Electronic Supplementary Material (ESI) for RSC Advances.

Support Information

Metabolite identification and pharmacokinetic study of Platycodi Radix (Jiegeng) *in vivo*

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Table S1 Main platycosides identified in total saponins by UPLC-Q/TOF-MS

Peak	Ret. Time (min)	Mode	MS (m/z)	MS/MS (m/z)	MW	Formula	Identification
1	11.73	Pos	1255.6434 $[M+H]^+$	1255, 1123, 521	1254.5881	$C_{58}H_{94}O_{29}$	Deapioplatycodin D3
		Neg	1253.5803 $[M-H]^-$	1253			
2	11.83	Pos	1093.5806 $[M+H]^+$	1093, 961, 683, 521	1092.5353	$C_{52}H_{84}O_{24}$	Deapioplatycodin D
		Neg	1091.5323 $[M-H]^-$	1901			
3	11.93	Pos	1297.6371 $[M+H]^+$	845, 683, 521	1296.5986	$C_{60}H_{96}O_{30}$	2″-*O*-deapioacetylplatycodin D2
		Neg	1295.9511 $[M-H]^-$	1295			
4	12.12	Pos	1387.6702 $[M+H]^+$	1387, 1255, 521	1386.6303	$C_{63}H_{102}O_{33}$	Platycodin D3
		Neg	1385.6190 $[M-H]^-$	1385			
5	12.22	Pos	1225.6217 $[M+H]^+$	1225, 1093, 961, 683, 521	1224.5775	$C_{57}H_{92}O_{28}$	Platycodin D
		Neg	1223.5737 $[M-H]^-$	1223			
6	12.30	Pos	1107.5664 $[M+H]^+$	1107, 975, 697, 535	1106.5145	$C_{52}H_{82}O_{25}$	Platyconic acid C
		Neg	1105.5062 $[M-H]^-$	1105			
7	12.41	Pos	1267.6388 $[M+H]^+$	1267, 1135, 1003, 683, 521	1266.5881	$C_{59}H_{94}O_{29}$	Platycodin A
		Neg	1265.5782 $[M-H]^-$	1265			
8	12.70	Pos	1239.6040 $[M+H]^+$	975, 697, 535	1238.5568	$C_{57}H_{90}O_{29}$	Platyconic acid A
		Neg	1237.5519 $[M-H]^-$	1237			
9	12.88	Pos	1281.6162 $[M+H]^+$	1149, 1017, 697 535	1280.5673	$C_{59}H_{92}O_{30}$	Platyconic acid B
		Neg	1279.5591 $[M-H]^-$	1279			
10	13.32	Pos	1429.7012 $[M+H]^+$	1429, 1297, 1165, 845, 683, 521	1428.6409	$C_{65}H_{104}O_{34}$	2″-*O*-acetylplatycodin D2
		Neg	1427.6244 $[M-H]^-$	1427			
11	14.52	Pos	845.4833 $[M+H]^+$	845, 683, 521	844.4457	$C_{42}H_{68}O_{17}$	Platycoside K

		Neg	843.4387 $[M-H]^-$	843			
12	14.72	Pos	683.4249 $[M+H]^+$	683, 521	682.3928	$C_{36}H_{58}O_{12}$	3-*O*-β-D-glucopyranosylplatycodigenin
		Neg	681.3878 $[M-H]^-$	681			
13	15.43	Pos	697.4044 $[M+H]^+$	697, 535	696.3615	$C_{36}H_{56}O_{13}$	3-*O*-β-D-glucopyranosylplatyconic acid
		Neg	695.3668 $[M-H]^-$	695			

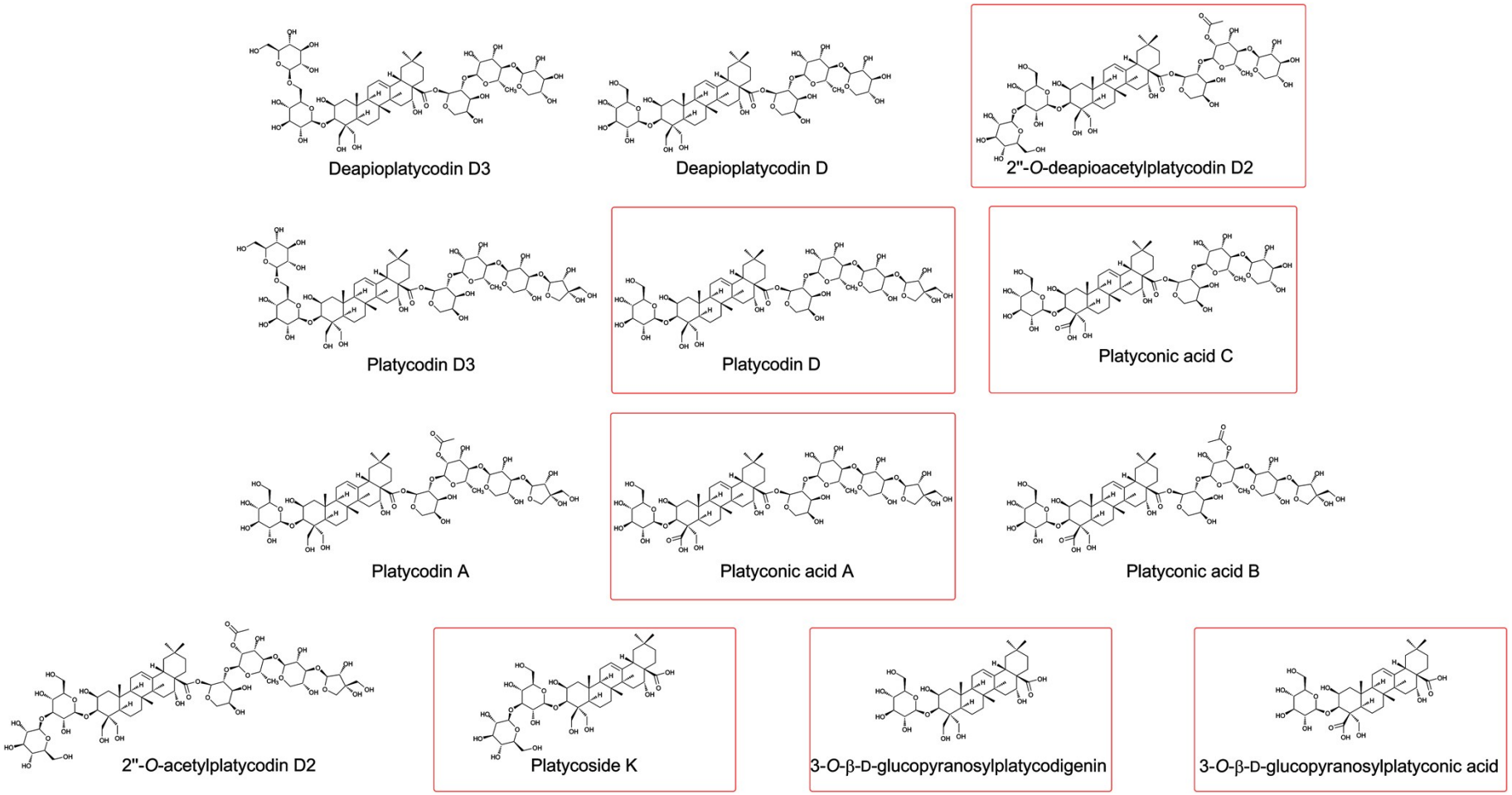

Fig. S1 Structures of platycosides in total saponins (platycosides in plasma were markered by red frame).

Structure identification of GP

GP was an amorphous powder and its molecular formula was assigned to be $C_{36}H_{58}O_{12}$ based on the high-resolution spectrum. The spectral features and physicochemical properties revealed it to be a triterpenoid saponin. The ^{1}H NMR spectrum (pyridine-d_5, 600 MHz) showed five tertiary methyl groups (δ 1.02, 1.06, 1.15, 1.51 and 1.78) and one olefinic proton (δ 5.67, br s). The ^{13}C NMR spectrum (pyridine-d_5, 600 MHz) showed five sp^3 carbons at δ 17.57, 18.23, 24.70, 27.20 and 33.35, and two sp^2 olefinic carbons at δ 122.71 and 145.05, and one carboxyl carbon at δ 180.06, and five oxygenated methene and methine carbons at δ 69.59, 86.15, 74.74, 65.03 and 63.58. The information of ^{1}H and ^{13}C NMR spectrum indicated that it possessed a 2,3,16,23,24-pentahydroxyolean-12-ene-28-oci acid as aglycon. The chemical shifts. of C-3 (δ 86.15) and C-28 (δ 180.06) revealed that it was a monodesmosidic glycoside. On the basis of the above evidence and literature, GP was identified to be 3-*O*-β-D-glucopyranosyl-2,3,16,23,24-pentahydroxyolean-12-ene-28-oic acid.

Table S2 ^{1}H and ^{13}C NMR spectrum data (δ) of GP and GPA

Position	GP		Position	GPA	
	δ_C	δ_H		δ_C	δ_H
1	45.06		1	45.49	
2	69.59	4.73 (1H, m)	2	69.97	5.12 (1H,m)
3	86.15	4.61 (1H, m)	3	81.19	4.72 (1H, m)
4	47.17		4	56.74	
5	48.11		5	49.12	
6	19.23		6	20.02	
7	33.67		7	33.32	
8	40.24		8	39.91	
9	47.67		9	47.54	
10	37.54		10	37.04	
11	24.17		11	24.29	
12	122.71	5.67 (1H, br s)	12	122.41	5.66 (1H, br s)
13	145.05		13	145.30	
14	42.37		14	42.26	
15	36.25		15	36.22	
16	74.74	5.23 (1H, br s)	16	74.72	5.24 (1H, br s)
17	48.95		17	48.82	
18	41.60		18	41.42	
19	46.47		19	47.22	
20	31.07		20	31.08	
21	36.07		21	36.07	
22	32.90		22	32.93	
23	63.58		23	62.67	
24	65.03		24	176.31	
25	18.23	1.51 (3H, s)	25	15.64	1.65 (3H, s)
26	17.57	1.06 (3H, s)	26	17.43	1.09 (3H, s)
27	27.20	1.78 (3H, s)	27	27.28	1.84 (3H, s)
28	180.06		28	179.99	
29	33.35	1.02 (3H, s)	29	33.37	1.05 (3H, s)
30	24.70	1.15 (3H, s)	30	24.72	1.18 (3H, s)
1’	106.34		1’	106.70	5.40 (1H, d. J = 7.8 Hz)
2’	75.27		2’	75.38	
3’	78.75		3’	78.60	
4’	71.62		4’	71.56	
5’	78.70		5’	78.52	
6’	62.55		6’	62.56	

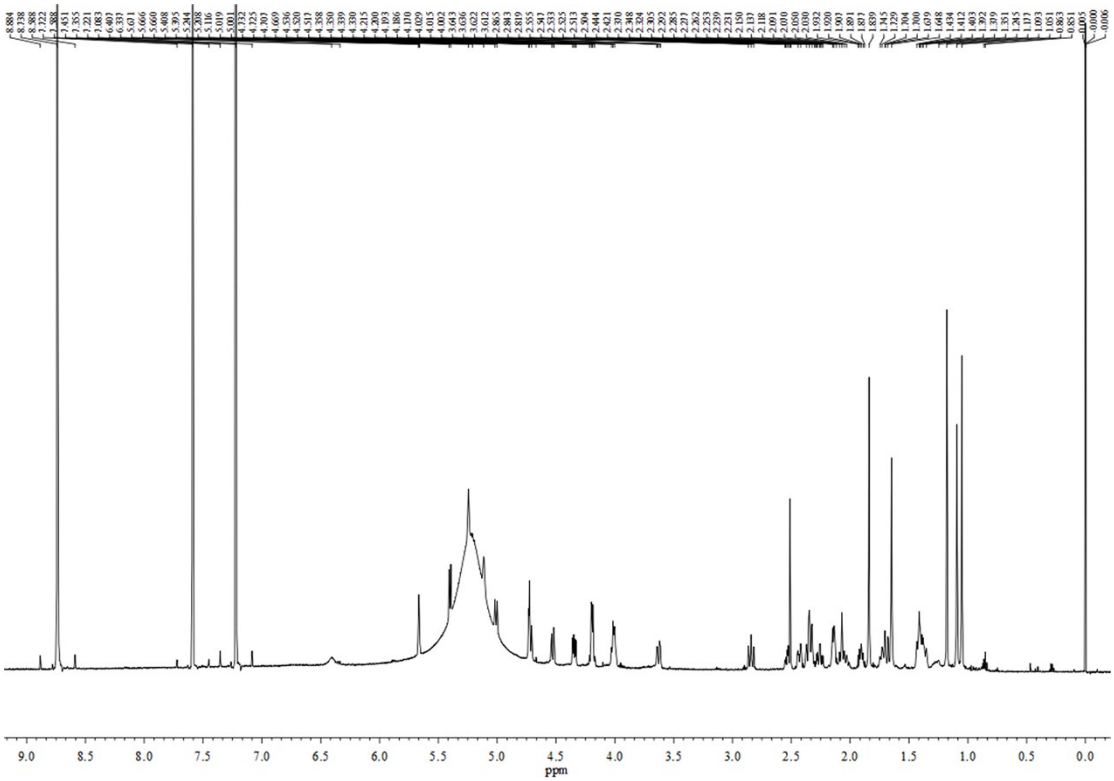

Fig. S2 ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum of GPA.

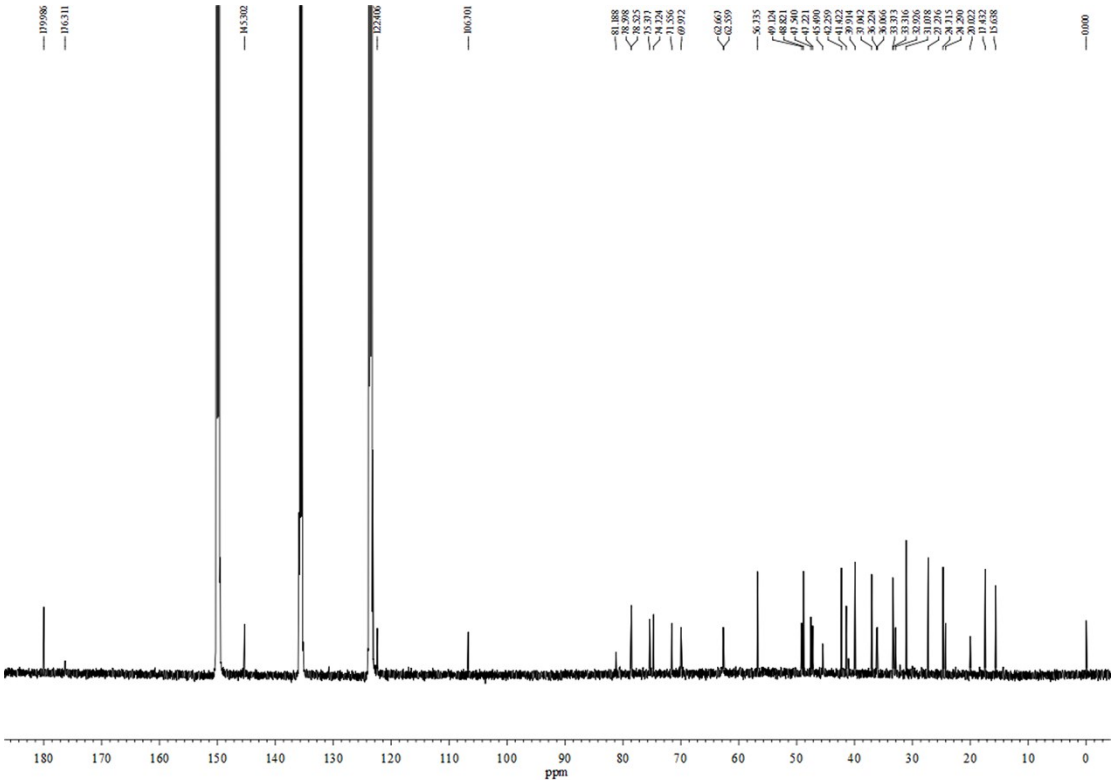

Fig. S3 ^{13}C NMR (pyridine-d_5, 600 MHz) spectrum of GPA.

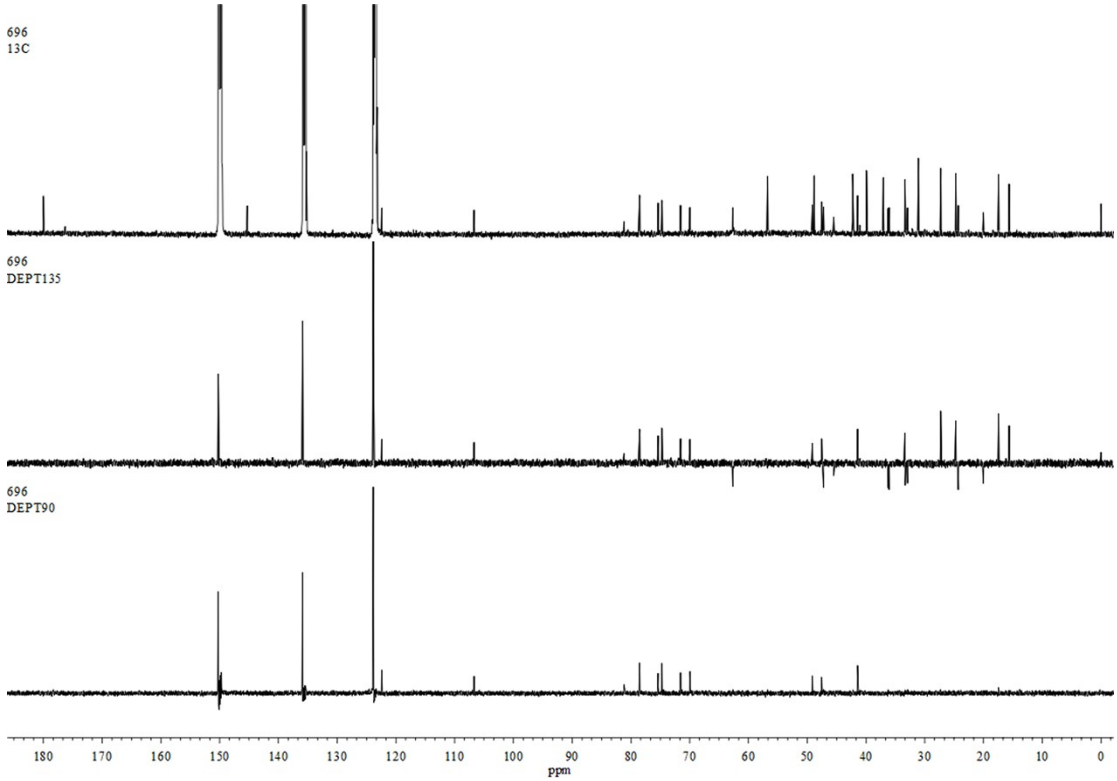

Fig. S4 DEPT spectrum of GPA.

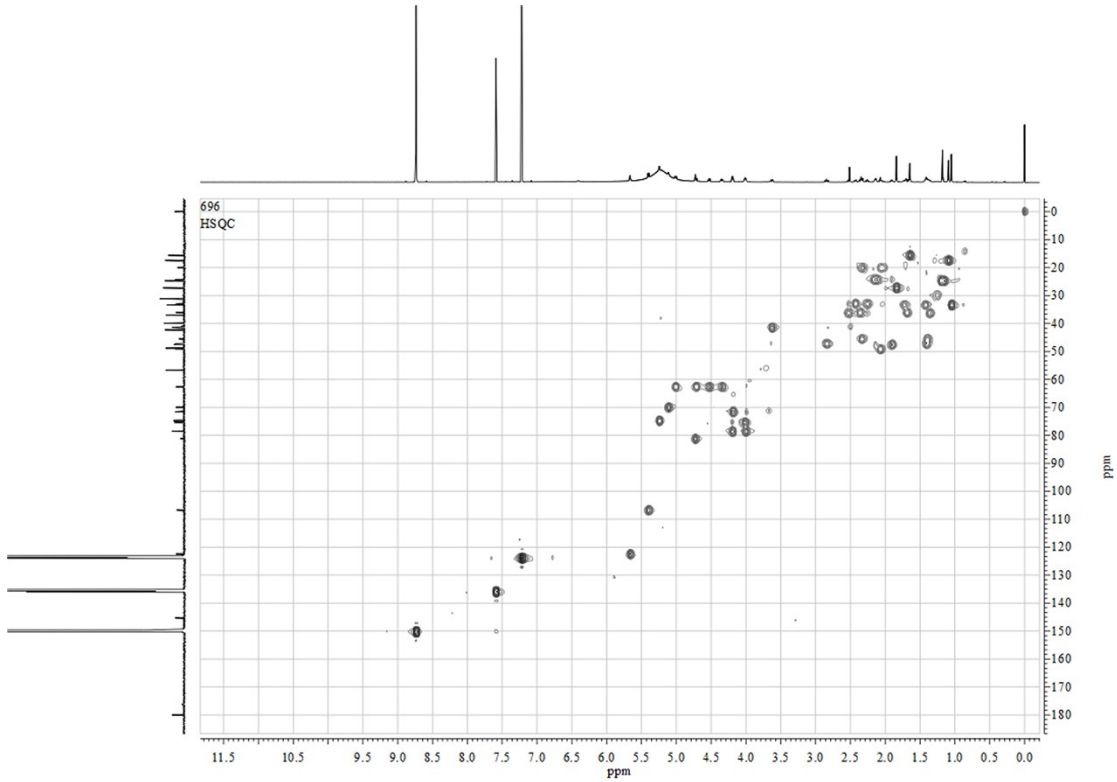

Fig. S5 HSQC spectrum of GPA.

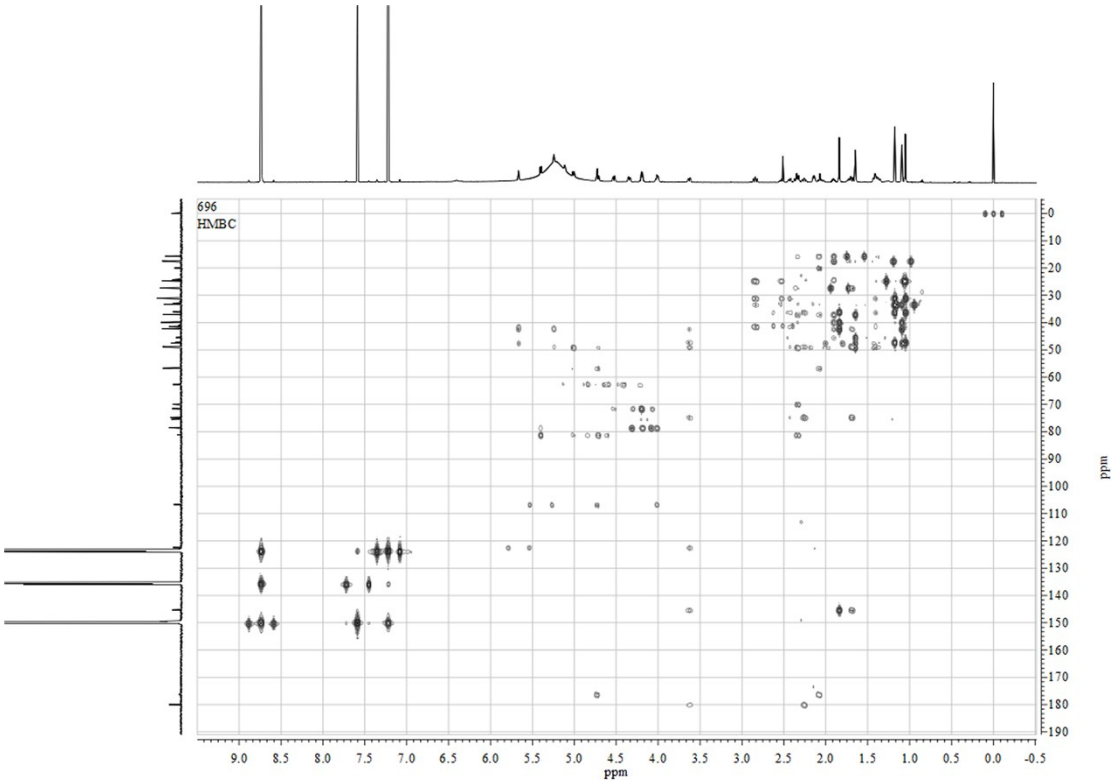

Fig. S6 HMBC spectrum of GPA.

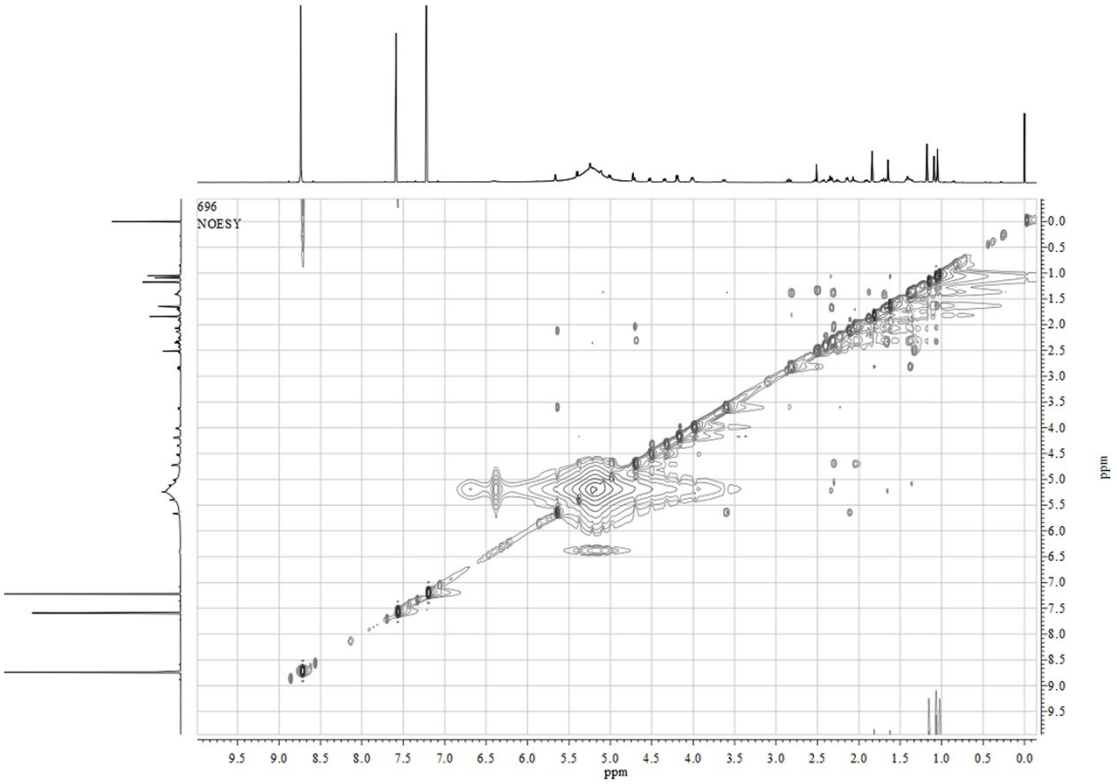

Fig. S7 NOSY spectrum of GPA.

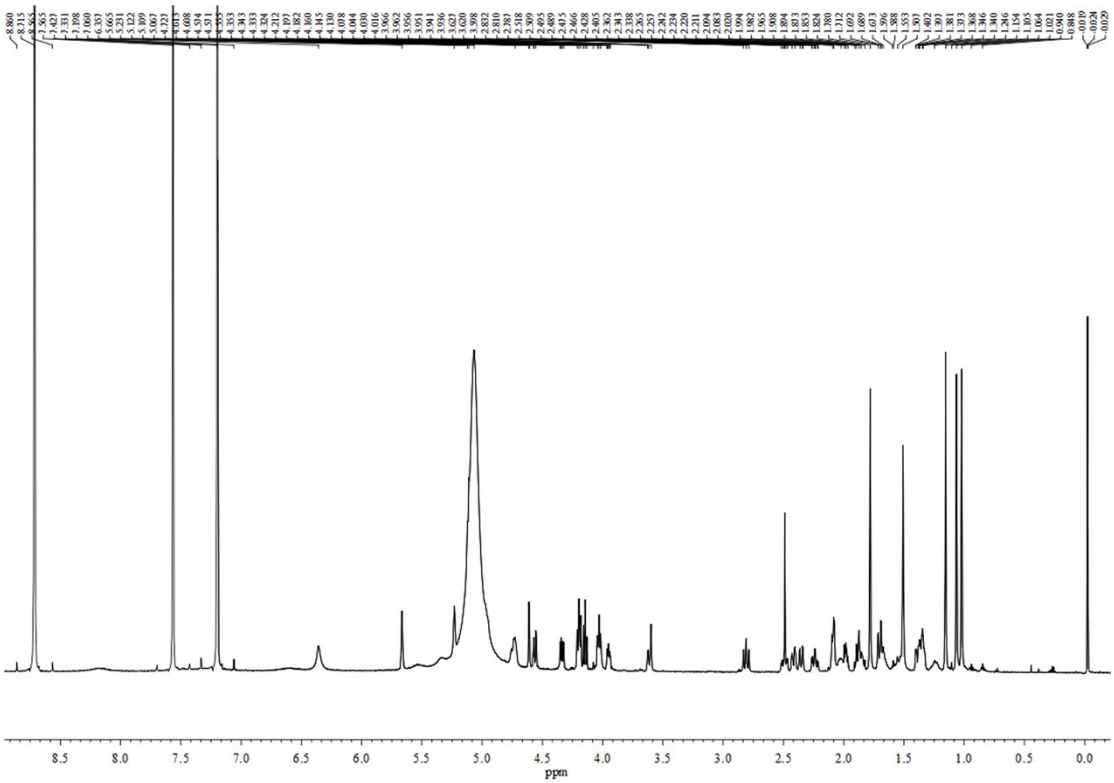

Fig. S8 ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum of GP.

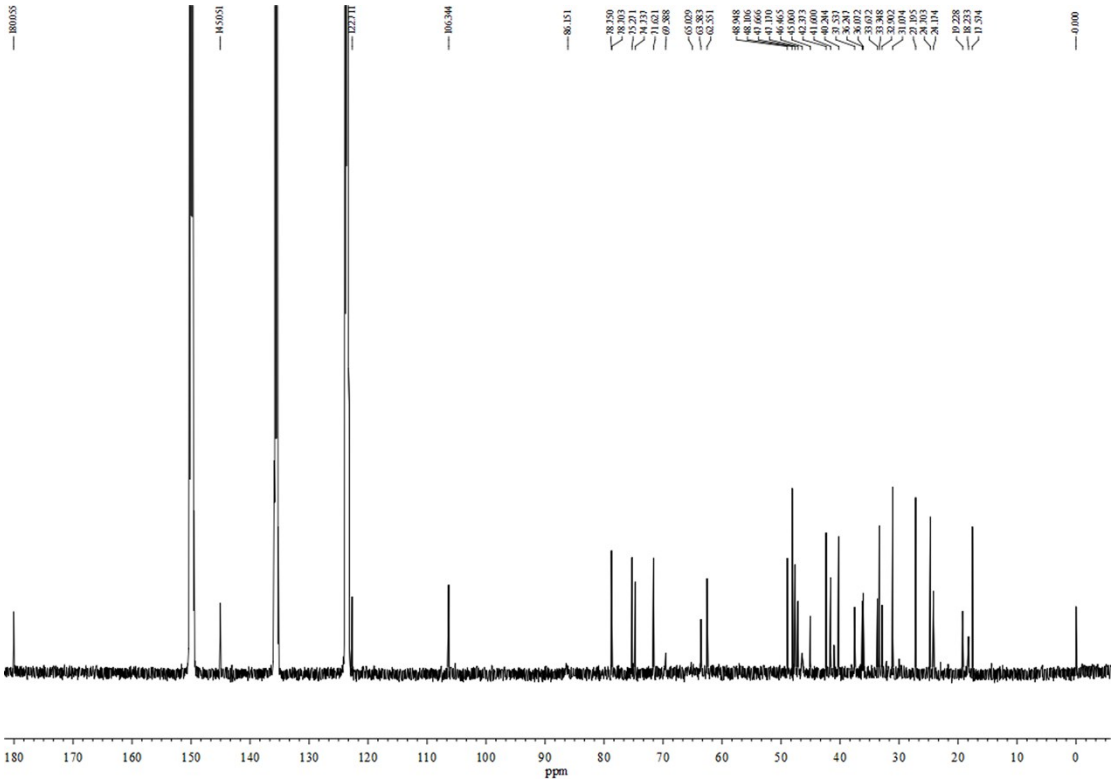

Fig. S9 ^{13}C NMR (pyridine-d_5, 600 MHz) spectrum of GP.

Table S3 Optimized MRM parameters for analytes and IS

Analytes	Mass	Prec ion (*m/z*)	Prod ion (*m/z*)	CE (V)
GP	682.3928	683.5	485.5	10
GPA	696.3615	697.7	517.4	15
IS	638.4394	603.3	423.3	9

Table S4 Regression data and LLOQs of analytes in plasma samples.

Analytes	Range (μg/L)	Linear regression equation	r^2	LLOQ (μg/L)
GP	0.25-4940.00	$y = 0.0064x - 0.0909$	0.9997	0.247
GPA	0.25-4992.00	$y = 0.0006x + 0.0035$	0.9995	0.250

Table S5 Extraction recovery and matrix effect of analytes and IS in plasma samples (*n* = 3).

Analytes	Spiked concentration(μg/L)	Extraction recovery		Matrix effect	
		Mean± SD (%)	RSD (%)	Mean± SD (%)	RSD (%)
GP	2.47	95.41±3.71	3.88	107.76±3.89	3.61
	247.00	94.06±2.10	2.24	101.91±1.83	1.79
	2470.00	98.53±1.41	1.43	107.05±0.92	0.86
GPA	2.50	96.57±1.13	1.17	102.09±2.94	2.88
	249.60	95.87±2.26	2.36	94.95±1.50	1.58
	2496.00	94.90±5.35	5.35	98.11±8.06	8.22
IS	500.00	98.03±1.83	1.87	97.32±4.42	4.54

Table S6 Stability of f analytes and IS in plasma samples (mean ± SD, *n* = 3).

Analytes	Conc. (μg/L)	Room temperature 24 h		Auto-sampler 24 h		Freeze-thraw cycles		-20 °C 14 days	
		Precision (%)	Accuracy (%)	Precision (%)	Accuracy (%)	Precision (%)	Accuracy (%)	Precision (%)	Accuracy (%)
GP	2.47	2.27	-11.37	1.11	2.26	0.44	-8.4	1.89	6.61
	247.00	0.34	-2.64	2.25	0.37	1.11	0.98	1.84	3.27
	2470.00	3.06	3.61	2.67	-0.38	4.84	-1.01	3.83	-4.3
GPA	2.50	3.55	1.72	6.59	2.4	0.39	1.31	2.66	-7.49
	249.60	3.97	-3	4.74	-2.83	3.67	2.56	3.61	-1.2
	2496.00	1.08	2.42	2.03	-0.6	1.32	-5.93	2.77	5.82