Supplementary data

Two new phenolic glycosides with anti-complementary activity from the roots of *Sanguisorba officinalis* L.

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Abstract: *Sanguisorba officinalis* L. is a traditional herbal plant that belongs to the genus *Sanguisorba* and the family Rosaceae. Two new phenolic glycosides (1–2), ten known phenolics (3–12), and six known monoterpenoid glycosides (13–18) were isolated from the roots of *S. officinalis* using silica gel column and preparative middle pressure liquid chromatography (MPLC). The chemical structures were elucidated based on extensive spectroscopic experiments, including 1D and 2D NMR as well as HR-ESI-MS, and comparison with those reported in the literature. Compounds 3–5, and 13 were isolated from the Rosaceae family and compound 7 was obtained from the genus *Sanguisorba* for the first time. Additionally, all compounds were evaluated for their anti-complementary activities against the classical pathway. Furthermore, compounds 1, 5, 9, and 14 showed significant anti-complementary activities with the 50% hemolytic inhibition concentrations (CH₅₀) values of 0.40 ± 0.03, 0.57 ± 0.01, 0.51 ± 0.07, and 0.53 ± 0.05 mM, respectively.

Keywords: *Sanguisorba officinalis* L.; Rosaceae; phenolic glycoside; monoterpenoid glycoside; anti-complementary activity

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Table S1: Anti-complementary activity through the classical pathway (CP) of compounds 1–18

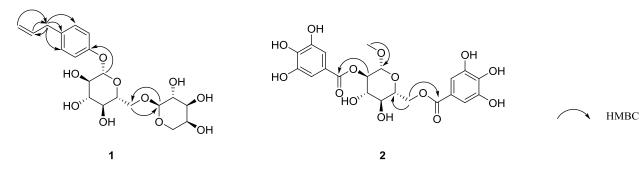


Figure S1: The key HMBC correlations of compounds 1–2

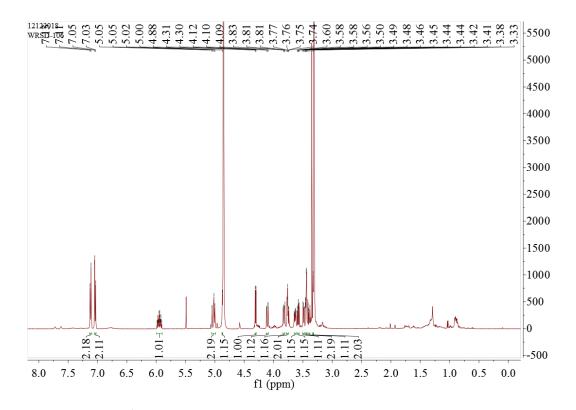


Figure S2: ¹H NMR spectrum of compound **1** in methanol- d_4 (500 MHz)

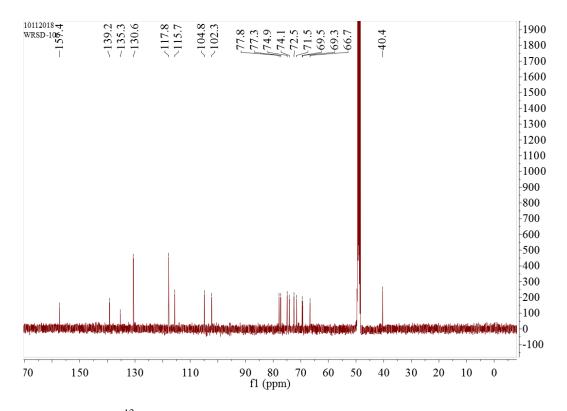


Figure S3: ¹³C NMR spectrum of compound **1** in methanol- d_4 (125 MHz)

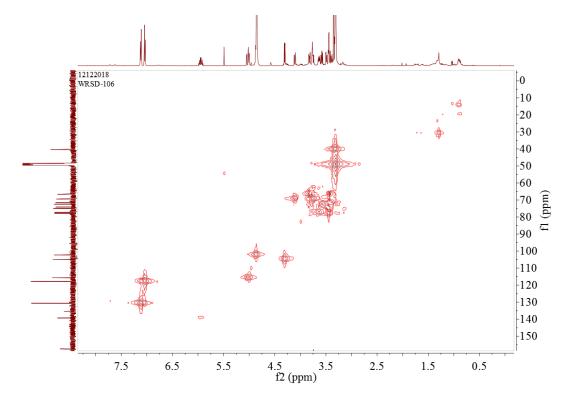


Figure S4: HMQC spectrum of compound 1 in methanol- d_4

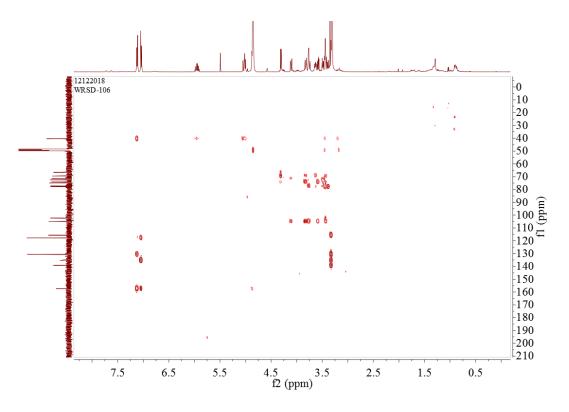


Figure S5: HMBC spectrum of compound $\mathbf{1}$ in methanol- d_4

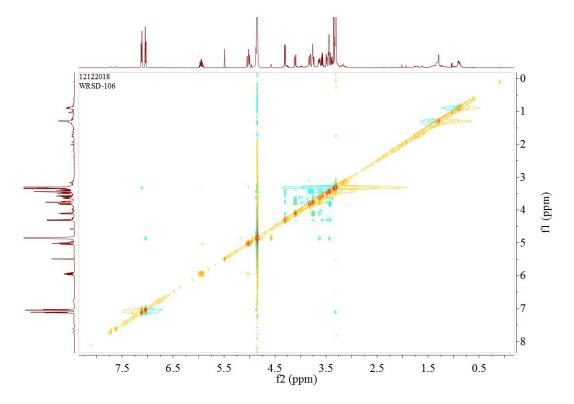


Figure S6: NOESY spectrum of compound 1 in methanol- d_4

Mass Spectrum SmartFormula Report

Analysis Info

 Analysis Name
 D:\Data\20190313\WRSD-106_P1-A-3_01_10849.d

 Method
 Ic-ms4-hr-low.m

 Sample Name
 WRSD-106

 Comment
 WRSD-106

Acquisition Date 3/13/2019 11:47:17 PM

Operator zlwei

Instrument / Ser# micrOTOF-Q II 10351

Scan End 1200 m/z Set Collision Cell RF 100.0 Vpp Set Divert Valve Was) Vmin	200 °C 5.0 l/min Waste	Set Dry Heater Set Dry Gas Set Divert Valve	4500 V -500 V 100.0 Vpp	lon Polarity Set Capillary Set End Plate Offset Set Collision Cell RF	ESI Active 50 m/z 1200 m/z	Source Type Focus Scan Begin Scan End
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			451.1570			
		295.1034				
133.0524	201.0916		. Lulu	589.1989	670.2253	

Meas. m/z	π	Formula	Score	m/z	err (mDa)	err (ppm)	mSigma	rdb	e ⁻ Conf	N-Rule
451.1570	- 4	C 20 H 28 Na O 10	96.12	451.1575	0.4	en (ppin) 1.0	10.9	6.5	even	ok
401.1070										
	2	C 22 H 27 O 10	17.80	451.1599	2.8	6.3	11.7	9.5	even	ok
	3	C 18 H 23 N 6 O 8	100.00	451.1572	0.2	0.3	15.3	10.5	even	ok
	4	C 21 H 24 N 4 Na O 6	38.93	451.1588	1.8	3.9	16.7	11.5	even	ok
	5	C 17 H 27 N 2 O 12	55.52	451.1559	-1.2	-2.6	18.3	5.5	even	ok
	6	C 19 H 19 N 10 O 4	45.02	451.1585	1.5	3.3	19.0	15.5	even	ok
	7	C 17 H 20 N 10 Na O 4	63.75	451.1561	-0.9	-2.0	19.1	12.5	even	ok
	8	C 15 H 15 N 16 O 2	51.02	451.1558	-1.2	-2.6	21.9	16.5	even	ok
	9	C 18 H 16 N 14 Na	73.60	451.1575	0.4	0.9	24.0	17.5	even	ok
	10	C 16 H 24 N 6 Na O 8	22.91	451.1548	-2.3	-5.0	24.3	7.5	even	ok
	11	C 14 H 19 N 12 O 6	17.39	451.1545	-2.5	-5.6	26.0	11.5	even	ok
	12	C 13 H 16 N 16 Na O 2	5.74	451.1534	-3.6	-8.0	28.5	13.5	even	ok
	13	C 15 H 28 N 2 Na O 12	5.80	451.1534	-3.6	-8.0	28.6	2.5	even	ok
	14	C 22 H 20 N 8 Na O 2	9.56	451.1601	3.1	6.9	28.6	16.5	even	ok
	15	C 20 H 15 N 14	12.00	451.1599	2.8	6.3	30.3	20.5	even	ok
	16	C 11 H 11 N 22	3.93	451.1532	-3.9	-8.6	31.1	17.5	even	ok
	17	C 13 H 23 N 8 O 10	3.69	451.1532	-3.9	-8.6	34.1	6.5	even	ok
	18	C 29 H 23 O 5	6.80	451.1540	-3.0	-6.7	44.4	18.5	even	ok
	19	C 7 H 16 N 20 Na O 3	2.88	451.1606	3.6	8.0	53.0	9.5	even	ok
	20	C 5 H 11 N 26 O	3.83	451.1604	3.3	7.4	53.4	13.5	even	ok
	21	C 30 H 19 N 4 O	14.03	451.1553	-1.7	-3.8	57.2	23.5	even	ok

Figure S7: HR-ESI-MS of compound 1

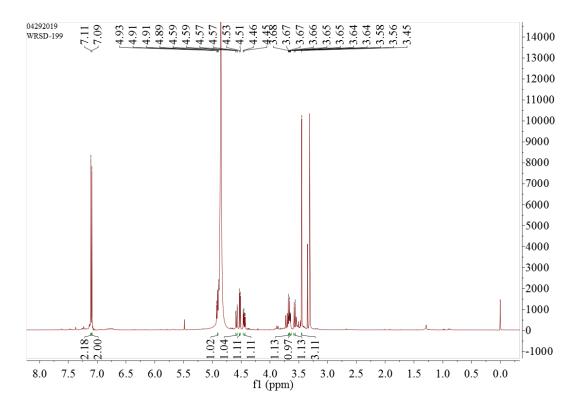


Figure S8: ¹H NMR spectrum of compound **2** in methanol- d_4 (500 MHz)

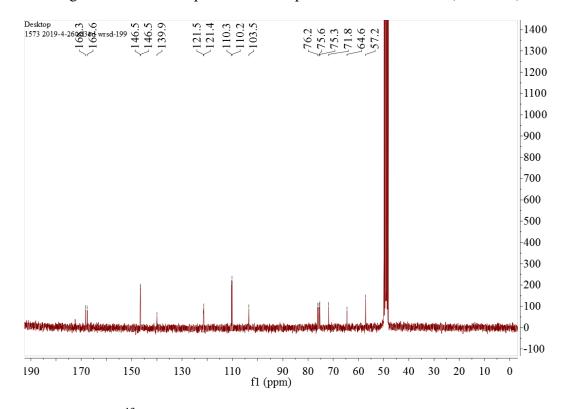


Figure S9: ¹³C NMR spectrum of compound **2** in methanol- d_4 (125 MHz)

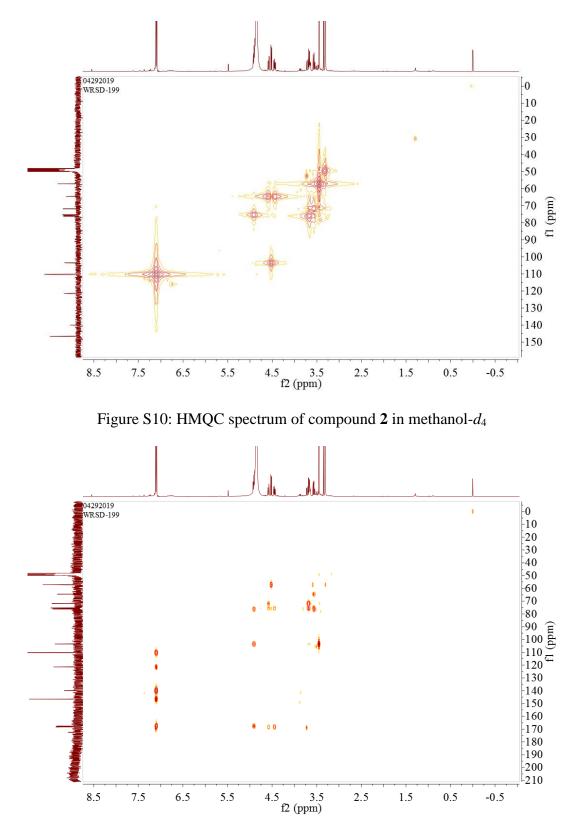


Figure S11: HMBC spectrum of compound 2 in methanol- d_4

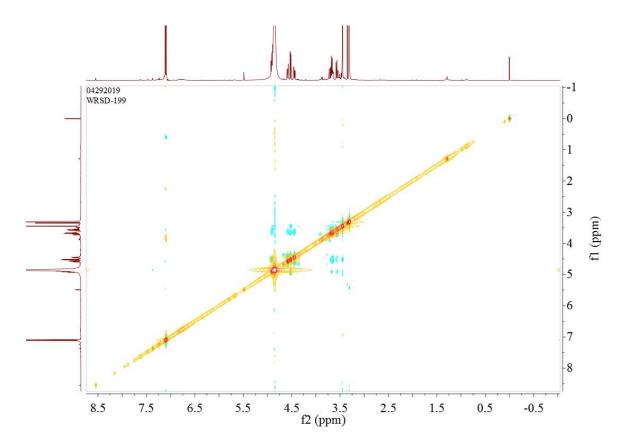


Figure S12: NOESY spectrum of compound 2 in methanol- d_4

	Mass	Spectrum	Sm	artFor	mula	Rep	oort			
Method Ic	:\Users\zlwei\D -ms3-hr-low.m SD-199	9esktop∖data\W 1	SD-199_	P1-B-2_0	1_12633) Operat	.d or zlw	0 2019/6/ ei OTOF-G		21:42:4 888.10	
Acquisition Para	amet									_
Source Type Focus Scan Begin Scan End	ESI Active 50 m/z 1500 m/z	lon Polari Set Capill Set End Pi Golfset Collis Gell RF	ary 45 ate -5	ositive 500 V 500 V 00.0 Vpp	Se Se Se	et Dry G			Bar 廢 I/min	
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×10 ⁴										
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4										
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2			P							
2			P							
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1	420	449.0716 440 46		480	499(10)	59	520		540	п
0400		440 460			500					
0 400 Meas. m/z	# Ion Formu	440 480	[ppm]	mSigma ≢	500 # mSigma	Score	rdb e	-	540	٤u
1 0 400		440 460			500		rdb e 30.5 e	- C		łu
1 0 400 Meas. m/z	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5	440 460 a m/z err 467.0788 467.0815 467.0847	[ppm] -6.3 -0.5 6.3	mSigma # 17.2 23.1 34.1	500 # mSigma 1 2 3	Score 13.47 100.00 9.08	rdb e 30.5 e 29.5 e 21.5 e	ven		2u
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855	[ppm] -6.3 -0.5 6.3 8.1	mSigma # 17.2 23.1 34.1 45.9	# mSigma 1 2 3 4	Score 13.47 100.00 9.08 3.66	rdb e 30.5 e 29.5 e 21.5 e 33.5 e	ven ven ven		ł
1 0 400 Meas. m/z	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885	[ppm] -6.3 -0.5 6.3 8.1 5.9	mSigma # 17.2 23.1 34.1 45.9 7.0	# mSigma 1 2 3 4 1	Score 13.47 100.00 9.08 3.66 40.98	rdb e 30.5 e 29.5 e 33.5 e 22.5 e	ven ven ven ven		łu
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H18N3O12	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885	[ppm] -6.3 -0.5 6.3 8.1 5.9 5.9	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8	# mSigma # mSigma 2 3 4 1 2	Score 13.47 100.00 9.08 3.66 40.98 48.55	rdb e 30.5 e 29.5 e 21.5 e 33.5 e 22.5 e	ven ven ven ven ven		lu
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H18N3O12	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885	[ppm] -6.3 -0.5 6.3 8.1 5.9	mSigma # 17.2 23.1 34.1 45.9 7.0	# mSigma 1 2 3 4 1	Score 13.47 100.00 9.08 3.66 40.98	rdb e 30.5 e 29.5 e 21.5 e 33.5 e 22.5 e 11.5 e	ven ven ven ven		l
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C18H6N17O2 2 C18H18N3O12 3 C15H10N1306 4 C25H14N3O7 5 C28H10N7O3	440 46 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0872 468.0826 468.0840	[ppm] -6.3 -0.5 6.3 8.1 5.9 5.9 3.0 -6.6 -3.8	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6	+	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91	rdb e 30.5 e 21.5 e 33.5 e 22.5 e 11.5 e 17.5 e 20.5 e	ven ven ven ven ven ven ven ven		łu
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H16N3O12 3 C15H10N13O6 4 C25H14N3O7 5 C28H10N7O3 6 C30H14NO5	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0885 468.0826 468.0840 468.0866	[ppm] -6.3 -0.5 6.3 8.1 5.9 3.0 -6.6 -3.8 2.0	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 41.6 48.1	# mSigma # mSigma 2 3 4 1 2 3 4 5 6	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56	rdb e 30.5 e 29.5 e 33.5 e 22.5 e 11.5 e 20.5 e 25.5 e 24.5 e	ven ven ven ven ven ven ven ven ven		tu
Meas. m/z 400 468.0857	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C18H6N17O2 2 C18H18N3O12 3 C18H10N13O6 4 C28H14N3O7 5 C28H14N3O7 6 C30H14N05 7 C31H10N5O	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0885 468.0872 468.0840 468.0840 468.0886 468.0880	[ppm] -6.3 -0.5 6.3 8.1 5.9 3.0 -6.6 -3.8 2.0 4.8	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 48.1 59.6	# mSigma 1 2 3 4 1 2 3 4 5 6 6 7	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56 22.19	rdb e 30.5 e 29.5 e 33.5 e 22.5 e 11.5 e 17.5 e 20.5 e 24.5 e 29.5 e	ven ven ven ven ven ven ven ven ven ven		2
1 400 Meas. m/z 467.0818	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H16N3O12 3 C15H10N13O6 4 C25H14N3O7 5 C28H10N7O3 6 C30H14NO5	440 460 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0885 468.0826 468.0840 468.0866	[ppm] -6.3 -0.5 6.3 8.1 5.9 3.0 -6.6 -3.8 2.0	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 41.6 48.1	# mSigma # mSigma 2 3 4 1 2 3 4 5 6	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56	rdb e 30.5 e 29.5 e 21.5 e 22.5 e 11.5 e 17.5 e 20.5 e 24.5 e 28.5 e	ven ven ven ven ven ven ven ven ven		2
Meas. m/z 400 468.0857	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H18N3O12 3 C15H10N13O6 4 C25H14N3O7 5 C26H10N7O3 6 C30H14N05 7 C31H10N5O 1 C34H15N2O3	440 46 a m/z err 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0885 468.0826 468.0840 468.0860 468.0880 468.0880 469.077	[ppm] -6.3 -0.5 6.3 8.1 5.9 5.9 3.0 -6.6 -3.8 2.0 4.8 1.7	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 48.1 59.6 18.1	# mSigma 1 2 3 4 1 2 3 4 1 2 3 4 5 6 7 7 1	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56 22.19 100.00	rdb e 30.5 e 29.5 e 21.5 e 22.5 e 17.5 e 22.5 e 17.5 e 24.5 e 28.5 e 28.5 e 29.5 e	ven ven ven ven ven ven ven ven ven ven		2
Meas. m/z 467.0818 468.0857	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C16H6N17O2 2 C18H18N3O12 3 C18H10N13O6 4 C25H14N3O7 5 C26H10N7O3 6 C30H14N3O7 7 C31H10N5O 1 C34H15N2O3 3 C29H15N4O5 4 C23H15N405 4 C25H15	440 46 440 46 467.0788 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0885 468.0826 468.0840 468.0860 468.0880 468.0880 468.0880 499.1077 499.1037 499.1037	[ppm] -6.3 -0.5 6.3 8.1 5.9 5.9 -6.6 -3.8 2.0 -6.6 4.8 1.7 -3.7 -6.4 8.1	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 48.1 59.6 18.1 20.3 23.9 46.0	# mSigma 1 2 3 4 1 2 3 4 5 6 7 7 1 2 3 4 5 6 7 1 2 3 4 4 4 4 3 4 4 4 4 4 4 4 4 4 4 4 4 4	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56 22.19 100.00 50.85 14.74 3.24	rdb e 30.5 e 29.5 e 33.5 e 33.5 e 11.5 e 20.5 e 29.5 e 29.5 e 29.5 e 29.5 e 29.5 e 29.5 e 29.5 e	ven ven ven ven ven ven ven ven ven ven		
Meas. m/z 467.0818 468.0857	# Ion Formul 1 C29H7N8 2 C33H11N2O2 3 C22H11N8O5 4 C38H11 1 C18H6N17O2 2 C18H18N3O12 3 C18H10N13O6 4 C28H14N3O7 5 C28H14N3O7 5 C39H14N05 7 C31H10N5O 1 C34H15N2O3 2 C39H11N8O 3 C29H15N4O5	440 46 440 46 467.0788 467.0788 467.0815 467.0847 467.0855 468.0885 468.0885 468.0826 468.0840 468.0860 468.0860 468.0880 469.1077 499.1037 499.1037	[ppm] -6.3 -0.5 8.1 5.9 3.0 -6.6 -3.8 2.0 4.8 1.7 -6.4	mSigma # 17.2 23.1 34.1 45.9 7.0 12.8 15.1 24.6 41.6 48.1 59.6 18.1 20.3 23.9	↓	Score 13.47 100.00 9.08 3.66 40.98 48.55 100.00 27.45 41.91 79.56 22.19 100.00 50.85 14.74 3.24	rdb e 30.5 e 29.5 e 33.5 e 22.5 e 22.	ven ven ven ven ven ven ven ven ven ven		tu

Figure S13: HR-ESI-MS of compound 2

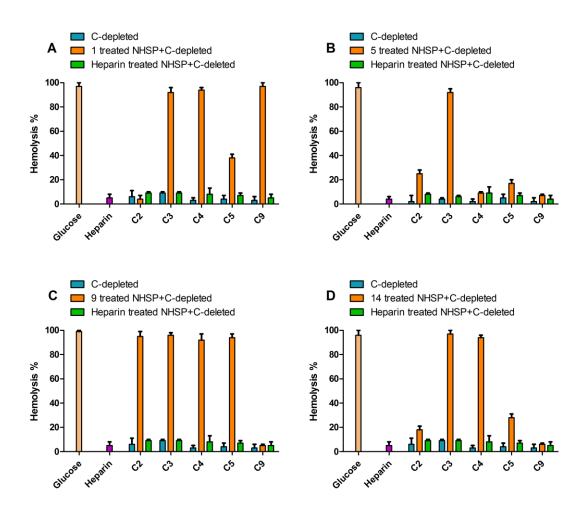


Figure S14: Targets of compounds **1** (A), **5** (B), **9** (C), and **14** (D) in complement activation cascade. 1-, 5-, 9-, and 14-treated sera were mixed with various complement-depleted (C-depleted) sera, and the capacity to restore hemolytic capacity of depleted sera by the CP was estimated by adding sheep antibody-sensitized erythrocytes. Data were expressed as mean \pm SD (n = 3).

Compounds	CH ₅₀ (mM)
1	0.40 ± 0.03
2	0.98 ± 0.06
3	NE
4	2.08 ± 0.27
5	0.57 ± 0.01
6	1.76 ± 0.08
7	NE
8	1.51 ± 0.21
9	0.51 ± 0.07
10	NE
11	NE
12	1.46 ± 0.24
13	1.54 ± 0.12
14	0.53 ± 0.05
15	0.90 ± 0.07
16	NE
17	NE
18	NE
Heparin ^b	0.30 ± 0.02

Table S1: Anti-complementary activity through the classical pathway (CP) of compounds $1-18^{a}$

^aData were expressed as mean \pm SD (n = 3); CH₅₀ stand for the 50% hemolytic inhibition concentrations through the classic pathway; NE denotes that this compound has no inhibitory effect at the maximal concentration tested.

^bHeparin was used as the positive controls (mg/mL).