

Supplementary information

Table S1. Stability and repeatability of UPLC-Q/TOF MS method validation using QC sample

NO	RT (min)	<i>m/z</i>	Stability			Repeatability		
			RSD (%) _{RT}	RSD (%) _{<i>m/z</i>}	RSD (%) _p	RSD (%) _{RT}	RSD (%) _{<i>m/z</i>}	RSD (%) _p
1 (ESI-)	1.22	283.0669	0.4428	0.0018	10.8532	0.6547	0.0036	11.3818
2 (ESI-)	7.64	514.2836	0.0106	0.0016	5.8795	0.5474	0.0034	6.8646
3 (ESI-)	13.82	319.2262	0.7601	0.0033	11.8316	0.6854	0.0045	13.0684
4 (ESI+)	1.97	167.0938	0.4353	0.0015	12.8432	0.0470	0.0021	7.8945
5 (ESI+)	3.76	206.1063	0.8476	0.0012	5.6983	0.8092	0.0035	12.1545
6 (ESI+)	11.74	468.3088	0.0243	0.0029	11.3403	0.7631	0.0033	11.1542

The RSD (%)_{RT}, RSD (%)_{*m/z*} and RSD (%)_p values representing for the RSD of retention time, *m/z* and peak areas of the selected ions based on UPLC-Q/TOF MS method.

Table S2 Identification of significantly differential metabolites in the mice plasma and their related pathways.

VIP	m/z	Quasi-molecular ion	Formula	Error (ppm)	Metabolite	Model trend ^a	Treatment trend ^b CA	Treatment trend ^b EPD	Related pathway
1.39	1028.2610	[M-H] ⁻	C ₃₇ H ₅₈ N ₇ O ₁₉ P ₃ S	-3.1	3-Oxo-OPC6-CoA	(*)↓	(*)↑	(*)↑	alpha-Linolenic acid metabolism
1.19	674.5101	[M-H] ⁻	C ₃₇ H ₇₄ NO ₇ P	-3.5	PE(14:0/P-18:0)	(*)↓	(*)↑	(*)↑	Glycerophospholipid metabolism
1.03	179.0448	[M-H] ⁻	C ₈ H ₈ N ₂ O ₃	-4.4	Nicotinuric acid	(*)↑	(*)↓	(*)↓	Nicotinate and nicotinamide metabolism
1.33	611.1434	[M-H] ⁻	C ₂₀ H ₃₂ N ₆ O ₁₂ S ₂	-1.1	Glutathione, oxidized	(*)↑	(#)↓	(*)↓	Glutathione metabolism
1.12	135.0305	[M-H] ⁻	C ₅ H ₄ N ₄ O	3.7	Hypoxanthine	(*)↑	(*)↓	(*)↓	Purine metabolism
1.54	211.9969	[M-H] ⁻	C ₄ H ₈ NO ₇ P	4.7	4-Phospho-L-aspartate	(*)↑	(*)↓	(*)↓	Glycine, serine and threonine metabolism
1.57	252.0740	[M-H] ⁻	C ₉ H ₁₁ N ₅ O ₄	3.2	D-(+)-Neopterin	(*)↑	(*)↓	(*)↓	Folate biosynthesis
1.52	283.0669	[M-H] ⁻	C ₁₀ H ₁₂ N ₄ O ₆	-3.2	Xanthosine	(*)↓	(*)↑	(*)↑	Purine metabolism;
1.37	322.0436	[M-H] ⁻	C ₉ H ₁₄ N ₃ O ₈ P	-1.1	5'-CMP	(*)↓	(*)↑	(*)↑	Pyrimidine metabolism
1.50	514.2836	[M-H] ⁻	C ₂₆ H ₄₅ NO ₇ S	-0.5	Taurocholic acid	(*)↑	(*)↓	(*)↓	Primary bile acid biosynthesis Bile secretion
1.53	313.1062	[M-H] ⁻	C ₁₄ H ₁₄ N ₆ O ₃	4.5	Dihydropteroic acid	(*)↑	(*)↓	(*)↓	Folate biosynthesis
1.53	380.2557	[M-H] ⁻	C ₁₈ H ₄₀ NO ₅ P	-2.1	Sphinganine-phosphate	(*)↑	(*)↓	(*)↓	Sphingolipid metabolism
1.54	319.2262	[M-H] ⁻	C ₂₀ H ₃₂ O ₃	-3.1	8(R)-HETE	(*)↑	(*)↓	(*)↓	Arachidonic acid metabolism
1.41	433.2249	[M-H] ⁻	C ₁₇ H ₃₄ N ₆ O ₅ S	3.9	Glutathionylspermidine	(*)↑	(#)↓	(*)↓	Glutathione metabolism
1.56	327.2324	[M-H] ⁻	C ₂₂ H ₃₂ O ₂	0.4	Docosahexaenoic acid	(*)↓	(*)↑	(*)↑	Biosynthesis of unsaturated fatty acids
1.55	279.2320	[M-H] ⁻	C ₁₈ H ₃₂ O ₂	-0.9	Linoleic acid	(*)↑	(*)↓	(*)↓	Linoleic acid metabolism Biosynthesis of unsaturated fatty acids
1.20	151.0394	[M+H] ⁺	C ₈ H ₆ O ₃	-1.2	Phenylglyoxylic acid	(*)↑	(*)↓	(*)↓	Phenylalanine metabolism
1.16	175.1238	[M+H] ⁺	C ₁₁ H ₁₄ N ₂	0.9	N-Methyltryptamine	(*)↓	(#)↓	(*)↑	Tryptophan metabolism
1.07	136.0767	[M+H] ⁺	C ₈ H ₉ NO	3.0	2-Phenylacetamide	(*)↑	(*)↓	(*)↓	Phenylalanine metabolism
1.14	154.0471	[M+H] ⁺	C ₅ H ₄ N ₄ O ₂	3.2	Xanthine	(*)↑	(*)↓	(*)↓	Purine metabolism
1.32	167.0938	[M+H] ⁺	C ₉ H ₁₁ NO ₂	-1.2	Phenylalanine	(*)↑	(*)↓	(*)↓	Phenylalanine metabolism
1.42	206.1063	[M+H] ⁺	C ₁₁ H ₁₂ N ₂ O ₂	2.9	L-Tryptophan	(*)↓	(#)↑	(*)↑	Tryptophan metabolism
1.29	468.3088	[M+H] ⁺	C ₂₂ H ₄₆ NO ₇ P	-0.7	LysoPC(14:0)	(*)↑	(*)↓	(*)↓	Glycerophospholipid metabolism
1.24	516.3068	[M+H] ⁺	C ₂₆ H ₄₆ NO ₇ P	-4.5	LysoPC(18:4)	(*)↑	(*)↓	(*)↓	Glycerophospholipid metabolism
1.26	494.3247	[M+H] ⁺	C ₂₄ H ₄₈ NO ₇ P	0.1	LysoPC(16:1)	(*)↑	(*)↓	(*)↓	Glycerophospholipid metabolism
1.29	570.3536	[M+H] ⁺	C ₃₀ H ₅₂ NO ₇ P	-4.1	LysoPC(22:5)	(*)↑	(*)↓	(*)↓	Glycerophospholipid metabolism

^a compared to normal group. ^b compared to model group. Arrow (↑) indicates relative increase in signal. Arrow (↓) indicates relative decrease in signal. Asterik (*) represents a statistically significant difference (P<0.05), while pound key (#) represents no statistically significant difference.

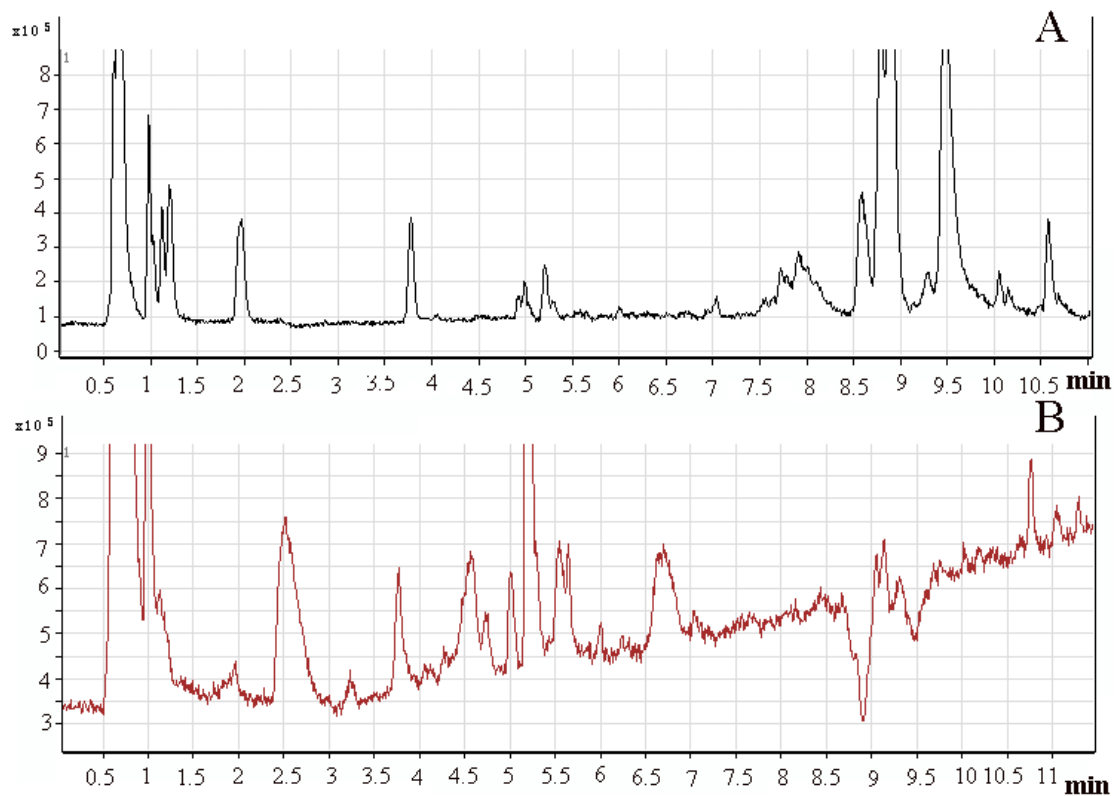


Fig. S1. The magnification of typical total ion chromatograms (TIC) of normal mice in (A) ESI⁺ mode and (B) ESI⁻ mode during 0-11 min.