New Sucrose Phenylpropanoid Esters from *Polygonum perfoliatum*

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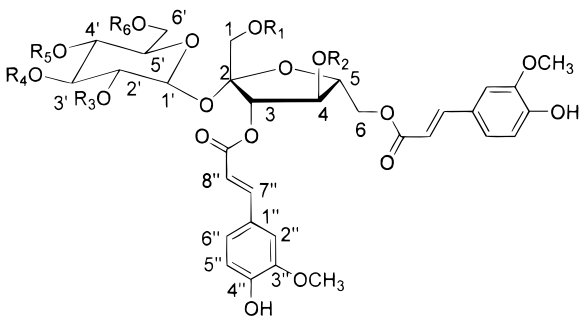
Five diferuloyl esters of sucrose, 6′-acetyl-3,6-diferuloylsucrose (helonioside B) (**1**); 2′,4′,6′-triacetyl-3,6-diferuloylsucrose (**2**); 1,2′,4′,6′-tetraacetyl-3,6-diferuloylsucrose (**3**); 1,2′,6′-triacetyl-3,6-diferuloylsucrose (**4**); and 2′,6′-diacetyl-3,6-diferuloylsucrose (**5**), were isolated, along with the 1,3,6-tri-*p*-coumaroyl-6′-feruloylsucroses, vanicoside A and vanicoside B, from the whole plant of *Polygonum perfoliatum* by various chromatographic methods. The structures of these phenylpropanoid glycosides were determined on the basis of their NMR and mass spectroscopic data. Compound **1** is a known compound, but **2**−**5** are new members of this class.

Phenylpropanoid esters of sucrose are common secondary metabolites in plants, which often show diverse biological activities.[1−3] In previous work on the genus *Polygonum*, we isolated two potent protein kinase C (PKC) inhibitory phenylpropanoid esters of sucrose, vanicosides A and B, from *P. pensylvanicum*, along with the inactive homologue, hydropiperoside.[4,5] Hydropiperoside was a known compound that had been isolated previously from *P. hydropiper*.[6] In subsequent work, we also isolated vanicosides C−F from *P. pensylvanicum*.[7] The biological activity of vanicosides A and B triggered a study of several other *Polygonum* species for similar, potential PKC inhibitors. *P. perfoliatum* (Polygonaceae), also known as speedweed or mile-a-minute plant, is a vine-type weed originally found in Asia, where there are reports of its use in raising white cell and platelet counts.[8] It is believed to have been introduced into the United States in the 1940s.[9] It is invasive and currently considered to be a major problem weed. The HPLC chromatogram of the ethanolic extract of *P. perfoliatum*, when compared to the chromatogram of the extract of *P. pensylvanicum*, as well as chromatograms of the isolated vanicosides, suggested that phenylpropanoid esters of sucrose related to the vanicosides were present in this plant. The ethanolic extract of *P. perfoliatum* was fractionated by chromatographic techniques, resulting in the isolation of vanicosides A and B,[10] four neoflavonoids,[11] and five diferuloyl esters of sucrose (**1**−**5**). Ester **1** was determined to be helonioside B, previously isolated from *Lilium longiflorum*,[12] but **2**−**5** were new compounds.

Results and Discussion

The dried whole plant of *P. perfoliatum* was ground to a powder and extracted with 95% EtOH in a Soxhlet extractor. Because the phenylpropanoid esters of sucrose of interest are very polar compounds, the dark gel, after evaporation, was triturated with petroleum ether to remove the majority of chlorophyll and nonpolar components. The remaining brown solid was then extracted with acetone. The acetone was removed in vacuo, and the resulting dark gel was subjected to column chromatography over Si gel to give relatively enriched fractions. These fractions were subjected to further column chromatography, dry column chromatography, flash column chromatography, and preparative TLC, as required, to isolate vanicosides A and B[10] and sucrose esters **1**−**5**.



	R_1	R_2	R_3	R_4	R_5	R_6
1	H	H	H	H	H	$COCH_3$
2	H	H	$COCH_3$	H	$COCH_3$	$COCH_3$
3	$COCH_3$	H	$COCH_3$	H	$COCH_3$	$COCH_3$
4	$COCH_3$	H	$COCH_3$	H	H	$COCH_3$
5	H	H	$COCH_3$	H	H	$COCH_3$

The electrospray HRMS of **1** gave an $[M - H]^-$ ion at *m/z* 735.1917, indicating a molecular formula of $C_{34}H_{40}O_{18}$. The ^1H NMR (Table 1) and COSY spectra of **1** indicated the presence of two feruloyl moieties, one acetyl moiety, and a sucrose moiety. The chemical shifts of the sucrose protons, and the subsequent downfield shifts of the C-1, C-3, C-2′, C-3′, and C-4′ protons in the ^1H NMR spectrum of the octaacetate (**6**) derived from **1**, indicated that the three ester moieties were located at C-3 and C-6 of the fructose moiety and C-6′ of the pyranose moiety. HMBC experiments, showing correlations between H-3, one 7″ proton, one 8″ proton, and one carbonyl carbon, confirmed that one of the feruloyl groups was located at C-3. The remaining feruloyl group was assigned to C-6 and the acetyl group to C-6′ based upon the fragmentation pattern in the negative ion LRFABMS. The fragment ion at *m/z* 531 ($[C_{26}H_{27}O_{12}]^-$) was due to the fructose ring with two feruloyl esters ($C_{34}H_{40}O_{18} - C_2H_3O - C_6H_{10}O_5$). Further fragmentation of this ion gave fragment ions at *m/z* 513 (−18, H_2O) and *m/z* 337 (−194, ferulic acid), similar to fragmentation patterns obtained from vanicosides A and B and hydropiperoside.[5] Thus, the second feruloyl group must be at C-6 and the acetyl group at C-6′. If a feruloyl ester was located at C-6′ and an acetyl group at C-6, there would be fragment ions due to the fructose ring at *m/z* 397, 379, and 333 (−60, acetic acid); no ions were detected at

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Table 1. ^{1}H NMR Chemical Shifts (δ in ppm, J in Hz at 300 MHz) for **1**−**6**[a]

C	**1**	**2**	**3**	**4**	**5**	**6**
1	3.60 m	3.43 d (11.7)	4.00 m	4.00 m	3.40 d (11.9)	4.15 m
		3.64 d (11.7)	4.18 m	4.20 m	3.57 d (11.9)	4.35 m
3	5.45 d (8.5)	5.55 d (7.7)	5.45 d (8.2)	5.49 d (8.5)	5.59 d (8.3)	5.65 d (6.3)
4	4.50 m	4.50 m	4.50 m	4.50 m	4.50 m	5.55 m
5	4.40 m	4.39 m	4.20 m	4.40 m	4.40 m	4.42 m
6	4.20 m	4.15 m	4.20 m	4.20 m	4.20 m	4.45 m
	4.50 m	4.50 m	4.50 m	4.50 m	4.50 m	4.55 m
1′	5.40 d (3.7)	5.60 d (3.7)	5.63 d (3.7)	5.56 d (3.6)	5.54 d (3.7)	5.72 d (3.5)
2′	3.44 dd (3.7, 10.1)	4.66 dd (3.7, 10.1)	4.72 dd (3.7, 10.1)	4.60 m	4.58 m	4.85 dd (3.6, 10.4)
3′	3.70 dd (9.7, 9.7)	4.00 m	4.00 m	3.86 m	3.88 m	5.45 dd (9.7, 10.3)
4′	3.30 dd (9.8, 9.8)	4.82 dd (9.3, 10.3)	4.85 dd (9.3, 10.2)	3.40 dd (9.7, 9.7)	3.40 m	5.00 dd (9.6, 10.1)
5′	4.20 m	4.30 m	4.26 m	4.20 m	4.22 m	4.35 m
6′	4.08 m	4.08 m	4.07 m	4.08 m	4.08 m	4.15 m
	4.50 m	4.18 m	4.18 m	4.18 m	4.50 m	4.35 m
2″	7.32, 7.35 each d (1.9)	7.34, 7.36 each d (1.9)	7.36, 7.38 each d (1.9)	7.34, 7.36 each d (1.9)	7.35 m	7.45, 7.50 each d (1.8)
5″	6.85, 6.86 each d (8.1)	6.84, 6.85 each d (8.1)	6.86, 6.89 each d (8.2)	6.84, 6.85 each d (8.1)	6.85, 6.86 each d (8.1)	7.10, 7.15 each d (8.1)
6″	7.12, 7.18 each dd (1.8, 8.2)	7.10−7.20 m	7.10−7.20 m	7.15, 7.19 each dd (1.8, 8.2)	7.13, 7.18 each dd (1.9, 8.2)	7.24−7.34 m
7″	7.60, 7.65 each d (15.9)	7.64, 7.68 each d (16.0)	7.62, 7.68 each d (15.9)	7.62, 7.67 each d (15.9)	7.61, 7.68 each d (16.0)	7.70, 7.75 each d (16.0)
8″	6.41, 6.44 each d (15.9)	6.45, 6.48 each d (15.9)	6.45, 6.48 each d (15.9)	6.46, 6.47 each d (15.9)	6.45, 6.47 each d (15.9)	6.60, 6.64 each d (16.0)
OCH_3	3.88, 3.90 each s	3.92 (2) s	3.92 (2) s	3.88, 3.90 each s	3.88, 3.90 each s	3.90 (2) s
$COCH_3$	1.98	1.90, 2.00−2.10 (2)	1.90, 2.00−2.10 (3)	1.90, 2.00−2.10 (2)	2.00−2.10 (2)	1.78, 1.90, 2.00, 2.04, 2.06, 2.07, 2.26 (2) each s

[a] Compounds **1**−**5** in Me_2CO-d_6, **6** in $CDCl_3$.

these *m*/*z* values. Based upon these data, **1** was identified as 6′-acetyl-3, 6-diferuloyl sucrose, also known as helonioside B.[12]

The structure elucidations of **2**−**5** were based upon the structure of **1**. The presence of two feruloyl moieties in each compound, **2**−**5**, was easily recognized by the characteristic ^{1}H NMR (Table 1) and COSY spectra in the region between δ 6 and δ 8. The ^{1}H NMR data for **2**−**5** (Table 1) also showed the characteristic resonances for a sucrose moiety, albeit with different chemical shifts for individual protons due to the substitution pattern. Finally, each spectrum indicated a different number of acetyl groups for each compound, although the exact number was difficult to determine in each case due to overlap with residual solvent resonances. Acetylation of each individual compound, **2**−**5**, however, resulted in the same octaacetate (**6**), identical to the octaacetate derived from **1**. These data indicated that the two feruloyl moieties in **2**−**5** were located at C-3 and C-6, as in **1**, and the structures differed only in the location and number of acetyl moieties.

The electrospray HRMS of **2** gave an $[M - H]^-$ ion at *m*/*z* 819.2086, indicating a molecular formula of $C_{38}H_{44}O_{20}$, and suggesting, in conjunction with the NMR data, a sucrose substituted with two feruloyl esters and three acetyl esters. The ^{1}H NMR and COSY spectra for the sucrose ring protons of **2** were similar to the ^{1}H NMR and COSY spectra of **1** (Table 1). Two doublets at δ 3.43 and δ 3.64 were coupled only to each other (J = 11.7 Hz) and were assigned to the two C-1 protons. The chemical shift of these protons suggested that C-1 was substituted by a hydroxyl moiety, not an acetate. Acetylation of **2** gave an octaacetate (**6**) identical to that obtained from acetylation of **1**, indicating that the two feruloyl moieties were located at C-3 and C-6 of the fructofuranose moiety in **2**. Comparison of the ^{1}H NMR spectrum of **2** with the spectrum of **6** identified downfield chemical shifts in the octaacetate spectrum for the 1-H_2 and 4-H resonances, but not for the 3-H and 6-H resonances. These data confirmed that the 3- and 6-positions were substituted by the feruloyl esters, and that the 1- and 4-positions bore hydroxyl moieties. In the spectrum of **2**, the chemical shifts of the 2′-H and 4′-H, δ 4.66 and δ 4.82, respectively, were shifted significantly downfield compared to the chemical shifts of the 2′-H and 4′-H, δ 3.44 and δ 3.3, in the spectrum of **1**. A downfield chemical shift was then observed for the 3′-H in the ^{1}H NMR spectrum of **6**. These data confirmed that the three acetyl groups were at the 2′-, 4′-, and 6′-positions. Therefore, **2** was determined to be 2′,4′,6′-triacetyl-3,6-diferuloylsucrose.

The electrospray HRMS of **3** showed an $[M - H]^-$ ion at *m*/*z* 861.2373, indicating a molecular formula of $C_{40}H_{46}O_{21}$, and suggesting, in conjunction with the NMR data, a sucrose substituted with two feruloyl and four acetyl esters. As noted above, **3** and **1** gave the same octaacetate (**6**), allowing the two feruloyl groups of **3** to be assigned to C-3 and C-6 of the fructofuranose moiety. The ^{1}H NMR (Table 1) and COSY spectra of **3** revealed additional downfield chemical shifts for the 1-H_2, 2′-H, and 4′-H resonances, in addition to the downfield shifts of the 3-H, 6-H_2, and 6′-H_2, when compared to the corresponding proton shifts in the spectrum of **1**. Comparison of the ^{1}H NMR spectrum of **3** to that of **6** showed significant downfield chemical shifts only for the 4-H and the 3′-H, relative to the spectrum of **3**, in the spectrum of **6**. Therefore, the four acetyl groups were located at C-1, C-2′, C-4′, and C-6′, and the structure of **3** was established as 1,2′,4′,6′-tetraacetyl-3,6-diferuloylsucrose.

The electrospray HRMS of **4** showed an $[M - H]^-$ ion at *m/z* 819.2232, indicating a molecular formula of $C_{38}H_{44}O_{20}$ and suggesting, in conjunction with the NMR data, a sucrose substituted with two feruloyl and three acetyl esters. Because acetylation of **4** again resulted in **6**, the two feruloyl groups were located at C-3 and C-6 of the fructofuranose moiety in **4**. The ^{1}H NMR (Table 1) and COSY spectra of **4** revealed additional downfield chemical shifts for the 1-H_2 and 2′-H resonances when compared to the spectrum of **1**. The ^{1}H NMR spectrum of **6** exhibited downfield chemical shifts for the 4-H, 3′-H, and 4′-H resonances relative to the spectrum of **4**. From these data, the structure of **4** was established as 1,2′,6′-triacetyl-3,6-diferuloylsucrose.

Finally, the electrospray HRMS of **5** showed an $[M - H]^-$ ion at *m/z* 777.1976, indicating a molecular formula of $C_{36}H_{42}O_{19}$ and suggesting, in conjunction with the NMR data, that **5** was a sucrose substituted with two feruloyl moieties and only two acetyl esters. Once again, acetylation of **5** resulted in **6**, confirming that the two feruloyl groups in **5** must be sited at C-3 and C-6 of the fructofuranose moiety. The ^{1}H NMR and COSY spectra of **5** revealed downfield chemical shifts for only the 6′-H_2 and the 2′-H resonances. The ^{1}H NMR spectrum of **6** exhibited additional downfield chemical shifts for the 1-H_2, 4-H, 3′-H, and 4′-H resonances. Therefore, **5** was established as 2′,6′-diacetyl-3,6-diferuloylsucrose.

Thus, in addition to vanicosides A and B and four 4-phenyldihydrocoumarins,[11] *P. perfoliatum* has been shown to produce phenylpropanoid glycosides **1**−**5**. These glycosides are homologues of helonioside B (**1**), a phenylpropanoid glycoside previously isolated from a different genus.[12] Glycosides **1**−**5** have not yet been subjected to bioassays.

Experimental Section

General Experimental Procedures. Routine NMR spectra were recorded at Virginia Commonwealth University on a General Electric QE−300 spectrometer at 300 MHz (^{1}H) in acetone-d_6 or $CDCl_3$. IR data were obtained from a Perkin-Elmer 1600 series FTIR. Positive and negative ion HRMS were acquired in the Department of Chemistry of Virginia Commonwealth University using an IonSpec 4.7 T Fourier Transform Ion Cyclotron Resonance mass spectrometer equipped with an electrospray injector at 0.2 μL/min. Negative ion LRMS were acquired using a JEOL SX-102/102 four-sector tandem mass spectrometer at Philip Morris USA Research Laboratories in Richmond, VA.

Plant Material. Whole plants of *P. perfoliatum* were collected in Reston, Virginia, in August 1994 and August 1997, and were identified by Claudia Thompson-Diehl of the Reston Association in collaboration with Dr. Nathan Hartwig of Pennsylvania State University. Reference specimens (VCU 8159401 and VCU 8229701) were preserved at Virginia Commonwealth University.

Extraction and Isolation. The dried, ground, whole plant (4 kg) was extracted with 95% EtOH (12 L) in a Soxhlet extractor for 24 h. (Room-temperature extraction gave the same product mixture, but in lower yield.) The EtOH was evaporated to give a dark gel. This gel was extracted with petroleum ether (35−60 °C) (800 mL × 3) to remove most of the chlorophyll. The remaining light yellow solid was again extracted with Me_2CO (800 mL × 3). The dark acetone solution was evaporated and dried by vacuum to a dark gel. This gel was separated by column chromatography over Si gel eluted successively with CH_2Cl_2, 5% MeOH in CH_2Cl_2, 10% MeOH in CH_2Cl_2, and 15% MeOH in CH_2Cl_2, collected in six fractions.

The fifth fraction was applied to dry column chromatography over Si gel, eluted by 5% MeOH in CH_2Cl_2, 10% MeOH in CH_2Cl_2, and 15% MeOH in CH_2Cl_2. One fraction, eluted with 5% MeOH in CH_2Cl_2, was applied to dry column chromatography packed with Si gel and eluted with CH_2Cl_2/CH_3CN/MeOH (8:1:1). The combined fractions were subjected to repeated preparative TLC over Si gel, developed multiple times with CH_2Cl_2/CH_3CN/MeOH (7:2:1) and CH_2Cl_2/MeOH (10:1) to give **1** (10.5 mg).

The third fraction was applied to dry column chromatography packed with Si gel, eluted with CH_2Cl_2/hexane/EtOAc (6:3:1) and CH_2Cl_2/hexane/MeOH (6:3:1), collected in two fractions. The second fraction was filtered through charcoal to remove chlorophyll. The yellowish filtrate was applied to dry column chromatography CH_2Cl_2/EtOAc (7:3), 5% MeOH in CH_2Cl_2, and 15% MeOH in CH_2Cl_2. All the fractions were examined by TLC and combined to give four fractions. The resulting third and fourth fractions were applied to repeated preparative TLC over Si gel and developed with CH_2Cl_2/hexane/MeOH (6:3:2) to give relatively separated fractions. These fractions were applied again to repeated preparative TLC over Si gel, eluted by CH_2Cl_2/MeOH (9:1), 7% MeOH in CH_2Cl_2, and CH_2Cl_2/CH_3CN (3:2), or CH_2Cl_2 (9:1) in MeOH and CH_2Cl_2/hexane/MeOH (9:3:1) to give **2** (4.2 mg), **3** (2.5 mg), **4** (1 mg), and **5** (3.3 mg).

6′-Acetyl-3,6-diferuloylsucrose (helonioside B) (1): yellowish glass; IR (KBr) ν_{max} 3412, 1707, 1631, 1602; ^{1}H NMR, see Table 1; ^{13}C NMR (Me_2CO-d_6, data from HMQC and HMBC) δ 58.3 (OCH_3), 67.1, 67.5 (C-1, C-6, C-6′), 73.5 (C-4′), 73.8 (C-5′), 74.9 (C-2′), 76.8 (C-4, C-3′), 81.1 (C-3), 82.9 (C-5), 94.1 (C-1′), 102.5 (C-2), 113.1 (C-2″), 117.1 (C-8″), 117.7 (C-5″), 125.5, 126.0 (C-6″), 127.4 (C-1″), 147.6, 148.2 (C-7″), 148.7 (C-3″), 150.4 (C-4″), 166.8 (C-9″); HR ES−MS *m/z* 735.1917 $[M - H]^-$ ($C_{34}H_{40}O_{18}$−H req 735.2136); negative ion FABMS 735, 693, 675, 559, 541, 531, 513, 337.

2′,4′,6′-Triacetyl-3,6-diferuloylsucrose (2): yellowish glass; IR (KBr) ν_{max} 3413, 1743, 1719, 1631, 1602; ^{1}H NMR, see Table 1; HR ES−MS *m/z* 819.2086 $[M - H]^-$ ($C_{38}H_{44}O_{20}$−H req 819.2347).

1,2′,4′,6′-Tetraacetyl-3,6-diferuloylsucrose (3): yellowish glass; IR (KBr) ν_{max} 3424, 1737, 1719, 1632, 1602; ^{1}H NMR, see Table 1; HR ES−MS *m/z* 861.2373 $[M - H]^-$ ($C_{40}H_{46}O_{21}$−H req 861.2453).

1,2′,6′-Triacetyl-3,6-diferuloylsucrose (4): yellowish glass; IR (KBr) ν_{max} 3413, 1737, 1719, 1637, 1602; ^{1}H NMR, see Table 1; HR ES−MS: *m/z* 819.2232 $[M - H]^-$ ($C_{38}H_{44}O_{20}$−H req 819.2347).

2′,6′-Diacetyl-3,6-diferuloylsucrose (5): yellowish glass; IR (KBr) ν_{max} 3401, 1719, 1654, 1631, 1601; ^{1}H NMR, see Table 1; HR ES−MS *m/z* 777.1976 $[M - H]^-$ ($C_{36}H_{42}O_{19}$−H req 777.2241).

1,4,2′,3′,4′,6′,4″,4‴-Octacetyl-3,6-diferuloylsucrose (6): Individual samples (0.5−2 mg) of **1**−**5** were each mixed with 1 mL of pyridine and stirred to dissolve, and 1 mL of acetic acid anhydride was then added. Each solution was stirred under ambient temperature for 24 h. Each solution was poured into ice-water and extracted with chloroform three times. The combined chloroform layer from each sample was washed with water, dried with anhydrous magnesium sulfate, and evaporated in a vacuum to give **6**: IR (KBr) ν_{max} 1748, 1637, 1602; ^{1}H NMR, see Table 1.

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References and Notes

(1) Jimenez, C.; Riguera, R. *Nat. Prod. Rep.* **1994**, 591−606.
(2) Kernan, M. A.; Amarquaye, A.; Chen, J. L.; Chan, J.; Sesin, D. F.; Parkinson, N.; Ye, Z.; Barrett, M.; Bales, C.; Stoddart, C. A.; Sloan, B.; Blanc, P.; Limbach, C.; Mrisho, S.; Rozhon, E. J. *J. Nat. Prod.* **1998**, *61*, 564−570.
(3) Qian-Cutrone, J.; Huang, S.; Trimble, J.; Li, H.; Lin, P.; Alam, M.; Klohr, S. E.; Kadow, K. F. *J. Nat. Prod.* **1996**, *59*, 196−199.
(4) Zimmermann, M. L.; Sneden, A. T. *J. Nat. Prod.* **1994**, *57*, 236−242.
(5) Sneden, A. T.; Zimmermann, M. L.; Sumpter, T. L. *J. Mass Spectrom.* **1995**, *30*, 1628−1632.
(6) Fukuyama, Y.; Sato, T.; Miura, I.; Asakawa, Y.; Takemoto, T. *Phytochemistry* **1983**, *22*, 549−552.
(7) Brown, L. L.; Larson, S. R.; Sneden, A. T. *J. Nat. Prod.* **1998**, *61*, 762−766.
(8) Ren, Y. C. *Zhong Hua Nei Ke Za Zhi* **1977**, 46 (Translated by C. S. Cheung).
(9) Oliver, J. D. *Bull. Ecol. Soc. Am.* **1994**, *75*, 169−170.
(10) Vanicosides A and B were isolated by preparative TLC from selected fractions of an initial extract of *P. perfoliatum* and identified by spectroscopic techniques followed by comparison to authentic samples. The yield of vanicoside A was 415 mg/kg, and the yield of vanicoside B was 1.39 g/kg.
(11) Sun, X.; Sneden, A. T. *Planta Med.* **1999**, *65*, 671−673.
(12) Nakano, K.; Murakami, K.; Takaishi, Y.; Tomimatsu, T. *Chem. Pharm. Bull.* **1986**, *34*, 5005−5010.

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