Electronic Supplementary Material (ESI) for RSC Advances.
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Supplementary Material Table 1. Identified compounds in Fugan Fang extract

NO.	Identified Compounds	Negative ion (m/z)		Positive ion (m/z)		Molecular		Fragment ions (m/z)	Plant origin
		Adduct	Error (ppm)	Adduct	Error (ppm)	Weight (Da)	Composition		
1	Gentiobiose	-H	-0.5	+Na	0.3	342	$C_{12}H_{22}O_{11}$	365[M+Na]$^{+}$,203[M+Na-Glc]$^{+}$,185[a]	Radix Gentianae
2	Gentianose	-H	-0.6	+Na	-0.2	504	$C_{18}H_{32}O_{16}$	527[M+Na]$^{+}$, 365[M+Na-Glc]$^{+}$, 203[M+Na-2Glc]$^{+}$[a]	Radix Gentianae
3	Gallic acid	-H	-0.7			170	$C_7H_6O_5$	169[M-H]$^{-}$, 125[M-H-CO2]$^{-}$[a]	Flos Carthami
4	Protocatechuic acid	-H	0.2			154	$C_7H_6O_4$	153[M-H]$^{-}$, 109[M-HCOO]$^{-}$, 91[M-HCOO-H2O]$^{-}$[b]	Radix Angelicae Sinensis and Caulis Spatholobi
5	Catechin	-H	0.2	+H	-0.3	290	$C_{15}H_{14}O_6$	289[M-H]$^{-}$,245[M-H-COO]$^{-}$,203,109[b]	Caulis Spatholobi
6	Caffeic acid	-H	-0.1			180	$C_9H_8O_4$	179[M-H]$^{-}$, 135[M-HCOO]$^{-}$	Radix Angelicae Sinensis
7	6-Hydroxykaempferol -3,6-di-O-β-glucoside -7-O-β-glucuronide	-H	2.2			802	$C_{33}H_{38}O_{23}$	801[M-H]$^{-}$,625[M-H-GA]$^{-}$,463[M-H-GA-Glc]$^{-}$, 301[M-H-GA-2Glc]$^{-}$[a]	Flos Carthami
8	6-Hydroxykaempferoltri -O-glucoside	-H	2.2			788	$C_{33}H_{40}O_{22}$	787[M-H]$^{-}$,625[M-H-Glc]$^{-}$,463[M-H-2Glc]$^{-}$,301[M-H-3Glc]$^{-}$[a]	Flos Carthami
9	Safflomin A	-H	0.5	+H	-0.3	612	$C_{27}H_{32}O_{16}$	613[M+H]$^{+}$, 595[M+H-H_2O]+, 415, 289	Flos Carthami
10	Chlorogenic acid	-H	0.1			354	$C_{16}H_{18}O_9$	353[M-H]$^{-}$, 191[M-H-C9H6O3]$^{-}$[a]	Flos Carthami
11	Loganic acid or 8-hydroxy-10-hydrosweroside	-H	0.7	+H	1	376	$C_{16}H_{24}O_{10}$	375[M-H]$^{-}$, 213[M-H-Glc]$^{-}$,169[M-H-Glc-COO]$^{-}$	Radix Gentianae
12	Hydroxysafflor yellow A	-H	0.5	+H	-0.3	612	$C_{27}H_{32}O_{16}$	613[M+H]$^{+}$, 451[M+H-Glc]$^{+}$,433, 313， 211[ab]	Flos Carthami
13	Chlorogenic acid isomer	-H	0.1			354	$C_{16}H_{18}O_9$	353[M-H]$^{-}$, 191[M-H-C9H6O3]$^{-}$[a]	Flos Carthami

14	Epicatechin	-H	0.2	+H	-0.3	290	$C_{15}H_{14}O_6$	289[M-H]$^-$,245[M-H-COO]$^-$,203,109[b]	Caulis Spatholobi
15	Gentiopicroside	-H	-0.5	+H	-0.2	356	$C_{16}H_{20}O_9$	357[M+H]$^+$,195[M+H-Glc]$^+$,177[M+H-Glc-H2O]$^+$, 149,121[+ab]	Radix Gentianae
16	Protocatechuic acid isomer	-H	0.2			154	$C_7H_6O_4$	153[M-H]$^-$, 109[M-HCOO]$^-$, 91[M-HCOO-H2O]$^-$[b]	Radix Angelicae Sinensis and Caulis Spatholobi
17	Sweroside	-H	-0.6	+H	0	358	C16H22O9	359[M+H]$^+$，197[M+H-Glc]$^+$,179[M+H-Glc-H2O]$^+$, 127[ab]	Radix Gentianae
18	Daidzin			+H	-0.6	416	$C_{21}H_{20}O_9$	417[M+H]$^+$，255[M+H-Glc]$^+$	Caulis Spatholobi
19	Gentianine	-H	-0.6			175	$C_{10}H_9NO_2$	174[M-H]$^-$, 131[M-H-C2H4O]$^-$, 87	Radix Gentianae
20	6-Hydroxykaempferol-di-O-glucoside	-H	1.9			626	$C_{27}H_{30}O_{17}$	625[M-H]$^-$,463[M-H-Glc]$^-$, 301[M-H-2Glc]$^-$[a]	Flos Carthami
21	P-coumaric acid	-H	0.1			164	$C_9H_8O_3$	163[M-H]$^-$, 119[M-H-COO]$^-$, 93[b]	Flos Carthami
22	Calycosin-7-O-β-D-glucoside	-H	-0.1	+H	-0.4	446	$C_{22}H_{22}O_{10}$	447[M+H]$^+$，285[M+H-Glc]$^+$，270[M+H-Glc-CH3]$^+$[ab]	Radix Astragali and Caulis Spatholobi
23	Ferulic acid	-H	1.1			194	$C_{10}H_{10}O_4$	193[M-H]$^-$,178[M-H-CH_3]$^-$, 134[M-H-CH3-COO]$^-$[ab]	Radix Angelicae Sinensis
24	6-Hydroxykaempferol-3- O-β-D-glucopyranoside or Isoquercitrin	-H	-0.3	+H	-0.6	464	$C_{21}H_{20}O_{12}$	463[M-H]$^-$, 301[M-H-Glc]$^-$,271[a]	Flos Carthami
25	Tinctormine	-H	1.3			593	$C_{27}H_{31}NO_{14}$	592[M-H]$^-$, 472, 244[a]	Flos Carthami
26	Rutin	-H	0.6			610	$C_{27}H_{30}O_{16}$	609[M-H]$^-$, 301[M-H-rutinose]$^-$[a]	Flos Carthami
27	6-Hydroxykaempferol-3- O-β- D-glucopyranoside or Isoquercitrin	-H	-0.3	+H	-0.6	464	$C_{21}H_{20}O_{12}$	463[M-H]$^-$, 301[M-H-Glc]$^-$,271[a]	Flos Carthami
28	Calycosin-7-O-β- D-glc-6″-O-malonate			+H	1.4	532	$C_{25}H_{24}O_{13}$	533[M+H]$^+$, 285[M+H−$C_3H_2O_3$−Glc]$^+$, 270, 253[a]	Radix Astragali

29	Cartormin	-H	0.2	+H	0.3	575	$C_{27}H_{29}NO_{13}$	576[M+H]$^+$, 414[M+H-Glc]$^+$, 354, 276	Flos Carthami
30	Kaempferol-3-O-rutinose	-H	1.7	+H	-0.8	594	$C_{27}H_{30}O_{15}$	593, 285[M-H-rutinose]$^-$,257[a]	Flos Carthami
31	Ononin			+H	-0.2	430	$C_{22}H_{22}O_9$	431[M+H]$^+$, 269[M+H-Glc]$^+$, 254, 237, 226[a]	Radix Astragali and Caulis Spatholobi
32	(6αR, 11αR)-9,10-dimethoxypterocarpan-3- O-β-D-glucoside			+H	-0.1	462	$C_{23}H_{26}O_{10}$	463[M+H]$^+$, 167[M+H-Glc]$^+$, 152[a]	Radix Astragali
33	Calycosin-7- O-β-D-glucoside-6"- O-acetate			+H	-0.6	488	$C_{24}H_{24}O_{11}$	489[M+H]$^+$, 285[M+H−C2H2O−Glc]$^+$, 270, 253[a]	Radix Astragali
34	Daidzein	-H	0.6	+H	-0.9	254	$C_{15}H_{10}O_4$	253[M-H]-, 224[M-H-CHO]-, 208,132[a]	Caulis Spatholobi
35	(3R)-2′-hydroxy-3′,4′- dimethoxy-isoflavan-7- O-β-D-glucoside	-H	0.5	+H	-0.6	464	$C_{23}H_{28}O_{10}$	465[M+H]$^+$,303[M+H-Glc]$^+$, 167[a]	Radix Astragali
36	Rindoside			+Na	-0.5	798	$C_{35}H_{42}O_{21}$	821[M+Na]+, 523, 505, 321[a]	Radix Gentianae
37	Quercetin	-H	0.0			302	$C_{15}H_{10}O_7$	301[M-H]$^-$, 273, 179, 165, 151[b]	Flos Carthami
38	Calycosin	-H	0.5	+H	-0.2	284	$C_{16}H_{12}O_5$	285[M+H]$^+$, 270[M+H-CH_3]$^+$, 253[M+H-CH3OH]$^+$, 225, 213[ab]	Radix Astragali and Caulis Spatholobi
39	Trifloroside	-H	3.0	+Na	0.3	782	$C_{35}H_{42}O_{20}$	805[M+Na]$^+$, 507, 321[a]	Radix Gentianae
40	(6aR, 11aR)-3-hydroxy-9,10-dimethoxypterocarpan	-H	1.7	+H	3.2	300	$C_{17}H_{16}O_5$	301[M+H]$^+$,167,152,134[a]	Radix Astragali
41	Senkyunolide F	-H	0.1	+H	-0.6	206	$C_{12}H_{14}O_3$	205[M-H]$^-$, 161, 131, 106	Radix Angelicae Sinensis
42	Formononetin	-H	1.9	+H	0.4	268	$C_{16}H_{12}O_4$	269[M+H]$^+$, 254[M+H-CH_3]$^+$, 226[M+H-CH3-CO]$^+$,197[ab]	Radix Astragali

									and Caulis Spatholobi
43	Astragaloside V/Astragaloside VI	-H	-1.6	+Na	-1	947	$C_{47}H_{78}O_{19}$	969[M+Na]$^{+}$, 789[M+Na-H20-Glc]$^{+a}$	Radix Astragali
44	Ligustilide （E）			+H	0.2	190	$C_{12}H_{14}O_2$	191[M+H]$^{+}$, 173[M+H-H_2O]+, 163[M+H-H2O-CO]$^{+}$,145^{a}	Radix Angelicae Sinensis
45	Astragaloside V/ Astragaloside VI	-H	-1.0	+Na	-1	947	$C_{47}H_{78}O_{19}$	969[M+Na]$^{+}$, 789[M+Na-$H_2$0-Glc]$^{+a}$	Radix Astragali
46	Astragaloside IV	-H	-0.8	+Na	-0.6	784	$C_{41}H_{68}O_{14}$	807[M+Na]$^{+}$, 627[M+Na-$H_2$0-Glc]$^{+ab}$	Radix Astragali
47	Astragaloside III	-H	-0.8	+Na	-0.8	784	$C_{41}H_{68}O_{14}$	807[M+Na]$^{+}$, 627[M+Na-$H_2$0-Glc]$^{+ab}$	Radix Astragali
48	Astragaloside II			+Na	-0.7	826	$C_{43}H_{70}O_{15}$	849[M+Na]$^{+}$, 669.40	Radix Astragali
49	isoAstragaloside II			+Na	-0.7	826	$C_{43}H_{70}O_{15}$	849[M+Na]$^{+}$, 669.40	Radix Astragali
50	Ligustilide （Z）			+H	0.2	190	$C_{12}H_{14}O_2$	191[M+H]$^{+}$, 173[M+H-H_2O]$^{+}$, 163[M+H-H2O-CO]$^{+}$, 145^{a}	Radix Angelicae Sinensis
51	Astragaloside Ⅰ			+Na	-2	868	$C_{45}H_{72}O_{16}$	891[M+Na]$^{+}$, 831,711^{b}	Radix Astragali
52	Isoastragaloside I			+Na	-2.7	868	$C_{45}H_{72}O_{16}$	891[M+Na]$^{+}$, 831,711^{b}	Radix Astragali
53	Cyclocephaloside Ⅱ			+Na	-0.7	826	$C_{43}H_{70}O_{15}$	849[M+Na]$^{+}$, 669.40	Radix Astragali

Supplementary Material Table 2. Calibration curve, linear range and LLOQ for calycosin-7-O-β-D-glucoside, ononin, ferulic acid, p-coumaric acid, gentiopicroside, sweroside, formononetin, and protocatechuic acid in plasma (n = 5)

Compounds	R	Linear range(ng/mL)	Calibration curve	LLOQ^{a}(ng/mL)	LOD^{b}(ng/mL)
Calycosin-7-O-β-D-Glucopyranoside	0.9992	0.5-161	y=0.481x+0.0418	0.5	0.2
Ononin	0.9990	0.28-88.8	y=0.833x+0.0771	0.28	0.1
Ferulic acid	0.9990	2-640.9	y=0.0194x+0.028	2	1

p-Coumaric acid	0.9991	10.1-3230	y=0.0382x+0.0624	10.1	6
Gentiopicroside	0.9985	1.8-578.4	y=0.125x+0.0999	1.8	0.2
Sweroside	0.9992	0.65-206	y=0.294x+0.0658	0.65	0.2
Formononetin	0.9990	0.1-33	y=0.423x+0.0323	0.1	0.05
Protocatechuic acid	0.9991	4-1280	y=0.0156x+0.105	4	2.5

a. lower limit of quantitation (the lowest point on the calibration curve).

b. limit of detection

Supplementary Material Table 3. Precision and accuracy of calycosin-7-O-β-D-glucoside, ononin, ferulic acid, p-coumaric acid, gentiopicroside, sweroside, formononetin, and protocatechuic acid from QC samples prepared in rat plasma (mean ± SD)

Compounds	Nominal concentration (ng/mL)	Intraday (n = 5)			Interday (n = 5*3)		
		Measured concentration (ng/mL)	Precision (%)	Accuracy (%)	Measured concentration (ng/mL)	Precision (%)	Accuracy (%)
Calycosin-7-O-β-D-Glucopyranoside	1.01	1.08 ± 0.02	1.8	107.1	1.03 ± 0.06	6.0	101.7
	16.1	16.50 ± 0.52	3.2	102.5	16.10 ± 1.07	6.6	100.0
	129	130.00 ± 5.74	4.4	100.8	122.60 ± 2.61	2.1	95.0
Ononin	0.555	0.56 ± 0.02	2.8	101.7	0.60 ± 0.04	6.2	107.8
	8.88	9.01 ± 0.18	2.0	101.4	9.14 ± 0.51	5.6	102.9
	71	71.58 ± 2.10	2.9	100.8	67.96 ± 0.78	1.2	95.7
Ferulic acid	4	3.95 ± 0.11	2.7	98.7	3.91 ± 0.10	2.7	97.7
	64	67.44 ± 2.80	4.1	105.4	67.22 ± 4.58	6.8	105.0
	512	523.40 ± 19.10	3.6	102.2	515.40 ± 8.71	1.7	100.7
p-Coumaric acid	20.2	19.10 ± 0.66	3.5	94.6	18.92 ± 0.67	3.5	93.7
	323	346.40 ± 12.54	3.6	107.2	338.00 ± 8.00	2.4	104.6
	2580	2656.00 ± 104.55	3.9	102.9	2576.00 ± 70.21	2.7	99.8
Gentiopicroside	3.62	3.73 ± 0.15	3.9	103.1	3.58 ± 0.19	5.3	98.9
	57.8	58.86 ± 2.85	4.8	101.8	58.82 ± 1.86	3.2	101.8
	463	468.60 ± 24.46	5.2	101.2	467.40 ± 7.60	1.6	101.0
Sweroside	1.29	1.37 ± 0.04	2.6	105.9	1.35 ± 0.07	4.9	105.0
	20.6	21.46 ± 1.24	5.8	104.2	21.56 ± 0.99	4.6	104.7
	165	169.40 ± 8.71	5.1	102.7	166.00 ± 1.73	1.0	100.6
Formononetin	0.206	0.21 ± 0.01	4.5	100.3	0.21 ± 0.01	3.6	100.6
	3.3	3.36 ± 0.16	4.8	101.9	3.35 ± 0.19	5.7	101.5
	26.4	26.66 ± 0.94	3.5	101.0	26.10 ± 0.37	1.4	98.9

Protocatechuic acid	8	7.64 ± 0.16	2.1	95.6	7.79 ± 0.60	7.8	97.4
	128	135.20 ± 4.76	3.5	105.6	131.60 ± 3.91	3.0	102.8
	1020	1074.00 ± 47.75	4.4	105.3	1056.00 ± 45.61	4.3	103.5

Supplementary Material Table 4. Extraction recovery, matrix effect and long-term stability of calycosin-7-O-β-D-glucoside, ononin, ferulic acid, p-coumaric acid, gentiopicroside, sweroside, formononetin, and protocatechuic acid in rat plasma (n = 5)

Compounds	Nominal concentration (ng/mL)	Recovery (%) (mean ± SD)	RSD	Matrix effect (%) (mean ± SD)	RSD	Stability(%) (mean ± SD)	RSD
Calycosin-7-O-β-D-Glucopyranoside	1.01	93.6 ± 1.5	1.6	91.0 ± 2.3	2.5	85.1 ± 5.6	6.6
	16.1	95.2 ± 2.3	2.4	94.0 ± 2.2	2.3	101.1 ± 5.1	5.0
	129	89.3 ± 3.5	4.0	99.7 ± 3.6	3.6	89.6 ± 2.7	3.0
Ononin	0.555	96.0 ± 4.9	5.1	110.1 ± 3.5	3.2	97.5 ± 6.9	7.1
	8.88	96.5 ± 2.7	2.8	93.0 ± 2.5	2.7	102.9 ± 6.3	6.1
	71	85.4 ± 1.1	1.3	103.2 ± 3.3	3.2	85.7 ± 0.9	1.1
Ferulic acid	4	97.6 ± 4.4	4.5	92.0 ± 6.3	6.9	103.0 ± 8.6	8.3
	64	91.3 ± 2.6	2.9	93.4 ± 1.3	1.4	112.5 ± 9.9	8.8
	512	93.6 ± 0.8	0.9	95.5 ± 2.6	2.7	100.0 ± 3.2	3.2
p-Coumaric acid	20.2	90.2 ± 4.0	4.4	91.8 ± 6.6	7.2	105.1 ± 14.6	13.9
	323	89.7 ± 3.6	4.0	89.7 ± 1.4	1.5	85.9 ± 7.8	9.1
	2580	93.7 ± 8.2	8.7	87.1 ± 1.9	2.2	100.8 ± 1.1	1.1
Gentiopicroside	3.62	93.7 ± 5.7	6.1	91.6 ± 1.3	1.5	89.3 ± 4.1	4.6
	57.8	92.1 ± 1.2	1.3	95.8 ± 3.2	3.4	102.8 ± 5.9	5.7
	463	86.3 ± 5.0	5.8	95.7 ± 3.8	4.0	90.1 ± 8.8	9.7
Sweroside	1.29	94.8 ± 0.7	0.8	91.0 ± 4.1	4.5	104.7 ± 7.7	7.3
	20.6	95.1 ± 2.1	2.2	98.8 ± 0.6	0.6	108.8 ± 11.0	10.2
	165	92.1 ± 5.6	6.1	94.4 ± 6.7	7.1	88.5 ± 2.3	2.6
Formononetin	0.206	95.1 ± 12.3	12.9	93.6 ± 6.5	6.9	92.6 ± 4.6	4.9
	3.3	92.8 ± 5.1	5.5	96.1 ± 1.0	1.1	98.8 ± 11.0	11.1
	26.4	91.2 ± 3.4	3.7	98.5 ± 4.5	4.6	87.8 ± 8.2	9.4
Protocatechuic acid	8	94.6 ± 3.3	3.5	98.9 ± 2.6	2.6	88.7 ± 7.2	8.2

	128	90.0	±	1.2	1.4	108.4	±	5.4	5.0	100.8	±	4.6	4.5
	1020	92.2	±	4.4	4.7	90.4	±	4.3	4.8	106.3	±	10.5	9.8
Wogonoside (IS+)	135	95.5	±	2.2	2.3	96.1	±	3.2	3.3				
Rhein (IS-)	135	91.0	±	2.4	2.6	97.7	±	4.7	4.8				