Tables:

Table S1.   Results of linear regression of calibration curves

of the four analytes in rat plasma

Analyte	Linear range(ng/ml)	Regression equation	R^2	LLOQ(ng/ml)
hesperidin	0.5-200	Y=0.0104X-0.00132	0.9993	0.5
hesperitin	0.5-200	Y=0.0369X-0.0266	0.9985	0.5
naringin	0.5-200	Y=0.006X+0.00253	0.9986	0.5
naringenin	0.5-200	Y=0.0874X-0.0709	0.9995	0.5
β-sitosterol	50-5000	Y=0.00919X+0.00508	0.9987	50

Table S2. Summary of accuracy and precision of hesperidin, hesperitin, naringin,

naringenin and β-sitosterol in plasma (mean± SD, intra-day: 6 replicates at each

concentration; inter-day: 6 replicates per day for 3 days).

Analyte	Added (ng/mL)	Intra-day (n=6)			Inter-day (n=18)		
		Mersured (ng/mL)	Accuracy (R.E., %)	Precision (R.S.D., %)	Mersured (ng/mL)	Accuracy (R.E., %)	Precision (R.S.D., %)
hesperidin	0.50	0.54±0.028	7.41	5.18	0.58±0.047	13.79	8.10
	50.0	52.20±3.31	4.21	6.34	54.24±2.83	7.82	5.22
	150	157.4±9.36	4.70	5.95	160.45±10.75	6.51	6.70
hesperitin	0.50	0.51±0.041	1.96	8.04	0.53±0.029	5.66	5.47
	50.0	54.30±2.15	7.92	3.96	55.19±6.64	9.40	12.03
	150	161.25±11.4	6.98	7.11	158.93±9.94	5.61	6.25
naringin	0.50	0.56±0.037	10.71	6.61	0.55±0.029	9.09	5.27
	50.0	53.65±5.83	6.81	10.87	51.99±3.74	3.83	7.19
	150	154.28±7.38	2.77	4.78	157.31±7.92	4.65	5.03
naringenin	0.50	0.58±0.068	13.79	11.72	0.56±0.058	10.71	10.36
	50.0	55.91±3.94	10.57	7.05	53.35±4.16	6.28	7.78
	150	144.53±10.2	-3.78	7.09	148.81±8.87	-0.80	5.96
β-sitosterol	50.0	52.8±3.27	5.60	5.18	55.9±5.77	11.8	10.3
	1000	1062±82.6	6.20	7.77	1097±90.3	9.70	8.23
	4000	4166±178.6	4.15	4.28	4236±211.6	5.90	4.99

Table S3. Absolute matrix effect and extraction recovery data

of the analytes and I.S. in rat plasma (n=6).

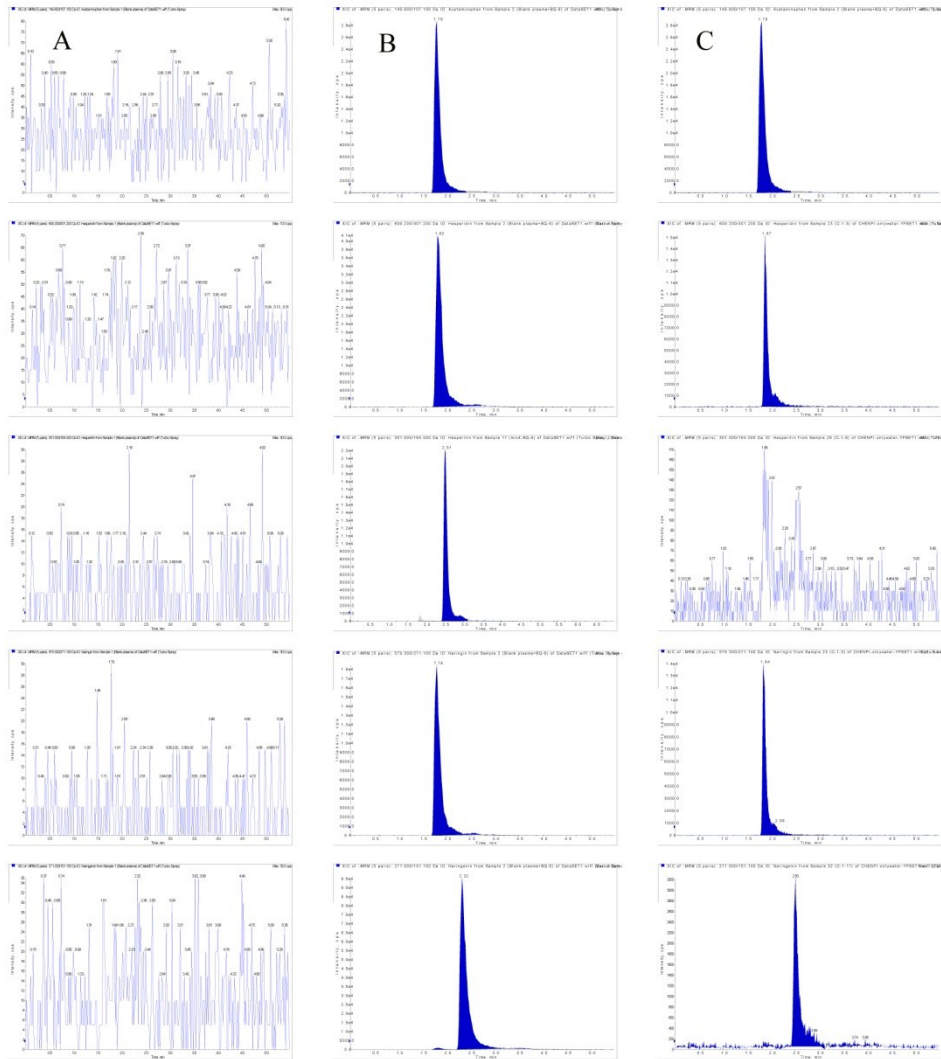| Analyte	Added(ng/mL)	Recovery		Matrix effect	
		Mean(%)	Precision(R.S.D., %)	Mean(%)	Precision(R.S.D., %)
hesperidin	0.5	90.1	11.3	97.6	10.4
	50	92.7	8.66	102.1	7.89
	150	94.8	7.89	98.9	6.11
hesperitin	0.5	95.1	8.52	96.1	10.03
	50	94.8	5.02	101.4	5.55
	150	96.7	7.41	99.1	6.24
naringin	0.5	87.2	9.57	101.9	13.31
	50	89.3	9.12	102.3	7.77
	150	93.9	10.1	99.8	5.82
naringenin	0.5	82.2	7.81	97.6	10.9
	50	85.6	9.22	97.1	8.01
	150	89.8	7.89	98.7	6.71
β-sitosterol	50	88.5	10.2	99.6	7.22
	1000	95.3	7.44	97.8	11.5
	4000	91.7	6.23	102.3	7.12
Acetaminophen	50	85.1	4.67	101.6	4.89
nitrendipine	50	88.7	5.67	99.6	6.21

Figure S1. Representative chromatograms of (A) blank plasma; (B) blank plasma spiked with acetaminophen (IS,250 ng/mL), hesperidin (10 ng/mL), hesperitin (10 ng/mL), naringin (10ng/mL) and naringenin(10 ng/mL); (C) plasma sample from a rat 0.5 h after oral administration of Chenpi at a dose of 2 g/kg.
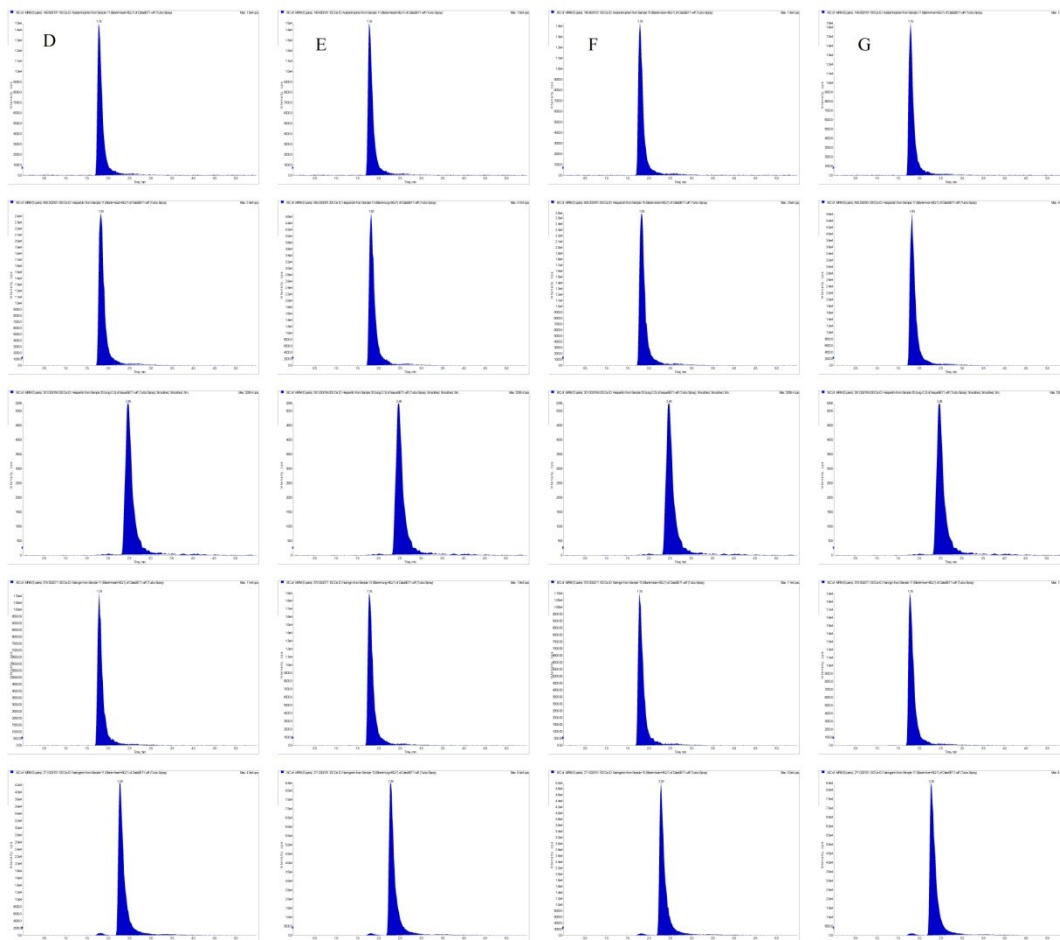
Figure S2. Representative chromatograms of acetaminophen(IS,250 ng/mL), hesperidin (20 ng/mL), hesperitin (20 ng/mL), naringin(20 ng/mL) and naringenin(20 ng/mL) in heart (D)，lung (E)，brain (F)and liver (G).
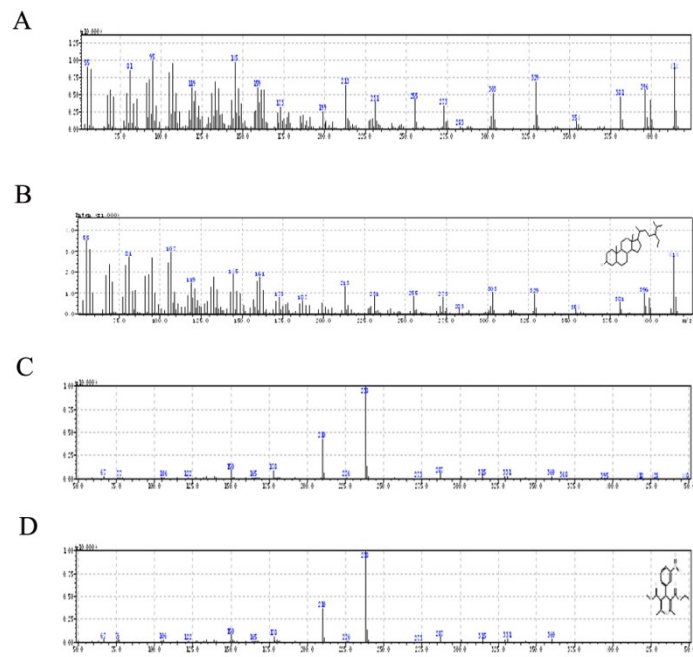
A

B

C

D

Figure S3. Mass spectrums of β-sitosterol (a), β-sitosterol in GC/MS database (b),   nitrendipine
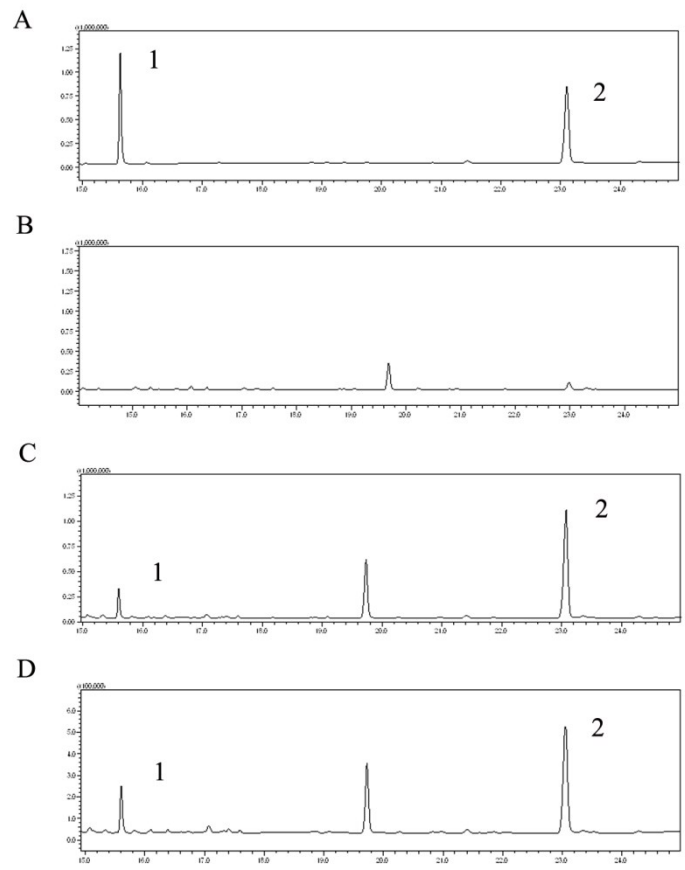
(c), nitrendipine in GC/MS database (d)

Figure S4. SIM chromatogram of (A) standard substance, (B) blank plasma, (C) blank plasma spiked with the analytes and I.S. (D) plasma sample obtained at 12 h after oral administration of Chenpi-Banxia: β-sitosterol (1), nitrendipine (2)