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FOUR NEW PRENYLATED FLAVONOIDS FROM AERIAL PARTS OF GLYCYRRHIZA URALENSIS[1]

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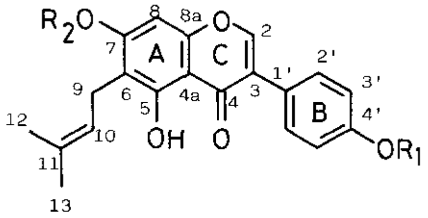
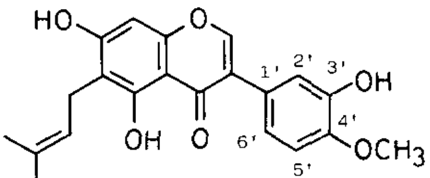
Abstract ---- Three new prenylated isoflavones were isolated from the aerial parts of Glycyrrhiza uralensis Fisch. et DC. (Leguminosae) and the structures of the new compounds, gancaonins B, C, and D, were elucidated as 5,7,3'-trihydroxy-4'-methoxy-6-prenylisoflavone, (E)-5,7,4'-trihydroxy-8-(3-hydroxymethyl-2-butenyl)isoflavone, and (E)-5,7,3'-trihydroxy-4'-methoxy-8-(3-hydroxymethyl-2-butenyl)isoflavone, respectively. Gancaonin E, from the same material, was confirmed as 5,7,3',4'-tetrahydroxy-8,5'-diprenylflavanone. Gancaonin A, 5,7-dihydroxy-4'-methoxy-6-prenylisoflavone, was isolated for the first time as a natural product. Four known phenolic compounds, scopoletin, formononetin, lupiwighteone, and sigmoidin B, were also isolated.

Licorice, the root of various species of Glycyrrhiza (Leguminosae), has long been employed as a flavoring and sweetening agent as well as a very important crude drug. The constituents of the crude drug have been studied by many investigators, and a series of prenylated phenolic compounds have been reported.[2] On the constituents of the aerial part of Glycyrrhiza sp., a few papers have been reported on the constituents of the aerial part of G. glabra,[3] G. acanthocarpa,[4] and G. astragalina,[5] while no paper has been reported on G. uralensis. In the course of our studies on the isoprenoid-substituted phenols from the crude drug,[6] we have undertaken the studies on the phenolic compounds of aerial parts of G. uralensis. This paper describes the structural characterization of three new prenylated isoflavones (**2**-**4**) and a new prenylated flavanone (**5**), together with the isolation of



1 : $R_1 = CH_3$, $R_2 = H$
1a : $R_1 = CH_3$, $R_2 = COCH_3$
10 : $R_1 = R_2 = H$



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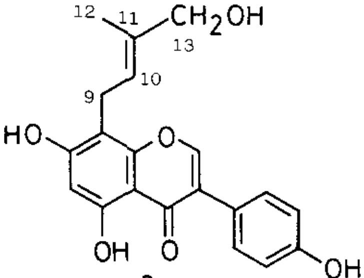

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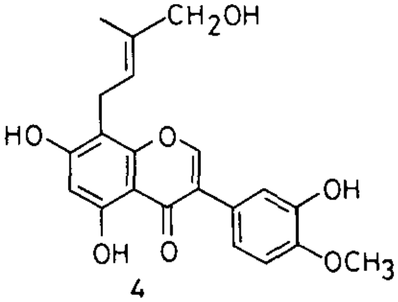

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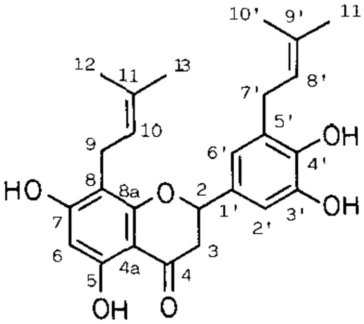

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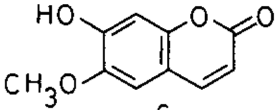

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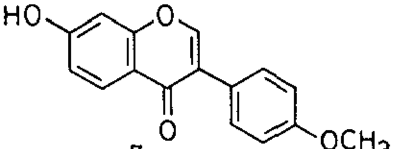

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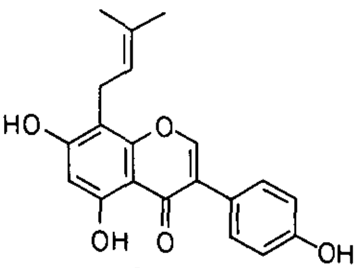

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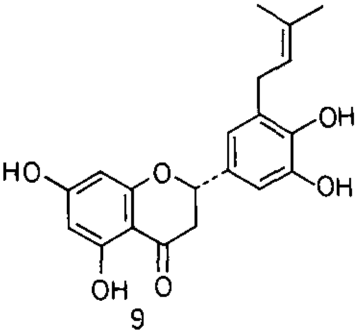

9

gancaonin A (1) and other known phenolic compounds.

From an ethanol extract of the aerial parts of G. uralensis Fisch. et DC., *gancaonins* A (**1**), B (**2**), C (**3**), D (**4**), and E (**5**) were isolated as well as four known phenolic compounds, scopoletin (**6**), formononetin (**7**), lupiwighteone (**8**),[7] and sigmoidin B (**9**).[8]

Gancaonin A (**1**), pale yellow prisms, mp 213-217 °C, $C_{21}H_{20}O_5$, gave a dark green color with methanolic ferric chloride, and was positive to the Gibbs test, while negative to the magnesium-hydrochloric acid test. The uv spectrum of **1** resembled those of isoflavone derivatives.[9] The ^1H nmr spectrum showed the characteristic singlet signal at δ8.24 (C-2-H), and showed the signals of the following protons: 1) protons in a γ,γ-dimethylallyl (prenyl) group, δ1.64 (3H, br s), 1.75 (3H, br s), 3.27 (2H, br d, J = 7 Hz), 5.21 (1H, br t, J = 7 Hz), 2) protons in a methoxyl group, δ3.80 (3H, s), 3) A_2B_2 type aromatic protons, δ6.98 (2H, d, J = 9 Hz), 7.49 (2H, d, J = 9 Hz), 4) an aromatic proton, δ6.47 (1H, s), 5) proton in hydroxyl group, δ13.15 (1H, s). The ^{13}C nmr spectrum of 1 was analyzed and compared with that of wighteone (**10**).[10] The chemical shift values of the carbon atoms of **1** were similar to those of the relevant carbon atoms of **10** except for the signals of the carbon atoms at the C-1', 3', 4', and 5' positions (Table 1). From these results, the formula 1 was suggested for the structure of gancaonin A. This results were further supported by the following results. Comparison between the ^1H nmr spectra of **1** and of its monoacetate (1a) indicated that the acetylation of the hydroxyl group at the C-7 position caused downfield shift (~0.49 ppm) of the proton at the C-8 position. The location of the prenyl group was confirmed by the following long-range selective ^1H decoupling (LSPD) technique.[11] When the proton in the hydroxyl group at δ13.15 (C-5-OH) was weakly irradiated, the broad singlet signal at δ111.32 (C-6) changed to doublet-triplet like signal. From these results, gancaonin A (1) can be characterized as the formula **1**. While Jain et al. reported the synthesis of **1**,[12] gancaonin A was isolated for the first example as a natural product.

Gancaonin B (2), pale yellow prisms, mp 206-209 °C, $C_{21}H_{20}O_6$, gave the similar results to gancaonin A (1) for the color reaction tests. The uv spectrum of **2** resembled that of **1**. In the ^{13}C nmr spectrum of **2**, the chemical shift values of the carbon atoms were similar to those of the relevant carbon atoms of **1** except for the signals of the carbon atoms of the B-ring (Table 1). Two oxygenated carbon signals were observed at δ146.35 and 147.84, suggesting that **2** has a 3',4'-dioxygenated

Table 1. ^{13}C Nmr data of **1**-**5**, **8**, and **10**

C	**1**	**2**	**10**$^{a)}$	**3**	**4**$^{b)}$	**8**	**5**
2	153.70	153.71	153.8	153.77	154.66	153.78	79.92
3	122.03	122.19	122.3	122.10	123.62	122.07	43.58
4	180.19	180.19	180.4	180.55	181.94	180.55	197.55
4a	104.45	104.40	104.4	104.58	106.29	104.57	103.39
5	158.99	158.94	159.0	159.66	161.64	159.61	162.99
6	111.32	111.25	111.2	98.58	99.52	98.58	96.39
$(J_{^{13}C6\text{-}OH5})$				(7 Hz)		(7 Hz)	(7 Hz)
7	162.11	162.06	162.1	161.69	162.38	161.66	164.96
8	93.08	93.01	93.0	105.79	106.99	105.97	108.36
8a	155.46	155.38	155.5	154.93	154.66	154.89	161.06
1'	123.31	123.81	121.5	121.39	125.14	121.40	131.04
2'	130.13	116.65	130.3	130.06	116.99	130.04	111.96
3'	113.81	146.35	115.2	115.10	147.28	115.09	145.33
4'	159.29	147.84	157.5	157.39	148.58	157.38	144.15
5'	113.81	112.49	115.2	115.10	112.37	115.09	129.08
6'	130.13	119.89	130.3	130.06	121.23	130.04	119.83
9	21.12	21.07	21.2	20.51	21.58	21.02	22.31
10	122.35	122.29	122.3	121.16	122.58	122.21	123.59*
11	130.54	130.51	130.7	135.53	136.64	130.88	131.24**
12	17.62	17.60	17.8	13.51	13.83	17.58	17.87***
13	25.37	25.35	25.6	66.34	68.27	25.30	25.91****
7'							29.07
8'							123.71*
9'							132.55**
10'							17.92***
11'							25.89****
OCH_3	55.21	55.93			56.39		
solvent	A	A	B	A	C	A	C

Solvent, A: measured in DMSO-d_6 at 60 °C, B: in DMSO-d_6 at 30 °C, C: in acetone-d_6 at 30 °C.

a): Data from K.R. Markham et al. (ref. 10), b): the datum was obtained only from complete decoupling spectrum, *-****: assignments may be interchanged.

phenyl partial structure.[10] The presence of a prenyl group, methoxyl group, and ABC type aromatic protons in the structure was supported by the ^{1}H nmr spectrum. The location of a prenyl group at the C-6 position was confirmed by the LSPD technique as described in the case of 1, and the location of the methoxyl group was also confirmed by the nuclear Overhauser effect (nOe) measurement as follows: when the methoxyl proton signal was irradiated, the proton signal at the C-5' (δ7.00) increased by 19% in area. From the above results, gancaonin B can be characterized as the formula **2**.

Gancaonin C (**3**), pale yellow prisms, mp 213°C, $C_{20}H_{18}O_6$, gave a dark green color with methanolic ferric chloride, while was negative to the Gibbs test. The uv spectrum suggested the compound (**3**) to be an isoflavone derivative.[9] In the ^{13}C nmr spectrum of **3**, the chemical shift values of the carbon atoms of **3** were similar to those of the relevant carbon atoms of lupiwighteone (**8**) except for the signals of the isoprenoid moiety (Table 1). The ^{1}H nmr spectrum showed the signals of the following protons: 1) protons in a 3-hydroxymethyl-2-butenyl group, δ1.83 (3H, br s), 3.50 (2H, br d, J = 7 Hz), 3.91 (2H, br s), 5.52 (1H, br t, J = 7 Hz), 2) A_2B_2 type aromatic protons, δ6.91 (2H, d, J = 9 Hz), 7.47 (2H, d, J = 9 Hz), 3) an aromatic proton, δ6.37 (1H, s), 4) an olefinic proton, δ8.27 (1H, s), 5) proton in a hydroxyl group, δ12.98 (1H, s). The chemical shift values of these protons except those of the isoprenoid moiety were similar to those of the relevant protons of **8**.[8] The stereochemistry of the 3-hydroxymethyl-2-butenyl moiety was confirmed as E configuration by the chemical shift values of the methyl and hydroxymethyl carbon atoms,[13] δ13.51 and 66.34, respectively, and by the nOe measurement as follows: when the methylene proton signal at δ3.91 was irradiated, the proton signal at δ5.52 increased by 12% in area. From these results, gancaonin C can be characterized as the formula 3.

Gancaonin D (**4**), pale yellow needles, mp 234-236°C, $C_{21}H_{20}O_7$, showed a similar uv spectrum to that of **3**. The ^{13}C nmr spectrum of **4** also showed that the chemical shift values were substantially similar to those of the relevant carbon atoms of **3** except for the those of the B-ring carbons (Table 1). The 3',4'-dioxygenated phenyl structure for the B-ring of **4** was supported by the chemical shift values of the two oxygenated carbon atoms (δ147.28, 148.58).[10] The ^{1}H nmr spectrum showed the signals of the following protons: 1) protons in a 3-hydroxymethyl-2-butenyl group, δ1.82 (3H, br s), 3.50 (2H, br d, J = 7.5 Hz), 3.91 (2H, br s), 5.52 (1H, br t, J = 7.5 Hz), 2) ABC type aromatic protons, δ7.00 (1H, d, J = 8 Hz), 7.06 (1H, dd, J = 2 and

8 Hz), 7.16 (1H, d, J = 2 Hz), 3) an aromatic proton, δ6.38 (1H, s), 4) an olefinic proton, δ8.28 (1H, s), 5) protons in a methoxyl group, δ3.89 (3H, s), 6) proton in hydroxyl group, δ12.99 (1H, s). The chemical shift values of the protons except for those of the ABC type aromatic and methoxyl protons were similar to those of the relevant protons of **3**. The location of a methoxyl group was confirmed by the nOe measurement as follows: the signal at δ6.99 (C-5'-H) increased by 12.5% in area on irradiation at the methoxyl proton signal. The stereochemistry of the 3-hydroxylmethyl-2-butenyl moiety was confirmed as *E* configuration by the chemical shift values of the methyl and hydroxymethyl carbon atoms,[13] δ13.83 and 68.27, respectively. From these results, gancaonin D can be characterized as formula **4**.

Gancaonin E (**5**), colorless prisms, mp 203-207°C, $[\alpha]_D$ 0°, $C_{25}H_{28}O_6$, exhibited positive results in ferric chloride reaction, magnesium hydrochloric acid test, and sodium borohydride test. The uv spectrum of **5** resembled those of flavanone derivatives. The ^1H nmr spectrum of **5** showed the characteristic proton signals at C-2 and C-3 positions of a flavanone skeleton [δ2.74 (1H, dd, J = 3 and 17 Hz), 3.07 (1H, dd, J = 12.5 and 17 Hz), 5.36 (1H, dd, J = 3 and 12.5 Hz)]. The spectrum also showed the signals of the following protons: 1) protons in two prenyl groups, δ1.62 (6H, br s), 1.72 (6H, br s), 3.22 (2H, br d, J = 7 Hz), 3.36 (2H, br d, J = 7 Hz), 5.20 (1H, br t, J = 7 Hz), 5.36 (1H, overlapping with the proton signal at C-2), 2) an aromatic proton, δ6.02 (1H, s), 3) *meta*-coupled two aromatic protons, δ6.84 (1H, dd, J = 2 and *ca*. 0.6 Hz),[14] 6.92 (1H, d, J = 2 Hz), 4) proton in hydroxyl group, δ12.14. In the ^{13}C nmr spectrum, the signals of the two oxygenated carbon atoms in the B-ring were observed at δ145.33 and 144.15 to support the B-ring being of a 3',4'-dioxygenated phenyl structure.[10] The location of one of the prenyl groups was confirmed by the following LSPD technique. When the proton in the hydroxyl group at δ12.14 was weakly irradiated the double doublet signal at δ96.39 (J = 161 and 7 Hz) changed to doublet (J = 161 Hz). This result suggests that the prenyl group is located at the C-8 position. From these results, gancaonin E can be characterized as formula **5**.

EXPERIMENTAL

Abbreviations: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet, br = broad, sh = shoulder, infl = inflection. The general procedures followed and the instruments used are described in our previous paper.[15]

Plant Materials

Aerial parts of Glycyrrhiza uralensis Fisch. et DC. (Leguminosae) were collected in Heilongjiang province, Zhaozhou prefecture, China, in August 1987. The material was identified by Prof. K.-Z. Fu, Heilongjiang Institute of Chinese Traditional Medicine. The sample has been deposited in the *herbarium of Heilongjiang* Institute of Drug Control.

Isolation of Gancaonins A (**1**), B (**2**), C (**3**), D (**4**), E (**5**), and Other Phenolic Compounds from the Aerial Parts of Glycyrrhiza uralensis.

The dried aerial parts of G. uralensis (6 Kg) were exhaustively extracted with ethanol at room temperature. Evaporation of the extract to dryness yielded 590 g of the residue. This residue (300 g) was chromatographed on Amberlite XAD-2 (1 l), successively, with H_2O, methanol and benzene as an eluent. After the methanol eluted fractions were combined and the solution was washed with n-hexane, the methanol layer was evaporated to give a residue (94 g). This residue (94 g) was chromatographed on silica gel (500 g) with benzene-methanol as an eluent, each fraction (eluent volume 500 ml) being monitored by tlc. The fractions 9-10 eluted with benzene were evaporated to give 0.95 g of residue, from which gancaonin A (**1**, 110 mg) was obtained by recrystallization from benzene-acetone. From the fractions 14-15 (1.3 g of residue) eluted with benzene, gancaonin B (**2**, 60 mg) was obtained by using preparative tlc (solvent system, benzene-ether=4:1, silica gel). From the fraction 64 (1 g) eluted with benzene-methanol (99.3:0.7), scopoletin (**6**, 5 mg) was obtained. The collected fraction (fractions 66-80, 1 g) eluted with benzene-methanol=99.3:0.7-99:1 was purified by preparative tlc (benzene-acetone =4:1) to give gancaonin E (**5**, 25 mg). From the fractions 87-88 (0.4 g) eluted with benzene-methanol (98:2), formononetin (**7**, 10 mg) was obtained. The collected fraction (fractions 90-118, 6.6 g) eluted with benzene-methanol=98:2-95:5 was purified by preparative tlc (chloroform-acetone=6:1, benzene-ethyl acetate=3:1, n-hexane-acetone=3:2) to give lupiwighteone (**8**, mp 141-143°C, 19 mg)[7] and sigmoidin B (**9**, mp 215-217°C, 21 mg).[8] The collected fraction (fractions 141-142, 4 g) eluted with benzene-methanol=92.5:7.5 was purified by preparative *tlc (chloroform-methanol*=10:1, benzene-ether=1:1, benzene-acetone=1:1) to give gancaonins C (**3**, 10 mg) and D (**4**, 1 mg). Physical and spectral data of these known compounds were identified with the relevant published data.

Gancaonin A (**1**).

Compound **1** was recrystallized from benzene-acetone to give pale yellow prisms, mp 213-217°C, identical with the literature value (mp 215-217°C),[12] $FeCl_3$ test: dark green, Mg-HCl test: negative, Zn-HCl test: negative, and Gibbs test: positive. Uv λ_{max}^{MeOH} nm (*log* ε): *214 (4.44)*, 267 *(4.48)*, 330 (sh 3.54). Uv $\lambda_{max}^{MeOH+AlCl_3}$ (after 2h): 215 (sh 4.54), 240 (sh 4.55), 274 (4.57), 320 (sh 3.91), 380 (3.44). Uv $\lambda_{max}^{MeOH+AcONa}$: 273 (4.66), 337 (4.15). Ir $\nu_{max}^{KBr}cm^{-1}$: 3300, 1660 (sh), 1650, 1625, 1610, 1570, 1510. EI-Ms (probe), 70 eV, m/z (relative intensity): 353 $[M+1]^+$ (19%), 352 $[M]^+$ (81), 337 (19), 323 (5), 309 (100), 297 (90), 284 (5), 254 (2), 132 (4), 117 (2), 69 (3). High-resolution-Ms (HR-Ms), m/z: 352.1292 $[M]^+$ ($C_{21}H_{20}O_5$ requires: 352.1311). ^1H Nmr (DMSO-d_6, 60°C): δ1.64, 1.75 (each 3H, s, C-11-CH_3), 3.27 (2H, br d, J = 7 Hz, C-9-Hx2), 3.80 (3H, s, OCH_3), 5.21 (1H, br t, J = 7 Hz, C-10-H), 6.47 (1H, s, C-8-H), 6.98 (2H, d, J = 9 Hz, C-3'-H and C-5'-H), 7.49 (2H, d, J = 9 Hz, C-2'-H and C-6'-H), 8.24 (1H, s, C-2-H), 13.15 (1H, s, C-5-OH).

Gancaonin A Monoacetate (**1a**).

A mixture of **1** (10 mg), acetic anhydride (0.1 ml), and pyridine (0.1 ml) was kept at room temperature for 10 min and treated as usual. Gancaonin A monoacetate was crystallized from methanol-ether to give **1a** (9 mg), colorless prisms, mp 112-114°C. $FeCl_3$ test: green. EI-Ms, m/z (rel. int.): 395 $[M+1]^+$ (22%), 394 $[M]^+$ (81), 351 (60), 339 (25), 309 (100), 297 (95), 284 (5), 254 (2), 132 (4), 43 (16). ^1H Nmr (DMSO-d_6, 60°C): δ1.63, 1.72 (each 3H, br s, C-11-CH_3), 2.32 (3H, s, OAc), 3.25 (2H, br d, J = 7 Hz, C-9-Hx2), 3.80 (3H, s, OCH_3), 5.09 (1H, br t, J = 7 Hz, C-10-H), 6.96 (1H, s, C-8-H), 7.01 (2H, d, J = 9 Hz, C-3'-H and C-5'-H), 7.52 (2H, d, J = 9 Hz, C-2'-H and C-6'-H), 8.47 (1H, s, C-2-H), 13.25 (1H, s, C-5-OH).

Gancaonin B (**2**).

Compound **2** was recrystallized from benzene to give pale yellow prisms, mp 206-209°C. $FeCl_3$ test: dark green, Mg-HCl test: negative, Zn-HCl test: negative, and Gibbs test: positive. Uv λ_{max}^{MeOH} nm (log ε): 206 (4.56), 216 (sh 4.55), 267 (4.41), 290 (sh 4.11), 340 (sh 3.41). Uv $\lambda_{max}^{MeOH+AlCl_3}$ (after 2h): 273 (4.41), 320 (sh 3.86), 380 (3.34). Uv $\lambda_{max}^{MeOH+AcONa}$: 274 (4.37), 338 (3.90). Ir ν_{max}^{KBr} cm^{-1}: 3400 (sh), 3200, 1660 (sh), 1650 (sh), 1640, 1620, 1560, 1515. EI-Ms, m/z (rel. int.): 369 $[M+1]^+$ (18%), 368 $[M]^+$ (77), 353 (16), 339 (5), 325 (100), 313 (85), 300 (4), 165 (2), 69 (5). HR-Ms, m/z: 368.1248 $[M]^+$ ($C_{21}H_{20}O_6$ requires: 368.1260). ^1H Nmr (DMSO-d_6, 60°C): δ1.63, 1.73 (each 3H, br d, J = 1 Hz, C-11-CH_3), 3.25 (2H, br d, J = 7 Hz, C-9-Hx2), 3.80 (3H, s, OCH_3), 5.19 (1H, br t, J = 7 Hz, C-10-H), 6.44 (1H, s, C-8-H), 6.93 (1H, dd, J = 2 and 8 Hz, C-6'-H), 6.96 (1H, d, J = 8 Hz, C-5'-H), 7.04 (1H, d, J = 2 Hz, C-2'-H), 8.24 (1H, s, C-2-H), 13.17 (1H, s, C-5-OH). ^1H Nmr (acetone-d_6): δ1.65 (3H, br d, J = 1 Hz, C-11-CH_3), 1.78 (3H, br d, J = 0.7 Hz, C-11-CH_3), 3.37 (2H, br d, J = 7 Hz, C-9-Hx2), 3.88 (3H, s, OCH_3), 5.28 (1H, br t, J = 7 Hz, C-10-H), 6.50 (1H, s, C-8-H), 7.00 (1H, d, J = 8 Hz, C-5'-H), 7.05 (1H, dd, J = 2 and 8 Hz, C-6'-H), 7.14 (1H, d, J = 2 Hz, C-2'-H), 8.16 (1H, s, C-2-H), 13.34 (1H, s, C-5-OH).

Gancaonin C (**3**).

Compound **3** was recrystallized from benzene-acetone to give pale yellow prisms, mp 213°C. $FeCl_3$ test: dark green and Gibbs test: negative. Uv λ_{max}^{MeOH} nm (log ε): 204 (4.52), 210 (sh 4.46), 220 (sh 4.32), 265 (4.58), 300 (sh 3.85), 334 (3.51). Uv $\lambda_{max}^{MeOH+AlCl_3}$: 204 (4.61), 220 (sh 4.40), 230 (sh 4.32), 240 (sh 4.15), 278 (4.62), 315 (sh 3.75), 389 (3.61). Uv $\lambda_{max}^{MeOH+AcONa}$: 277 (3.49), 332 (2.79). Ir ν_{max}^{KBr} cm^{-1}: 3250, 1650, 1620, 1600, 1570, 1510. EI-Ms, m/z (rel. int.): 355 $[M+1]^+$ (23%), 354 $[M]^+$ (100), 323 (99), 321 (78), 283 (50), 270 (48), 165 (12), 153 (5). HR-Ms, m/z: 354.1093 $[M]^+$ ($C_{20}H_{18}O_6$ requires: 354.1103). ^1H Nmr (DMSO-d_6, 60°C): δ1.74 (3H, br s, C-11-CH_3), 3.38 (2H, br d, J = 7 Hz, C-9-Hx2), 3.78 (2H, br s, C-13-Hx2), 5.40 (1H, br t, J = 7 Hz, C-10-H), 6.33 (1H, s, C-6-H), 6.82 (2H, d, J = 8 Hz, C-3'-H and C-5'-H), 7.39 (2H, d, J = 8 Hz, C-2'-H and C-6'-H), 8.32 (1H, s, C-2-H), 12.84 (1H, s, C-5-OH). ^1H Nmr(acetone-d_6): δ1.83 (3H, br s, C-11-CH_3), 3.50 (2H, br d, J = 7 Hz, C-9-Hx2), 3.91 (2H, br s, C-13-Hx2), 5.52 (1H, br t, J = 7 Hz, C-10-H), 6.37 (1H, s, C-6-H), 6.91 (2H, d, J = 9 Hz, C-3'-H and C-5'-H), 7.47 (2H, d, J = 9 Hz, C-2'-H and C-6'-H), 8.27 (1H, s, C-2-H), 12.98 (1H, s, C-5-OH).

Gancaonin D (**4**).

Compound **4** was recrystallized from benzene-acetone to give pale yellow needles, mp 234-236°C. $FeCl_3$ test: dark green. Uv λ_{max}^{MeOH} nm (log ε): 206 (4.36), 215 (infl 4.32), 266 (4.30), 290 (sh 3.78), 340 (sh 3.28). Uv $\lambda_{max}^{MeOH+AlCl_3}$: 208 (4.40), 278 (4.33), 315 (sh 3.53), 389 (3.35). Uv $\lambda_{max}^{MeOH+AcONa}$: 277 (4.24), 332 (3.60). EI-Ms, m/z (rel. int.): 385 $[M+1]^+$, (26 %), 384 $[M]^+$ (100), 366 (29), 353 (71), 313 (20). HR-Ms, m/z: 384.1181 $[M]^+$ ($C_{21}H_{20}O_7$ requires: 384.1209). ^1H Nmr (acetone-d_6): δ1.82 (3H, br s, C-11-CH_3), 3.50 (2H, br d, J = 7.5 Hz, C-9-Hx2), 3.89 (3H, s, OCH_3), 3.91 (2H, br s, C-13-Hx2), 5.52 (1H, br t, J = 7.5 Hz, C-10-H), 6.38 (1H, s, C-6-H), 7.00 (1H, d, J = 8 Hz, C-5'-H), 7.06 (1H, dd, J = 2 and 8 Hz, C-6'-H), 7.16 (1H, d, J = 2 Hz, C-2'-H), 8.28 (1H, s, C-2-H), 12.99 (1H, s, C-5-OH).

Gancaonin E (**5**).

Compound 5 was recrystallized from benzene-methanol to give colorless prisms, mp 203-207°C, $[\alpha]_D$ 0°(methanol, c = 0.095). $FeCl_3$ test: green, Mg-HCl test: reddish violet, Zn-HCl test: pale yellow, and $NaBH_4$ test: reddish violet. Uv λ_{max}^{MeOH} nm (log ε): 206 (4.67), 225 (sh 4.32), 240 (sh 4.02), 292 (4.10), 336 (3.42). Uv $\lambda_{max}^{MeOH+AlCl_3}$: 208 (4.71), 225 (sh 4.39), 240 (sh 4.02), 314 (4.27), 391 (3.53). Uv $\lambda_{max}^{MeOH+AlCl_3+HCl}$: 206 (4.70), 225 (sh 4.42), 313 (4.25), 384 (3.52). Uv $\lambda_{max}^{MeOH+AcONa}$: 285 (sh 3.77), 332 (4.19). Ir ν_{max}^{KBr} cm^{-1}: 3440, 1640, 1610 (sh), 1600. EI-Ms, m/z(rel. int.): 425 $[M+1]^+$ (28%), 424 $[M]^+$ (100), 409 (16), 381 (13), 369 (23), 356 (4), 205 (38), 177 (23), 165 (52), 148 (14), 69 (14). HR-Ms, m/z: 424.1880 $[M]^+$ ($C_{25}H_{28}O_6$ requires: 424.1886). ^1H Nmr (acetone-d_6): δ1.62 (6H, br s, C-11-CH_3 and C-9'-CH_3), 1.72 (6H, br s, C-11-CH_3 and C-9'-CH_3), 2.74 (1H, dd, J = 3 and 17 Hz, C-3-H), 3.07 (1H, dd, J = 12.5 and 17 Hz, C-3-H), 3.22 (2H, br d, J = 7 Hz, C-9-Hx2), 3.36 (2H, br d, J = 7 Hz, C-7'-Hx2), 5.20 (1H, br t, J = 7 Hz, C-10-H), 5.36 (1H, overlapping with the signal of C-2-H, C-8'-H), 5.36 (1H, dd, J = 3 and 12.5 Hz, C-2-H), 6.02 (1H, s, C-6-H), 6.84 (1H, dd, $J_{2'-6'}$ = 2.1 Hz and $J_{6'-7'a}$ = 0.55 Hz, C-6'-H, digital resolution: 0.061 Hz),[16] 6.92 (1H, d, $J_{2'-6'}$ = 2.1 Hz, C-2'-H, digital resolution: 0.061 Hz), 12.14 (1H, s, C-5-OH).

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