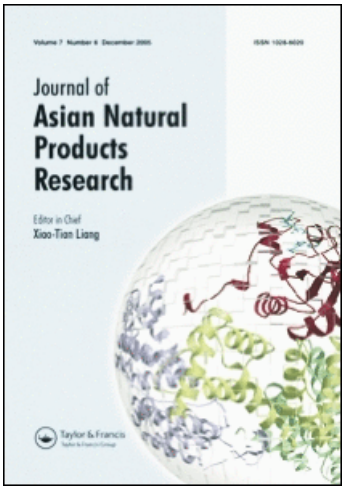

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Sabian, a novel flavonoid from *Sabia yunnanensis*

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Sabian, a novel flavonoid from *Sabia yunnanensis*

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A novel flavonoid, [2-(3,4-dihydroxy-phenyl)-3,5,7-trihydroxy-4-oxo-4*H*-chromen-8-yl]-[8-hydroxy-7-(*E*-4-hydroxy-3-methyl-but-2-enyl)-2,2-dimethyl-chroman-5-yl]-acetic acid methyl ester (10), trivially named sabian, along with 11 known compounds, have been isolated from the stems and leaves of *Sabia yunnanensis*. Their structures were established on the basis of spectral analysis.

Keywords: *Sabia yunnanensis*; Flavonoid; Sabian; Chroman

1. Introduction

Sabia yunnanensis Franch. is a folk medicinal herb, distributed in Yunnan Province of China, used for the treatment of rheumatism and tumefaction [1]. To our knowledge, no phytochemical study on this plant has been reported. In the present paper, we describe the isolation and characterization of a novel flavonoid, sabian (10), together with 11 known compounds, namely, ferulic acid (1) [2], syringic acid (2) [3], sinapic acid (3) [3], tyrosol (4) [4], daphnetin (5) [5], *p*-hydroxybenzoic acid (6) [6], *p*-hydroxycinnamic acid (7) [7], glycosmisic acid (8) [8], fraxetin (9) [9], 2,5-dihydroxybenzoic acid (11) [10] and skimmin (12) [5].

2. Results and discussion

Compound 10, obtained as yellow powder, showed positive reaction to Mg-HCl test. Its UV spectrum in methanol showed characteristic absorptions at 260, 272 (sh) (band II), and 378 nm (band I), indicating a flavonol skeleton. Analysis with the usual flavonoid diagnostic reagent suggested the presence of free hydroxyl groups at positions C-5, C-7, C-3′ and C-4′ [11]. The molecular formula $C_{34}H_{34}O_{12}$ was deduced from the evidences given by ESIMS and HRESIMS. The ESIMS spectrum exhibited two quasi-molecular ion peaks at *m*/*z* 657 $[M + Na]^+$ and 633 $[M - H]^-$, and the HRESIMS spectrum exhibited a quasi-molecular ion peak at *m*/*z* 657.1948 $[M + Na]^+$ (calcd: 657.1942). The IR band at 3292 cm^{-1} and 1691 cm^{-1} indicated the presence of hydroxyl and carbonyl.

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In the ^{1}H NMR spectrum, nine downfield signals (δ 12.65, 1H, s, 5′-OH; δ 11.12, 1H, br s, 7′-OH; δ 9.67, 1H, s, 4″-OH; δ 9.45, 1H, s, 3′-OH; δ 9.24, 1H, s, 3″-OH; δ 7.66, 1H, d, $J = 1.7$ Hz, H-2″; δ 7.15, 1H, dd, $J = 8.4$, 1.7 Hz, H-6″; δ 6.78, 1H, d, $J = 8.4$ Hz, H-5″; δ 6.34, 1H, s, H-6′) suggested the presence of a quercetin moiety. The 15 corresponding carbon signals of quercetin moiety were also found in ^{13}C NMR spectrum. In the HMBC spectrum, the singlet at δ 6.34 in ^{1}H NMR spectrum showed correlations with C-10′, C-5′, C-7′ and C-8′ of quercetin moiety, which indicated this singlet belonged to H-6′ and the quercetin moiety was 8′-substituted. It was further supported by the correlations of 5′-OH with C-6′, C-5′ and C-10′.

Two downfield proton signals (δ 6.21, 1H, s, H-6‴ and 7.86, 1H, s, 8‴-OH) in the ^{1}H NMR spectrum, together with the six downfield carbon signals at δ 126.3 (C-5‴), 120.0 (C-6‴), 124.3 (C-7‴), 142.8 (C-8‴), 141.6 (C-9‴) and 118.8 (C-10‴) in ^{13}C NMR spectrum, indicated the presence of a penta-substituted benzene moiety. The signals of two mutually coupled methylenes were observed at δ 1.81 (2H, t, $J = 6.8$ Hz, H-3‴), 2.58 and 2.84 (each 1H, dt, $J = 16.8$, 6.8 Hz, H-4‴a and H-4‴b), suggesting an isolated C_2 chain as a partial structure of 10. In the HMBC spectrum, the correlations of two methyls at δ 1.24 and 1.32 (each 3H, s) with C-2‴, C-3‴, the correlations of H-3″ with the two methyls, C-2‴ and C-4‴, together with the correlations between H-4‴ and C-2‴, C-3‴, C-10‴, C-5‴, C-9‴, suggested that the penta-substituted benzene moiety was a substituted 2,2-dimethyl chroman moiety. The correlations of the OH at δ 7.86 with C-7‴, C-8‴, C-9‴ in the HMBC revealed that the OH located at C-8‴ of the chroman moiety. The ^{1}H NMR spectrum showed a methyl (δ 1.36, 3H, s, 3⁗-CH_3), a hydroxymethyl (δ 3.57, 2H, s, H-4⁗ and 4.52, 1H, br s, 4⁗-OH), a methylene (δ 2.95 and 3.05, each 1H, dd, $J = 14.8$, 7.6 Hz, H-1⁗a and H-1⁗b) coupled with an olefinic proton (δ 5.24, 1H, t, $J = 7.6$ Hz, H-2⁗). In the HMBC spectrum, the correlations of the hydroxymethyl with C-2⁗, C-3⁗, the correlations of the methyl at δ 1.36 with C-2⁗, C-3⁗ and hydroxymethyl, together with the correlations of the methylene with C-2⁗, C-3⁗ and C-6‴, C-7‴, C-8‴, indicated the existence of 4-hydroxy-3-methyl-but-2-enyl which attached to C-7‴ of the chroman moiety. In the NOESY spectrum (figure 1), the correlation between H-2⁗ and H-4⁗ indicated the 4-hydroxy-3-methyl-but-2-enyl was *E* configuration.

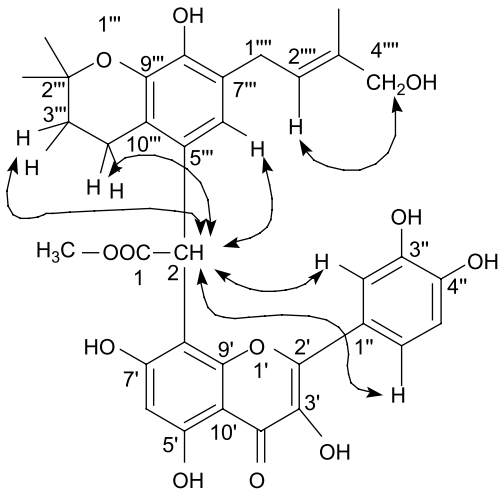

Figure 1. Some key NOESY correlations of 10.

The ^{1}H NMR spectrum also showed the signals of a methoxy (δ 3.50, 3H, s) and a methine (δ 5.39, 1H, s, H-2). And, the carbon signals at δ 172.8 (C-1), δ 52.5 (1-OCH_3), δ 41.6 (C-2) in the ^{13}C NMR spectrum were observed. In the HMBC spectrum, the correlations of the methine signal at δ 5.39 with C-7′, C-8′, C-9′, C-5‴, C-6‴, C-10‴ and C-1 indicated that the methine attached to C-8′ of the quercetin moiety, to C-5‴ of the substituted chroman moiety and to C-1 of the methoxycarbonyl at the same time. Furthermore, the NOESY correlations of H-2 with H-2″, H-6″, H-6‴, H-4‴, H-3‴ also confirmed that the quercetin moiety and the substituted chroman moiety attached to the methine.

Consequently, compound 10 was elucidated as [2-(3,4-dihydroxy-phenyl)-3,5,7-trihydroxy-4-oxo-4*H*-chromen-8-yl]-[8-hydroxy-7-(*E*-4-hydroxy-3-methyl-but-2-enyl)-2,2-dimethyl-chroman-5-yl]-acetic acid methyl ester, trivially named sabian. Its ^{1}H NMR and ^{13}C NMR spectra (table 1) were completely assigned by detailed HMQC, HMBC and NOESY experiments.

Table 1. NMR spectra data of 10 in DMSO-d_6 (600 MHz for ^{1}H, 150 MHz for ^{13}C).

Position	*^{1}H*	*^{13}C*	*HMBC* [a]
1		172.8	
1-OCH_3	3.50, 3H, s	52.5	1
2	5.39, 1H, s	41.6	1, 7′, 8′, 9′, 5‴, 6‴, 10‴
2′		147.8	
3′		136.2	
3′-OH	9.45, 1H, s		2′, 3′, 4′
4′		176.7	
5′		159.9	
5′-OH	12.65, 1H, s		5′, 6′, 10′
6′	6.34, 1H, s	98.4	5′, 7′, 8′, 10′
7′		162.0	
7′-OH	11.12, 1H, br s		
8′		105.9	
9′		153.9	
10′		103.6	
1″		122.4	
2″	7.66, 1H, d(1.7)	116.4	2′, 3″, 4″, 6″
3″		145.5	
3″-OH	9.24, 1H, s		2″, 3″, 4″
4″		148.3	
4″-OH	9.67, 1H, s		3″, 4″, 5″
5″	6.78, 1H, d(8.4)	115.9	1″, 3″, 4″
6″	7.15, 1H, dd(8.4, 1.7)	120.0	2′, 2″, 4″
2‴		73.9	
2‴-2 × CH_3	1.24 and 1.32, each 3H, s	26.8	2‴, 3‴
3‴	1.81, 2H, t(6.8)	32.9	2‴, 4‴, 10‴, 2‴-2 × CH_3
4‴ 4‴a	2.58, 1H, dt(16.8, 6.8)	20.1	2‴, 3‴, 5‴, 9‴, 10‴
	4‴b	2.84, 1H, dt(16.8, 6.8)	
5‴		126.3	
6‴	6.21, 1H, s	120.0	8‴, 10‴, 2, 1‴
7‴		124.3	
8‴		142.8	
8‴-OH	7.86, 1H, s		7‴, 8‴, 9‴
9‴		141.6	
10‴		118.8	
1‴′ 1‴′a	3.05, 1H, dd(14.8, 7.6)	28.1	6‴, 7‴, 8‴, 2‴′, 3‴′
	1‴′b	2.95, 1H, dd(14.8, 7.6)	
2‴′	5.24, 1H, t(7.6)	122.5	1‴′, 4‴′, 3‴′-CH_3
3‴′		136.2	
3‴′-CH_3	1.36, 3H, s	13.9	2‴′, 3‴′, 4‴′
4‴′	3.57, 2H, s	67.0	2‴′, 3‴′
4‴′-OH	4.52, 1H, br s		

[a] Carbon atoms correlated with proton.

3. Experimental

3.1 General experimental procedure

Melting points were recorded on a XRC-1 micro-melting point apparatus (Scientific Instruments Factory, Sichuan University) and are uncorrected. Optical rotations were measured on a Perkin-Elmer model 341 polarimeter. UV spectra were obtained on a Perkin-Elmer Lambda 35 UV spectrometer. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer. ^{1}H NMR, ^{13}C NMR, HMBC and NOESY spectra were performed on a Bruker Avance 600 spectrometer. Chemical shift values are in ppm (δ) with TMS as internal standard. ESIMS were acquired with a Finnigan LCQ^{DECA} mass spectrometer. HRESIMS was obtained on Bruker Dalonics Apex II mass spectrometer. Column chromatography was performed with silica gel (200–300 mesh, Qingdao Marine Chemical Inc., China) and polyamide (200 mesh, Linjiang Chemical Inc., Jiangsu, China). 732 R-SO_3H cation exchange resin was acquired from Tianjin Nankai Chemical Factory, China.

3.2 Plant material

Stems and leaves of *Sabia. yunnanensis* were collected in Aziyingxiang, Songming County, Yunnan Province, China in April 2001, and identified by Professor Guoda Tao, Kunming Institute of Botany, Chinese Academy of Sciences. A voucher specimen (No. (2001)0502) is deposited in the corresponding author's laboratory, Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, China.

3.3 Extraction and isolation

The air-dried and powdered stems and leaves of *S. yunnanensis* (18 kg) were extracted with MeOH (90%)/H_2O (10%) at room temperature (3 × 7 d). After evaporation of solvent under reduced pressure, 2150 g of viscous residue was obtained. 1630 g of this residue was suspended in MeOH (90%)/H_2O (10%) and partitioned with petroleum ether. The solvent of the MeOH fraction was evaporated under reduced pressure, and then the MeOH fraction was suspended in H_2O and successively partitioned with EtOAc and n-BuOH to give *n*-BuOH extracts (380 g). 280 g of *n*-BuOH extract was dissolved in water and applied to a column filled with 732 cation exchange resin, eluted with H_2O, MeOH/ammonia water (1:1) and ammonia water successively. The H_2O eluate (220 g) was subjected to column chromatography over silica gel (200–300 mesh) eluting with $CHCl_3$/MeOH (15:1 to 1:1) to give 7 fractions on the basis of TLC analyses. Fraction 2 was subjected to silica gel column chromatography eluting with petroleum ether/EtOAc (4:1), and then repeatedly chromatographed over polyamide column to give compound 1 (28 mg), compound 2 (88 mg), compound 3 (47 mg), compound 4 (27 mg), and compound 5 (18 mg). Fraction 3 was subjected to silica gel column chromatography eluting with petroleum ether/EtOAc (2.5:1) yielding 7 subfractions. Subfraction 1 was column chromatographed over silica gel eluting with $CHCl_3$/MeOH (60:1) to give compound 6 (14 mg) and compound 7 (32 mg). Subfraction 2 was column chromatographed over silica gel eluting with $CHCl_3$/MeOH (40:1) to give compound 8 (4 mg). Subfraction 3 was subjected to polyamide column chromatography eluting with $CHCl_3$/MeOH (30:1) to yield compound 9 (16 mg) and

compound 10 (11 mg). Fraction 4 was column chromatographed over silica gel eluting with $CHCl_3$/MeOH (15:1) to give compound 11 (59 mg) and compound 12 (23 mg).

3.3.1 Sabian (10). Yellow amorphous powder; mp: 176–178°C; $[\alpha]_D^{20} + 4.5$ (c 0.2, CH_3COCH_3); UV (MeOH) λ_{max} ($\log \varepsilon$) 259 (4.36), 272 (sh) (4.21), 378 (4.22) nm, (MeOH—NaOMe) 284, 334 (sh), 444 nm, (MeOH—$AlCl_3$) 275, 304 (sh), 452 nm, (MeOH—$AlCl_3$—HCl) 273, 305 (sh), 370 (sh), 436 nm, (MeOH—NaOAc) 258 (sh), 272, 328 (sh), 387 nm; IR (KBr) ν_{max}: 3292, 1691, 1651, 1601, 1558, 1520 cm^{-1}; NMR data, see table 1; ESIMS *m/z*: 633 $[M - H]^-$ and 657 $[M + Na]^+$, HRESIMS *m/z*: 657.1948 $[M + Na]^+$ (calcd for $[C_{34}H_{34}O_{12} + Na]^+$, 657.1942).

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