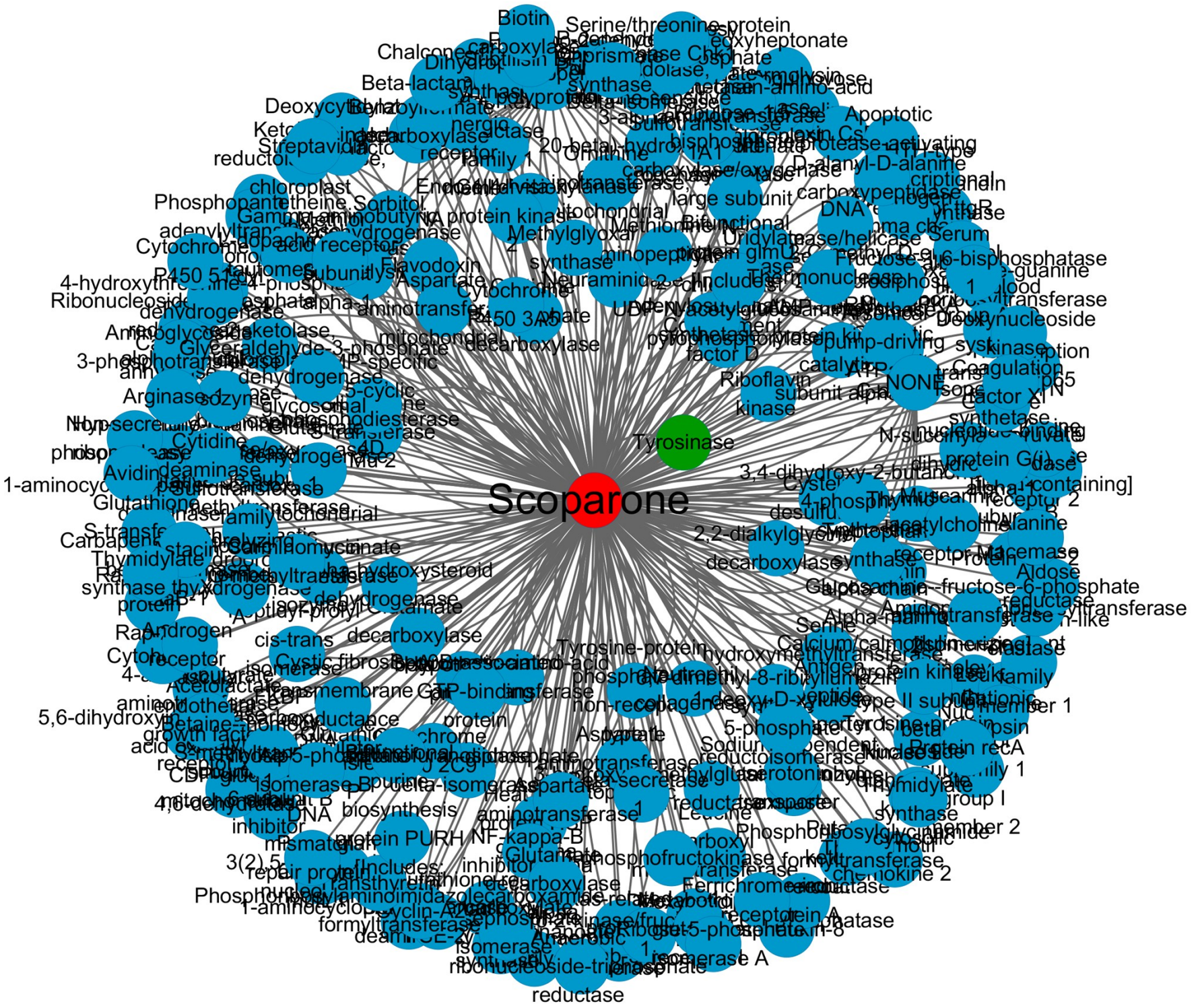
Electronic Supplementary Material (ESI) for RSC Advances.

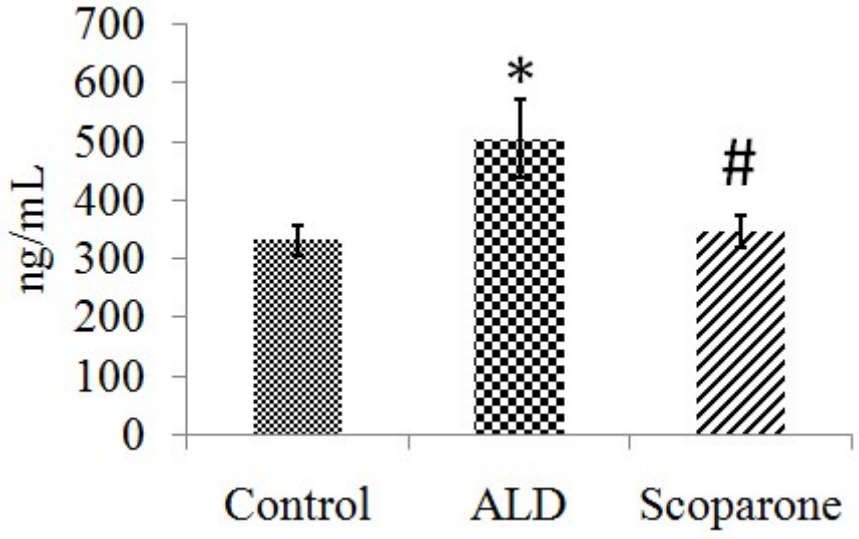
Supplementary Table 1. Identification and trends of change for differential metabolites

NO	Rt(min)	m/z determined	m/z calculated	HMDB	Ion form	Molecular Formula	Metabolite Name	Trend	VIP	T'TEST
1	0.57	146.1653	146.1657	HMDB01257	$[M+H]^+$	$C_7H_{19}N_3$	Spermidine	↓	1.00	0.0069
2	0.86	126.0222	126.0225	HMDB00251	$[M+H]^+$	$C_2H_7NO_3S$	Taurine	↓	3.00	0.0062
3	2.10	188.0911	188.0923	HMDB12150	$[M+H]^+$	$C_8H_{13}NO_4$	2-Keto-6-acetamidocaproate	↓	1.39	0.0096
4	2.70	122.0263	122.0276	HMDB00574	$[M+H]^+$	$C_3H_7NO_2S$	L-Cysteine	↓	1.42	0.0001
5	3.17	109.0286	109.0290	HMDB12133	$[M+H]^+$	$C_6H_4O_2$	1,2-Benzoquinone	↑	1.45	0.0143
6	3.32	168.0662	168.0661	HMDB01545	$[M+H]^+$	$C_8H_9NO_3$	Pyridoxal	↓	1.42	0.0010
7	3.33	315.1193	315.1206	HMDB01412	$[M+H]^+$	$C_{14}H_{14}N_6O_3$	7,8-Dihydropteroic acid	↓	1.61	0.0006
8	3.74	210.0742	210.0766	HMDB00735	$[M+H]^+$	$C_{10}H_{11}NO_4$	Hydroxyphenylacetylglycine	↓	4.90	0.0041
9	3.92	184.0972	184.0974	HMDB00068	$[M+H]^+$	$C_9H_{13}NO_3$	Epinephrine	↑	2.46	0.0442
10	4.67	474.1725	474.1737	HMDB00972	$[M+H]^+$	$C_{20}H_{23}N_7O_7$	10-Formyltetrahydrofolate	↑	1.54	0.0060
11	4.87	235.1081	235.1083	HMDB02339	$[M+H]^+$	$C_{12}H_{14}N_2O_3$	5-Methoxytryptophan	↑	1.38	0.0038
12	5.10	190.0504	190.0504	HMDB00715	$[M+H]^+$	$C_{10}H_7NO_3$	Kynurenic acid	↓	8.04	0.0010
13	5.64	247.0949	247.0930	HMDB00497	$[M+H]^+$	$C_9H_{14}N_2O_6$	5,6-Dihydrouridine	↓	1.20	0.0040
14	6.22	233.1281	233.1290	HMDB01389	$[M+H]^+$	$C_{13}H_{16}N_2O_2$	Melatonin	↑	1.24	0.0013
15	7.37	300.0913	300.0944	HMDB02044	$[M+H]^+$	$C_{10}H_{13}N_5O_6$	8-Hydroxyguanosine	↓	1.28	0.0024
16	0.65	177.0400	177.0399	HMDB03466	$[M-H]^-$	$C_6H_{10}O_6$	L-Gulonolactone	↓	1.79	0.0241
17	0.65	195.0505	195.0505	HMDB00625	$[M-H]^-$	$C_6H_{12}O_7$	Gluconic acid	↓	7.42	0.0215
18	3.72	176.0375	176.0381	HMDB01015	$[M-H]^-$	$C_6H_{11}NO_3S$	N-Formyl-L-methionine	↓	1.23	0.0394
19	3.78	259.1292	259.1292	HMDB11171	$[M-H]^-$	$C_{11}H_{20}N_2O_5$	L-gamma-glutamyl-L-leucine	↑	1.31	0.0083
20	4.52	137.0602	137.0603	HMDB04284	$[M-H]^-$	$C_8H_{10}O_2$	Tyrosol	↑	2.08	0.0263
21	4.52	167.0341	167.0344	HMDB00130	$[M-H]^-$	$C_8H_8O_4$	Homogentisic acid	↑	3.44	0.0036
22	5.16	175.0607	175.0607	HMDB00402	$[M-H]^-$	$C_7H_{12}O_5$	2-Isopropylmalic acid	↑	2.37	0.0259
23	7.31	211.0600	211.0606	HMDB00913	$[M-H]^-$	$C_{10}H_{12}O_5$	Vanillactic acid	↓	1.03	0.0104
24	6.76	194.0452	194.0453	HMDB01229	$[M-H]^-$	$C_9H_9NO_4$	Dopaquinone	↑	1.87	0.0024

Note: ↑, ↓ compared with the control group



Supplemental Figure 1. Different independent machine learning systems for the targets prediction of scoparone based on network pharmacology approach. (●) The supplied ligand for the different target prediction systems. (●) The optimal receptor from different molecule-ducking methods. (●) All the targets from the different machine learning systems.



Supplemental Figure 2. The target verification of ELISA kit for tyrosinase. Data are expressed as mean ± SD.

*p<0.05, **p<0.01: Compared with control group; #p<0.05, ##p<0.01: Compared with ALD group.