Supplementary material

Investigating the basis for the antidepressant effects of Gleditsiae Spina using an integrated metabolomic strategy

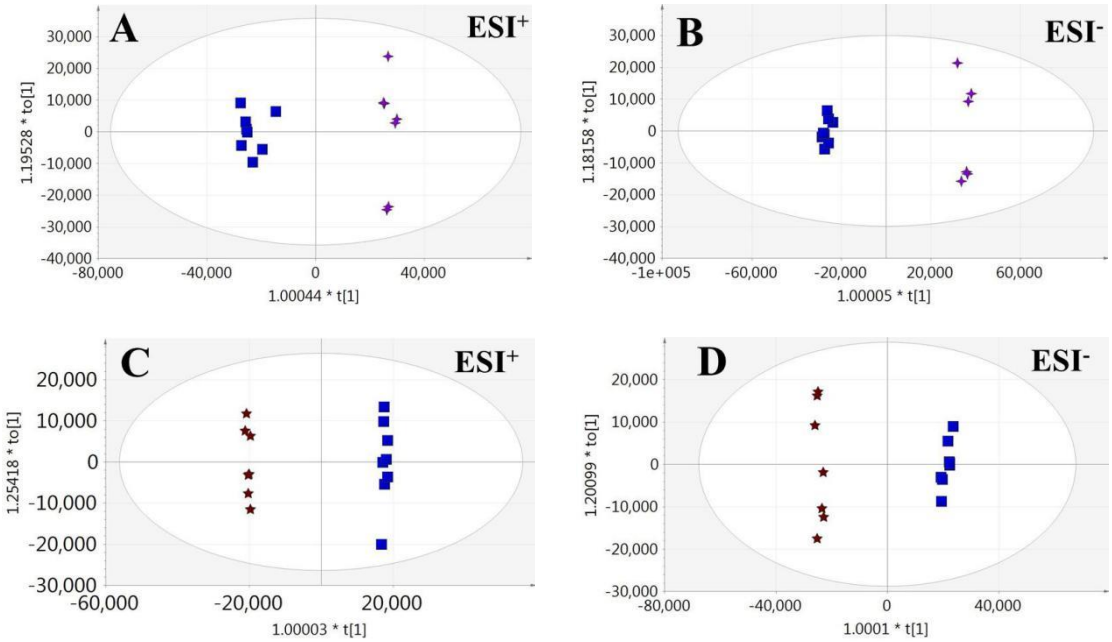

Figure 1. OPLS-DA score scatter plots obtained from Cor *vs.* GS and Cor *vs.* Tax groups

Cor group GS group Tax group. Corticosterone (Cor) / Gleditsiae Spina (GS) / Taxifolin (Tax) group

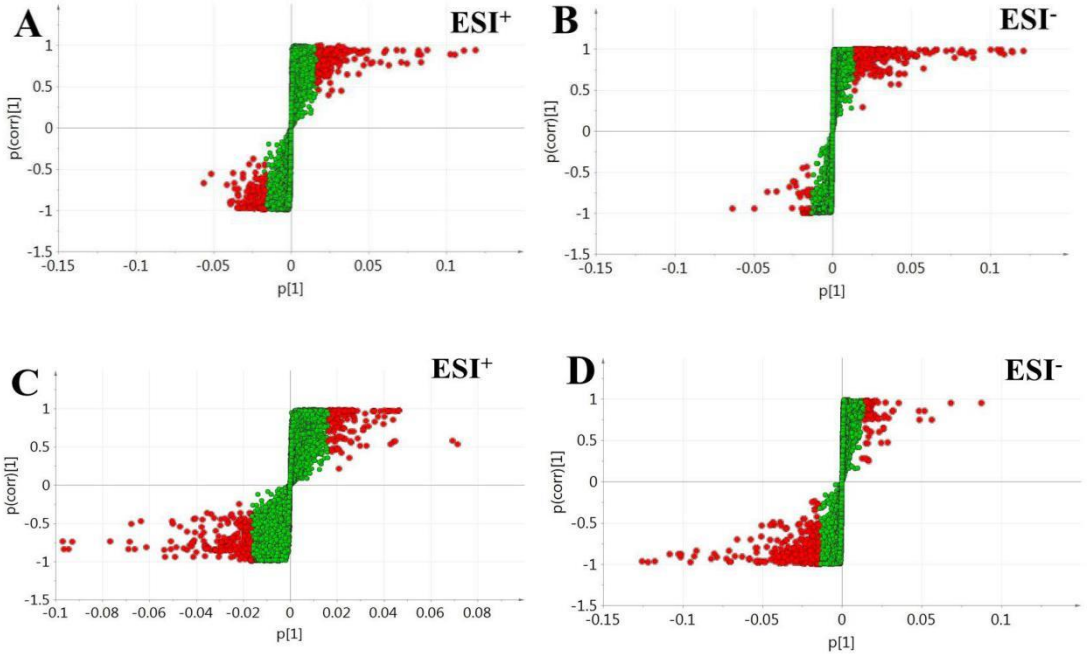

Figure 2. S-plots obtained from Cor *vs.* GS and Cor *vs.* Tax groups. Cor *vs.*GS group (A, B), Cor *vs.* Tax group (C, D). Corticosterone (Cor) / Gleditsiae Spina (GS) / Taxifolin (Tax) group. Corticosterone (Cor) / Gleditsiae Spina (GS) / Taxifolin (Tax) group

Table 1. Identification results for the candidate metabolites

NO.	Compound	Metabolic pathway	Cor *VS.* NC	GS *VS*. Cor	Tax *VS*. Cor	KEGG ID	VIP
1	Dimethyl sulfone	Sulfur metabolism	↑	↓		C11142	6.17066
2	(2R)-2-Hydroxy-2-methylbutanenitrile	Cyanoamino acid metabolism	↓	↑		C18796	3.8521
3	L-Asparagine	Alanine, aspartate and glutamate metabolism	↓	↑		C00152	3.72602
4	L-Carnitine	Bile secretion	↑	↓		C00318	3.88775
5	L-Phenylalanine	Phenylalanine metabolism	↓	↑		C00079	4.4782
6	Valproic acid	Bile secretion	↓	↑		C07185	4.73947
7	L-Arginine	Arginine and proline metabolism	↓	↑		C00062	4.10776
8	Nicotinuric acid	Nicotinate and nicotinamide metabolism	↓	↑		C05380	5.76193
9	L-Rhamnulose	Fructose and mannose metabolism	↓	↑		C00861	5.13939
10	Carnosine	Histidine metabolism	↓	↑		C00386	4.97201
11	2,5-Dioxopentanoate	Pentose and glucuronate interconversions	↓	↑		C00433	5.66226
12	D-Xylono-1,5-lactone	Pentose and glucuronate interconversions	↓	↑		C02266	3.93013
13	D-Ribulose	Pentose and glucuronate interconversions	↓	↑		C00309	3.90022
14	Protocatechuic acid	Phenylalanine, tyrosine and tryptophan biosynthesis	↓	↑		C00230	3.9968
15	L-Lyxonate	Pentose and glucuronate interconversions	↑	↑		C05412	4.53317
16	N-Formyl-L-methionine	Cysteine and methionine metabolism	↓	↑		C03145	3.89345

17	3-Succinoylpyridine	Nicotinate and nicotinamide metabolism	↓	↑		C19569	27.8304
18	Kynurenic acid	Tryptophan metabolism	↓	↑		C01717	3.80428
19	Pantothenic acid	beta-Alanine metabolism	↓	↑		C00864	3.92848
20	Uric acid	Purine metabolism	↓	↑		C00366	4.36208
21	Nicotinic acid	Nicotinate and nicotinamide metabolism	↑		↓	C00253	4.4257
22	N-Acetylputrescine	Arginine and proline metabolism	↓		↑	C02714	7.73004
23	Creatine	Arginine and proline metabolism	↓		↑	C00300	10.8636
24	Beta-Leucine	Amino acid metabolism	↓		↑	C02486	8.89876
25	1-Methylnicotinamide	Nicotinate and nicotinamide metabolism	↓		↑	C02918	3.76094
26	Spermidine	Arginine and proline metabolism	↓		↓	C00315	4.14856
27	2-Aminomuconic acid	Tryptophan metabolism	↓		↑	C02220	8.68034
28	Isopropylmaleate	2-Oxocarboxylic acid metabolism	↓		↑	C02631	3.83732
29	L-Tyrosine	Phenylalanine metabolism	↓		↑	C00082	2.79789
30	L-2-Amino-3-oxobutanoic acid	Glycine, serine and threonine metabolism	↓		↑	C03508	5.06574
31	Succinic acid	Citrate cycle (TCA cycle)	↓		↑	C00042	5.14972
32	1-Pyrroline-4-hydroxy-2-carboxylate	Arginine and proline metabolism	↓		↑	C04282	3.66263
33	Gentisic acid	Tyrosine metabolism	↓		↑	C00628	3.9916
34	N-Acetyl-L-glutamic acid	Phenylalanine metabolism	↓		↑	C00624	6.23205
35	Citric acid	Citrate cycle (TCA cycle)	↓		↓	C00158	3.61806
36	Cytidine monophosphate	Pyrimidine metabolism	↓		↑	C00055	3.58052
37	Urocanic acid	Histidine metabolism	↓		↑	C00785	4.05068
38	Gulonic acid	Pentose and glucuronate interconversions	↓	↑	↑	C00800	5.83653
39	L-Proline/D-Proline	Arginine and proline metabolism	↓	↑	↑	C00148	5.86336

40	Betaine	Glycine, serine and threonine metabolism	↓	↑	↑	C00719	4.37995
41	Trigonelline	Nicotinate and nicotinamide metabolism	↓	↑	↑	C01004	4.1958
42	L-Methionine	Cysteine and methionine metabolism	↓	↑	↑	C00073	7.69545
43	Phenylacetylglycine	Phenylalanine metabolism	↓	↑	↑	C05598	8.53192
44	Hippuric acid	Phenylalanine metabolism	↓	↑	↑	C01586	20.0937
45	5-Methoxyindoleacetate	Tryptophan metabolism	↓	↑	↑	C05660	20.2399
46	N-Acetyl-L-phenylalanine	Phenylalanine metabolism	↓	↑	↑	C03519	9.40148
47	Cortisol	Cortisol synthesis and secretion	↑	↓	↓	C00735	8.54345
48	Taurine	Taurine and hypotaurine metabolism	↓	↑	↑	C00245	6.77779
49	2-Hydroxyethanesulfonate	Taurine and hypotaurine metabolism	↓	↑	↑	C05123	9.68046
50	3-Hydroxy-L-proline	Arginine and proline metabolism	↓	↑	↑	C19706	3.77696
51	2-Phenylacetamide	Phenylalanine metabolism	↓	↑	↑	C02505	4.60703
52	Oxoglutaric acid	Citrate cycle (TCA cycle)	↓	↑	↑	C00026	3.96066
53	Allantoin	Purine metabolism	↓	↑	↑	C02348	13.5615
54	3-(3-Hydroxyphenyl)propanoic acid	Phenylalanine metabolism	↓	↑	↑	C11457	6.42793
55	cis-Aconitic acid	Citrate cycle (TCA cycle)	↓	↑	↓	C00417	3.77027
56	Xanthurenic acid	Tryptophan metabolism	↓	↑	↑	C02470	6.81071
57	5-L-Glutamyl-taurine	Taurine and hypotaurine metabolism	↓	↑	↑	C05844	5.22165
58	Sulfate	Purine metabolism	↑	↓	↓	C00059	7.11853