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QUERCETIN 5,4′-DIMETHYL ETHER FROM *RHODODENDRON ELLIPTICUM*

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Key Word Index—*Rhododendron ellipticum*; Ericaceae; quercetin; myricetin; quercitrin; myricitrin; hyperin; quercetin 3-glucoside; quercetin 5,4′-dimethyl ether.

Abstract—From the leaf of *Rhododendron ellipticum* β-carotene, sitosterol, uvaol, quercetin, myricetin, quercitrin, myricitrin, hyperin, quercetin 3-glucoside, and the new aglycone quercetin 5,4′-dimethyl ether were characterized by spectroscopic analysis and/or comparison with authentic samples.

INTRODUCTION

The leaf of *Rhododendron ellipticum* Max. is used in Taiwan as a folk medicine to treat high blood pressure [1, 2]. It is found in mountainous areas 160–700 m above sea level. In this study, we have attempted to identify the chemical constituents of *R. ellipticum* which have not been reported previously.

RESULTS AND DISCUSSION

The air-dried and powdered leaves of *R. ellipticum* were extracted with 50% ethanol. The crude extracts were partitioned with *n*-hexane, chloroform, *n*-butanol, and water followed by chromatographic separation on silica gel. β-Carotene, sitosterol, and uvaol were obtained from the *n*-hexane layer and uvaol was also found in the chloroform layer. The *n*-butanol layer gave seven compounds: quercetin, myricetin, quercitrin, myricitrin, hyperin, quercetin 3-glucoside, and quercetin 5,4′-dimethyl ether. All the above compounds were identified by spectroscopic data and with authentic samples except the last one. Quercetin 5,4′-dimethyl ether recrystallized from methanol as yellow needles and gave a molecular ion peak at m/z 330. Two other fragments at m/z 167 $[A_1 + 1]^+$ and 151 $[B2]^+$ representing ring A and ring B portions of the molecule, respectively, indicated that a methoxyl group was present in both rings. To further elucidate the substitution pattern, we carried out UV spectral analysis. The neutral spectrum in methanol gave three bands: 213, 267 and 367 nm, respectively. Band II showed a bathochromic shift from 56 to 423 nm on addition of NaOMe and shifted from 54 to 421 nm with $AlCl_3$. Band I shifted 5 nm to 272 nm when NaOAc was added. The above evidence suggested that the C-3 and C-7 hydroxy groups were not methylated and C-4′ was substituted [3–5].

The ^1H NMR spectrum showed protons H-6 and H-8 as two doublets with a coupling constant of 2.1 Hz at 6.42 and 6.34 ppm, respectively. Proton H-6′ (7.37 ppm, J = 8.2, 2.2 Hz) was coupled with both H-2′ (7.48 ppm, J = 2.2 Hz) and H-5′ (6.86 ppm, J = 8.2 Hz). The remaining two three-proton signals at 3.79 and 3.69 ppm were assigned to two methoxyl groups. By carefully comparing the chemical shift differences between H-2′, H-5′ and H-6′ of quercetin and quercetin 5,3′-dimethyl ether, we concluded that the B ring methoxyl group has to be at the C-4′ position [4]. From the ^{13}C NMR spectrum data we found a large chemical shift difference: 3.95 ppm between C-3′ (148.0 ppm) and C-4′ (151.9 ppm). If C-3′ is methylated, the difference would be much smaller in this system [5, 6]. Analysis of the HETCOR experiment further supported these assignments.

EXPERIMENTAL

General. ^1H and ^{13}C NMR : 400 and 100.6 MHz, respectively, with DMSO-d_6 hydrogen (2.49 ppm) and carbon (39.5 ppm) residual as int. standard. CC was carried out on Kieselgel 60 or Sephadex LH-20. TLC were performed on Kieselgel 60 F_{254} and/or polyamide DC-11.

Plant material. Leaves of *R. ellipticum* (6.2 kg) were collected from Nan-Tou, Taiwan in September, 1989. They were identified by Mr Nien-Yung Chiu, Institute of Chinese Pharmaceutical Sciences, China Medical College and a voucher specimen is deposited at the herbarium of this institute.

Extraction and isolation. The air-dried leaves (5.56 kg) were extracted with 50% EtOH (3 × 15 l). The crude extract (1.8 kg) was partitioned between *n*-hexane/H_2O (25 g), $CHCl_3$/H_2O (14.61 g) and *n*-butanol/H_2O (445 g). The *n*-hexane layer gave β-carotene, sitosterol, and uvaol.

The chloroform layer was subjected to silica gel CC and yielded only uvaol. The *n*-butanol layer was chromatographed by silica gel with a gradient of $CHCl_3$ to MeOH and/or Sephadex LH-20 (CH_2Cl_2, MeOH, 1:1) and gave 7 compounds: quercetin, myricetin, quercitrin, myricitrin, hyperin, quercetin 3-glucoside, and quercetin 5,4′-dimethyl ether.

Quercetin 5,4′-dimethyl ether. Mp 320–322° (MeOH), brilliant yellow fluorescence on Kieselgel 60 F_{254} (R_f 0.67; $CHCl_3$–MeOH–H_2O, 80:20:3 and R_f = 0.36; EtOAc–*n*-hexane, 100:2), on polyamide DC-11 (R_f 0.19; toluene–MeCOEt–MeOH, 13:5:3); EIMS *m/z* (rel. int.): 331 (22.7), 330 $[M]^+$ (100), 310 (22.7), 167 (20), 151 (25.5), UV λ_{max}^{MeOH} nm: 213, 267, 367; + NaOMe 235, 284, 327 (sh), 378 (sh), 423; + $AlCl_3$ 216, 271, 306 (sh), 349, 412; + $AlCl_3$ + HCl 206, 266, 361; + NaOAc 223, 272, 378; + H_3BO_3 269, 372; IR ν (KBr) cm^{-1}: 3390, 3170, 1615, 1600, 1580, 1500, 1430, 1360. ^1H NMR (DMSO-d_6) δ ppm: 7.48 (*d*, 1H, H-2′, J = 2.2 Hz), 7.37 (*dd*, 1H, H-6′, J = 2.2, 8.2 Hz), 6.86 (*d*, 1H, H-5′, J = 8.2 Hz), 6.42 (*d*, 1H, H-8, J = 2.1 Hz), 6.34 (*d*, 1H, H-6, J = 2.1 Hz), 3.79 (*s*, 3H, 5-OMe), 3.69 (*s*, 3H, 4′-OMe). ^{13}C NMR (DMSO-d_6) δ ppm: 177.2 (C-4), 162.5 (C-7), 160.8 (C-5), 158.1 (C-9), 151.9 (C-4′), 148.0 (C-3′), 145.2 (C-2), 137.5 (C-3), 121.3 (C-1′), 120.0 (C-6′), 115.7 (C-2′), 115.2 (C-5′), 105.3 (C-10), 96.1 (C-6), 94.8 (C-8), 59.2 (C-5-OMe), 55.9 (C-4′-OMe).

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