

Table S1. The regression equations, correlation coefficient (*r*), linear ranges and LLOQs for the determination of seven analytes in rat plasma.

Analytes	Linear regression equations	<i>r</i>	Linear range (ng/mL)	LLOQ (ng/mL)
Gallic acid	$Y = 0.607 \times 10^{-1} X + 1.004 \times 10^{-1}$	0.996 6	0.1-50.0	0.1
Danshensu	$Y = 3.499 \times 10^{-1} X - 9.966 \times 10^{-3}$	0.996 3	0.5-250.0	0.5
Rosmarinic acid	$Y = 2.090 X + 5.049 \times 10^{-2}$	0.997 1	0.1-50.0	0.1
Salvianolic acid A	$Y = 2.197 \times 10^{-1} X + 1.650 \times 10^{-2}$	0.996 9	0.1-50.0	0.1
Aloe emodin	$Y = 2.793 \times 10^{-1} X + 4.519 \times 10^{-3}$	0.997 2	1.0-500.0	1.0
Rhein	$Y = 2.181 \times 10^{-1} X - 1.274 \times 10^{-1}$	0.997 6	1.0-500.0	1.0
Emodin	$Y = 1.218 \times 10^{-1} X + 6.569 \times 10^{-3}$	0.998 0	0.1-50.0	0.1

Table S2. Precision and accuracy for seven analytes in rat plasma (n=18, 6 replicates per day for 3 days).

Analytes	Nominal concentration (ng/mL)	Intra-day			Inter-day		
		Measured concentration (ng/mL)	Precision (% RSD)	Accuracy (% RE)	Measured concentration (ng/mL)	Precision (% RSD)	Accuracy (% RE)
Gallic acid	0.1	0.09 ± 0.00	4.36	-5.80	0.10 ± 0.01	9.85	-3.74
	0.2	0.21 ± 0.01	6.27	7.45	0.22 ± 0.01	6.68	8.69
	2.5	2.35 ± 0.12	5.30	-6.11	2.36 ± 0.10	4.33	-5.78
	40.0	40.62 ± 2.18	5.25	4.05	41.64 ± 1.73	4.15	4.09
Danshensu	0.5	0.50 ± 0.01	2.79	0.65	0.50 ± 0.01	3.00	-0.27
	1.0	1.05 ± 0.05	4.74	5.29	1.04 ± 0.04	4.09	4.19
	12.5	11.45 ± 0.35	3.06	-8.37	11.63 ± 0.51	4.41	-6.98
	200.0	218.80 ± 8.37	3.82	9.40	215.30 ± 9.36	4.35	7.65
Rosmarinic acid	0.1	0.10 ± 0.01	3.57	-0.43	0.10 ± 0.00	3.57	0.92
	0.2	0.21 ± 0.00	1.40	6.67	0.21 ± 0.01	2.69	5.75
	2.5	2.35 ± 0.10	4.21	-5.98	2.38 ± 0.10	4.10	-4.70
	40.0	43.98 ± 1.74	3.95	9.94	43.80 ± 1.50	3.42	9.51
Salvianolic acid A	0.1	0.10 ± 0.01	5.21	-3.10	0.10 ± 0.01	6.51	-2.04
	0.2	0.21 ± 0.01	6.54	7.23	0.21 ± 0.01	5.65	6.74
	2.5	2.40 ± 0.08	3.29	-3.90	2.41 ± 0.09	3.55	-3.74
	40.0	41.93 ± 1.35	3.23	4.83	42.67 ± 1.42	3.32	6.67
Aloe emodin	1.0	0.95 ± 0.04	4.50	-4.59	0.96 ± 0.04	3.84	-3.87
	2.0	2.16 ± 0.10	4.77	8.01	2.15 ± 0.08	3.73	7.36
	25.0	23.44 ± 0.42	1.78	-6.23	23.81 ± 1.00	4.19	-4.75

	400.0	431.80 ± 5.33	1.24	7.95	423.81 ± 14.15	3.34	5.95
	1.0	1.00 ± 0.02	1.54	-0.31	1.00 ± 0.01	1.16	-0.16
Rhein	2.0	2.04 ± 0.07	3.28	2.20	2.05 ± 0.05	2.59	2.32
	25.0	24.78 ± 1.12	4.51	-0.88	24.63 ± 0.85	3.43	-1.47
	400.0	432.01 ± 11.90	2.75	8.00	428.28 ± 16.37	3.82	7.07
	0.1	0.10 ± 0.01	6.68	-0.98	0.10 ± 0.01	6.63	-0.02
Emodin	0.2	0.20 ± 0.01	3.15	2.41	0.20 ± 0.01	4.08	-0.29
	2.5	2.54 ± 0.12	4.56	1.43	5.52 ± 0.12	4.60	0.61
	40.0	40.67 ± 1.65	4.0	1.67	40.83 ± 1.26	3.09	2.08

Table S3. Extraction recovery and matrix effect for seven analytes and IS in rat plasma (n=6).

Analytes	Spiked concentration (ng/mL)	Extraction Recovery		Matrix Effect	
		Mean (%)	RSD (%)	Mean (%)	RSD (%)
Gallic acid	0.2	88.71	4.62	94.84	5.62
	2.5	88.70	4.95	101.78	6.20
	40.0	81.71	6.77	100.33	4.73
Danshensu	1.0	87.08	8.34	97.81	6.11
	12.5	81.38	4.14	99.93	6.80
	200.0	87.10	6.41	96.70	3.99
Rosmarinic acid	0.2	82.37	8.21	99.73	5.48
	2.5	87.83	6.60	100.83	3.92
	40.0	89.30	6.30	104.43	5.19
Salvianolic acid A	0.2	90.82	6.14	97.10	3.56
	2.5	87.35	5.31	102.38	5.74
	40.0	89.50	8.58	102.95	4.16
Aloe emodin	2.0	85.88	5.69	101.35	6.69
	25.0	84.49	5.58	101.62	8.26
	400.0	85.38	4.57	96.23	6.11
Rhein	2.0	82.93	4.05	94.85	5.01
	25.0	88.22	4.41	100.97	5.83
	400.0	85.86	5.34	99.81	5.18
Emodin	0.2	88.98	8.10	100.26	3.96
	2.5	87.36	5.94	97.81	7.54
	40.0	87.00	7.75	95.27	4.42
Carbamazepine	100.0	83.94	6.13	100.44	7.36

Table S4. Stability of the seven analytes in rat plasma under different storage conditions (n=6).

Analytes	Spiked concentration (ng/mL)	Room temperature 4 h		Auto-sampler 24h		Three freeze-thraw cycles		Stored at 4°C for 24h		Stored at -20 °C for 14 days	
		RE (%)	RSD (%)	RE (%)	RSD (%)	RE (%)	RSD (%)	RE (%)	RSD (%)	RE (%)	RSD (%)
Gallic acid	0.2	1.83	5.68	7.16	3.33	4.78	8.92	6.71	9.40	8.09	4.68
	2.5	-4.96	3.00	-6.94	2.21	-4.89	2.89	-4.02	4.06	-3.88	4.89
	40.0	4.88	2.31	5.58	2.20	3.73	3.55	0.24	2.65	0.58	3.61
Danshensu	1.0	6.01	3.70	5.25	5.59	3.75	4.49	2.50	2.36	4.06	4.13
	12.5	-6.15	3.61	-5.74	3.83	-5.97	3.39	-6.11	2.96	-6.23	2.83
	200.0	5.27	3.17	8.18	3.26	9.43	3.40	6.56	3.79	4.01	2.69
Rosmarinic acid	0.2	5.02	5.28	6.42	4.75	7.64	3.65	6.46	4.35	5.70	3.33
	2.5	-5.17	1.84	-3.12	1.84	-2.50	2.12	-3.52	2.30	-4.83	2.34
	40.0	8.09	3.02	8.91	2.52	9.07	2.34	6.62	2.59	8.15	4.28
Salvianolic acid A	0.2	4.69	7.27	4.82	5.48	4.11	4.24	6.23	4.35	4.81	4.97
	2.5	-6.00	4.19	-4.20	4.93	-5.51	4.78	-6.38	4.90	-4.68	5.86
	40.0	5.83	3.72	5.35	3.16	5.05	3.85	4.09	3.65	6.71	4.10
Aloe emodin	2.0	7.61	3.62	9.85	2.15	9.90	2.71	9.48	3.63	8.43	3.38
	25.0	-4.09	3.65	-5.88	4.31	-5.78	3.79	-3.62	3.83	-2.82	3.46
	400.0	3.96	5.11	7.06	3.43	9.53	3.02	6.32	4.46	6.04	4.80
Rhein	2.0	1.69	1.13	3.29	2.49	3.69	2.38	2.47	2.24	1.39	2.48
	25.0	-4.71	2.85	-3.40	4.88	-1.86	4.41	-0.64	3.13	0.16	2.62

	400.0	2.12	4.67	4.89	4.66	7.09	4.37	5.25	3.85	4.16	1.80
	0.2	2.17	3.64	0.38	4.65	1.64	4.57	-0.52	5.69	-0.06	6.62
Emodin	2.5	0.60	1.98	0.29	4.41	-0.05	4.61	-0.55	3.88	2.73	2.07
	40.0	6.20	2.81	4.65	3.53	5.05	4.01	6.41	2.84	3.30	2.30

Table S5. The MS information of the meatbolins derived from the seven prototypal components

Metabolin	Formula	RT(min)	ES/expected(m/z)	ES/measured(m/z)	Delta (ppm)	Fragment Ion(m/z)
M1-1	C ₇ H ₄ O	11.43	105.03349	105.03353	-0.368	105.03[M+H] ⁺ ,81.03[M+H-2C] ⁺ ,77.04[M+H-CO] ⁺ ,53.04[M+H-CO-2C] ⁺
M1-2	C ₈ H ₄ O ₃	31.7	149.02332	149.02296	-2.419	149.02[M+H] ⁺ ,121.03[M+H-CO] ⁺ ,93.03[M+H-CO-CO] ⁺ ,65.04[M+H-CO-CO-CO] ⁺
M1-3	C ₉ H ₉ NO ₃	11.43	180.06551	180.06525	-1.498	180.07[M+H] ⁺ ,105.03[M+H-C ₂ H ₅ NO ₂] ⁺ ,95.05[M+H-C ₃ H ₃ NO ₂] ⁺ ,81.03[M+H-C ₃ H ₃ NO ₂ -CH ₂] ⁺ ,77.04[M+H-C ₂ H ₅ NO ₂ -CO] ⁺ ,53.04[M+H-C ₃ H ₃ NO ₂ -CH ₂ -CO] ⁺
M1-4	C ₉ H ₈ O ₃	2.5	165.05462	165.05429	-2.003	165.05[M+H] ⁺ ,147.04[M+H-H ₂ O] ⁺ ,123.04[M+H-CO-CH ₂] ⁺ ,119.05[M+H-H ₂ O-CO] ⁺ ,103.05[M+H-H ₂ O-CO ₂] ⁺ ,95.05[M+H-CO-CH ₂ -CO] ⁺ ,91.05[M+H-H ₂ O-CO-CO] ⁺ ,77.04[M+H-CO-CH ₂ -CO-H ₂ O] ⁺
M2-1	C ₉ H ₈ O ₂	4.13	149.05970	149.05943	-1.852	149.06[M+H] ⁺ ,131.05[M+H-H ₂ O] ⁺ ,121.06[M+H-C ₂ H ₄] ⁺ ,107.05[M+H-H ₂ O-2C] ⁺ ,103.05[M+H-H ₂ O-CO] ⁺ ,95.05[M+H-H ₂ O-3C] ⁺ ,79.05[M+H-H ₂ O-2C-CO] ⁺ ,65.04[M+H-H ₂ O-2C-CO-CH ₂] ⁺
M2-2	C ₉ H ₆ O ₃	26.65	163.03897	163.03870	-1.660	163.04[M+H] ⁺ ,135.04[M+H-CO] ⁺ ,133.03[M+H-CH ₂ O] ⁺ ,105.03[M+H-CH ₂ O-CO] ⁺ ,92.03[M+H-CH ₂ O-CO-CH] ⁺ ,79.05[M+H-CO-CO-CO] ⁺ ,53.04[M+H-CO-CO-CO-C ₂ H ₂] ⁺
M2-4	C ₁₀ H ₈ O ₄	21.14	193.04953	193.04929	-1.271	193.05[M+H] ⁺ ,149.02[M+H-CH ₃ CHO] ⁺ ,139.04[M+H-CO-C ₂ H ₂] ⁺ ,121.03[M+H-CH ₃ CHO-CO] ⁺ ,65.04[M+H-CH ₃ CHO-CO-CO-CO] ⁺

M2-5	C ₁₁ H ₁₅ N O ₄	7.17	226.10738	226.10692	-2.054	226.10[M+H] ⁺ ,208.09[M+H-H ₂ O] ⁺ ,190.08[M+H-H ₂ O-H ₂ O] ⁺ ,166.08[M+H-H ₂ O-H ₂ O-2C] ⁺ ,138.09[M+H-H ₂ O-H ₂ O-2C-CO] ⁺
M2-6	C ₁₄ H ₁₈ N ₂ O ₅	10.61	295.12884	295.12823	-2.095	295.13[M+H] ⁺ ,278.10[M+H-NH ₃] ⁺ ,232.10[M+H-NH ₃ -C H ₂ O ₂] ⁺ ,166.09[M+H-C ₅ H ₇ NO ₃] ⁺ ,130.05[M+H-NH ₃ -C ₉ H ₈ O ₂] ⁺ ,120.08[M+H-C ₅ H ₇ NO ₃ -CH ₂ O ₂] ⁺ ,103.05[M+H-C ₅ H ₇ NO ₃ -CH ₂ O ₂ -NH ₃] ⁺ ,84.04[M+H-NH ₃ -C ₉ H ₈ O ₂ -CH ₂ O ₂] ⁺
M2-7	C ₁₄ H ₂₀ N ₂ O ₅	6.45	297.14449	297.14383	-2.249	297.14[M+H] ⁺ ,279.13[M+H-H ₂ O] ⁺ ,255.13[M+H-H ₂ O-2C] ⁺ ,210.11[M+H-H ₂ O-2C-CH ₃ ON] ⁺ ,192.10[M+H-H ₂ O-2C-CH ₃ ON-H ₂ O] ⁺ ,126.05[M+H-H ₂ O-2C-CH ₃ ON-H ₂ O-C ₅ H ₆] ⁺
M3-3	C ₉ H ₈ O ₃	2.58	165.05462	165.05444	-1.095	165.05[M+H] ⁺ ,147.0434[M+H-H ₂ O] ⁺ ,123.0437[M+H-C O-CH ₂] ⁺ ,119.0489[M+H-H ₂ O-CO] ⁺ ,103.0541[M+H-H ₂ O-CO ₂] ⁺ ,95.0488[M+H-CO-CH ₂ -CO] ⁺ ,91.0543[M+H-H ₂ O-CO-CO] ⁺ ,77.0385[M+H-CO-CH ₂ -CO-H ₂ O] ⁺
M5-1	C ₁₅ H ₁₄ O ₃	23.56	243.10157	243.1012	-1.649	243.10[M+H] ⁺ ,123.04[M+H-C ₈ H ₈ O] ⁺ ,107.05[M+H-C ₈ H ₈ O ₂] ⁺ ,95.05[M+H-C ₈ H ₈ O-CO] ⁺ ,79.05[M+H-C ₈ H ₈ O-CO ₂] ⁺
M5-2	C ₂₁ H ₂₂ O ₈	29.01	403.13874	403.1376	-2.838	403.14[M+H] ⁺ ,373.09[M+H-CH ₃ -CH ₃] ⁺ ,327.09[M+H-C H ₃ -CH ₃ -CO-H ₂ O] ⁺
M6-2	C ₁₅ H ₁₀ O ₅	25.72	271.06009	271.0593	-2.840	271.06[M+H] ⁺ ,225.06[M+H-CO ₂ -H ₂ O] ⁺ ,135.04[M+H-C ₇ H ₄ O ₃] ⁺

Note: Some metabolites may be derived from different prototypal components, M2-3 and M1-4 were identified as the same metabolites. Similarly, M3-1 with M2-1; M3-2 with M2-2; M3-4 with M2-4; M3-5 with M2-5; M3-6 with M2-6; M3-7 with M2-7; M4-1 with M2-2; M4-2 with M1-4; M4-3 with M2-4; M4-4 with M2-5; M4-5 with M2-6; M4-6 with M2-7; M6-1 with M5-1; M7-1 with M5-1; M7-2 with M5-2, were also the same metabolites.