

Supplemental materials:

Supplemental Table S1 The key differential metabolites between HHF-fed-THF-treated and HFF-fed-vehicle-treated rats presented by metabolomics analysis.

NO	Metabolites	VIP values ^a	<i>p</i> -values	Fold Change ^b	KEGG ID
1	4-aminobutanoic acid	1.61	0.02	0.45	C00334
2	Amphetamine	2.08	0.00	0.34	C07514
3	Oxalic acid	1.58	0.02	0.26	C00209
4	ethylene glycol	1.46	0.05	-1.85	C01380
5	Diethanolamine	1.49	0.03	-0.97	C06772
6	cyclopentanol	1.92	0.00	-0.33	C02020
7	cyclohexanol	1.93	0.01	-0.93	C00854
8	Phenylalanine	1.58	0.01	-1.11	C02057
9	2-oxobutanoic acid	1.49	0.02	-0.53	C00109
10	DL-Ornithine	1.48	0.02	0.62	C07997
11	L-Serine	1.44	0.03	-1.02	C00077
12	Ethanolamine	1.46	0.02	1.05	C00189
13	D-Lyxose	1.57	0.03	0.63	C00476
14	D-Erythrose	1.50	0.02	-1.61	C01796
15	L-Tyrosine	1.52	0.01	-0.59	C00082
16	Palmitic Acid	1.84	0.00	-0.50	C00249
17	Pentadecylic acid	1.57	0.03	1.17	C16537
18	Stearic acid	1.85	0.01	-0.53	C01530
19	L-Tryptophan	1.65	0.01	-0.52	C00078
20	Cadaverine	1.76	0.01	-1.68	C01672
21	D-Xylose	1.90	0.00	1.36	C00181
22	Batyl alcohol	2.17	0.01	-0.75	C13858
23	D-Threose	1.68	0.01	-0.98	C06463
24	4-Hydroxybutanoic acid	1.96	0.05	-1.08	C00989
25	Urea	1.58	0.02	0.39	C00086
26	Lactic Acid	1.09	0.02	-0.75	C00186
27	L-Glutamine	1.77	0.02	-0.98	C00064
28	Pyroglutamic acid	1.73	0.02	-0.68	C01879
29	L-Aspartic acid	1.84	0.03	1.12	C00049
30	L-Valine	2.11	0.03	-0.55	C00183
31	L-Isoleucine	1.42	0.04	0.44	C00407
32	L-Serine	1.52	0.03	-0.69	C00065

^a Based on OPLS-DA results, the metabolites with variable influence on projection (VIP) values >1.0 and *p*-values < 0.05 were deemed as differential metabolites.

^b Fold change was calculated as the logarithm of the average mass response (area) ratio between the two groups (i.e., Fold change = $\log_2(\text{THF} / \text{HFF})$).

Supplemental Table S2 Primer sequences for RT-qPCR

Primers	Forward primer	Reverse primer	Size(bp)
SREBP-2	GATGATGCCGACTCTACTGCTGTG	AAGGTGACCGAGGAGCGTGAG	120
LDLR	CAAGGTGACATGGCTGGCAGAG	ATCTCGTCCTCCGTGGTCTTCTG	194
PCSK9	CAGGACGAGGACGGAGACTACG	CTTGGAGCAACGGCGGAAGG	114
PI3K	CTGTGCCTTCTGCCTTACGGTTG	GCAATCGTCGTGGCGTCCTTC	83
AKT1	GGCAGGAGGAGGAGACGATGG	TTCATGGTCACACGGTGCTTGG	109
IRS1	AGCAACAGCAGCAGCAGTCTTC	ACTCTTCCGAGCCAGTCTTCTTC	189

Supplemental methods

Quantitative profiling of THF, a mixed extract of *Panax notoginseng* and *Coptis chinensis*

1.1 Quantitative profiling of *Panax notoginseng* saponins

The temperature of the column was set at 25 °C, and the flow rate was 1.0 ml/min. The injection volume was 10 µL. The detection wavelength was 203 nm, and the acetonitrile (A) and water (B) were used as the mobile phase. The gradient program for the ginsenoside samples was optimized as follows: 0-20 min, 20% A; 20-45 min, 20-46% A; 45-55 min, 46-55% A.

1.2 Quantitative profiling of *Coptis chinensis* alkaloids

The temperature of the columns was set at 30 °C, and the flow rate was 1.0 ml/min. The injection volume was 10 µL. The detection wavelength was 345 nm, and acetonitrile-0.05mol/L KH₂PO₄ solution was used as the mobile phase (0.31g of sodium dodecyl sulfate was added per 100mL, and the pH value was adjusted by phosphoric acid to 3.5). The elution procedure was designed to isocratic elution (0-60 min).

1.3 Linear regression was performed

by taking the sample quantity as the horizontal coordinate (X) and the peak area as the vertical coordinate (Y). The regression equations of ginsenoside Rg1, ginsenoside Rb1, ginsenoside Rd, ginsenoside Re, panax notoginseng saponin R1, coptidine, bamatine and berberine were obtained successively: $Y_1=18.6022X_1+0.0680$ ($r=0.9995$), $Y_2=36.8398X_2+0.0157$ ($r=0.9994$), $Y_3=43.8432X_3+0.0084$ ($r=0.9995$), $Y_4=42.1264X_4+0.0192$ ($r=0.9987$), $Y_5=52.9536+0.0680$ ($r=0.9993$), $Y_6=572.9329X_6-10.2098$ ($r=0.9999$), $Y_7=657.7388X_7-11.6213$ ($r=0.9999$), $Y_8=598.3541X_8-11.2877$ ($r=0.9998$).

The content of mixed extract was determined by external standard method.