Electronic Supplementary Material (ESI) for Food & Function.

Supplementary Table 1 The water consumption of rats during the experiment.

Groups	Water consumption (ml)										
	0W	1W	2W	3W	4W	5W	6W	7W	8W	12W	16W
C	24.7±2.0	29.0±0.8	32.0±1.6	34.4±1.1	38.0±0.9	41.6±0.8	44.3±0.9	46.8±0.6	47.7±1.1	47.1±1.0	47.0±1.2
Q1	25.4±1.5	28.2±1.0	32.2±1.7	33.8±0.9	38.5±1.6	41.7±0.9	44.1±0.9	47.5±1.6	47.7±1.1	47.4±1.1	47.3±1.3
Q2	24.5±2.5	28.7±0.5	31.8±1.1	33.9±1.3	38.2±1.1	41.5±0.8	44.4±1.0	46.8±1.3	47.8±1.1	46.9±1.4	46.9±1.4
A	25.9±2.4	29.4±1.0	31.7±1.3	33.7±1.2	39.1±1.3	42.1±0.9	44.7±0.8	47.8±1.8	48.2±1.8	47.9±1.4	47.0±1.3
AQ1	24.9±2.3	28.3±1.1	31.5±1.4	33.7±0.8	38.9±1.3	41.4±0.9	44.7±0.8	47.7±1.9	48.0±0.9	47.2±1.2	46.5±1.4
AQ2	24.7±2.0	28.3±1.0	31.7±1.3	34.1±1.1	38.7±1.7	42.1±1.0	44.2±0.8	47.5±1.6	48.1±1.0	47.0±1.4	47.2±1.3

C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group; W, weeks; 0 W, the week before treatment. Values expressed as mean ± SD (n = 10).

Supplementary Table 2 The body weight of rats at each time point and group (g).

	Body weight (g)					
Time point	C	Q1	Q2	A	AQ1	AQ2
0 weeks	220.7±12.0	215.8±9.4	213.7±14.7	220.8±13.5	214.1±15.0	215.2±14.8
4weeks	374.1±33.0	358.2±23.8	352.8±28.2	355.2±40.7	353.6±19.3	365.9±19.0
8weeks	467.3±51.0	439.9±29.2	436.5±42.1	435.1±58.6	437.3±35.0	463.5±32.7
12weeks	528.6±60.6	493.1±37.0	493.3±45.2	481.3±61.9	489.6±42.9	515.2±39.8
16weeks	566.5±49.6	530.1±33.7	531.1±38.8	500.4±49.6	514.9±32.1	534.6±42.5

C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group; Values expressed as mean ± SD (n = 10).

Supplementary Table 3 Summary of intensity values of biomarkers identified in Rats urine in positive mode

Groups	Peak intensity (mean ± SD, n = 10)				
	GAMA	AAMA	L-Cysteine	Vinylacetylglycine	1-Salicylate glucuronide
C	-	-	7.6±2.8	4671.6±634.3	129.2±51.0
Q1	-	-	10.3±3.4	4871.6±437.4	127.3±32.0
Q2	-	-	10.7±4.1	4891.6±196.2	120.3±33.4
A	2859.5±1234.7**	2233.71±1143.4**	103.4±59.4**	8711.6±1761.3**	403.1±160.6**
AQ1	2588.1±588.7**	1833.7±726.9**	98.4±59.5**	7461.7±1570.4**	351.0±92.2**
AQ2	1990.8±366.9** #	1423.7±421.7** ##	39.4±9.0* ##	5831.7±1392.2* ##	223.2±61.4* ##

C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group; –, not detected. Values expressed as mean ± SD (n = 10).

* Significantly different from control group at $p < 0.05$ (ANOVA).

** Significantly different from control group at $p < 0.01$ (ANOVA).

Significantly different from AA group at $p < 0.05$ (ANOVA).

Significantly different from AA group at $p < 0.01$ (ANOVA).

Supplementary Table 3（continue） Summary of intensity values of biomarkers identified in Rats urine in positive mode

Groups	Peak intensity (mean ± SD, n = 10)				
	3-Acetamidobutanal	2-Indolecarboxylic acid	Kynurenic acid	Isorhamnetin	Quercetin
C	14867.4±3676.5	32965.9±7984.3	105876.1±29998.9	-	-
Q1	13967.4±2603.3	32265.8±5400.9	95806.2±15051.4	195.1±59.22**	2372.8±717.8**
Q2	14057.4±2915.4	33365.8±4209.0	94873.0±17028.9	221.0±74.9**	2542.5±448.1**
A	6793.4±1115.1**	16989.9±3809.4**	44827.9±12476.7**	-	-
AQ1	8593.47±2543.5**	18890.1±3372.8**	55827.9±19887.1**	159.0±39.0** ##	1932.7±386.0** ##
AQ2	11993.5±3763.6* ##	27490.0±8643.3* ##	70246.2±26694.0** ##	193.0±131.6** ##	2074.7±599.1** ##

C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group; –, not detected. Values expressed as mean ± SD (n = 10).

* Significantly different from control group at $p < 0.05$ (ANOVA).

** Significantly different from control group at $p < 0.01$ (ANOVA).

Significantly different from AA group at $p < 0.01$ (ANOVA).

Supplementary Table 4 Summary of intensity values of biomarkers identified in Rats urine in negative mode

Groups	Peak intensity (mean ± SD, n = 10)							
	GAMA	iso-GAMA	7-Ketodeoxycholic acid	Cysteic acid	p-Cresol sulfate	L-Cysteine	Isorhamnetin	Quercetin
C	-	-	616.8±190.6	992.4±808.9	5.7±3.9	7.6±2.8	-	-
Q1	-	-	676.8±196.8	944.1±379.4	7.8±2.8	10.3±3.4	195.1±59.22**	2372.8±717.8**
Q2	-	-	697.7±168.0	953.7±216.8	9.5±3.5	10.7±4.1	221.0±74.9**	2542.5±448.1**
A	2859.5±1234.7**	1385.8±471.0**	1572.7±547.4**	2951.75±584.5**	311.67±50.8**	103.4±59.4**	-	-
AQ1	2588.1±588.7**	1241.6±273.0**	1372.±478.7**	2578.1±877.1**	285.6±55.9**	98.4±59.5**	159.0±39.0**##	1932.7±386.0**##
AQ2	1990.8±366.9**#	1088.4±298.4**#	962.7.±315.7*##	1600.2.2±398.2*##	35.2±9.4*##	39.4±9.0*##	193.0±131.6**##	2074.7±599.1**##

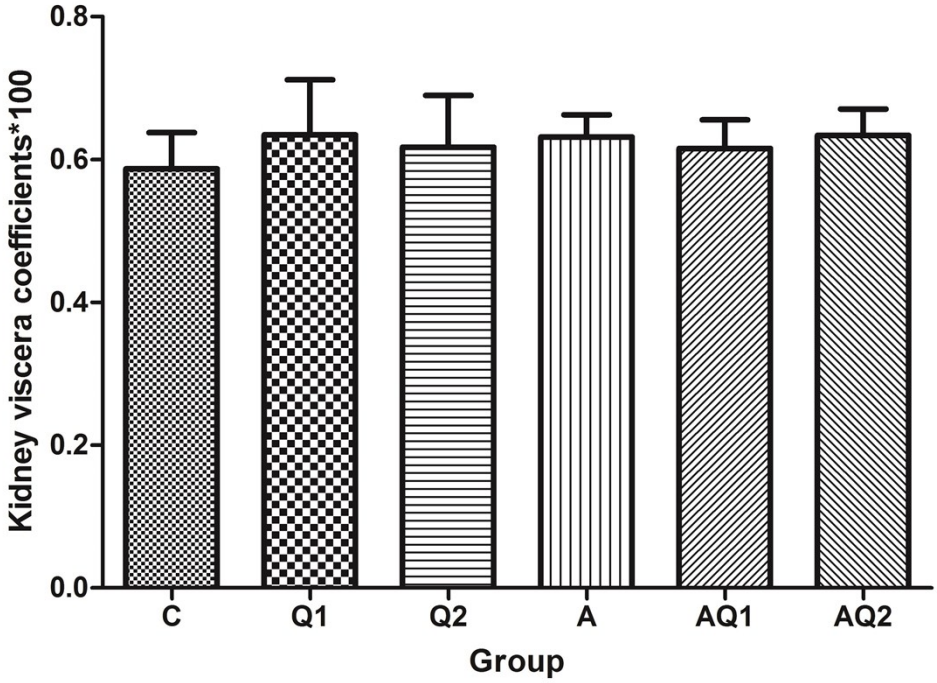
C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated Group; AQ2, high-dose quercetin plus AA-treated group; –, not detected. Values expressed as mean ± SD (n = 10).

* Significantly different from control group at $p < 0.05$ (ANOVA).

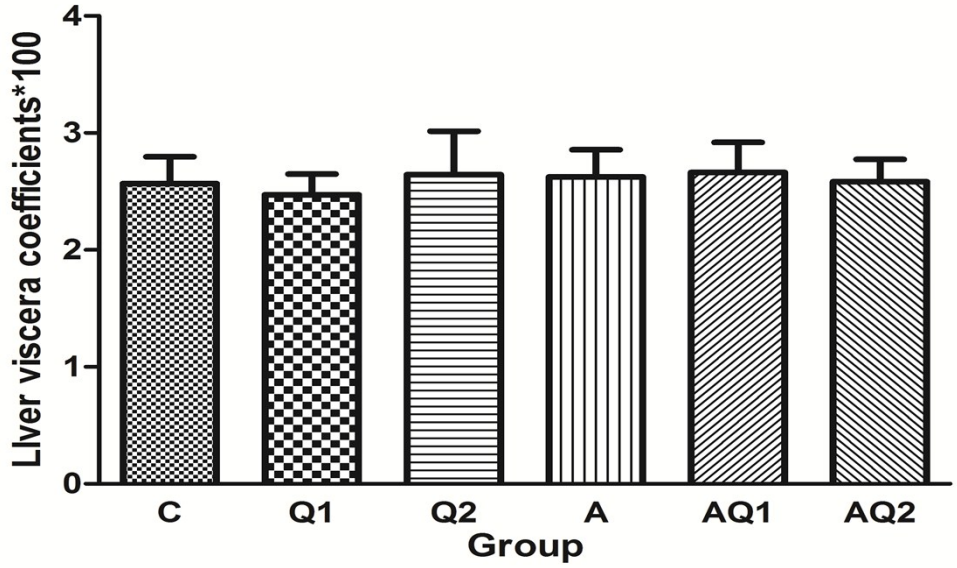
** Significantly different from control group at $p < 0.01$ (ANOVA).

Significantly different from AA group at $p < 0.05$ (ANOVA).

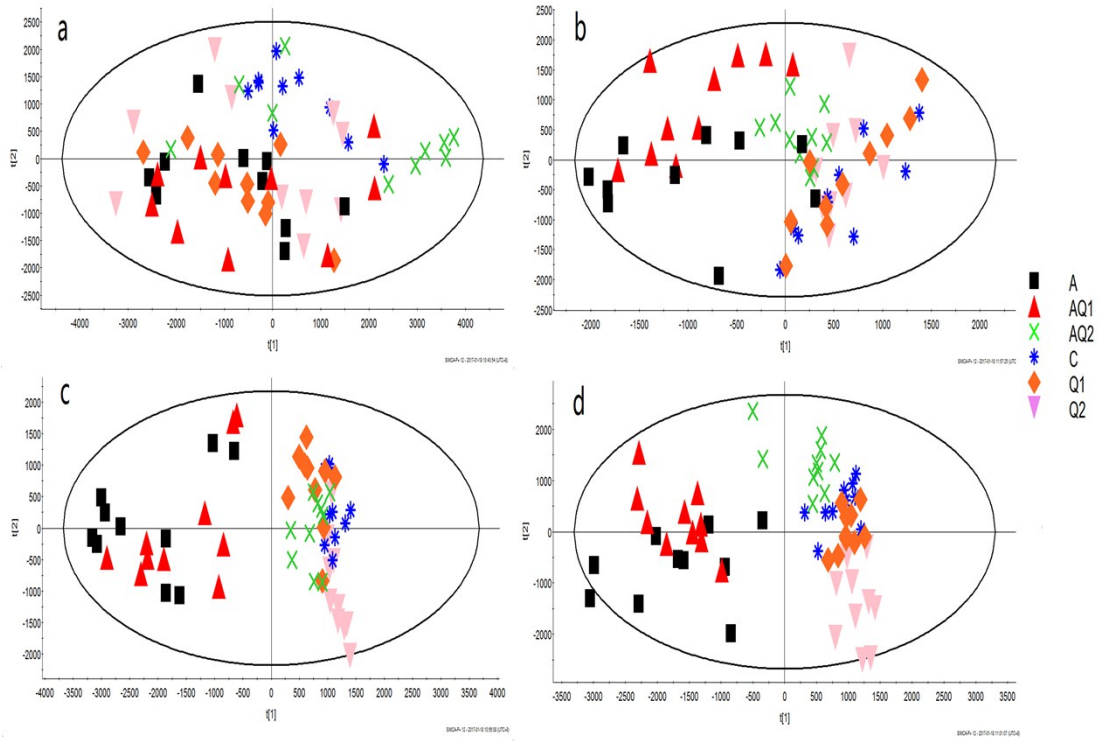
Significantly different from AA group at $p < 0.01$ (ANOVA).



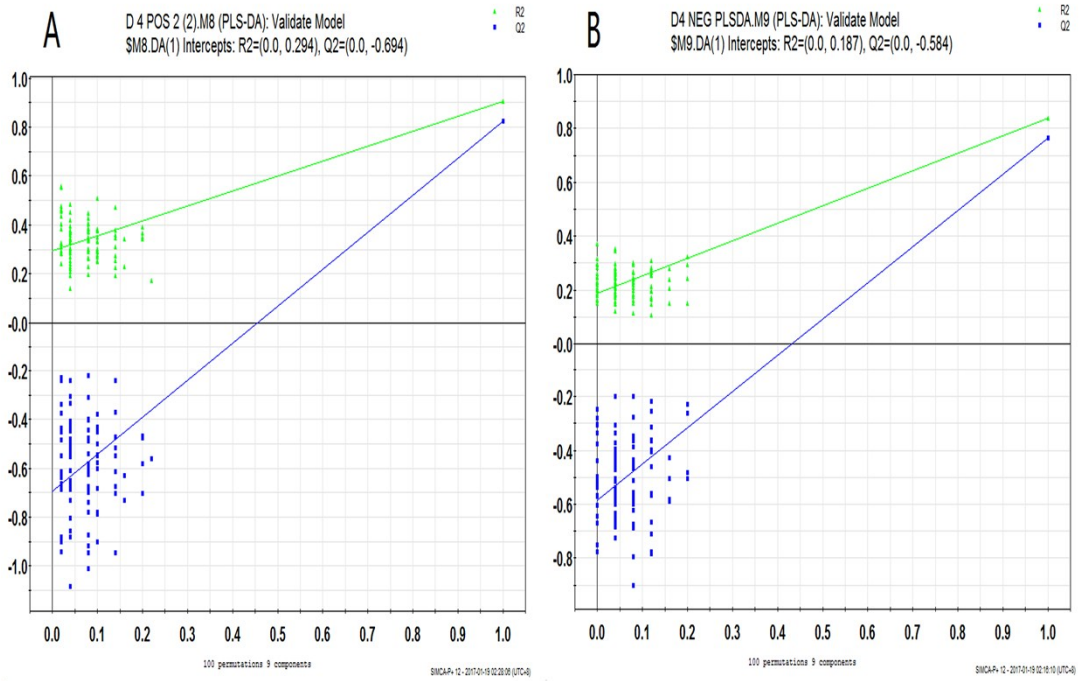
Supplementary Figure. 1. The kidney viscera coefficients of rats in each group at the end of experiment. C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group. Each bar represents means ± SD (one-way ANOVA).



Supplementary Figure.2. The liver viscera coefficients of rats in each group at the end of experiment. C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetin-treated group; A, AA-treated group; AQ1, low-dose quercetin plus AA-treated group; AQ2, high-dose quercetin plus AA-treated group. Each bar represents means ± SD (one-way ANOVA).

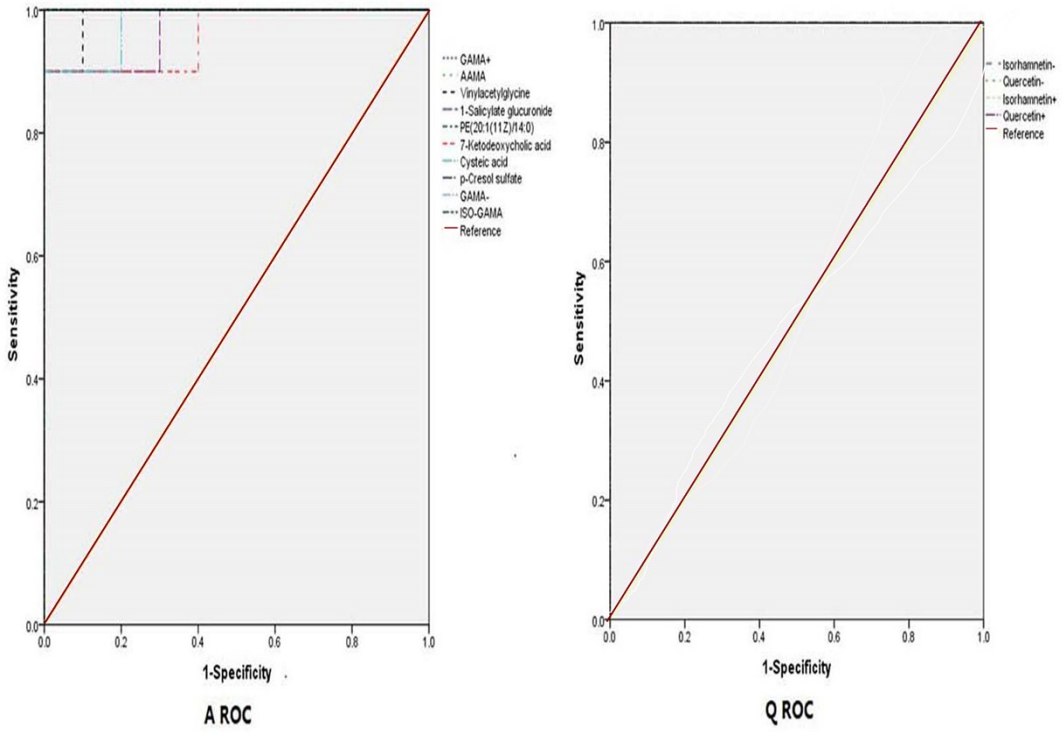


Supplementary Figure.3. PLS-DA scores plots obtained from the UPLE/ESI–Q-TOF/MS in negative mode of urine. *, control group; ■, AA-treated group; ▲, low-dose quercetin plus AA-treated Group ; ×,high-dose quercetin plus AA-treated group;, ◆,low-dose quercetin-treated group; ▼,high-dose quercetin-treated group ； a, 0 week before treatment; b, c and d derived at 4 weeks, 12 weeks and 16 weeks treatment, respectively.



Supplementary Figure.4. Permutation test result of the PLS-DA models after 16 weeks treatment

in the positive and negative modes. A, the positive mode; B, the negative mode. The R2Y value represents the goodness of fit of the model. The Q2 value represents the predictability of the models.



Supplementary Figure. 5. ROC analysis for the 15 metabolites after 16 weeks treatment.