Table S1 Assignments of peaks from HPLC-ELSD chromatogram of the Astragali Radix extract.

Peak No.	Compound
1	calycosin-7-O-β-D-glucoside
2	ononin
3	(6αR, 11αR)-9,10-dimethoxypterocarpan-3-O-β-D-glucoside
4	(3R)-2'-hydroxy-3',4'-dimethoxyisoflavan-7-O-β-D-glucoside
5	calycosin
6	astragaloside IV
7	astragaloside II
8	formononetin
9	astragaloside I

Table S2 ^{1}H NMR assignments of major metabolites in Astragali Radix extract

Key	Metabolites	δ	Key	Metabolites	δ
1	isoleucine	0.94 (t, J=7.2 Hz), 1.01 (d, J=7.2 Hz)	12	choline	3.20 (s)
2	leucine	0.96 (d, J=6.0 Hz), 0.97 (d, J=6.6 Hz)	13	sucrose	5.41 (d, J=3.6 Hz), 4.22 (d, J=9.0 Hz), 4.06 (t, J=8.4Hz)
3	valine	1.00 (d, J=7.2 Hz), 1.05 (d, J=6.6 Hz)	14	α-glucose	5.23 (d, J=3.6 Hz)
4	threonine	1.33 (d, J=7.2 Hz)	15	β-glucose	4.64 (d, J=7.8 Hz)
5	alanine	1.48 (d, J=7.2 Hz)	16	fumarate	6.53 (s)
6	arginine	1.66 (m), 1.73 (m)	17	uridine	7.88 (d, J=8.4 Hz), 5.91 (m)
7	acetate	1.93 (s)	18	hypoxanthine	8.20 (s), 8.18 (s)
8	proline	2.01 (m), 2.08 (m), 2.35 (m)	19	adenosine	8.34 (s), 8.22 (s)
9	succinate	2.45 (s)	20	formate	8.46 (s)
10	aspartate	2.82 (dd, J=3.6, 17.4 Hz), 2.69 (dd, J=9.0, 17.4 Hz)	21	trigonelline	9.13 (s), 8.84 (m), 8.08 (m)
11	asparagine	2.96 (dd, J=4.2, 17.4 Hz), 2.85 (dd, J=7.8, 16.8 Hz)			

Table S3 Effect of Astragali Radix on serum SOD, LA, BUN, CK and liver glycogen contents

Parameters	NS	AL	AM	AH
SOD (U/mL)	139.15±15.78	152.28±8.46	182.86±10.38	171.60±14.01
		$p^a = 0.557$	$p^a = 0.079$	$p^a = 0.223$
LA (mmol/L)	18.20±1.97	15.11±1.63	11.62±0.98*	12.11±1.24*
		p = 0.266	p = 0.014	p = 0.025
BUN (mmol/L)	26.24±3.42	18.60±2.83	17.46±2.53	16.22±3.46
		p = 0.103	p = 0.0538	p = 0.0544
CK (U/ml)	2.73±0.26	2.15±0.09	2.11±0.18	2.44±0.12
		p = 0.200	p = 0.195	p = 0.480
Hepatic glycogen	257.53±8.27	260.90±10.38	277.78±25.60	257.69±14.69
(ng/L)		p = 0.812	p = 0.492	p = 0.508

a. Compared with the NS group, * $p < 0.05$

Table S4 ^{1}HNMR assignments of major metabolites from rat serum and urine

Key	Metabolites	Moieties	Chemical shifts [a]	Samples [b]
1	lipid	CH_3, $(CH_2)_n$, $C{=}CCH_2C{=}C$, $CH{=}CH$	0.86(m), 1.28(m), 2.78(m), 5.30(m)	S
2	valine	γCH_3, $\gamma' CH_3$	0.99(d), 1.05(d)	S
3	isoleucine	δCH_3, γCH_3, $\gamma' CH_2$	0.94(t), 1.01(d), 1.27(m)	S
4	leucine	δCH_3, $\delta' CH_3$	0.96(d), 0.97(d)	S
5	β-OH-butyrate	γCH_3, half αCH_2, half αCH_2	1.20(d), 2.41(d), 2.31(d)	S
6	lactate	αCH, βCH_3	1.33(d), 4.12(q)	S, U
7	alanine	βCH_3	1.48(d)	S, U
8	lysine	βCH_2, δCH_2, γCH_2	1.90(m), 1.73(m), 1.45(m)	S
9	acetate	CH_3	1.92(s)	S, U
10	NAG [c]	CH_3	2.04(s)	S
11	OAG [c]	CH_3	2.14(s)	S

12	acetone	CH_3	2.23(s)	S
13	acetoacetate	CH_3	2.27(s)	S
14	pyruvate	CH_3	2.37(s)	S, U
15	succinate	CH_2	2.41(s)	S, U
16	glutamate	$\beta CH_2, \gamma CH_2$	2.06(m), 2.35(m)	S
17	glutamine	$\beta CH_2, \gamma CH_2$	2.14(m), 2.46(m)	S
18	citrate	half CH_2, half CH_2	2.54(d), 2.70(d)	S, U
19	dimethylglycine	N-CH_3, CH_2	2.92(s), 3.72(s)	S, U
20	choline	$N(CH_3)_3$	3.20(s)	S
21	PC [c]	$N(CH_3)_3$	3.21(s)	S
22	GPC [c]	$N(CH_3)_3$	3.22(s)	S
23	TMAO [c]	CH_3	3.26(s)	S
24	creatine	CH_3, CH_2	3.04(s), 3.94(s)	S
25	glycerol	CH_2OH, CH_2OH	3.66(dd), 3.56(dd)	S
26	glycine	CH_2	3.56(s)	S
27	glucose	1-CH	5.23(d), 4.65(d), 3.90(dd),	S
28	tyrosine	3 or 5-CH, 2 or 6-CH	6.90(d), 7.19(d)	S
29	histidine	2-CH, 4-CH	7.76(s), 7.06(s)	S
30	phenylalanine	2 or 6-CH, 3 or 5-CH	7.32(m), 7.42(m)	S
31	formate	CH	8.45(s)	S, U
32	pantothenate	CH_3, CH_3, CHOH	0.94(s), 0.90(s), 4.02(s)	U
33	methylamine	CH_3	2.61(s)	U
34	α-ketoglutarate	$\alpha CH_2, \beta CH_2$	2.44(t), 3.01(t)	U
35	dimethylamine	CH_3	2.73(s)	S, U
36	methylguanidine	CH_3	2.85(s)	U
37	TMA [c]	CH_3	2.88(s)	U
38	creatinine	CH_3, CH_2	3.04(s), 4.06(s)	U

39	malonate	CH_2	3.13(s)	U
40	taurine	S-CH_2, N-CH_2	3.27(t), 3.42(t)	U
41	betaine	$N(CH_3)_3$, CH_2	3.27(s), 3.90(s)	U
42	guanidinoacetate	CH_2	3.80(s)	U
43	malate	CH	4.31(dd)	U
44	allantoin	CH	5.38(s)	U
45	fumarate	CH=CH	6.53(s)	U
46	hippurate	CH_2, CH, CH, CH	3.98(d), 7.56(t), 7.49(t), 7.87(d)	U
47	trigonelline	1-CH, 2 or 4-CH, 3-CH	9.13(s), 8.84(dd), 8.08(d)	U
48	N-methylnicotinamide	2-CH, 4-CH, 6-CH, 5-CH, CH_3	9.29(s), 8.97(d), 8.91(dt), 8.19(m), 4.48(s)	U

a. s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, dd: doublet of doublet.

b. S represents serum and U represents urine.

c. NAG: N-acetylated glycoproteins; OAG: O-acetylated glycoproteins; PC: phosphatidylcholine; GPC: glycerophosphocholine; TMA: trimethylamine; TMAO: trimethylamine oxide .

Table S5 Comparison of relative integral levels of endogenous metabolites in NS and AM rats

δ_H	metabolites	NS	AM[a]	*p* value	sample[b]
4.65	glucose	0.62 ± 0.04	0.86 ± 0.14**	0.002	S
3.04	creatine	0.19 ± 0.05	0.44 ± 0.09*	0.016	S
3.55	glycine	0.68 ± 0.06	0.78 ± 0.10*	0.038	S
4.11	lactate	0.61 ± 0.10	0.46 ± 0.10**	0.002	S
3.20	choline	0.17 ± 0.02	0.13 ± 0.03*	0.024	S
3.22	PC	0.67 ± 0.10	0.59 ± 0.08	0.109	S
3.23	GPC	0.79 ± 0.08	0.66 ± 0.09	0.011	S

2.15	O-acetylated glycoproteins	1.19 ± 0.08	1.05 ± 0.12*	0.020	S
3.65	glycerol	0.24 ± 0.03	0.21 ± 0.05	0.089	S
1.21	β-OH-butyrate	0.25 ± 0.06	0.20 ± 0.03	0.055	S
3.56	glycine	1.17 ± 0.42	1.62 ± 0.34*	0.035	U
4.16	lactate	0.85 ± 0.06	0.77 ± 0.05*	0.012	U
2.56	citrate	2.17 ± 0.34	3.14 ± 0.58**	0.002	U
3.80	guanidinoacetate	1.56 ± 0.34	1.93 ± 0.40	0.071	U
5.40	allantoin	1.04 ± 0.45	1.36 ± 0.38	0.152	U
2.96	dimethylglycine	0.40 ± 0.08	0.60 ± 0.18*	0.016	U
2.76	DMA	0.64 ± 0.10	0.73 ± 0.07*	0.049	U
4.08	creatinine	1.62 ± 0.48	1.93 ± 0.42	0.191	U
3.92	betaine	1.26 ± 0.25	1.47 ± 0.21	0.087	U
4.32	malate	0.22 ± 0.07	0.30 ± 0.05*	0.028	U
1.96	acetate	9.66 ± 1.19	5.54 ± 2.52	0.070	U
8.48	formate	1.47 ± 0.57	0.76 ± 0.23	0.088	U
2.48	α-ketoglutarate	1.36 ± 0.36	1.14 ± 0.28	0.200	U
2.88	TMA	0.68 ± 0.07	0.63 ± 0.06	0.140	U
7.56	hippurate	0.45 ± 0.04	0.38 ± 0.02**	0.003	U

a. compared with NS group, *$p < 0.05$ and **$p < 0.01$.

b. S: serum; U: urine.

Figure S1 OPLS-DA score plot (A) and corresponding S-plot (B) of urine between the NS and AM group on the 21th day