioglucosides, only diospyroside (4), decuroside (5), and adicardin (6,7) are known to date. Hymexelsin is the fourth example.

The air-dried, powdered stem bark was exhaustively extracted with MeOH, and from the concentrated extract scopoletin and hymexelsin were isolated. Hymexelsin is a colorless, crystalline compound with an extremely bitter taste. Its color reactions and uv spectrum showed that it is a coumarin glycoside.

It analyzed for $C_{21}H_{26}O_{13}$. One methoxyl group was present, and on acetylation it gave a hexaacetate, $C_{33}H_{38}O_{19}$. Acid hydrolysis gave scopoletin as the aglycone. Glucose and apiose as the sugar components were identified by paper chromatographic comparison with authentic sugars obtained by the hydrolysis of adicardin and lanceolarin (7–9). Quantitative acid hydrolysis showed that hymexelsin contains scopoletin, glucose, and apiose in equimolar proportions.

Partial hydrolysis of hymexelsin with 0.5% H_2SO_4 at room temperature led to the selective cleavage of apiose giving scopolin (scopoletin 7-*O*-β-D-glucoside), $C_{15}H_{16}O_8$, thus indicating that the apiose and glucose are attached to the 7 position of scopoletin as a biose unit with glucose as the first sugar attached to the aglycone. Apiose is thus the terminal sugar of the biose unit attached to one of the hydroxyls of the glucose moiety. Apiose is known to occur in nature with a glycosidic linkage with either the 2- or 6-hydroxyl group of the glucose moiety. Hymexelsin was permethylated using Hakamori's method (10) followed by the acid hydrolysis of the resulting permethylate. The partial methyl ethers of the sugars were identical (pc) with those obtained from adicardin on similar treatment. Hymexelsin consumed 4.00 moles of periodate (11) while adicardin as a standard consumed 3.98 moles suggesting a glucose (6↔1) apiose glycosidic



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linkage. The ^{1}H-nmr spectra of hymexelsin and acetyl hymexelsin and the ^{13}C-nmr spectrum of hymexelsin (in DMSO-d_6) (Table 1) supported structure **1**.

HYMEXELSIN ACETATE.—Prepared with Ac_2O/pyridine, 100°, 2 h and separated from MeOH as colorless crystals, mp 105° (Found: C 53.2, H 5.0%; $C_{33}H_{38}O_{19}$ requires C 53.6, H 5.1%); ^{1}H nmr ($CDCl_3$, 90 MHz) 7.62 (1H, d, J=9.5 Hz, H-4), 6.22 (1H, d, J=9.5 Hz, H-3), 7.04 (1H, s, H-5), 6.93 (1H, s, H-8), 5.29 (1H, d, J=4.5 Hz, H-1′), 4.88 (1H, s, H-1″), 3.78 (3H, s, OMe), 1.99, 1.98, 1.97, 1.95, 1.94, 1.92 (18H, each a singlet, 6 OAc acetoxyls).

TABLE 1. ^{13}C-Chemical Shifts of Hymexelsin [**1**].

Scopoletin		D-Glucose		D-Apiose	
Carbon	ppm	Carbon	ppm	Carbon	ppm
2	160.9	1	99.7	1	109.2
3	113.3	2	72.9	2	75.4
4	144.2	3	76.4	3	78.7
5	109.8	4	69.7	4	73.4
6	145.9	5	76.1	5	63.4
7	149.6	6	67.5		
8	103.1				
9	148.8				
10	112.5				
−OMe	56.1				

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected. The uv and ir spectra were recorded on a Shimadzu MPS-5000 Spectrophotometer and Perkin-Elmer 253 instruments, respectively. The ^{1}H-nmr spectrum of hymexelsin was determined on a Perkin-Elmer 90 MHz instrument in DMSO-d_6 with that of its acetate in $CDCl_3$. ^{13}C-nmr of hymexelsin was recorded on a Bruker-spectrospin instrument at 25.16 MHz in DMSO-d_6.

ISOLATION OF HYMEXELSIN [**1**].—Fresh stem bark (2 kg) was exhaustively extracted with 95% MeOH (5 liters) in a blender. It was filtered and the filtrate condensed under reduced pressure.

The concentrate thus obtained, on refrigeration for 24 h, gave a buff-colored compound (2.3 g, 0.12%) which crystallized from dry MeOH as white crystals melting at 206°; $[\alpha]^{30}D$ −116° (c=1.0 in pyridine); uv λ max (MeOH) 228, 236, 250, 259, 292, 340 nm; ir ν max (KBr) 3400, 1660, 1610, 1290, 1020 cm^{-1}; ^{1}H nmr (DMSO-d_6, 90 MHz), 7.73 (d, J=9.5 Hz, H-4), 6.13 (1H, d, J=9.5 Hz, H-3), 7.08 (1H, s, H-5), 6.95 (1H, s, H-8), 5.12 (1H, d, J=4.75 Hz, H-1′), 4.9 (1H, d, J=3 Hz, H-1″), 4.60, 4.62, 4.68, 4.74 (4H, each a singlet, sugar hydroxyls), 4.42 (1H, t, 5″-OH), 3.78 (1H, s, 3″-OH), 3.85 (3H, s, OMe), 3.1–3.6 (9H, m, other sugar protons). It gave a positive Molisch test and a negative ferric reaction. Found: C 51.6, H 5.2%; $C_{21}H_{26}O_{13}$ requires C 51.8, H 5.3%.

ACID HYDROLYSIS OF HYMEXELSIN [**1**].—Hymexelsin (0.1 g) was refluxed with 1% aqueous H_2SO_4 for 3 h. The aglycone (0.04 g) was identified as scopoletin. The aqueous filtrate was tested by pc when glucose and apiose were identified as the sugars by comparison with authentic sugars obtained by the hydrolysis of adicardin (7) and lanceolarin (8,9).

Quantitative hydrolysis of hymexelsin gave 38.8% of the aglycone (expected 39.5%).

PARTIAL HYDROLYSIS OF HYMEXELSIN.—Partial hydrolysis of hymexelsin with 0.5% H_2SO_4 yielded apiose after 30 min. The reaction was complete in 12 h. Evaporation of the reaction mixture yielded scopolin, mp 218°, $[\alpha]^{30}D$ −88° (c=1.0 in pyridine). Found: C 54.1, H 5.0%; $C_{16}H_{18}O_9$ requires C 54.2, H 5.1%.

Scopolin on hydrolysis in the usual way yielded scopoletin and glucose.

PERMETHYLATION.—Hymexelsin (0.1 g) was permethylated by the Hakamori method (10) (DMSO, NaH, MeI, 4 h), and the permethylate hydrolyzed (7% H_2SO_4, 4 h). The sugar partial methyl ethers were identical with those obtained from adicardin by a similar procedure.

PERIODIC OXIDATION.—A spectrophotometric method (11) was followed; hymexelsin

consumed 4.00 moles of periodate, while under similar conditions adicardin consumed 3.98 moles (7).

ENZYMIC HYDROLYSIS OF **1** USING ALMOND EMULSIN (12).—β-Glycosidase gave apiose and glucose as monitored by pc.

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