

Supplementary Materials: Comparative Study on Excretive Characterization of Main Components in Herb Pair Noto Ginseng-Safflower and Single Herbs by LC-MS/MS

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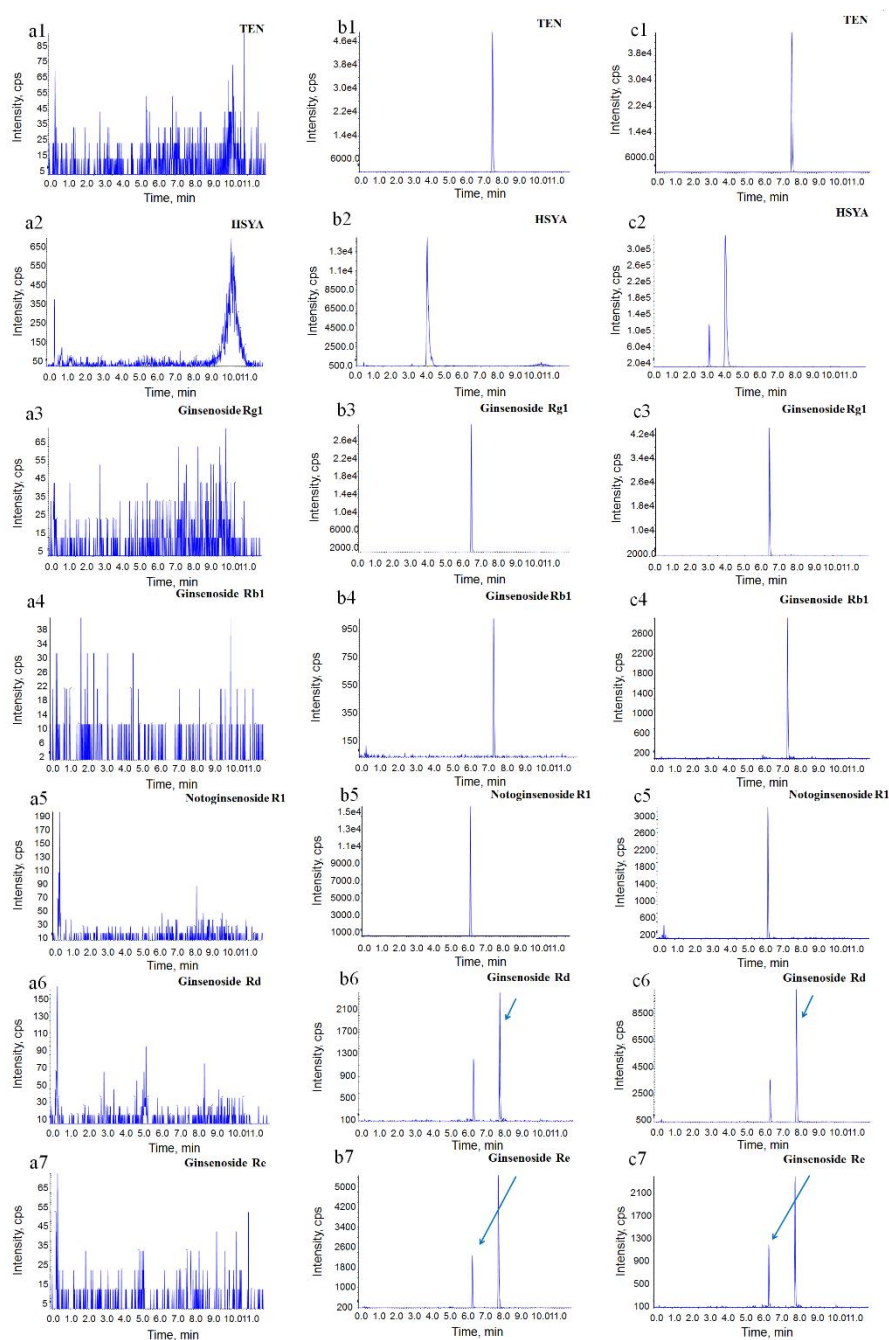


Figure S1. Representative LC-MS chromatograms of (a) blank rat urine, (b) rat urine spiked with 6 compounds solution (500 ng/mL) and IS (100 ng/mL), and (c) 6 compounds in the rat urine sample at 0–2 h after oral administration of CNS.

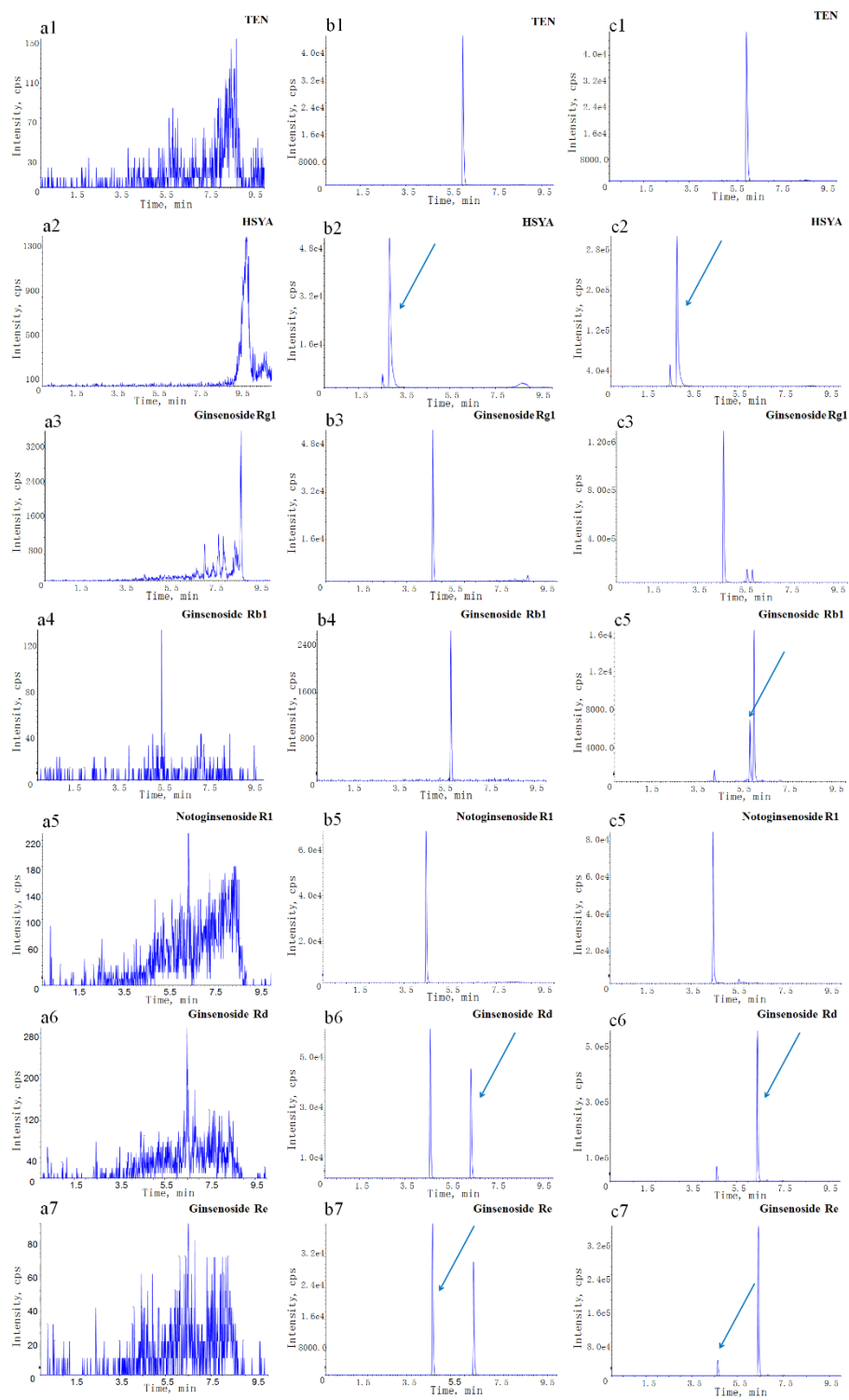


Figure S2. Representative LC-MS chromatograms of (a) blank rat feces, (b) rat feces spiked with 6 compounds solution (1000 ng/mL) and IS (100 ng/mL), and (c) 6 compounds in the rat feces sample at 8–12 h after oral administration of CNS.

Table S1. Stability of six compounds in rat urine ($n = 5$).

Compounds	QC conc. (ng/mL)	Stored at -80 °C for 1 months			Freeze-thawing 3 cycles			Room temperature for 24 h			Post-preparative stability at 4 °C for 96 h		
		Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy
		(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)
HSYA	10	11.2	8.6	12.5	10.1	10.8	1.5	11.3	9.4	13.2	9.6	13.4	-4.4
	200	173.2	9.4	-13.4	203.0	5.7	1.7	195.8	5.0	-1.9	173.4	10.0	-3.3
	5000	5657.5	8.4	13.2	5104.1	4.9	1.9	5110.0	8.6	2.2	5590.0	5.2	12.0
Ginsenoside Rg1	10	8.8	7.4	12.7	9.6	6.2	-4.3	9.3	10.7	-7.3	9.1	8.2	-8.2
	200	200.9	7.1	0.2	202.3	5.1	1.0	195.7	2.1	-0.4	200.0	4.1	0.1
	5000	5616.0	6.4	12.4	4664.0	3.9	-6.7	5482.1	3.3	9.7	4824.0	3.4	-3.5
Ginsenoside Rb1	1	1.0	7.2	9.2	1.0	7.3	14.9	1.1	10.8	-0.2	0.9	11.6	-5.5
	20	17.6	9.8	-12.5	18.3	7.3	-8.2	17.7	11.2	-11.7	21.6	3.4	8.2
	500	497.5	4.8	-0.6	427.0	2.0	-14.6	452.0	3.5	-9.6	430.0	2.6	-14.1
Notoginsenoide	1	1.1	5.2	14.8	0.9	11.0	-13.3	0.9	14.3	-1.1	1.0	14.7	-2.0
R1	20	17.4	12.4	-7.8	18.7	8.5	-7.0	21.0	10.8	5.0	19.8	7.7	-1.4
	500	501.5	5.4	0.3	436.5	5.8	-12.7	544.0	2.6	8.8	452.2	2.7	-9.5
Ginsenoside Rd	1	1.0	8.4	-6.3	1.1	9.9	5.6	1.0	14.1	-9.2	0.9	14.3	-2.1
	20	17.3	12.7	-13.8	18.3	2.1	-8.7	19.2	12.7	-4.2	19.4	4.7	-3.4
	500	479.1	5.56	-4.3	45.8	5.7	-8.4	473.3	4.1	-5.3	469.6	5.3	-6.2
Ginsenoside Re	1	0.9	13.0	9.7	1.0	9.1	6.2	0.8	14.9	-14.0	0.9	6.5	-13.7
	20	19.5	3.9	-2.3	18.3	3.5	-8.2	10.9	5.8	-3.0	18.1	5.9	-9.0
	500	437.4	5.6	-12.5	465.8	1.4	-6.8	509.0	3.2	1.7	427.3	2.2	-14.6

Table S2. Stability of six compounds in rat feces ($n = 5$).

Compounds	QC conc. (ng/mL)	Stored at -80 °C for 1 months			Freeze-thawing 3 cycles			Room temperature for 24 h			Post-preparative stability at 4 °C for 96 h		
		Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy	Calc. conc	Precision	Accuracy
		(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)	(ng/mL)	(%)	(%)
HSYA	5	4.7	5.9	-6.6	5.0	9.5	0.1	5.0	9.8	1.0	5.4	6.2	6.8
	200	189.3	4.0	-5.3	180.1	6.3	-9.9	178.8	4.1	-7.6	186.8	10.5	-6.4
	2000	2075.0	6.7	4.0	2068.3	4.7	-8.6	1891.7	6.3	-6.8	1783.3	5.0	-10.9
Ginsenoside Rg1	5	5.5	2.1	9.3	5.4	6.1	7.1	5.6	13.2	11.2	5.5	2.5	9.2
	200	214.5	3.1	7.3	203.9	4.2	2.0	217.3	4.1	3.0	212.7	5.4	6.4
	2000	1993.3	1.1	-0.2	1800.0	3.6	2.2	1790.0	3.7	0.4	1891.7	6.2	-5.5
Ginsenoside Rb1	5	5.5	4.5	9.5	5.5	1.2	10.0	4.8	9.7	-4.3	5.4	2.3	8.7
	200	183.3	2.6	-8.4	188.3	5.2	-5.7	186.2	3.3	-3.6	202.5	8.4	1.3
	2000	1903.3	4.4	-4.8	2138.3	3.4	-5.7	1965.0	5.8	-1.7	1881.7	5.8	-6.0
Notoginsenoside R1	5	5.3	4.4	6.2	5.4	3.1	8.7	5.4	4.8	7.3	5.5	2.6	10.5
	200	213.7	2.3	6.8	194.3	4.6	-2.9	213.3	2.7	2.1	214.0	5.0	6.9
	2000	1845.0	5.3	-7.8	1875.0	3.7	-2.1	1808.3	4.1	0.5	1828.3	4.9	-8.5
Ginsenoside Rd	5	5.0	9.4	-0.1	5.1	9.4	2.3	4.8	8.0	-3.8	5.3	5.1	5.4
	200	209.8	2.8	4.8	198.4	2.6	-0.9	213.8	3.9	2.7	209.2	7.6	4.7
	2000	1928.3	2.1	-3.6	1903.3	3.2	-1.4	1826.7	5.2	2.1	1835.0	3.7	-8.2

Ginsenoside Re	5	4.8	9.3	-3.7	5.4	4.5	7.3	5.0	6.2	0.6	5.3	7.0	5.9
	200	219.0	2.6	9.5	192.9	4.0	-3.6	217.2	2.9	4.6	212.8	3.2	6.5
	2000	2095.0	4.4	4.6	1905.0	4.7	-3.3	1866.7	4.8	3.6	1945.0	5.6	-2.6

Table S3. Mean urine excretion amount of HSYA after oral administration of safflower total flavonoids (SF) in rats ($n = 6$, mean \pm SD).

Time point (h)	HSYA Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	1.803 \pm 0.870	6.268 \pm 3.141	6.268 \pm 3.141	0.623 \pm 0.317
4	4.325 \pm 2.706	6.880 \pm 4.592	13.148 \pm 6.505	1.305 \pm 0.647
6	3.381 \pm 2.681	5.139 \pm 5.476	14.717 \pm 5.303	1.465 \pm 0.527
8	1.310 \pm 0.782	2.185 \pm 1.420	15.809 \pm 5.807	1.564 \pm 0.573
12	0.864 \pm 0.046	2.960 \pm 2.5891	18.769 \pm 6.103	1.861 \pm 0.608
24	0.825 \pm 0.828	8.442 \pm 8.803	27.211 \pm 12.281	2.691 \pm 1.210
36	0.201 \pm 0.136	0.864 \pm 0.722	28.075 \pm 12.431	2.782 \pm 1.235
48	0.050 \pm 0.046	0.269 \pm 0.285	28.344 \pm 12.378	2.809 \pm 1.228
72	0.022 \pm 0.014	0.126 \pm 0.043	28.470 \pm 12.357	2.822 \pm 1.220
96	0.018 \pm 0.019	0.031 \pm 0.038	28.501 \pm 12.334	2.822 \pm 1.225
120	0.035 \pm 0.045	0.070 \pm 0.091	28.562 \pm 12.270	2.837 \pm 1.216

Table S4. Mean urine excretion amount of HSYA after oral administration of the combination of NS and SF (CNS) in rats ($n = 6$, mean \pm SD).

Time point (h)	HSYA Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	3.367 \pm 3.471	4.713 \pm 3.816	4.713 \pm 3.816	0.473 \pm 0.387
4	4.299 \pm 4.350	5.787 \pm 2.672	9.054 \pm 2.878	0.902 \pm 0.288
6	1.851 \pm 1.081	2.915 \pm 1.407	11.240 \pm 2.799	1.111 \pm 0.284
8	2.374 \pm 2.051	3.567 \pm 3.630	13.469 \pm 5.034	1.332 \pm 0.503
12	4.148 \pm 6.221	3.442 \pm 2.613	16.481 \pm 6.950	1.634 \pm 0.696

24	0.453±0.548	1.562±1.307	18.044±7.031	1.783±0.701
36	0.198±0.296	0.340±0.319	18.373±7.165	1.821±0.715
48	0.039±0.042	0.195±0.178	18.568±7.270	1.841±0.726
72	0.066±0.139	0.133±0.278	18.701±7.480	1.857±0.748
96	0.031±0.045	0.062±0.089	18.763±7.536	1.864±0.759
120	0.057±0.114	0.041±0.052	18.804±7.544	1.864±0.756

Table S5. Mean urine excretion amount of ginsenoside Rg1 after oral administration of notoginseng total saponins (NS) in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rg1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	3.362±7.021	4.985±1.411	4.985±1.411	0.142±0.045
4	1.678±1.800	2.844±0.973	6.610±2.052	0.193±0.061
6	1.445±1.455	3.616±2.575	9.709±2.893	0.285±0.086
8	1.140±1.226	3.890±2.477	11.931±4.568	0.348±0.137
12	0.727±0.171	3.130±2.715	15.061±7.022	0.439±0.200
24	0.135±0.209	0.636±0.590	15.697±7.182	0.451±0.202
36	0.115±0.151	0.402±0.338	16.042±7.062	0.463±0.204
48	0.100±0.171	0.285±0.276	1.633±7.089	0.465±0.204
72	0.178±0.382	0.091±0.014	16.417±7.147	0.476±0.208
96	0.085±0.159	0.062±0.110	16.480±7.192	0.473±0.208
120	0.059±0.105	0.062±0.148	16.542±7.264	0.473±0.211

Table S6. Mean urine excretion amount of ginsenoside Rg1 after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rg1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	1.507 \pm 1.443	1.881 \pm 1.001	1.881 \pm 1.001	0.066 \pm 0.032
4	1.692 \pm 2.343	2.002 \pm 1.609	3.382 \pm 2.188	0.111 \pm 0.072
6	0.544 \pm 0.216	0.816 \pm 0.264	3.994 \pm 2.061	0.132 \pm 0.073
8	0.835 \pm 0.697	1.169 \pm 0.913	4.725 \pm 2.486	0.155 \pm 0.084
12	0.789 \pm 0.937	0.805 \pm 0.300	5.430 \pm 2.374	0.188 \pm 0.080
24	2.348 \pm 5.832	2.622 \pm 5.710	8.052 \pm 5.572	0.263 \pm 0.182
36	0.228 \pm 0.361	0.336 \pm 0.421	8.388 \pm 5.927	0.274 \pm 0.195
48	0.065 \pm 0.082	0.301 \pm 0.361	8.689 \pm 6.056	0.285 \pm 0.202
72	0.093 \pm 0.156	0.185 \pm 0.312	8.87 \pm 6.051	0.293 \pm 0.206
96	0.046 \pm 0.053	0.091 \pm 0.106	8.966 \pm 6.090	0.292 \pm 0.204
120	0.080 \pm 0.174	0.061 \pm 0.081	9.027 \pm 6.117	0.292 \pm 0.206

Table S7. Mean urine excretion amount of ginsenoside Rb1 after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rb1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.115 \pm 0.284	0.075 \pm 0.063	0.075 \pm 0.063	0.002 \pm 0.001
4	0.245 \pm 0.450	0.872 \pm 1.518	0.574 \pm 1.167	0.013 \pm 0.027
6	0.140 \pm 0.244	0.262 \pm 0.207	0.798 \pm 1.077	0.019 \pm 0.025
8	0.140 \pm 0.196	0.152 \pm 0.084	0.863 \pm 1.044	0.021 \pm 0.025
12	0.214 \pm 0.344	0.276 \pm 0.142	1.139 \pm 1.140	0.027 \pm 0.027

24	0.240±0.553	0.742±0.289	1.881±1.352	0.044±0.032
36	0.061±0.054	0.394±0.221	2.275±1.435	0.053±0.033
48	0.142±0.344	0.201±0.117	2.476±1.415	0.058±0.033
72	0.084±0.195	0.030±0.020	2.506±1.429	0.058±0.033
96	0.045±0.104	0.016±0.011	2.521±1.438	0.060±0.034
120	0.025±0.062	0.006±0.003	2.528±1.439	0.060±0.034

Table S8. Mean urine excretion amount of ginsenoside Rb1 after oral administration of CNS in rats ($n = 6$, mean \pm SD)´.

Time point (h)	Ginsenoside Rb1 Concentration (µg/mL)	Excretion amount (µg)	Accumulative excretion amount (µg)	Accumulative excretion percentage (%)
2	0.054±0.073	0.075±0.093	0.075±0.093	0.002±0.002
4	0.027±0.041	0.044±0.050	0.106±0.086	0.003±0.002
6	0.111±0.121	0.158±0.142	0.218±0.166	0.006±0.004
8	0.105±0.100	0.212±0.169	0.339±0.213	0.009±0.006
12	0.120±0.134	0.154±0.128	0.472±0.310	0.013±0.008
24	0.072 ±0.050	0.388±0.391	0.859±0.527	0.023±0.014
36	0.138±0.144	0.197±0.129	1.056±0.587	0.028±0.016
48	0.051±0.060	0.247±0.216	1.303±0.684	0.035±0.018
72	0.033±0.028	0.070±0.060	1.373±0.705	0.037±0.019
96	0.019±0.014	0.040±0.031	1.414±0.715	0.038±0.019
120	0.014±0.012	0.022±0.025	1.436±0.726	0.038±0.019

Table S9. Mean urine excretion amount of notoginsenoide R1 after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Notoginsenoside R1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.347 \pm 0.206	1.836 \pm 0.582	1.836 \pm 0.583	0.221 \pm 0.074
4	0.554 \pm 0.525	0.923 \pm 0.305	2.297 \pm 0.417	0.282 \pm 0.055
6	0.487 \pm 0.591	1.291 \pm 1.148	3.373 \pm 1.035	0.414 \pm 0.133
8	0.303 \pm 0.337	0.914 \pm 0.716	3.830 \pm 1.192	0.476 \pm 0.151
12	0.160 \pm 0.020	0.703 \pm 0.729	4.533 \pm 1.801	0.557 \pm 0.229
24	0.025 \pm 0.032	0.177 \pm 0.156	4.710 \pm 1.879	0.586 \pm 0.237
36	0.017 \pm 0.018	0.072 \pm 0.047	4.782 \pm 1.871	0.582 \pm 0.233
48	0.014 \pm 0.020	0.057 \pm 40.00	4.840 \pm 1.877	0.591 \pm 0.232
72	0.020 \pm 0.038	0.006 \pm 0.005	4.846 \pm 1.877	0.591 \pm 0.235
96	0.009 \pm 0.014	0.003 \pm 0.003	4.849 \pm 1.876	0.591 \pm 0.232
120	0.008 \pm 0.013	0.001 \pm 0.0001	4.850 \pm 1.876	0.593 \pm 0.231

Table S10. Mean urine excretion amount of notoginsenoide R1 after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Notoginsenoside R1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.499 \pm 0.465	0.637 \pm 0.317	0.637 \pm 0.317	0.091 \pm 0.043
4	0.664 \pm 1.002	0.750 \pm 0.709	1.200 \pm 0.836	0.174 \pm 0.122
6	0.195 \pm 0.094	0.301 \pm 0.152	1.426 \pm 0.803	0.201 \pm 0.115
8	0.264 \pm 0.226	0.454 \pm 0.236	1.653 \pm 0.940	0.231 \pm 0.134
12	0.159 \pm 0.204	0.177 \pm 0.097	1.808 \pm 0.888	0.252 \pm 0.123

24	0.480±0.130	0.554±0.128	2.361±1.275	0.334±0.182
36	0.021±0.037	0.037±0.053	2.399±1.316	0.345±0.186
48	0.007±0.005	0.033±0.019	2.432±1.326	0.341±0.196
72	0.008±0.011	0.016±0.022	2.447±1.325	0.342±0.193
96	0.004±0.003	0.009±0.007	2.456±1.328	0.342±0.193
120	0.005±0.004	0.006±0.003	2.462±1.328	0.342±0.196

Table S11. Mean urine excretion amount of ginsenoside Rd after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rd Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.017±0.039	0.022±0.025	0.022±0.025	0.002±0.003
4	0.033±0.069	0.008±0.003	0.027±0.029	0.003±0.003
6	0.010±0.018	0.021±0.020	0.048±0.039	0.006±0.004
8	0.009±0.012	0.082±0.123	0.097±0.129	0.011±0.015
12	0.028±0.019	0.076±0.083	0.173±0.206	0.020±0.024
24	0.034±0.063	0.106±0.109	0.279±0.198	0.032±0.023
36	0.017±0.033	0.041±0.012	0.311±0.182	0.036±0.021
48	0.012±0.019	0.048±0.045	0.359±0.187	0.041±0.021
72	0.012±0.023	0.013±0.018	0.372±0.200	0.043±0.023
96	0.006±0.010	0.008±0.013	0.379±0.211	0.044±0.024
120	0.003±0.006	0.007±0.012	0.386±0.221	0.044±0.025

Table S12. Mean urine excretion amount of ginsenoside Rd after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rd Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.022 \pm 0.042	0.005 \pm 0.005	0.005 \pm 0.005	0.001 \pm 0.001
4	0.009 \pm 0.015	0.005 \pm 0.007	0.009 \pm 0.008	0.001 \pm 0.001
6	0.017 \pm 0.016	0.018 \pm 0.018	0.024 \pm 0.023	0.003 \pm 0.003
8	0.038 \pm 0.075	0.010 \pm 0.009	0.029 \pm 0.024	0.004 \pm 0.003
12	0.053 \pm 0.110	0.019 \pm 0.016	0.045 \pm 0.040	0.006 \pm 0.005
24	0.315 \pm 0.787	0.058 \pm 0.066	0.103 \pm 0.083	0.014 \pm 0.011
36	0.041 \pm 0.068	0.011 \pm 0.009	0.114 \pm 0.086	0.015 \pm 0.011
48	0.030 \pm 0.070	0.021 \pm 0.024	0.135 \pm 0.096	0.018 \pm 0.013
72	0.016 \pm 0.035	0.004 \pm 0.004	0.139 \pm 0.098	0.018 \pm 0.013
96	0.016 \pm 0.036	0.005 \pm 0.005	0.144 \pm 0.100	0.019 \pm 0.013
120	0.010 \pm 0.017	0.004 \pm 0.004	0.148 \pm 0.101	0.019 \pm 0.013

Table S13. Mean urine excretion amount of ginsenoside Re after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Re Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.289 \pm 0.689	0.304 \pm 0.161	0.304 \pm 0.161	0.064 \pm 0.030
4	0.091 \pm 0.119	0.129 \pm 0.051	0.390 \pm 0.199	0.072 \pm 0.037
6	0.032 \pm 0.030	0.143 \pm 0.125	0.509 \pm 0.225	0.096 \pm 0.042
8	0.040 \pm 0.026	0.173 \pm 0.121	0.625 \pm 0.321	0.127 \pm 0.059
12	0.033 \pm 0.024	0.096 \pm 0.087	0.721 \pm 0.406	0.138 \pm 0.075

24	0.017±0.034	0.024±0.015	0.745±0.403	0.149±0.074
36	0.015±0.023	0.044±0.046	0.782±0.377	0.141±0.070
48	0.013±0.024	0.020±0.022	0.802±0.380	0.152±0.070
72	0.017±0.037	0.007±0.017	0.809±0.391	0.156±0.072
96	0.007±0.013	0.005±0.010	0.814±0.399	0.154±0.074
120	0.004±0.008	0.004±0.010	0.819±0.408	0.154±0.075

Table S14. Mean urine excretion amount of ginsenoside Re after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Re Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
2	0.086±0.088	0.133±0.062	0.133±0.062	0.028±0.013
4	0.070±0.089	0.100±0.090	0.193±0.131	0.041±0.028
6	0.039±0.027	0.064±0.030	0.231±0.118	0.049±0.025
8	0.041±0.035	0.072±0.033	0.289±0.121	0.061±0.026
12	0.035±0.041	0.035±0.015	0.324±0.110	0.069±0.023
24	0.369±0.963	0.058±0.054	0.381±0.153	0.081±0.032
36	0.024±0.038	0.030±0.037	0.411±0.177	0.087±0.037
48	0.006±0.007	0.03±0.038	0.447±0.206	0.095±0.044
72	0.005±0.007	0.013±0.017	0.460±0.207	0.097±0.044
96	0.003±0.005	0.008±0.012	0.468±0.217	0.099±0.046
120	0.004±0.008	0.004±0.005	0.472±0.219	0.100±0.046

Table S15. Mean feces excretion amount of HSYA after oral administration of SF in rats ($n = 6$, mean \pm SD).

Time point (h)	HSYA Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	2.409 \pm 0.352	43.994 \pm 12.319	43.994 \pm 12.319	4.352 \pm 1.224
8	1.954 \pm 0.115	36.072 \pm 10.358	80.066 \pm 21.692	7.922 \pm 2.151
12	2.144 \pm 0.142	39.052 \pm 8.681	119.118 \pm 30.243	11.784 \pm 2.995
24	0.791 \pm 0.082	14.632 \pm 4.256	133.750 \pm 33.764	13.233 \pm 3.346
36	0.975 \pm 0.039	17.848 \pm 4.279	151.598 \pm 37.989	15.001 \pm 3.762
48	0.060 \pm 0.002	1.109 \pm 0.297	152.707 \pm 38.286	15.115 \pm 3.794
72	0.031 \pm 0.002	0.570 \pm 0.162	153.277 \pm 38.442	15.161 \pm 3.803
96	ND	ND	153.277 \pm 38.442	15.156 \pm 3.807
120	ND	ND	153.277 \pm 38.442	15.159 \pm 3.802

Table S16. Mean feces excretion amount of HSYA after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	HSYA Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	1.646 \pm 2.261	21.013 \pm 30.299	21.012 \pm 30.299	2.084 \pm 3.005
8	2.095 \pm 0.121	31.265 \pm 8.953	52.277 \pm 28.669	5.171 \pm 2.844
12	1.660 \pm 0.349	24.260 \pm 6.796	76.537 \pm 34.048	7.572 \pm 3.374
24	1.829 \pm 0.220	27.706 \pm 9.755	104.243 \pm 34.486	10.316 \pm 3.415
36	0.737 \pm 0.037	11.040 \pm 3.298	115.284 \pm 36.570	11.401 \pm 3.623
48	0.688 \pm 0.047	10.267 \pm 3.026	125.551 \pm 38.391	12.422 \pm 3.804
72	0.068 \pm 0.028	1.049 \pm 0.586	126.560 \pm 38.340	12.521 \pm 3.795

96	0.017±0.016	0.274±0.283	126.874±38.274	12.556±3.795
120	ND	ND	126.874±38.274	12.556±3.796

Table S17. Mean feces excretion amount of ginsenoside Rg1 after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rg1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	1.508±0.256	21.063±5.410	21.063±5.410	0.612±0.145
8	0.473±0.016	6.792±2.122	27.855±7.375	0.798±0.216
12	1.087±0.088	15.587±4.879	43.442±12.025	1.244±0.343
24	2.041±0.055	29.239±8.754	72.682±20.662	2.071±0.592
36	2.020±0.054	28.977±8.942	101.659±29.524	2.904±0.845
48	2.084±0.047	30.041±9.594	131.700±39.092	3.751±1.111
72	0.116±0.008	1.673±0.554	133.372±39.629	3.801±1.132
96	0.023±0.001	0.327±0.104	133.700±39.733	3.814±1.133
120	0.022±0.002	0.315±0.110	134.015±39.837	3.824±1.132

Table S18. Mean feces excretion amount of ginsenoside Rg1 after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rg1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	1.105±1.515	14.286±20.907	14.286±20.907	0.474±0.681
8	1.708±0.054	25.666±7.933	39.952±21.244	1.303±0.695
12	1.109±0.221	16.908±6.636	56.860±20.559	1.864±0.675
24	0.980±0.138	14.504±4.143	71.363±24.096	2.331±0.796

36	0.959±0.040	14.365±4.335	85.729±27.211	2.802±0.894
48	0.943±0.049	14.173±4.533	99.901±30.374	3.265±0.994
72	0.324±0.249	5.212±4.367	105.113±30.466	3.431±0.996
96	0.024±0.024	0.396±0.402	105.509±30.482	3.441±0.996
120	ND	ND	105.509±30.482	3.442±0.994

Table S19. Mean feces excretion amount of ginsenoside Rb1 after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rb1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	1.082±0.156	15.357±4.697	15.357±4.697	0.361±0.113
8	0.767±0.029	11.066±3.551	26.423±8.057	0.624±0.192
12	2.064±0.137	29.724±9.595	56.148±17.467	1.312±0.411
24	2.184±0.090	31.223±9.132	87.371±26.505	2.043±0.622
36	0.920±0.048	13.350±4.715	100.721±31.049	2.354±0.725
48	1.022±0.052	14.806±5.076	115.527±36.105	2.692±0.846
72	0.120±0.009	1.710±0.525	117.237±36.600	2.731±0.854
96	0.019±0.004	0.264±0.103	117.502±36.686	2.741±0.854
120	0.017±0.003	0.252±0.100	117.753±36.774	2.745±0.858

Table S20. Mean feces excretion amount of ginsenoside Rb1 after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rb1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.555±0.763	7.072±10.199	7.072±10.199	0.192±0.275

8	1.079±0.431	15.499±6.228	22.570±15.790	0.607±0.426
12	0.899±0.096	13.492±4.335	36.062±14.935	0.968±0.409
24	0.802±0.025	12.018±3.497	48.081±16.475	1.282±0.443
36	0.548±0.036	8.141±2.259	56.222±17.772	1.501±0.476
48	0.552±0.030	8.316±2.614	64.538±19.434	1.723±0.522
72	0.455±0.377	7.325±6.432	71.863±19.005	1.923±0.515
96	0.021±0.020	0.350±0.350	72.213±19.048	1.931±0.512
120	ND	ND	72.213±19.048	1.931±0.513

Table S21. Mean feces excretion amount of notoginsenoside R1 after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Notoginsenoside R1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.654±0.107	9.116±2.220	9.116±2.220	1.112±0.274
8	0.819±0.021	11.769±3.631	20.885±5.710	2.552±0.705
12	0.734±0.058	10.516±3.227	31.400±8.858	3.843±1.083
24	0.852±0.028	12.201±3.654	43.602±12.487	5.331±1.532
36	1.949±0.092	28.179±9.578	71.781±21.933	8.772±2.685
48	0.486±0.014	7.000±2.190	78.781±24.115	9.637±2.956
72	0.081±0.006	1.167±0.367	79.948±24.475	9.773±2.992
96	0.015±0.001	0.222±0.076	80.170±24.552	9.806±3.001
120	0.015±0.002	0.212±0.077	80.382±24.620	9.826±3.017

Table S22. Mean feces excretion amount of notoginsenoside R1 after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Notoginsenoside R1 Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.498 \pm 0.687	6.325 \pm 9.106	6.325 \pm 9.106	0.891 \pm 1.272
8	0.579 \pm 0.146	8.872 \pm 3.877	15.196 \pm 6.994	2.135 \pm 0.983
12	0.286 \pm 0.016	4.255 \pm 1.140	19.451 \pm 7.478	2.726 \pm 1.057
24	0.430 \pm 0.169	6.198 \pm 2.470	25.649 \pm 9.940	3.594 \pm 1.392
36	0.817 \pm 0.034	12.178 \pm 3.423	37.827 \pm 11.858	5.305 \pm 1.667
48	0.807 \pm 0.056	12.106 \pm 3.723	49.933 \pm 14.254	6.992 \pm 2.001
72	0.116 \pm 0.021	1.766 \pm 0.672	51.699 \pm 14.529	7.243 \pm 2.035
96	0.044 \pm 0.042	0.713 \pm 0.707	52.411 \pm 14.487	7.342 \pm 2.034
120	ND	ND	52.411 \pm 14.487	7.342 \pm 2.033

Table S23. Mean feces excretion amount of ginsenoside Rd after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rd Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.752 \pm 0.079	10.755 \pm 3.385	10.755 \pm 3.385	1.232 \pm 0.395
8	0.605 \pm 0.022	8.721 \pm 2.813	19.476 \pm 6.086	2.244 \pm 0.706
12	0.602 \pm 0.049	8.676 \pm 2.808	28.152 \pm 8.861	3.232 \pm 1.024
24	0.670 \pm 0.034	9.562 \pm 2.795	37.713 \pm 11.637	4.331 \pm 1.342
36	0.505 \pm 0.014	7.290 \pm 2.427	45.004 \pm 14.004	5.174 \pm 1.612
48	0.704 \pm 0.026	10.151 \pm 3.361	55.154 \pm 17.338	6.332 \pm 1.991
72	0.122 \pm 0.005	1.753 \pm 0.562	56.907 \pm 17.892	6.534 \pm 2.048

96	0.017±0.001	0.241±0.076	57.148±17.967	6.563±2.059
120	0.015±0.002	0.223±0.076	57.371±18.037	6.589±2.068

Table S24. Mean feces excretion amount of ginsenoside Rd after oral administration of CNS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Rd Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.204±0.283	2.579±3.701	2.579±3.701	0.343±0.491
8	0.274±0.065	4.108±1.195	6.687±3.535	0.883±0.462
12	0.164±0.012	2.459±0.753	9.145±3.524	1.204±0.465
24	0.119±0.051	1.855±1.046	11.000±3.256	1.453±0.432
36	0.653±0.041	9.700±2.660	20.700±5.415	2.724±0.715
48	0.658±0.072	9.778±2.743	30.478±7.801	4.011±1.032
72	0.153±0.072	2.403±1.477	32.881±8.515	4.322±1.123
96	0.035±0.034	0.570±0.568	33.451±8.722	4.403±1.154
120	ND	ND	33.425±8.713	4.404±1.151

Table S25. Mean feces excretion amount of ginsenoside Re after oral administration of NS in rats ($n = 6$, mean \pm SD).

Time point (h)	Ginsenoside Re Concentration ($\mu\text{g/mL}$)	Excretion amount (μg)	Accumulative excretion amount (μg)	Accumulative excretion percentage (%)
4	0.323±0.043	4.585±1.408	4.585±1.408	0.852±0.261
8	0.455±0.018	6.563±2.122	11.148±3.459	2.063±0.644
12	0.401±0.027	5.759±1.787	16.907±5.229	3.122±0.971
24	0.430±0.015	6.150±1.850	23.057±7.062	4.266±1.305

36	0.421±0.018	6.105±2.098	29.162±9.141	5.397± 1.699
48	0.561±0.026	8.106±2.700	37.268±11.835	6.892±2.193
72	0.081±0.006	1.155±0.306	38.423±12.180	7.103±2.254
96	0.018±0.001	0.262±0.086	38.685±12.265	7.149±2.268
120	0.017±0.002	0.252±0.091	38.937±12.350	7.187±2.278

Table S26. Mean feces excretion amount of ginsenoside Re after oral administration of CNS in rats (*n* = 6, mean ± SD).

Time point (h)	Ginsenoside Re Concentration (µg/mL)	Excretion amount (µg)	Accumulative excretion amount (µg)	Accumulative excretion percentage (%)
4	0.087±0.124	1.098±1.616	1.098±1.616	0.234±0.345
8	0.267±0.204	3.705±2.813	4.802±4.393	1.022±0.936
12	0.330±0.026	4.873±1.226	9.675±4.726	2.051±1.001
24	0.366±0.020	5.459±1.584	15.135±5.426	3.203±1.152
36	0.367±0.026	5.435±1.413	20.570±6.347	4.364±1.343
48	0.354±0.028	5.282±1.513	25.852±7.369	5.469±1.568
72	0.168±0.069	2.615±1.424	28.467±7.628	6.027±1.613
96	0.044±0.043	0.717±0.713	29.184±7.675	6.182±1.623
120	ND	ND	29.184±7.675	6.182±1.623