Fig. S1 Scores plots of multivariate statistical analysis on urine samples. A. Partial least squares-discriminate analysis (PLS-DA) scores plot of normal (N) group versus model (M) group, B. PLS-DA scores plot of model (M) group versus memantine (M+Mem) group, C. PLS-DA scores plot of model (M) group versus chlorogenic acid (M+CGA) group, D. PLS-DA scores plot of N, M, M+Mem, M+CGA groups.

Table S1 Automatic modeling parameters for assessing modeling quality of PCA, PLS-DA and OPLS (n=6 in each group)

		Amount of components	R^2X	R^2Y	$Q^2(cum)$
M *vs.* N	PCA-X	2	0.667		0.466
	PLS-DA	2	0.646	0.988	0.955
	OPLS	2	0.646	0.988	0.955
M+Mem *vs.* M	PCA-X	2	0.645		0.347
	PLS-DA	3	0.705	0.998	0.998
	OPLS	2	0.626	0.979	0.942
M+CGA *vs.* M	PCA-X	2	0.68		0.466
	PLS-DA	2	0.622	0.995	0.967
	OPLS	2	0.622	0.995	0.967
N *vs.* M *vs.* M+Mem *vs.* M+CGA	PCA-X	2	0.523		0.377
	PLS-DA	6	0.715	0.967	0.785

Table S2 Differential metabolites among N, M, M+Mem, M+CGA comparison groups.

Metabolites	RT(min)	Mass	M vs N			M+Mem vs. M			M+CGA vs M		
			Fold change[a]	VIP[b]	T-test (p)	Fold change	VIP	T-test(p)	Fold change	VIP	T-test (p)
Beta-alanine	7.31	102	0.51	1.08	0.001	2.04	1.08	0.013	2.15	1.07	0.022
4-Aminobutanoic acid	15.31	174	0.28	1.01	0.008	—	—	—	—	—	—
Propanedioic acid	7.48	147	0.54	1.11	0.004	2.08	1.30	0.002	2.25	1.26	0.001
Threonine	16.82	218	0.36	1.31	<0.001	2.63	1.00	0.015	2.48	1.01	0.030
Serine	9.86	218	0.47	1.01	0.019	1.90	1.13	<0.001	3.42	1.10	0.004
Galactose	17.55	117	0.41	1.07	0.010	—	—	—	—	—	—
Myo-inositol	25.99	217	0.32	1.21	0.002	3.06	1.15	0.006	3.99	1.31	<0.001
D-lactic acid	5.38	117	0.32	1.10	0.019	—	—	—	—	—	—
Acetic acid	5.61	177	0.36	1.31	<0.001	3.47	1.41	<0.001	3.47	1.29	<0.001
Urea	7.12	171	0.29	1.20	0.003	—	—	—	—	—	—
Creatinine	13.65	115	0.21	1.36	<0.001	5.97	1.39	<0.001	4.76	1.25	<0.001
Proline	8.88	142	0.31	1.07	0.001	4.60	1.13	0.011	—	—	—
Oxalic acid	6.42	117	0.47	1.06	0.017	2.08	1.25	0.003	2.76	1.30	<0.001
Ascorbic acid	33.59	332	0.29	1.29	0.017	—	—	—	—	—	—
Asparagine	12.57	128	0.30	1.18	0.007	4.07	1.27	0.005	—	—	—
Alpha-alanine	6.01	116	0.34	1.18	0.006	2.55	1.09	0.010	2.90	1.09	0.014
Hippurate	19.40	105	11.05	1.29	<0.001	0.05	1.38	<0.001	0.11	1.27	<0.001
Ferulic acid	25.80	338	77.50	1.10	0.009	68.90	1.20	0.042	2.50	1.08	0.009
Kynurenic acid	25.43	318	0.40	1.15	0.015	2.37	1.26	<0.001	2.10	1.01	0.014

a. Values greater than 1 indicate higher levels in M group relative to N group; values less than 1 indicate higher levels in N group relative to M group, this comparison method was also applicable in other groups.

b. Variable importance in the projection (VIP) was obtained from OPLS-DA with a threshold of 1.0. The short dash line (-) indicates no significant variation