

CONSTITUTIONS OF FORSYTHOSIDES F AND G, NEW PHENOL GLYCOSIDES OF FORSYTHIA VIRIDISSIMA STEMS[†]

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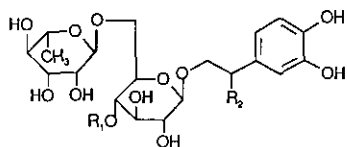
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Abstract — Two new phenol glycosides forsythoside F (1) and forsythoside G (2) have been isolated from Forsythia viridissima stems and their structures were established based on the spectroscopic data and chemical transformations. D-2-O-methylapiose was for the first time characterized in the natural product.

The crude drug Forsythiae Fructus is prescribed in the Oriental medicine as an antiinflammatory, a diuretic, a drainage or an antidote. Recent investigations have proven that the original plants of the drug contain a series of phenol glycosides which are primarily responsible to the antibacterial activity. Thus F. viridissima Lindley yielded forsythoside B (3) in the stems and acetoside (4) in the leaves,^{1,2)} while F. suspensa Vahl. afforded forsythoside A (5) in the leaves and forsythosides A, C (6), D (7) and E (8) in the fruits.³⁾ The result indicates further that F. viridissima is characterized by the presence of 3-rhamnosylglucose derivatives which contrasts to the 6-rhamnosylglucose derivatives in F. suspensa.

Our continued efforts to the investigation of pharmacologically active constituents resulted in isolation of two new phenol glycosides from F. viridissima stems, designated as forsythoside F (1) and forsythoside G (2) both having the 3-rhamnosylglucose part structure, and this article deals with their structure determination.

Forsythoside F (1), amorphous solid, $[\alpha]_D -70.9^\circ$ (MeOH), exhibited the ion peaks at m/z 757 ($[M+1]^+$) and 779 ($[M+Na]^+$), corresponding to the molecular formula of $C_{34}H_{44}O_{19}$, in the FAB-mass spectrum. Further, the 1H nmr spectrum (CD_3OD) of 1 displayed signals for a rhamnosyl group (δ



- 5 R₁ = Caffeoyl R₂ = H
- 6 R₁ = Caffeoyl R₂ = OH
- 7 R₁ = H R₂ = OH
- 8 R₁ = R₂ = H

1.08 3H d, J 6Hz; 5.15 1H d, J 2Hz), a phenethyl group (δ 2.77 2H t, J 7Hz; 6.5-7.3 3H m), a β -glucosyl group (δ 4.36 1H d, J 8Hz) a caffeoyl group (δ 6.25 and 7.56 1H each d, J 16Hz; 6.5-7.3 3H m) and one more aldosyl group (δ 4.22 1H d, J 7Hz). All of the structural features are very similar to those of forsythosid B (3) except the signal at δ 4.22 which

[†] In the memories of Professor Emeritus Tetsuji Kametani.

Table I. ^{13}C Signals of Sugar Carbons in Forsythoside F and the Related Compounds

		Forsythoside F	Acteoside	β -Xyloside	Forsythoside B
β -Glucosyl	C-1	103.9 (d 158)	104.0 (d)		103.9 (d)
	2	73.8 (d)	73.7 (d)		73.7 (d)
	3	80.4 (d)	80.3 (d)		79.6 (d)
	4	70.1 (d)	70.3 (d)		70.3 (d)
	5	74.5 (d)	76.1 (d)		74.3 (d)
	6	69.2 (t)	62.1 (t)		68.2 (t)
α -Rhamnosyl	C-1	103.0 (d 170)	102.9 (d)		102.9 (d)
	2	72.4 (d)	72.4 (d)		72.3 (d)
	3	72.4 (d)	72.4 (d)		72.3 (d)
	4	75.6 (d)	75.7 (d)		75.5 (d)
	5	70.2 (t)	70.1 (t)		70.2 (t)
	6	19.1 (q)	19.0 (q)		19.0 (q)
Pentosyl	C-1	105.5 (d 157)		105.6 (d)	111.0 (d)
	2	74.9 (d)		74.7 (d)	77.7 (d)
	3	78.0 (d)		77.8 (d)	80.3 (s)
	4	70.9 (d)		71.1 (d)	75.0 (t)
	5	67.0 (t)		66.8 (t)	65.3 (t)

Chemical shift δ (ppm) from TMS in pyridine- d_5 ; multiplicity and coupling constant in parenthesis differs from the data for the β -apiosyl group (δ 4.91 1H d, J 2.5Hz).¹⁾ Corresponding differences are also observed between the ^{13}C nmr spectra of 1 and 3, where the new signals at δ 105.5 (d), 74.9 (d), 78.0 (d), 70.9 (d) and 67.0 (t) are assignable most likely to a β -xylosyl group (Table I).⁴⁾

These analyses were substantiated by the following experiments. Thus acetylation of 1 with acetic anhydride in pyridine at room temperature overnight yielded the undecaacetate 1a (m/z 1218).

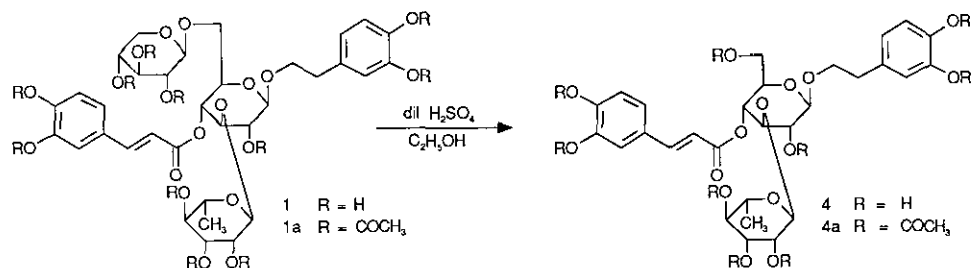


Table II. Selected ^1H Signals of Forsythoside F Acetate and the Related Compounds

Forsythoside F acetate (1a)	1.03 (d 6)	1.86, 1.92, 1.95, 1.99, 2.01 2.01, 2.08 2.25, 2.27, 2.28, 2.29 (all s)	2.84 (t 7)	4.33 (d 8) 4.49 (d 8) 5.00 (d 2)
F-Hydrolysate acetate (1b)	1.03 (d 6)	1.86, 1.93, 2.01, 2.08, 2.09 2.25, 2.27, 2.28, 2.30 (all s)	2.85 (t 7)	4.37 (d 8) 5.02 (d 2)
Acteoside acetate (4a)	1.03 (d 6)	1.85, 1.93, 2.01, 2.07, 2.09 2.26, 2.27, 2.29, 2.30 (all s)	2.85 (t 7)	4.37 (d 8) 5.02 (d 2)
Forsythoside A acetate (5a)	1.17 (d 6)	1.90, 1.93, 1.95, 1.95, 2.09 2.25, 2.27, 2.28, 2.30 (all s)	2.85 (t 7)	4.49 (d 8) 4.77 (d 2)

Chemical shift δ (ppm) from TMS in CDCl_3 ; multiplicity and coupling constant in parenthesis

On the other hand, partial hydrolysis of 1 with 2N sulfuric acid in 50% aqueous ethanol at the refluxing temperature for 1h furnished its dexylosyl derivative (4 35%), which was then acetylated similarly to the peracetate. The product did not coincide to the forsythoside A nonaacetate (5a) but identical to the acteoside nonaacetate (4a) (Table II).

Thus the β -xylosyl group was allocated on the C-6 of the glucose moiety, and consequently, the structure of forsythoside F was assigned as β -(3,4-dihydroxyphenyl)ethyl 4-caffeoyl-3- α -rhamnosyl-6- β -xylosylglucoside (1).

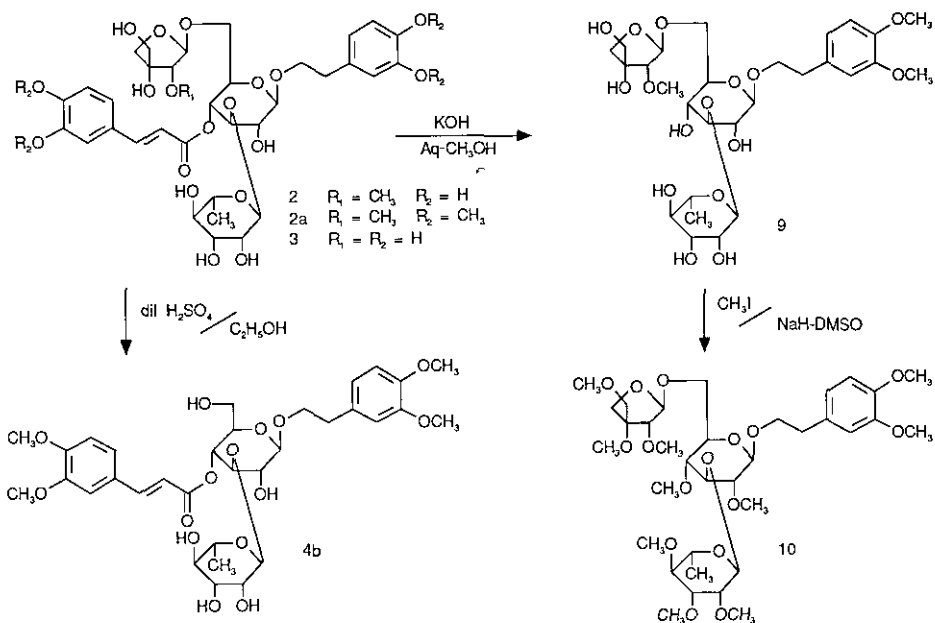
Forsythoside G (2) was isolated as its tetramethyl ether (2a), amorphous solid, $[\alpha]_D -69.1^\circ$ (MeOH), from a crude forsythoside B fraction treated with methyl iodide and potassium carbonate in acetone. The largest ion peak of 2a at m/z 825 ($[M-1]^+$) in the FD-mass spectrum indicated the molecular formula of $C_{39}H_{54}O_{19}$. The 1H nmr peaks of 2a (CD_3OD) at δ 1.09 (3H d, J 6Hz), 2.89 (2H t, J 7Hz), 3.41 (3H s), 3.78 (3H s), 3.82 (3H s), 3.84 (3H s), 3.85 (3H s), 4.37 (1H d, J 8Hz), 4.97 (1H d, J 2Hz), 5.19 (1H d, J 1Hz), 6.41 (1H d, J 16Hz), 6.8-7.3 (6H m), 7.67 (1H d, J 16Hz) and ^{13}C nmr spectrum (Table III) were very similar to those of forsythoside B (3) with additional signals at δ 3.41 (3H s) and 58.8 (1C q) compatible to an extra methoxyl group.

On hydrolysis with 2N sulfuric acid in aqueous ethanol, 2a yielded acteoside tetramethyl ether (4b 30%), while reaction with potassium hydroxide in methanol, it gave the deacyl derivative (9), $[\alpha]_D -68.9^\circ$ (MeOH). 9 was then methylated exhaustively with methyl iodide and sodium hydride in DMSO to furnish the permethyl ether (10), m/z 736, $[\alpha]_D -52.9^\circ$ (MeOH), being identical to the product obtained by the same treatment of 3.¹⁾ Further, the C-2 carbon signals for the apiose moieties in

Table III. ^{13}C Signals of Sugar Carbons in Forsythoside G and the Related Compounds

		Forsythoside G tetramethyl ether (2a)	Deacylforsy- thoside G di- methyl ether (9)	Forsythoside B tetramethyl ether (3a)	Deacylforsy- thoside B di- methyl ether
β -Glucosyl	C-1	103.9 (d)	104.0 (d)	103.9 (d)	104.2 (d)
	2	73.6 (d)	73.9 (d)	73.7 (d)	74.0 (d)
	3	80.2 (d)	83.7 (d)	80.1 (d)	83.5 (d)
	4	70.9 (d)	70.0 (d)	70.8 (d)	70.0 (d)
	5	74.1 (d)	76.7 (d)	74.4 (d)	76.9 (d)
	6	68.2 (t)	68.8 (t)	68.3 (t)	68.6 (t)
α -Rhamnosyl	C-1	102.9 (d)	102.8 (d)	102.9 (d)	102.8 (d)
	2	72.3 (d)	72.4 (d)	72.4 (d)	72.6 (d)
	3	72.3 (d)	72.3 (d)	72.4 (d)	72.5 (d)
	4	75.5 (d)	75.1 (d)	75.6 (d)	75.3 (d)
	5	70.1 (t)	69.8 (t)	70.2 (t)	69.8 (t)
	6	18.9 (q)	18.4 (q)	18.8 (q)	18.6 (q)
β -Apiosyl	C-1	110.8 (d)	108.9 (d)	110.9 (d)	111.0 (d)
	2	86.7 (d)	86.5 (d)	77.8 (d)	77.7 (d)
	3	80.6 (s)	80.5 (s)	80.3 (s)	80.4 (s)
	4	75.0 (t)	74.9 (t)	75.0 (t)	74.9 (t)
	5	65.1 (t)	65.1 (t)	65.3 (t)	65.3 (t)
Methoxyl		58.8 (q)	58.7 (q)		

Chemical shift δ (ppm) from TMS in pyridine- d_5 ; multiplicity in parenthesis



the ^{13}C nmr spectra of 2a and 9 showed apparent down field shifts due to alkylation (Table III), and hence, the structure of new sugar was assigned as 2-O-methylapiose. Consequently, the structure of forsythoside G was established as β -(3,4-dihydroxyphenyl)ethyl 4-caffeoyl-6- β -(2-O-methyl)apiosyl-3- α -rhamnosylglucoside (2).

ACKNOWLEDGEMENTS

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NOTE AND REFERENCES

- 1) K. Endo, K. Takahashi, T. Abe, and H. Hikino, *Heterocycles*, 1982, **19**, 261.
- 2) The plant previously assigned as *Forsythia koreana*¹⁾ was incorrect, and it should read *Forsythia viridissima*. Analysis of lignan derivatives also supported this identification.⁵⁾
- 3) K. Endo, K. Takahashi, T. Abe, and H. Hikino, *Heterocycles*, 1981, **16**, 1311; K. Endo and H. Hikino, *ibid.*, 1982, **19**, 2033; S. Nishibe, K. Okabe, H. Tsukamoto, A. Sakushima, and S. Hisada, *Chem. Pharm. Bull.*, 1982, **30**, 1048; S. Nishibe, K. Okabe, H. Tsukamoto, A. Sakushima, S. Hisada, H. Baba, and T. Akisada, *ibid.*, 1982, **30**, 4548.
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