Supplement

Table S1 The summary of the physical signs of model rats in different groups

Group	No.	Squinted eyes	Towered hair	Group bundling	Red paw	Fever	Thrombosis in the tail（cm）	Ear features
2h TG	1	●	●	●	●	●	-	Red ear, ear vein congestion,
	2	●	●	●	●	●	-	no ecchymosis
	3	●	●	●	●	●	0.6	
	4	●	●	●	●	●	1.5	
	5	●	●	●	●	●	0.9	
	6	●	●	●	●	●	-	
	7	●	●	●	●	●	-	
	8	●	●	●	●	●	-	
8h TG	1	○	○	○	○	○	2.6	Light red ear, ear vein
	2	○	○	○	○	○	1.5	dilatation, no ecchymosis
	3	○	○	○	○	○	-	
	4	○	○	○	○	○	1.6	ecchymosis in ears
	5	○	○	○	○	○	2.0	Light red ear, ear vein
	6	○	○	○	○	○	4.6	dilatation, no ecchymosis
	7	○	○	○	○	○	1.8	
	8	○	○	○	○	○	6.4	Ecchymosis in ears
24h	1	○	○	○	light	○	9.8	Ecchymosis in ears
TG					purple			
	2	○	○	○	○	○	3.9	Light red ear, ear vein
	3	○	○	○	light	○	7.6	dilatation, no ecchymosis
					purple			
	4	○	○	○	○	○	1.8	
	5	○	○	○	○	○	11.7	Ecchymosis in ears
	6	○	○	○	○	○	7.3	Ecchymosis in ears

7	○	○	○	purple	○	10.8	Ecchymosis in ears
8	○	○	○	○	○	3.2	Ecchymosis in ears

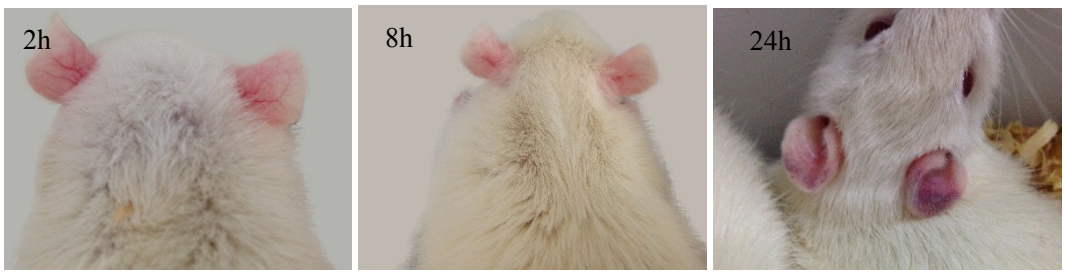
● represents the rats exhibit this physical signs; ○ represents the rats don’t exhibit this physical signs.

Table S2 The related information of the 23 differential amino acids

$m/z/t_R$	Identification	Pathway	Fold change (THBSS/Normal)		
			2h	8h	24h
170.0928/1.33	1-Methylhistidine	Histidine metabolism	0.90	-	-
173.0926/1.39	Glycylproline		0.39	-	-
116.0710/1.39	Proline	Arginnine and Proline metabolism	0.34	-	-
		Aminoacyl-tRNA biosynthesis			
181.0613/5.67	Nicotinuric acid		-	0.35	-
160.0608/2.10	Aminoadipic acid	Lysine degradation	-	-	0.62
173.0923/2.39	N-Acetylornithine	Arginine and proline metabolism	-	-	0.49
118.0615/0.82	Guanidoacetic acid	Arginine and proline metabolism	0.44	0.32	-
		Glycine, serine and threonine metabolism			
129.1027/1.09	L-Lysine	Biotin metabolism	0.45	0.28	-
		Aminoacyl-tRNA biosynthesis			
146.0929/1.42	4-Guanidinobutanoic acid	Arginine and proline metabolism	0.62	0.46	-
130.0504/1.48	Pyroglutamic acid	Glutathione metabolism	0.47	0.60	-
229.1189/1.27	Prolylhydroxyproline		0.50	0.37	-
156.0772/1.09	L-Histidine	Histidine metabolism	0.49	0.38	0.76
		Nitrogen metabolism			
		Aminoacyl-tRNA biosynthesis			
259.1658/2.86	Pipecolic acid	Lysine degradation	0.31	0.26	0.58
118.0867/0.83	L-Valine	Valine, leucine and isoleucine biosynthesis	0.6092	-	1.6348
		Pantothenate and CoA biosynthesis			
		Aminocayl-tRNA biosynthesis			
		Valine, leucine, and isoleucine 1degradation			
158.0816/5.74	2-Methylbutyrylglycine		1.48	-	0.46
216.9806/4.51	N-a-Acetylcitrulline		2.40	2.16	0.56
187.0719/1.47	N-Acetylglutamine		1.14	1.36	0.67
144.0659/4.38	Isobutyrylglycine		-	1.02	0.31
148.0611/0.80	L-Glutamic acid	Histidine metabolism	-	0.28	0.90
		Nitrogen metabolism			
		Alanine, aspartate and glutamate metabolism			
		Arginine and proline metabolism			
		Butanoate metabolism			
		D-Glutamine and D-glutamate metabolism			
		Glutathione metabolism			
		Porphyrin and chlorophyll metabolism			
		Aminoacyl-tRNA biosynthesis			
158.0815/5.57	Isovalerylglycine		1.75	1.47	-
192.0662/6.97	Phenylacetylglycine		1.67	1.44	-
205.0828/1.03	5-L-Glutamylglycine		-	-	2.33
168.0296/4.64	2-Furoylglycine		5.85	2.96	2.74

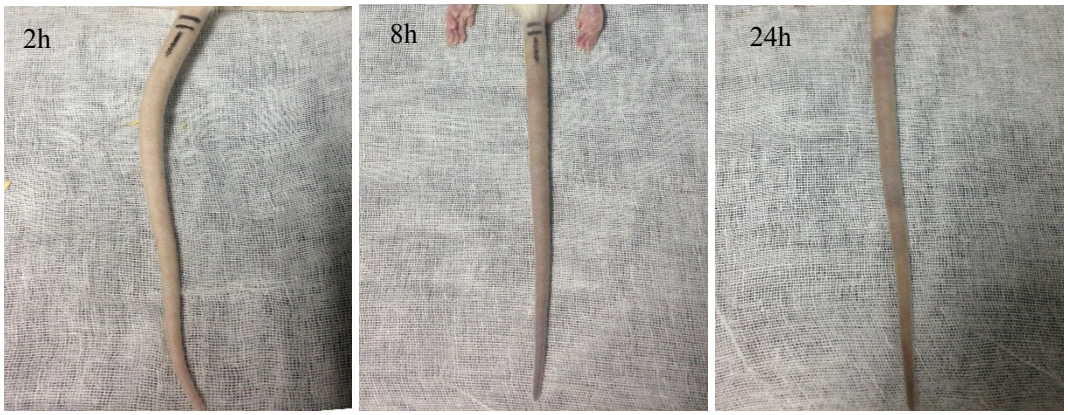
"-" represents this metabolite is not the differential metabolite at this time-point; THBSS, the toxic heat and blood stasis syndrome.

A. Physical signs of the 2h TG (squinted eyes, towered hair, group bundling)



B. The changes of the ear at different time-points

C. The changes of the paw at different time-points



D. The changes of the tail at different time-points

Fig. S1 The physical signs of model rats at different time points after modeling

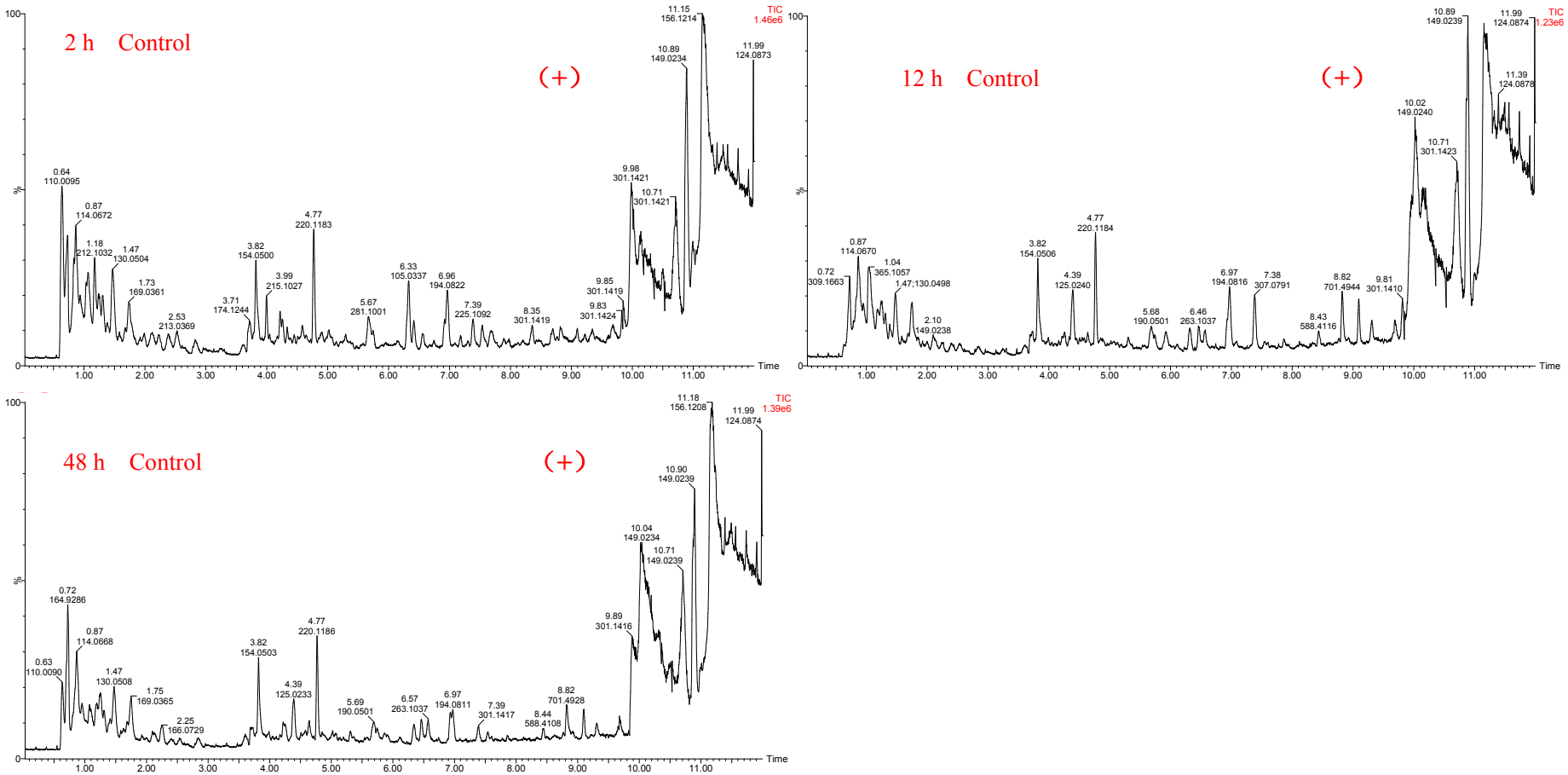


Fig. S2 The LC-MS profiling of the urine obtained from control rats at 2 h, 12 h and 48 h in positive mode

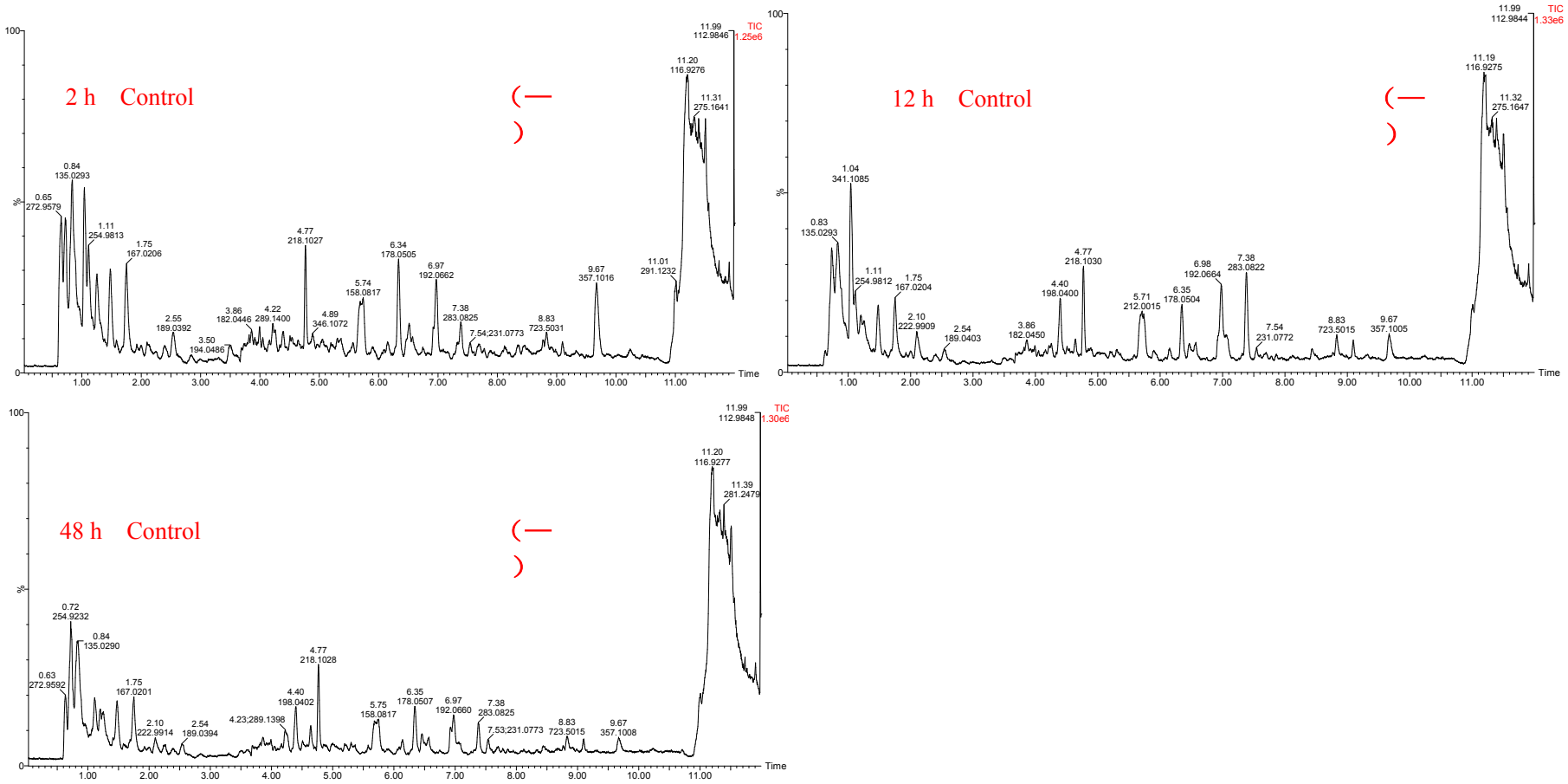


Fig. S3 The LC-MS profiling of the urine obtained from control rats at 2 h, 12 h and 48 h in negative mode

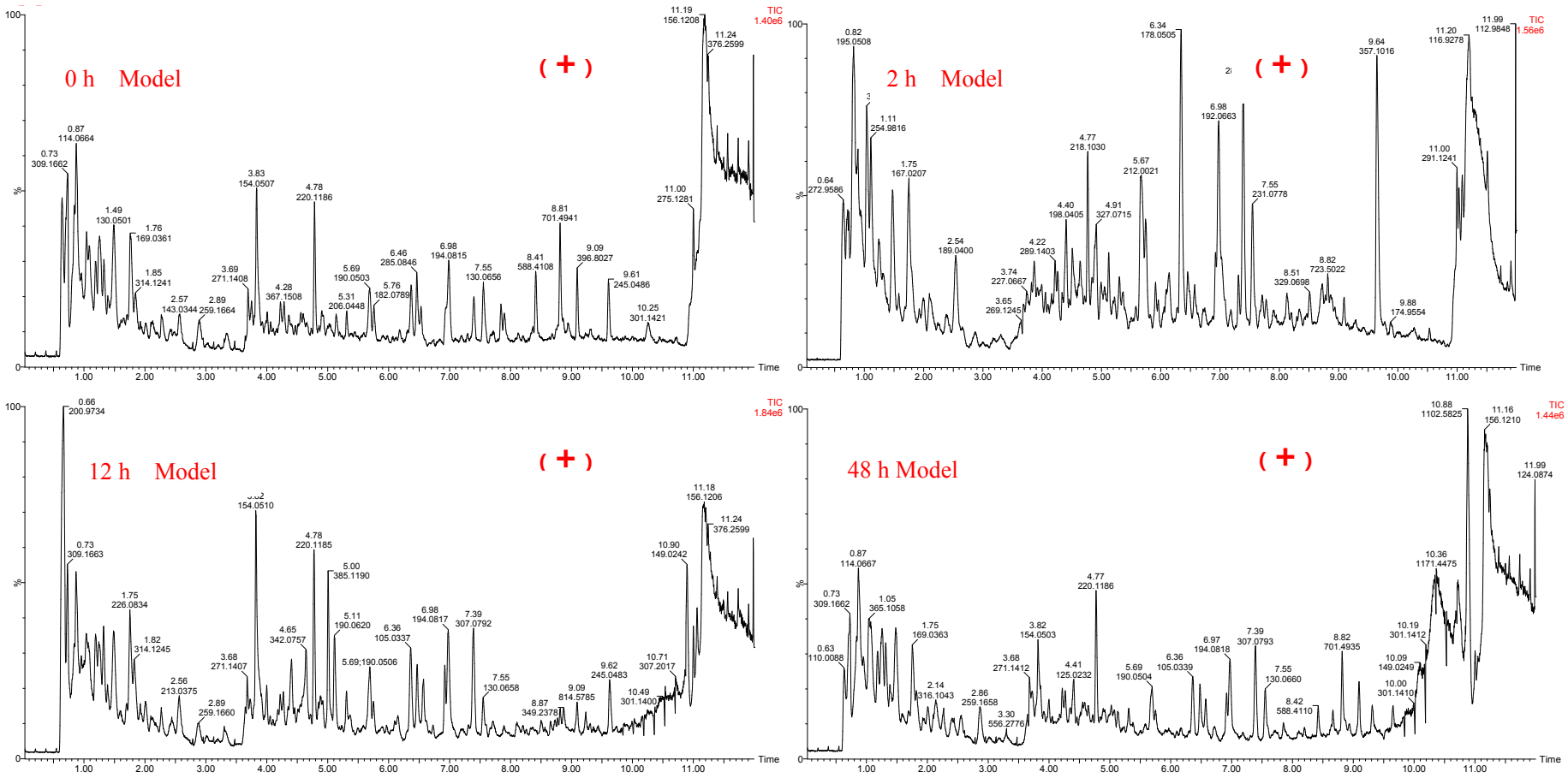


Fig. S4 The LC-MS profiling of the urine obtained from model rats at 0 h, 2 h, 12 h and 48 h in positive mode

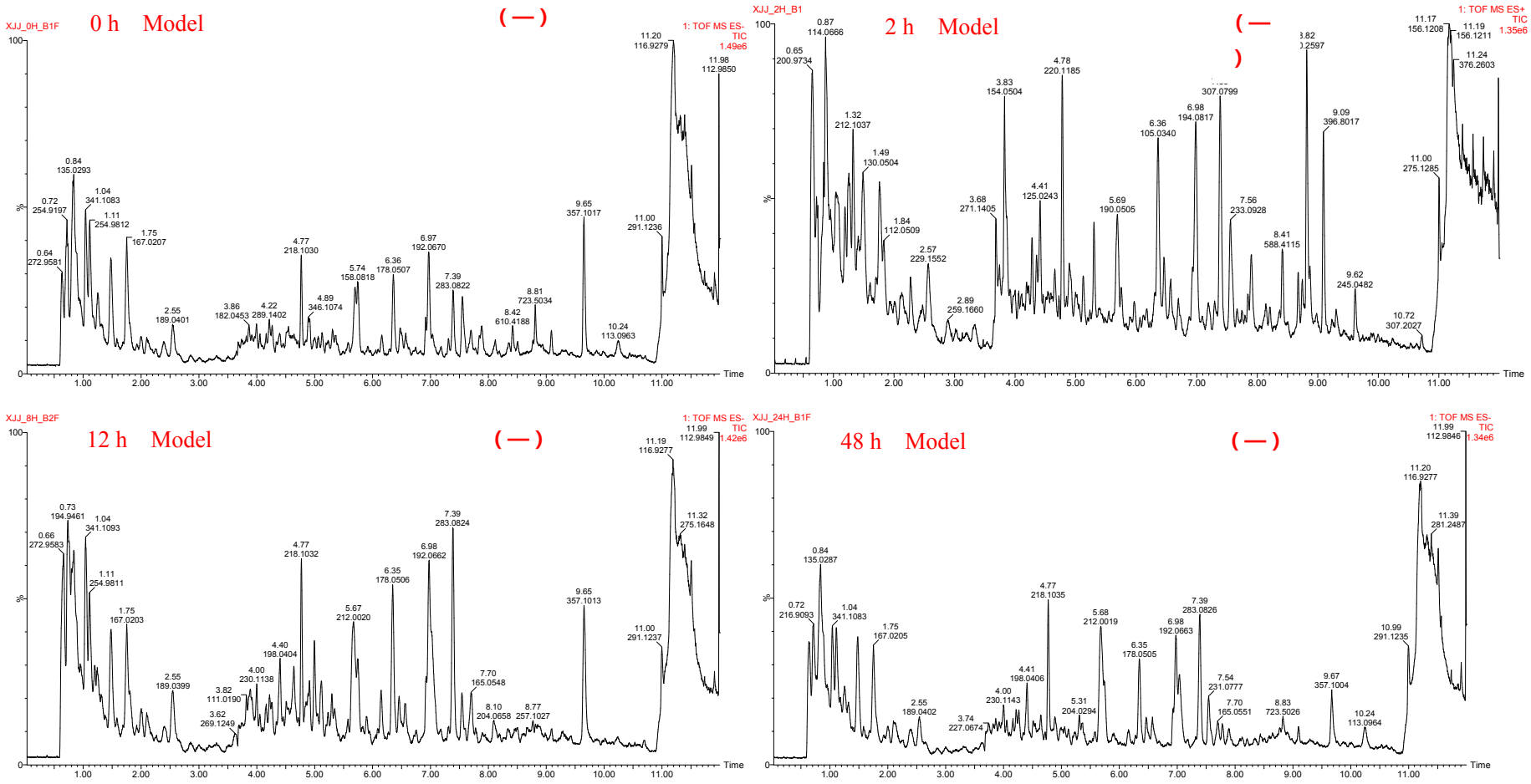
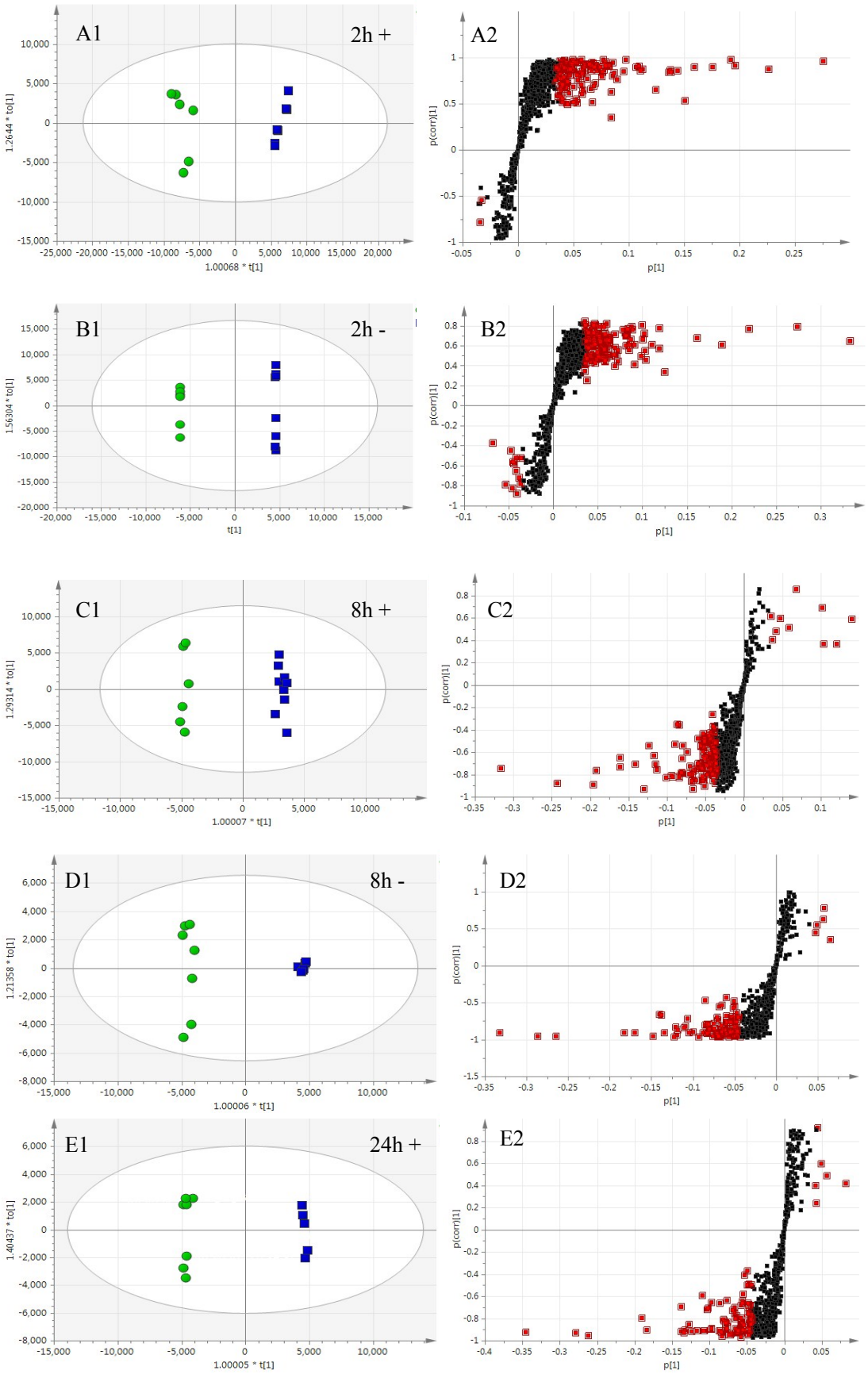


Fig. S5 The LC-MS profiling of the urine obtained from model rats at 0 h, 2 h, 12 h and 48 h in negative mode


A1
2h +
1.2644 * to[1]
1.00068 * t[1]
A2
p(corr)[1]
p[1]
B1
2h -
1.56304 * to[1]
t[1]
B2
p(corr)[1]
p[1]
C1
8h +
1.29314 * to[1]
1.00007 * t[1]
C2
p(corr)[1]
p[1]
D1
8h -
1.21358 * to[1]
1.00006 * t[1]
D2
p(corr)[1]
p[1]
E1
24h +
1.40437 * to[1]
1.00005 * t[1]
E2
p(corr)[1]
p[1]

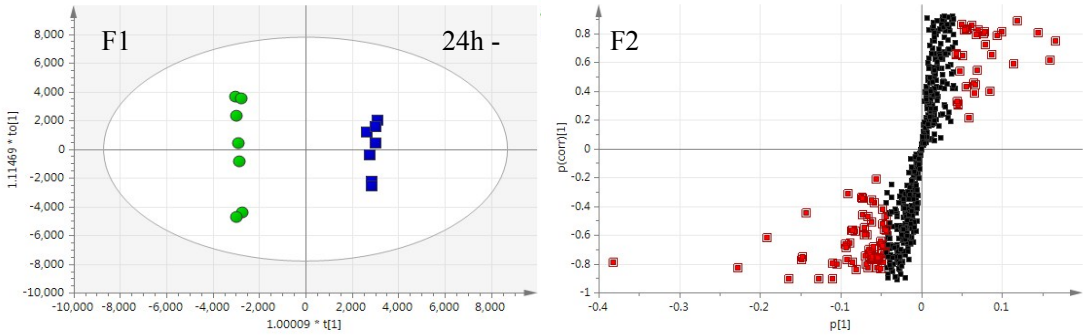


Fig. S6 OPLS-DA models and S-plots of the normal rats (●) and THBSS (■) at different time-points. (A, B) 2 h; (C, D) 8 h; (E, F) 24 h; in positive (A, C, E) and negative (B, D, F) mode

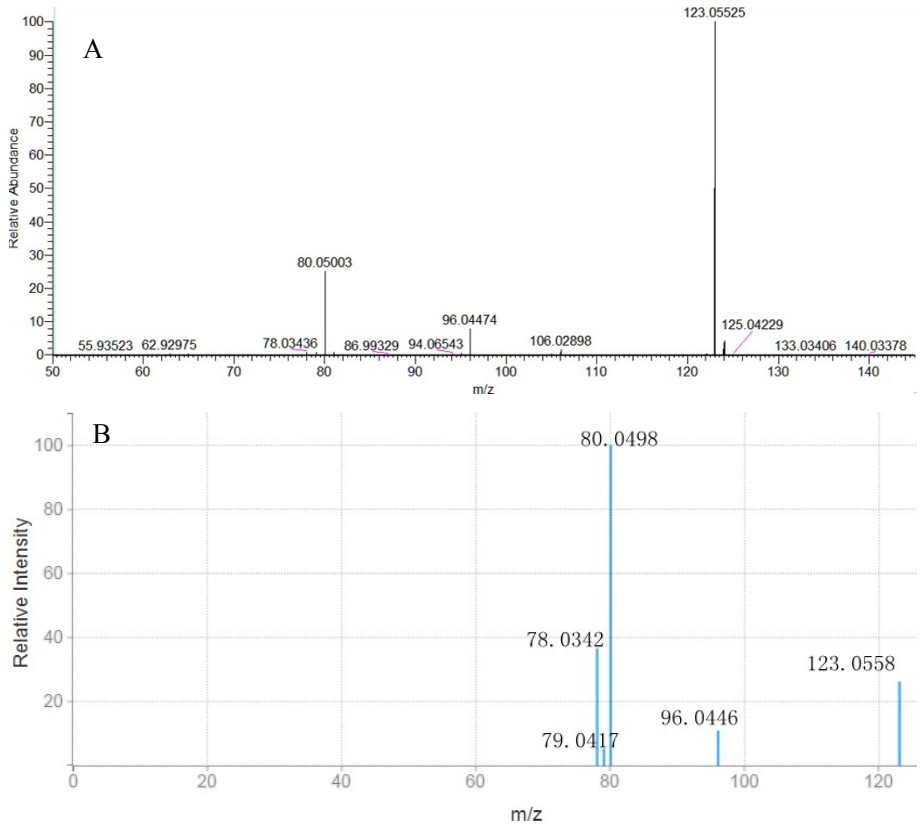


Fig. S7 Product ion spectra (A) metabolite **M1** in our research (B) Niacinamide in HMDB (UPLC Q-TOF Premier, Waters; 30V; Positive)

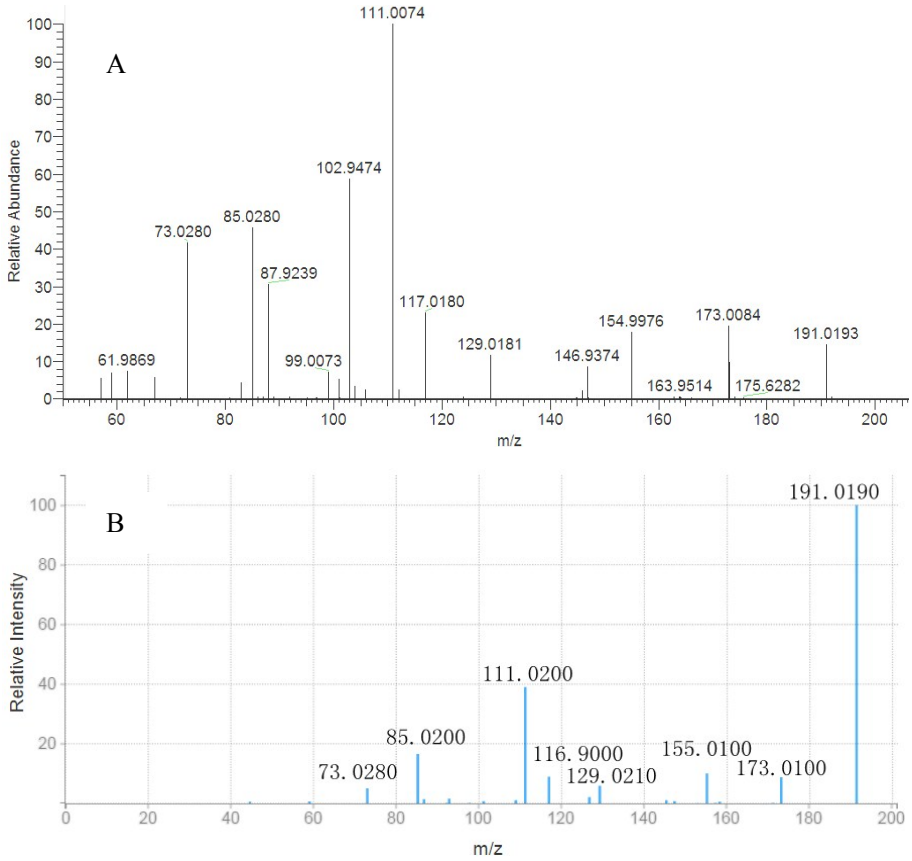


Fig. S8 Product ion spectra (A) metabolite **M2** in our research (B) Isocitric acid in HMDB (API3000 LC-ESI-QQ, Applied Biosystems; 20V; Negative)