

## Communications to the Editor

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SWEET AND BITTER GLYCOSIDES OF THE CHINESE PLANT DRUG, BAI-YUN-SHEN  
(ROOTS OF SALVIA DIGITALOIDES)

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From a Chinese plant drug, Bai-Yun-Shen (roots of Salvia digitaloides), a new sweet glycoside named baiyunoside (**1**) was isolated. The structure of the acid-unstable aglycone of **1** named baiyunol (**2**) was elucidated by MS and NMR spectroscopy especially by comparison with the <sup>13</sup>C chemical shifts of β-onocerin (**3**). The structure of **1** was determined to be β-D-xylopyranosyl(1→2)-β-D-glucopyranoside of **2** by MS and NMR spectroscopy. Besides this sweet principle (**1**), several bitter iridoid glucosides were also isolated from this plant. Two of these glucosides were identified as shanzhiside methyl ester (**13**) and its 8-O-acetate (=acetylbarlerin, **10**), respectively. A new glucoside (**9**) was formulated as 6-O-syringyl-8-O-acetyl shanzhiside methyl ester by the correlation with **13**.

KEYWORDS — Bai-Yun-Shen; Salvia digitaloides Diels; Labiatae; sweet glycoside; baiyunoside; labdane-type diterpene; <sup>13</sup>C-NMR; β-onocerin; iridoid glucoside; acylated shanzhiside methyl ester

We have been engaged in the investigation of the sweet principles of Chinese plants, i.e., a sweet steviol-glycoside, rubusoside from Chinese Rubus chingii Hu (Rosaceae),<sup>1)</sup> dihydrochalcone-glycosides, phlorizin and trilobatin from Lithocarpus litseifolius (Hance) Rehd. (Fagaceae)<sup>2)</sup> and trilobatin from Vitis piasezkii Maxim. and V. saccharifera Makino (Vitaceae)<sup>3)</sup>. The present communication deals with the chemical study of sweet and bitter glycosides of the Chinese plant drug "Bai-Yun-Shen", roots of Salvia digitaloides Diels (Labiatae) which has been used for women's diseases.

An aqueous suspension of the methanolic extract of the dried roots collected in Li-jiang, Yunnan, China, was washed with ether and then extracted with 1-butanol saturated with water. The butanolic fraction was chromatographed to give a new sweet principle named baiyunoside (**1**), white powder, C<sub>31</sub>H<sub>48</sub>O<sub>11</sub>, EI-MS as its hexa-acetate: M+ m/z 890, [α]<sub>D</sub><sup>26</sup> +13.8° (c=2.50, MeOH), UV λ<sub>max</sub><sup>EtOH</sup> 213nm (logε=3.8), yield: 0.11%. This glycoside (**1**) is about 500-fold sweeter than sucrose and its sweetness lasts more than one h.

On hydrolysis with crude hesperidinase,<sup>4)</sup> an acid unstable aglycone, named baiyunol (**2**), was obtained from **1** as colorless needles mp 85.5–86°C (from n-hexane), C<sub>20</sub>H<sub>30</sub>O<sub>2</sub>, EI-MS: M+ 302, [α]<sub>D</sub><sup>21</sup> +64.0° (c=1.47, CHCl<sub>3</sub>). It was not sweet. The UV

absorption maximum at 212nm (in MeOH) ( $\log \epsilon = 3.9$ ), strong ions at  $m/z$  81 and 95 in its EI-MS,  $^1\text{H-NMR}$  signals at  $\delta$  7.35(1H, t,  $J=1.8\text{Hz}$ ), 7.23(1H, broadened dd) and 6.30(1H, broadened dd) in  $\text{CDCl}_3$  as well as  $^{13}\text{C}$  signals at  $\delta$  125.5 (or 126.7) (s, 13-C), 110.8(d, 14-C), 142.6(d, 15-C) and 138.4(d, 16-C) in  $\text{CDCl}_3$  revealed the presence of a  $\beta$ -substituted furan ring<sup>5</sup>) in **2**. Further, multiplicities of the  $^{13}\text{C-NMR}$  signals of **2** demonstrated the presence of one carbonyl carbon, one tetra-substituted double bond, four methyls, six methylenes, two methines and two quaternary carbons. Its proton signals in  $\text{CDCl}_3$  at  $\delta$  0.81(3H, s), 0.97(3H, s), 1.02(3H, s), 1.61(3H, s) and 3.25(1H, dd,  $J=6.0$  and  $10.8\text{Hz}$ ) revealed the presence

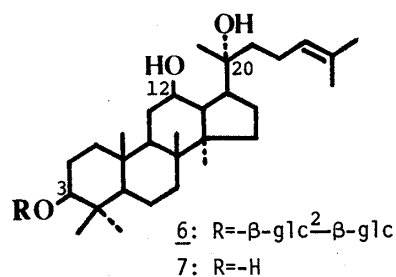
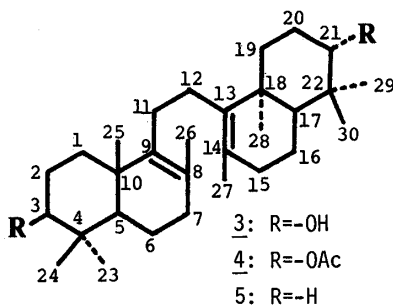
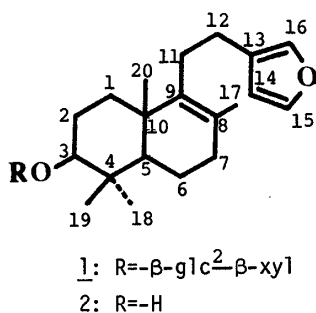


Table I.  $^{13}\text{C-NMR}$  Spectra of Aglycone Moieties (in Pyridine- $d_5$  at 25.15 MHz)

	1	2	3	1	2	3
C-1	35.3	35.5	36.3	C-11	29.0	29.2
2	27.2	29.2	29.1	12	26.1	26.1
3	89.3	78.1	78.0	13	126.1†	126.1†
4	38.7*	39.1*	39.2	14	111.5	111.4
5	51.6	51.4	51.4	15	143.3	143.3
6	18.9	19.5	19.4	16	139.0	139.1
7	34.0	34.1	34.6	17(26)	19.0	19.2
8	126.5†	126.6†	126.5	18(23)	28.0	28.7
9	139.9	140.1	141.1	19(24)	16.4	16.5
10	39.6*	39.5*	39.5	20(25)	20.2	20.3

( ); For **3**. \*,†; These signals may be reversed.

Table II.  $^{13}\text{C-NMR}$  Spectra of Sugar Moieties (in Pyridine- $d_5$  at 25.15 MHz)

	1 (inner)	6
glc-1	105.0	glc-1 105.1
2	83.8	2 83.5
3	78.3*	3 78.2*
4	71.4†	4 71.7
5	78.1*	5 78.0*
6	62.6	6 62.7†
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xyl-1	106.8	
2	76.5	
3	77.9	
4	71.0†	
5	67.4	

\*,†; These signals may be reversed.  
glc; -D-glucopyranosyl, xyl; -D-xylopyranosyl.

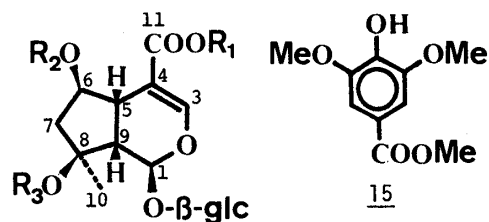


Table III.  $^{13}\text{C-NMR}$  Spectra of Iridoids (in Pyridine- $d_5$  at 25.15 MHz)

	9	16	10	13	9	16	10	13
C-1	95.1	94.9	95.8	94.9	$\eta$ -COOMe	51.1	51.3	51.1
3	153.6	152.6	152.9	152.3	OCOMe	170.5		170.9
4	107.7	109.3	108.9	110.6	OCOMe	21.9*		22.0
5	39.2	38.2	42.0	41.5				
6	78.1	78.3	74.7	76.6	1'	120.4	120.9	
7	44.7	48.1	47.4	48.8	2',6'	108.4	108.4	
8	88.3	77.7	88.6	78.3	3',5'	148.5	148.6	
9	49.7	51.3	49.6	51.1	4'	143.0	142.7	
10	21.5*	25.7	22.0	24.9	$\phi$ -OMe	56.4	56.4	
11	166.6†	167.1†	167.5	168.0	$\phi$ -COO	165.9†	166.4†	

\*,†; These signals may be reversed.

of three methyl groups on quarternary carbons, one allylic methyl group and one equatorial secondary hydroxyl group, respectively. This evidence suggests that **2** is a monohydroxy-labdane-type diterpene having a  $\beta$ -substituted furan ring. One of the present authors, Ageta, has investigated the  $^{13}\text{C}$ -NMR spectra of onocerane-type triterpenes in connection with his chemical studies of fern triterpenes, assigning the carbon signals of  $\beta$ -onocerin (**3**)<sup>6)</sup> derived from  $\alpha$ -onocerin<sup>7)</sup> by comparing them with those of its acetate (**4**) and  $\beta$ -onoceradiene (**5**)<sup>8)</sup> with consideration for the substitution and acetylation effects. As shown in Table I, it was found that the carbon signals of **2** other than those associated with its  $\beta$ -substituted furan moiety appeared at almost the same positions as those of **3** except for the slight differences in the chemical shift of the allylic methyl signal (C-17 for **2** and C-26 and -27 for **3**), leading to the formulation of **2** as illustrated in Chart 1. The  $^1\text{H}$ -NMR of **2** was consistent with this formulation. The chirality of the 3-equatorial-hydroxyl group of **2** was established as S-configuration by the modified Horeau's method.<sup>9)</sup> Accordingly, the absolute configuration of the skeleton of **2** should be the normal type.

On mineral acid hydrolysis, **1** yielded glucose and xylose. The EI-MS of the acetate of **1** exhibited fragment ions at  $m/z$  547 ((glucose-xylose)Ac<sub>6</sub>) and 259 ((xylose)Ac<sub>3</sub>). The coupling constants of two anomeric proton signals of **1** ( $\delta$  4.93 and 5.25 (1H d each,  $J=6.0\text{Hz}$ ) in  $\text{C}_5\text{D}_5\text{N}$ ) indicated the  $\beta$ -configuration of both glycosyl linkages. Inspection of the  $^{13}\text{C}$ -NMR spectrum of **1** in comparison with those of known glycosides revealed that signals due to the sugar moiety of **1** consisted of those due to a terminal  $\beta$ -xylopyranosyl unit and a 2-O-glycosylated  $\beta$ -glucopyranoside unit, the latter of which appeared at almost the same positions as those of the 2-O-substituted  $\beta$ -D-glucopyranosyl unit of the 3-O- $\beta$ -sophorosyl moiety of the prosapogenin (**6**) of Ginseng saponins<sup>10)</sup> as shown in Table II. It was revealed that the glycosylation shifts are significantly related to the combination of absolute configurations of an aglycone alcohol<sup>11)</sup> and a sugar moiety. On going from **2** to **1**, the glycosylation shift values of C-2, -3 and -4 as well as that of the anomeric carbon signal of the inner glucosyl unit were found to be almost identical with those for **6** from 20(R)-protopanaxadiol (**7**).<sup>11)</sup> This evidence led to the formulation of **1** including absolute configuration of the sugar moiety as  $\beta$ -D-xylopyranosyl(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranoside of **2**.

Besides this sweet principle (**1**), six bitter iridoid-glucosides, **8-13**, were isolated from this plant in yields of 0.02, 0.19, 0.28, 0.11, 0.17 and 0.03%, respectively. Glucoside (**13**), white powder,  $[\alpha]_{\text{D}}^{22} -123.3^\circ$  ( $c=3.8$ , MeOH), UV  $\lambda_{\text{max}}^{\text{MeOH}}$  236nm ( $\log \epsilon=3.9$ ) was identified as shanzhiside methyl ester which was previously isolated from *Mussaenda parviflora* Miquel.<sup>12)</sup> Glucoside (**10**), white powder,  $[\alpha]_{\text{D}}^{26} -84.8^\circ$  ( $c=1.28$ , MeOH), UV  $\lambda_{\text{max}}^{\text{MeOH}}$  234nm ( $\log \epsilon=4.0$ ),  $^1\text{H}$ -NMR in  $\text{C}_5\text{D}_5\text{N}$ :  $\delta$  1.65(3H, s, 10-CH<sub>3</sub>), 1.88(3H, s, OCOCH<sub>3</sub>), 3.60(3H, s, COOCH<sub>3</sub>), 5.32(1H, d,  $J=7.2\text{Hz}$ , anomeric H), 6.43(1H, d,  $J=1.0\text{Hz}$ , 1-H) and 7.68(1H, s, 3-H) afforded **13** on mild alkaline hydrolysis, being identical with 8-O-acetate of **13** named acetylbarlerin which was recently isolated from *Barleria prionitis* L..<sup>13)</sup>

On alkaline hydrolysis with 1N NaOH in methanol at room temperature, a new glucoside **9**, white powder,  $[\alpha]_{\text{D}}^{24} -71.0^\circ$  ( $c=1.01$ , MeOH), UV  $\lambda_{\text{max}}^{\text{MeOH}}$  221 and 276nm ( $\log \epsilon=4.2$  and 3.7) yielded shanzhiside (**14**) and methyl syringate (**15**). The  $^1\text{H}$ -NMR spectrum of **9** in  $\text{C}_5\text{D}_5\text{N}$  exhibited a signal at  $\delta$  1.93(3H, s, OCOCH<sub>3</sub>) along with

signals at  $\delta$  1.71(3H, s, 10-CH<sub>3</sub>), 3.60(3H, s, COOCH<sub>3</sub>), 3.83(6H, s, OCH<sub>3</sub>), 5.36(1H, d, J=7.2Hz, anomeric H), 6.31(1H, d, J=3.6Hz, 1-H), 7.69(2H, s, aromatic H) and 7.74(1H, d, J=1.2Hz, 3-H) indicating the presence of an acetoxy group which was supported by its <sup>13</sup>C-NMR spectrum (Table III). Mild hydrolysis of **9** with 0.1N NaOH in methanol at room temperature resulted in deacetylation, yielding **16** (a syringate of **13**), white powder,  $[\alpha]_D^{22}$  -117.3° (c=1.05, MeOH), UV  $\lambda_{\max}^{\text{MeOH}}$  221 and 275nm (log  $\epsilon$  =4.3 and 3.9), <sup>1</sup>H-NMR in C<sub>5</sub>D<sub>5</sub>N:  $\delta$  1.43(3H, s, 10-CH<sub>3</sub>), 3.55(3H, s, COOCH<sub>3</sub>), 3.80(6H, s, OCH<sub>3</sub>), 5.37(1H, d, J=7.2Hz, anomeric H), 6.07(1H, d, J=4.5Hz, 1-H), 7.74(1H, s, 3-H) and 7.78(2H, s, aromatic H). As shown in Table III, on going from **13** to **16**, the signal due to 6-C was deshielded by 1.7 ppm and that due to 4-, 5- and 11-C were shielded, leading to the formulation of **16** as 6-O-syringate of **13**. On going from **13** to **9**, signals due to both 6- and 8-C were displaced downfield and those due to 4-, 5-, 7-, 9-, 10- and 11-C were shielded. It follows that **9** can be formulated as 6-O-syringyl-8-O-acetyl shanzhiside methyl esters. The structures elucidation of **8**, **11** and **12** are being studied.

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