GALLOYL-OXYPAEONIFLORIN, SUFFRUTICOSIDES A, B, C, AND D, FIVE NEW ANTIOXIDATIVE GLYCOSIDES, AND SUFFRUTICOSIDE E, A PAEONOL GLYCOSIDE, FROM CHINESE MOUTAN CORTEX

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Five new antioxidative glycosides named galloyl-oxypaeoniflorin, suffruticosides A, B, C, and D, and a new paeonol glycoside named suffruticoside E have been isolated from Chinese Moutan Cortex, the root cortex of *Paeonia suffruticosa* ANDREWS, together with antioxidative galloyl-paeoniflorin. Their structures were elucidated on the basis of chemical and physicochemical evidences. Galloyl-oxypaeoniflorin, galloyl-paeoniflorin, suffruticosides A, B, C, and D showed more potent radical scavenging and antioxidative effects than α-tocopherol.

KEYWORDS *Paeonia suffruticosa*; Moutan Cortex; Paeoniaceae; galloyl-oxypaeoniflorin; suffruticoside; radical scavenging effect; antioxidative principle

Moutan Cortex(Botanpi in Japanese), the root cortex of *Paeonia suffruticosa* ANDREWS(Paeoniaceae), is one of the most important crude drugs known as an analgesic, a sedative, an antiinflammatory agent, and remedy for female diseases in Chinese traditional medicine, and it is prescribed particularly in various Chinese preparations used for treatment of "Oketsu" syndrome (blood stagnation). Chemical studies on Moutan Cortex have been carried out by many investigators, and the presence of paeonol[1] and its glycosides, paeonoside,[2] paeonolide,[3] and apiopaeonoside,[4] as well as various monoterpene glycosides,[5,6] paeoniflorin, oxypaeoniflorin, benzoyl-paeoniflorin, and benzoyl-oxypaeoniflorin has so far been reported.

During the course of chemical studies on the bioactive constituents of Moutan Cortex,[6] we isolated five new antioxidative glycosides named galloyl-oxypaeoniflorin(2) and suffruticosides A(5), B(6), C(8), and D(9) from Chinese Moutan Cortex. This paper deals with evidence for their structures. In addition, a new paeonol glycoside, suffruticoside E(10), was chemically elucidated.

By monitoring with a radical scavenging effect on α,α-diphenylpicrylhydrazyl(DPPH)radical,[7] five new active principles, galloyl-oxypaeoniflorin (2 , 0.0010% from the crude drug), suffruticosides A (5 , 0.0004%), B(6 , 0.0003%), C(8 , 0.0002%), and D (9 , 0.0004%)were isolated from Chinese Moutan Cortex by use of various chromatographic separations together with suffruticoside E (10, 0.0005%) and galloyl-paeoniflorin[8] (3, 0.0005%).

Galloyl-oxypaeoniflorin (2), white powder, $[\alpha]_D$ -27.3° (EtOH), $C_{30}H_{32}O_{16}$,[9] UV(EtOH): 215(17000), 267(9500) nm, IR (KBr): 3450, 1701, 1653, 1609 cm^{-1}, was shown to possess one each of *p*-hydroxybenzoyl group and galloyl group in its ^1H NMR spectrum.[10] Comparison of ^{13}C NMR data for 2 with those for oxypaeoniflorin (1)[6] and benzoyl-oxypaeoniflorin[6] led us to presume the structure of 2 as having 6'-galloyl group. The SIMS spectrum of 2 showed the quasimolecular ion peak at m/z 649(M+H)$^+$ and the fragment ion peak (i , m/z 315, $C_{13}H_{15}O_9$) formed from 6'-galloyl glucosyl moiety. Furthermore, the selective alkaline hydrolysis of 2 with 1% KOH liberated 1 together with gallic acid. Based on this evidence, the structure of galloyl-oxypaeoniflorin(2) has been clarified as shown.

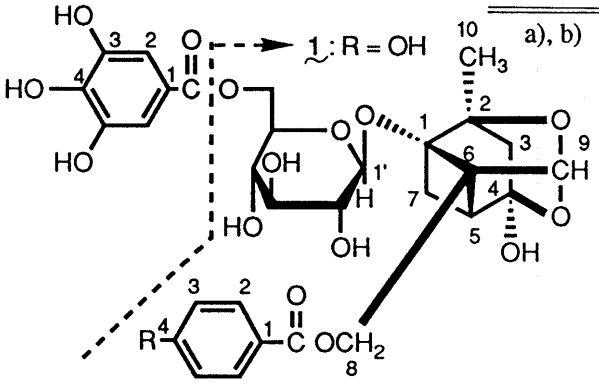
Suffruticoside A(5), white powder, $[\alpha]_D$ -57.8° (MeOH), $C_{27}H_{32}O_{16}$, UV (EtOH): 219(30000), 272(16000) nm, IR(KBr): 3450, 1703, 1651, 1605 cm^{-1}, liberated apiopaeonoside(7) and gallic acid on alkaline hydrolysis. The FAB-MS spectrum of 5 showed the quasimolecular ions at m/z 635(M+Na)$^+$ and m/z 613(M+H)$^+$, and the fragment ion peak at m/z 285 (ii) formed from the oligosaccharide moiety was observed. The ^1H NMR spectrum of 5 showed signals ascribable to two anomeric protons and galloyl-bearing methylene protons [δ 4.83, 4.80 (2H, ABq, J=11Hz, 4"-H_2]. Comparison of ^{13}C NMR data for 5 with those for 7 led us to consider that the galloyl group in 5 is attached to 4"-OH of apiofuranosyl moiety and consequently the structure of suffruticoside A(5) has been determined.

The structures of suffruticosides B(6),[11] C(8),[12] and D(9)[13] have been elucidated in the same manner. Upon the alkaline hydrolysis, 6 liberated 7 and gallic acid, whereas similar treatment of 8 and 9 furnished paeonolide(11) and gallic acid

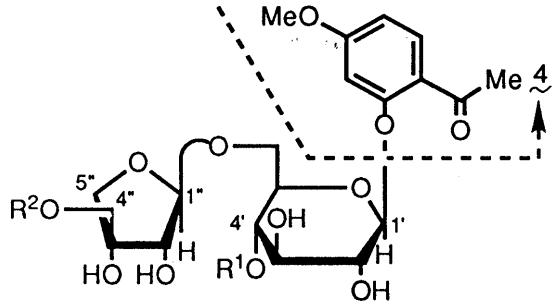
Table I. ^{13}C NMR Data for 2, 5, 6, 8, 9 and 10 (75 MHz, pyridine-d_5, δc)

		2			5	6	8	9	10
Monoterpene moiety	C-1	88.8	Paeonol moiety	C-1	121.9	122.1	122.0	121.9	121.8
	C-2	85.9		C-2	160.0	159.9	159.9	159.8	159.7
	C-3	44.6		C-3	102.4	102.3	102.0	102.2	101.6
	C-4	105.9		C-4	164.8	164.9	164.8	164.8	164.8
	C-5	43.6		C-5	108.0	108.4	108.4	108.9	108.8
	C-6	71.5		C-6	132.1	132.2	132.1	132.1	135.6
	C-7	22.6		Me	32.3	32.4	32.3	32.3	32.3
	C-8	60.6		C=O	197.2	197.0	197.2	197.0	197.1
	C-9	101.5		OMe	55.6	55.7	55.6	55.8	55.8
	C-10	19.7	β-D-Gluco-	C-1'	102.4	102.4	102.5	101.7	101.8
β-D-Gluco-	C-1'	100.0	pyranosyl	C-2'	74.6 a)	74.6 a)	74.5	74.1	73.3
pyranosyl	C-2'	74.7	moiety	C-3'	78.4 a)	76.0	78.6	75.9 a)	88.3
moiety	C-3'	78.0		C-4'	71.5	72.3	71.0	72.3	69.2
	C-4'	71.2		C-5'	77.2	74.9 a)	77.5	75.3 a)	77.0
	C-5'	75.0		C-6'	69.1	68.5	70.4	69.4	69.7
	C-6'	64.4	α-L-Arabino-	C-1"	110.6	111.2	106.0	105.6	105.9
p-Hydroxy-	C-1	121.1 a)	pyranosyl	C-2"	78.3	77.7	72.0 a)	71.9	72.2
benzoyl	C-2	132.2	or β-D-apio-	C-3"	78.8 a)	80.2	72.6 a)	74.5	75.3
moiety	C-3	115.9	furanosyl	C-4"	67.4	65.4	72.8	69.1	69.2
	C-4	163.4	moiety	C-5"	74.6	75.1	64.8	66.7	66.8
	C=O	166.5 b)		C-1	120.8	120.7	121.2	120.7	
Galloyl	C-1	121.0 a)	Galloyl	C-2	110.2	110.5	110.3	110.5	
moiety	C-2	110.0	moiety	C-3	147.5	147.6	147.4	147.5	
	C-3	147.4		C-4	141.0	141.2	140.8	141.2	
	C-4	140.9		C=O	167.0	166.7	167.0	166.9	
	C=O	167.0 b)	β-D-Gluco-	C-1'''					105.5
			pyranosyl	C-2'''					74.3
			moiety	C-3'''					78.1
				C-4'''					71.4
				C-5'''					78.6
				C-6'''					62.3

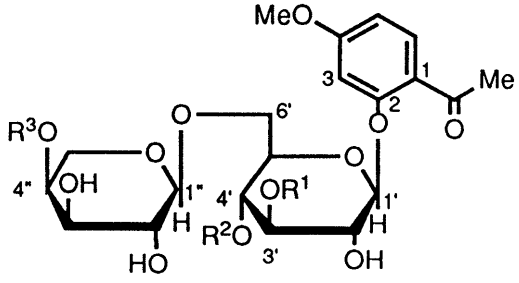
a), b) Assignments may be interchangeable within the same column.



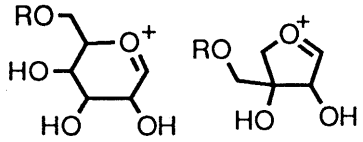
galloyl-oxypaeoniflorin (2) : R = OH
galloyl-paeoniflorin (3) : R = H



suffruticoside A (5) : R^1 = H, R^2 = galloyl
suffruticoside B (6) : R^1 = galloyl, R^2 = H,
apiopaeonoside (7) : $R^1 = R^2$ = H



suffruticoside C (8) :
$R^1 = R^2$ = H, R^3 = galloyl
suffruticoside D (9) :
$R^1 = R^3$ = H, R^2 = galloyl
suffruticoside E (10) :
R^1 = β-D-glucopyranosyl, $R^2 = R^3$ = H
paeonolide (11) : $R^1 = R^2 = R^3$ = H



i : R = galloyl ii : R = galloyl

as the common products. The FAB-MS spectrum of 6, 8, and 9 showed quasimolecular ion peaks at m/z 635(M+Na)$^+$ and m/z 613(M+H)$^+$, and fragment ion peaks formed from the oligosaccharide moiety. Finally, the ^{1}H and ^{13}C NMR examination of 6, 8, and 9 has led to the formulation of suffruticosides B(6), C(8), and D(9).

Suffruticoside E(10), white powder, $[\alpha]_D$ -47.8° (H_2O), $C_{26}H_{38}O_{17}$, UV(EtOH): 215(17000), 268(9600) nm, IR(KBr): 3450, 1661, 1605 cm^{-1}, liberated paeonol(4) together with D-glucose and L-arabinose in a 2:1 ratio on acid hydrolysis. The ^{1}H and ^{13}C NMR signals of 10 could be analyzed completely by use of ^{1}H-^{1}H-COSY, ^{1}H-^{13}C-COSY and HOHAHA experiments : δ 4.56(dd, J=2, 12Hz, 6'-H), 4.32(dd, J=7, 7Hz, 3'-H), 4.81(d, J=8Hz, 1"-H), 5.33(d, J=8Hz, 1"'-H), 5.60(d, J=7Hz, 1'-H), 7.25(d, J=2Hz, 3-H). The NOEs were observed between the following pairs of protons : 3-H&1'-H ; 3'-H&1"'-H ; 6'-H&1"-H. Based on this evidence together with ^{13}C NMR analysis, the structure of suffruticoside E(10) was determined as shown.

As given in Table II, galloyl-oxypaeoniflorin(2), galloyl-paeoniflorin(3), suffruticosides A(5), B(6), C(8), and D(9) showed more potent radical scavenging effects than α-tocopherol, and oxypaeoniflorin(1) was found to exhibit a weak radical scavenging effect.

Table II. Radical Scavenging Effect on DPPH Radical for Constituents from Moutan Cortex

Compounds	50 % Reduc. (10^{-8}M)
Oxypaeoniflorin(1)	85.48
Galloyl-oxypaeoniflorin(2)	2.87
Galloyl-paeoniflorin(3)	2.69
Suffruticoside A(5)	3.10
Suffruticoside B(6)	3.33
Apiopaeonoside(7)	No effect
Suffruticoside C(8)	3.30
Suffruticoside D(9)	2.54
Suffruticoside E(10)	No effect
Paeonolide(11)	No effect
Paeoniflorin	No effect
α-Tocopherol	4.88

Amount required for 50% reduction of DPPH (2×10^{-7}M, 0.079mg) solution; Measurement in acetic acid buffer (pH 5.5).

Furthermore, the antioxidative activity of those compounds was examined by the Ferric thiocyanate method,[14] and all of those compounds showed stronger activity than α-tocopherol at a concentration of 0.002%. These antioxidative glycosides might be useful as natural antioxidants because of their water solubility.

REFERENCES AND NOTES

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