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STUDIES OF THE CONSTITUENTS OF SCUTELLARIA SPECIES. I. THE FLAVONOID GLUCURONIDES OF "BO YE HUANG CHIN", SCUTELLARIA IKONNIKOVII JUZ.

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Seven flavonoid glucuronides (1-7) were isolated from "Bo Ye Huang Chin" (薄葉黄芩), the whole herb of Scutellaria ikonnikovii Juz.(Labiatae). A new glucuronyl flavone named ikonnikoside I (1) was formulated as 5,6,2'-trihydroxy-7-O-glucuronyl flavone. Other compounds (2-7) were identified as norwogonin-8-O-glucuronide (2), scutellarin (3), 5,2'-dihydroxy-7-O-glucuronylflavone (4), baicalin (5), norwogonin-7-O-glucuronide (6) and chrysin-7-O-glucuronide (7).

KEYWORDS— Bo Ye Huang Chin; Scutellaria ikonnikovii; Labiatae; flavone; ikonnikoside I; 5,6,2'-trihydroxy-7-O-glucuronyl-flavone; norwogonin-8-O-glucuronide

The Chinese crude drug "Bo Ye Huang Chin"(薄葉黄芩) is the dried whole herb of Scutellaria ikonnikovii Juz.(Labiatae), which grows plentifully in the northern part of Jilin province. "Bo Ye Huang Chin", as well as Scutellalria baicalensis George., has been used in Chinese traditional medicine for the treatment of epigastric pain and hypoglycemia. Also, anti-phlogistic, anti-hypertensive, and diuretic activities[1] have been suggested. An antipyretic effect achieved by using it together with Bupleurum root has also been suggested. Since 1899 the chemical constituents of Scutellaria species have been studied, and a typical flavonoid of S. altissima, scutellarin (5) was first reported by Goldschmiedt and Zerner.[2] Tomimori et al.[3] isolated twentythree flavonoids from both S. baicalensis and S. revularis.

In this paper, we report the isolation and the structural elucidation of several flavonoid glucuronides from S. ikonnikovii, including a new compound.

Dried whole herbs (1.5 kg) collected in 1986 at Tae Nan of Jilin prov., China, were extracted with hot 95% aq. EtOH, and the concentrated extracts were loaded on a Diaion HP-20 column and eluted with 50% aq. MeOH to obtain a fraction in which flavonoid is concentrated. The concentrated eluant was chromatographed on an HPLC dimethylamino bonded silica gel column (Senshu Pak SN-432N, 20 x 200mm)[4] to get a highly acidic fraction by the solvent gradient system (THF(100%)-60 min THF(77.7%), AcOH(2.9%), H_2O(19.4%)). The mixture was further purified by successive chromatography with an ODS column (Senshu Pak ODS-3251N, 8 x 250mm) using the solvent gradient system (3% AcOH (80%), CH_3CN (20%)-60 min 3% AcOH (20%), CH_3CN (80%)).

Ikonnikoside I(1), a new flavone glucuronide, was obtained as yellow needles (MeOH), $C_{21}H_{18}O_{11}$, giving a positive Mg-HCl test; mp 175-176°C, $UV_{\lambda max}^{MeOH}$ nm: 275, 336; $UV_{\lambda max}^{MeOH+NaOAc}$ nm: 275, 334. The UV spectrum absorption maxima at 275nm as band I and 336nm as band II, the ^1H NMR singlet signal at δ7.06(1H, H-3) and the ^{13}C NMR signal at δ108.54(C-3) suggest a flavone skeltone. A 5,6,7-trihydroxylated structure on the A-ring is supported by the absence of proton signals for H-5, H-6 and H-7, and the presence of one chelated hydroxyl signal (δ12.65), a proton signal for H-8 at δ6.98, and a methine carbon signal for an unsubstituted C-8 at δ93.62 (Table I). A complex resonance at δ6.99-7.38 (3H), a double doublet signal at δ7.85 (1H, J=6.6, 1.4Hz) and a quarternary carbon signal at δ 156.63 are assignable to the B-ring having one hydroxyl group. The complete asssignment of all carbons of the aglycone and the sugar unit was determined in comparison with those of 5 as shown in Table I. Compound 1, having a 7-glucuronyl group, exhibited no bathochromic shift of band II in the UV spectrum when NaOAc was added. On the basis of these results in comparison with baicalin (5), 1 was determined to be 5,6,2'-trihydroxy-7-O-glucuronylflavone (1).

Norwogonin-8-O-glucuronide (2), $C_{21}H_{18}O_{10}$, a flavone glucuronide, was obtained as light yellow needles (MeOH), mp 202-203°C; Mg-HCl test (positive). In comparing the ^1H NMR spectroscopic data of 2 and 6, a singlet signal at δ6.23 and a complex signal at δ7.52-8.23 were assigned to H-6 and five protons in the B-ring, respectively. These data showed that 2 has a flavone skeltone with an unsubstituted B-ring, as do wogonin-7-O-glucuronide methyl ester,[3a] norwogonin[3b] and 5,8-dihydroxy-7-glucuronylflavone (6).[3b] The chelated hydroxyl also appeared at δ12.64 in 2 as in 1. The ^{13}C NMR spectrum of 2 revealed six hexuronyl signals which were different from those of 1 and 3-7 (Table I). In order to determine the sugar moiety, the carbonyl group of hexuronyl residue in 2 was reduced with the carbodiimide reagent[5] and sodium borohydride to give a corresponding hexosyl compound (8) whose structure was determined as 5,7-dihydroxy-8-O-glucosylflavone in comparison with the ^{13}C and ^1H NMR spectra of 6. Consequently the structure of 2 was assigned to 5,7-dihydroxy-8-O-glucuronylflavone (2)[6].

Other flavonoids (3-7) were identified by their physical and spectral data in comparison with known flavonoids. The ^1H and ^{13}C NMR spectra of 3-7 are listed in Table I and II.

Table I. ^{13}C NMR Spectral Data for Compounds 1-8 (δ in DMSO-d_6)

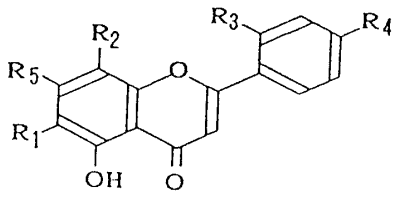
Compounds	1	2	3	4	5	6	7	8
Carbons								
2	161.69	163.10	164.05	163.07	163.59	163.56	163.80	162.89
3	108.54	106.68	102.35	105.34	104.78	105.03	105.54	106.66
4	182.45	181.77	182.25	182.20	182.64	182.62	182.25	181.63
5	146.40	157.42	146.74	161.00	146.73	151.45	161.18	157.18
6	130.32	99.78	130.46	99.37	130.84	99.16	99.51	99.43
7	149.20	159.48	148.91	161.73	149.27	152.17	163.11	159.03
8	93.62	125.77	93.77	94.69	94.32	127.51	94.94	125.67
9	151.20	149.57	151.06	157.34	151.76	144.71	157.20	149.40
10	105.81	103.05	105.80	109.12	106.18	105.57	105.71	102.87
1'	117.30	130.70	121.09	117.35	130.91	130.91	130.67	130.57
2'	156.63	126.89	128.29	157.08	126.45	126.58	126.58	126.84
3'	117.05	129.18	115.92	116.82	129.25	129.21	129.25	128.90
4'	132.72	131.92	161.24	132.84	132.00	132.18	132.27	131.83
5'	119.32	129.18	115.92	119.13	129.25	129.21	129.25	128.90
6'	128.40	126.89	128.29	128.25	126.45	126.58	126.58	126.84
1''	100.06	104.69	100.30	99.45	100.75	101.23	99.76	104.45
2''	72.76	73.61	72.79	72.96	71.93	72.98	72.93	74.03
3''	75.17	75.64	75.03	74.11	75.66	74.63	74.72	75.99
4''	71.34	72.01	71.49	71.89	71.85	71.83	71.65	69.02
5''	75.27	76.52	75.36	76.32	75.82	75.54	76.14	77.22
6''	170.20	170.86	170.68	172.02	171.14	172.01	171.00	60.40

Table II. ^{1}H NMR Spectral Data for Compounds 1-8 (δ in DMSO-d_6)

Compounds	1	2	3	4	5	6	7	8
Protons								
anomeric	5.15 1H d J=7.3Hz	4.77 1H d J=7.7Hz	5.17 1H d J=7.3Hz	5.23 1H d J=6.9Hz	5.10 1H d J=6.9Hz	5.02 1H d J=7.3Hz	5.18 1H bs	4.65 1H d J=7.7Hz
3	7.06 1H s	6.97 1H s	6.99 1H s	7.13 1H s	7.04 1H s	7.01 1H s	7.06 1H s	6.99 1H s
A-ring								
6		6.23 1H s		6.44 1H d J=2.2Hz		6.65 1H s	6.48 1H bs	6.23 1H s
8	6.98 1H s		6.80 1H s	6.82 1H d J=2.2Hz	7.00 1H s		6.90 1H bs	
5-OH	12.65 1H s	12.64 1H s	12.73 1H s	12.86 1H s	12.58 1H s	12.20 1H s	12.60 1H s	12.66 1H s
B-ring								
3'	7.06 1H d J=7.7Hz			7.07 1H d J=8.0Hz				
4'	7.37 -7.40 1H m			7.39 1H t				
5'	6.97 -7.01 1H m			6.98 1H t				
6'	7.85 1H dd J=6.6, 1.4Hz			7.83 1H d J=8.0Hz				
3',5'			6.94 2H d J=8.4Hz					
3',4',5'		7.52 -7.59 3H m			7.52 -7.60 3H m	7.58 -7.64 3H m	7.50 -7.60 3H m	7.08 -7.59 3H m
2',6'		8.23 2H d J=7.3Hz	7.91 2H d J=8.4Hz		8.07 2H d J=8.0Hz	8.10 -8.15 2H m	8.00 -8.11 2H m	8.29 2H d J=6.2Hz

Fig. 1. Structures of Compounds 1-8

	R_1	R_2	R_3	R_4	R_5
1	OH	H	OH	H	OGlcA
2	H	OGlcA	H	H	OH
3	OH	H	H	OH	OGlcA
4	H	H	OH	H	OGlcA
5	OH	H	H	H	OGlcA
6	H	OH	H	H	OGlcA
7	H	H	H	H	OGlcA
8	H	OGlc	H	H	OH



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