Supplementary Table 1 The results from CV-ANOVA of the positive PLS-DA model

	SS	DF	MS	F	P	SD
Total corrected	59	59	1			1
Regression	49.96	12	4.16	21.6373	3.52e-015	2.04

CV: cross-validation; ANOVA: analysis of variance; SS, sum of squares of deviation from mean； DF, degrees of freedom; MS, mean square; SD, standard deviation.

Supplementary Table 2 The results from CV-ANOVA of the negative PLS-DA model

	SS	DF	MS	F	P	SD
Total corrected	59	59	1			1
Regression	40.69	10	4.07	10.89	1.91e-009	2.02

CV: cross-validation; ANOVA: analysis of variance; SS, sum of squares of deviation from mean； DF, degrees of freedom; MS, mean square; SD, standard deviation.

Supplementary Table 3 Renal biomarkers identified after treatment in positive and negative mode.

Retention time (min)	Measured mass (Da)	Calculated mass (Da)	Mass error (Da)	Elemental composition	Scan mode	Metabolite
1.05	203.1153	203.1158	−0.0005	C9H17NO4	+	L -Acetylcarnitine [a, b]
1.18	168.0278	168.0283	−0.0005	C5H4N4O3	+	Uric acid [a, b]
1.54	153.0404	153.0407	−0.0003	C5H9N3O4	+	6,8-Dihydroxypurine [a]
1.68	136.0749	136.0757	−0.0008	C8H9NO	+	2-Phenylacetamide [a,b]
2.07	136.0382	136.0385	−0.0003	C5H4N4O	+	Hypoxanthine [a, b]
2.07	283.0918	283.0917	0.0001	C10H13N5O5	+	Guanosine [a, b]
2.50	166.0854	166.0863	−0.0009	C10H12N4O6	+	L -Phenylalanine [a, b]
2.68	384.1147	384.1150	−0.0003	C14H17N5O8	+	Succinyladenosine [a]
2.69	219.1100	219.1107	−0.0007	C9H17NO5	+	Pantothenic acid [a, b]
3.14	205.0966	205.0972	−0.0006	C11H12N2O2	+	Tryptophan [a, b]
11.34	495.3331	495.3325	0.0006	C24H50NO7P	+	LPC(16:0) [a]
11.50	521.3494	521.3481	0.0013	C26H52NO7P	+	LPC(18:1(9z)) [a]
1.78	268.0728	268.0808	−0.0026	C10H12N4O5	-	Inosine [a, b]
7.69	564.3318	564.3307	0.0011	C26H50NO7P	-	LPC(18:2(9z,12z))[a]

Note: [a] The metabolite was confirmed by comparison to the metabolites of the Human Metabolome Database (HMDB). [b] The metabolite was identified by comparison to the standard.

Supplementary Table 4 Mass fragment information of potentional biomarkers.

Metabolite identification	Scan mode	Accurate mass (Da)	Fragmentation pattern (Da)
L-Acetylcarnitine	+	203.12	144.04, 130.02, 100.11
Uric acid	+	168.03	151.86, 150.86, 125.95, 95.99
6,8-Dihydroxypurine	+	153.04	135.03, 111.02, 110.03
2-Phenylacetamide	+	136.07	135.07, 120.04, 119.05, 118.07, 92.06, 91.05, 90.05
Hypoxanthine	+	136.04	118.98, 109.93, 93.99, 92.05, 82.03
Guanosine	+	283.09	213.33, 182.03, 172.20, 152.05, 136.05
L -Phenylalanine	+	166.09	121.08, 120.08, 118.07, 103.05
Succinyladenosine	+	384.11	252.07, 234.06, 206.07, 192.05, 136.06
Pantothenic acid	+	219.11	202.20, 184.10, 132.40, 102.80, 83.30, 71.10
Tryptophan	+	205.10	189.07, 188.07, 187.09, 147.06, 146.12
LPC(16:0)	+	495.33	478.33, 184.07, 104.11
LPC(18:1(9z))	+	521.35	504.48, 445.44, 339.12, 258.08, 184.00, 104.08, 86.08
Inosine	−	268.07	249.40, 149.96, 133.85, 135.10, 108.04
LPC(18:2(9z,12z))	−	564.33	505.27, 504.27

Supplementary Table 5 Intensities of metabolites identified in the positive and negative mode

Group	Hypoxanthine	Succinyladenosine	Urid acid	Guanosine	6,8-Dihydroxypurine	L -Acetylcarnitine	L -Phenylalanine
C	22945.5±5004.6	1846.4±302.0	79002.0±14123.2	744.4±108.7	8493.2±1285.2	33639.1±4479.4	4141.4±496.9
Q1	22755.5±5373.2	1833.6±452.5	80969.1±11252.8	744.5±133.7	8443.5±1283.3	34517.0±4459.0	4027.6±413.4
Q2	20395.0±2387.2	1785.7±290.0	73802.2±11286.3	632.7±109.0	7486.8±1287.8	36371.1±4839.9	3886.3±417.8
A	36855.6±5134.9**	2571.4±348.2**	109024.5±10204.3**	1160.8±163.7**	15568.1±3029.3**	22804.4±3138.1**	6479.8±674.0**
AQ1	34797.0±5996.5**	2447.4±507.8**	106366.8±19789.9**	1141.5±170.3**	14084.5±2741.6**	22796.8±2918.5**	6275.4±720.7**
AQ2	29339.1±3964.0**, ##	2202.0±368.2*, #	95198.3±17852.3*, #	893.0±114.2*, ##	10542.5±2628.5*, ##	27896.4±3619.4**, ##	5290.5±862.7**, ##

C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetintreated 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).

* Significantly different from the control group at $p < 0.05$ (one-way ANCOVA). ** Significantly different from the control group at $p < 0.01$ (one-way ANCOVA).

Significantly different from the AA group at $p < 0.05$ (one-way ANCOVA). ## Significantly different from the AA group at $p < 0.01$ (one-way ANCOVA).

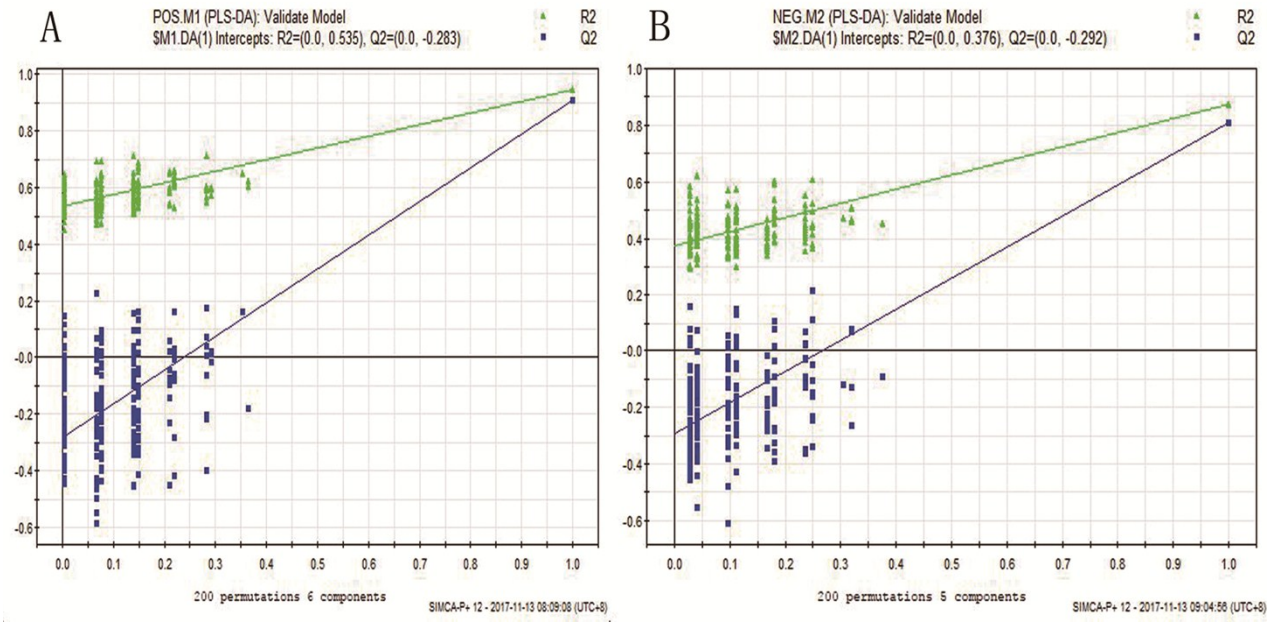
Supplementary Table 5 (continue) Intensities of metabolites identified in the positive and negative mode

Group	Pantothenic acid	Tryptophan	LPC(16:0)	LPC(18:1(9z))	2-Phenylacetamide	Inosine	LPC(18:2(9z,12z))
C	1316.3±273.9	1363.3±259.7	79790.2±9067.0	5728.4±490.3	31691.6±5421.5	20739.5±1742.1	3881.5±567.3
Q1	1334.6±259.21	1368.4±276.6	80943.0±8033.0	5704.8±691.0	31301.4±8029.2	20345.7±2695.7	3865.5±634.4
Q2	1428.7±250.8	1273.7±250.7	78016.6±8394.4	5611.3±772.8	32727.9±5969.8	19994.7±2601.7	3710.2±611.0
A	914.5±134.8**	2265.2±504.3**	109462.3±16443.8**	9235.2±1302.0**	20163.8±3802.9**	47775.6±5273.0**	5186.9±937.8**
AQ1	910.1±111.8**	2058.6±481.4**	106384.5±15989.8**	9185.5±1129.2**	21962.8±3064.4**	45204.2±5927.9**	5136.6±889.8**
AQ2	1123.7±158.8*, #	1783.6±391.7*, ##	94432.3±8997.8**, ##	6930.2±835.2**, ##	26193.0±3573.6*, #	33503.4±4841.5*, #	4537.5±494.5*, #

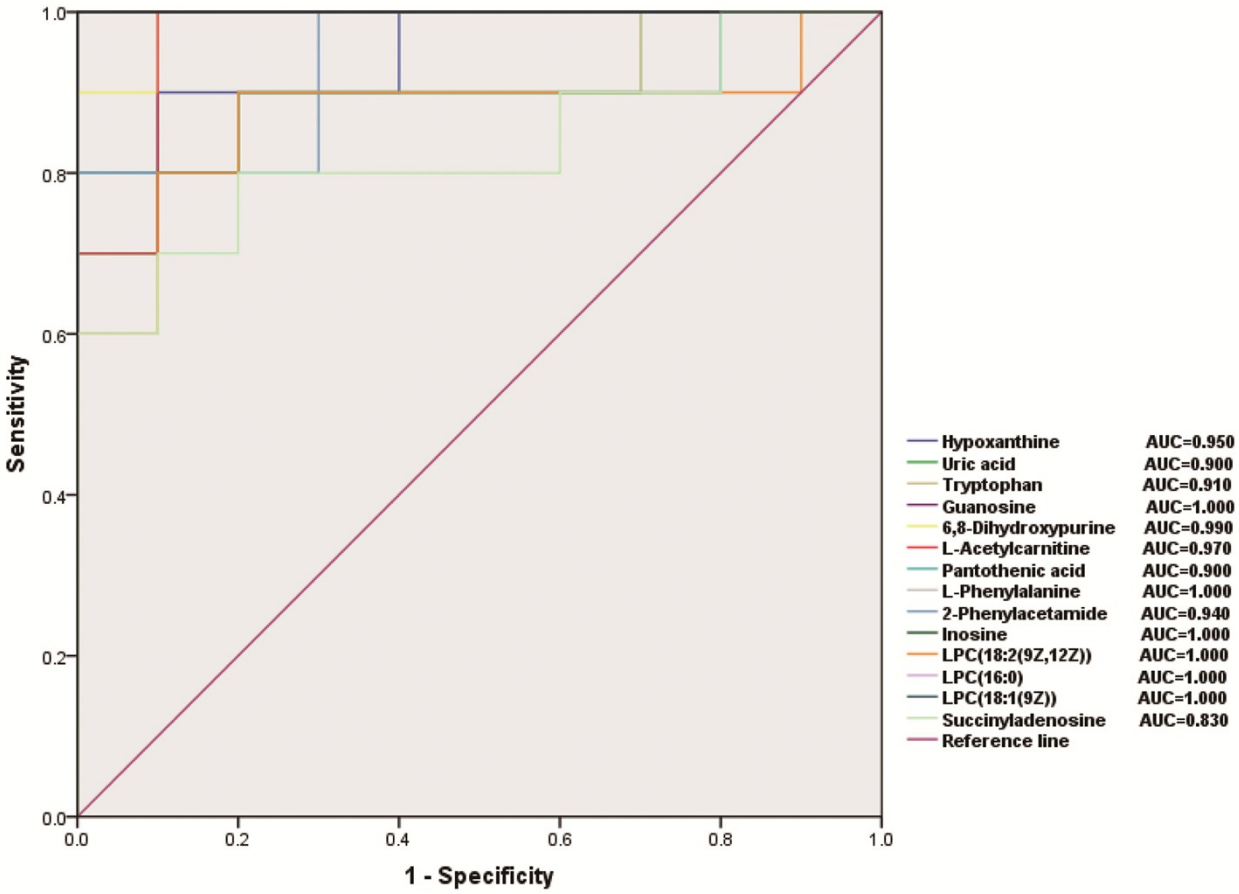
C, control group; Q1, low-dose quercetin-treated group; Q2, high-dose quercetintreated group; A, AA-treated group; AQ1, low-dose quercetin plus AA treated group; AQ2, high-dose quercetin plus AA-treated group. Values expressed as mean ± SD (n = 10).

* Significantly different from the control group at $p < 0.05$ (one-way ANCOVA). ** Significantly different from the control group at $p < 0.01$ (one-way ANCOVA).

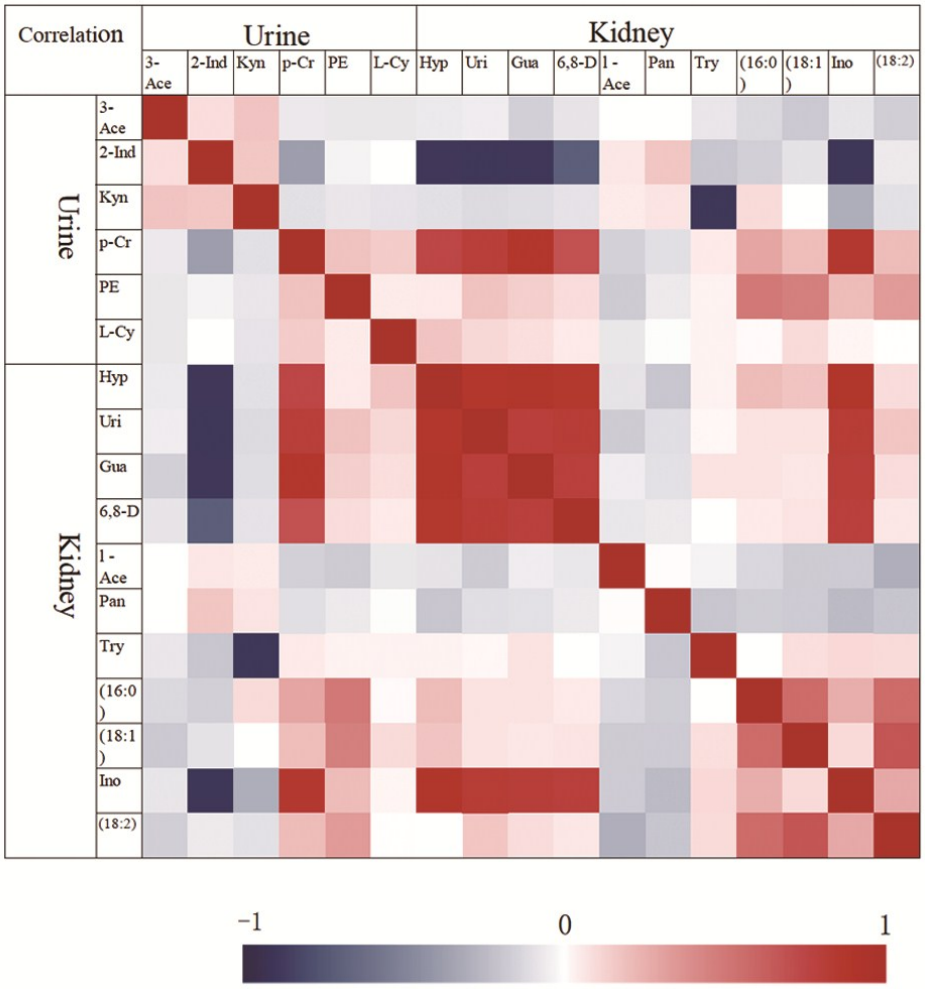
Significantly different from the AA group at $p < 0.05$ (one-way ANCOVA). ## Significantly different from the AA group at $p < 0.01$ (one-way ANCOVA).



Supplementary Figure 1. 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 2. ROC analysis for discrimination of the group AQ1 and group C for the 14 metabolites



Supplementary Figure 3.Integration of urine and kidney metabolites correlations.

The pixel maps were derived from correlations between kidney and urine metabolites found to be significantly different with AA treatment. The cutoff value of 0.70 was applied to the absolute value of the coefficient [r] for displaying the strong correlations between metabolites. Correlation values are displayed as a color-coded pixel map according to correlation value (gradient of red colors for positive correlations and gradient of blue colors for negative correlations). Keys: 3-Ace, 3-Acetamidobutanal; 2-Ind, 2-Indolecarboxylic acid; Kyn, Kynurenic acid;p-Cr, p-Cresol sulfate; PE, phosphatidylethanolamine; L-Cy, L-Cysteine; Hyp, Hypoxanthine; Uri, Urid acid; Gua, Guanosine; 6,8-D, 6,8-Dihydroxypurine; l-Ace, l-Acetylcarnitine; Pan, Pantothenic acid; Try, Tryptophan;(16:0), lysophosphatidylcholine(16:0); (18:1), lysophosphatidylcholine(18:1(9z)); Ino, Inosine; (18:2), lysophosphatidylcholine(18:2(9z,12z)).