SUPPLEMENTARY METHODS

Reagents and chemicals

Laboratory animal diet (No. 0608SH06130232D) was purchased from SPF (Beijing) Biotechnology Co., Ltd (Beijing, China). Fenofibrate capsules (No. 32779) were purchased from French Libofoni Pharmaceutical Biological Technology Co., Ltd. (Paris, France). Commercial kits for the determination of total cholesterol (TC, No. A111-1-1), triglyceride (TG, No. A110-1-1), alanine transaminase (ALT, No. C009-2-1), aspartate transaminase (AST, No. C010-2-1), LDL-C (No. A113-1-1), high-density lipoprotein cholesterol (HDL-C, No. A112-1-1), superoxide dismutase (SOD, No. A001-3-2), and glutathione (GSH, No. A006-2-1) were purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China). Tumor necrosis factor-alpha (TNF-α, No. MM-0180R2), interleukin-6 (IL-6, No. MM-0190R1), and interleukin-1β (IL-1β, No. MM-0047R1) ELISA Kit were obtained from Jiangsu Meimian Industrial Co., Ltd. (Jiangsu, China). 40 g/L Paraformaldehyde fix solution, hematoxylin and eosin (HE) stain kit (No. G1121), and Oil red O dye (No. G1261) were purchased from Wuhan Servicebio Technology Co., Ltd. (Wuhan, China). The HepG2 human hepatocellular cell was purchased from the Cell Resource Center, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences. (Beijing, China). Dulbecco's Modified Eagle Medium (DMEM; No.6124477) was purchased from Grand Island Biological Company Co., Ltd. (NY, USA). Sodium oleate (No. S817542) was purchased from Shanghai Macklin Biochemical Co., Ltd. (Shanghai, China). Sodium palmitate (No. P9767) was purchased from Sigma-Aldrich (PA, USA). RIPA Lysis Buffer（No.240007014） was purchased from Solarbio Co., Ltd. (Beijing, China). Tris Buffered Saline Tween (TBST; No. 240011012) was purchased from Solarbio Co., Ltd. (Beijing, China). Ultrasensitive ECL Detection Kit (No. 230718E01-02) was obtained from UElandy Co., Ltd. (Suzhou, China). PageRuler™ Plus Prestained Protein Ladder, 10 to 180 kDa (26616) was purchased from Thermo Fisher Scientific Co., Ltd. (Waltham, MA, USA). β-actin (No. 20536-1-AP) and anti-MAOA (No.

10539-1-AP) were purchased from Proteintech Group, Inc. (Wuhan, China). Goat anti-Rabbit IgG(H+L) (No. Bs-0295G-HRP), anti-NOS2 (No. Bs-0162R), and anti-MIF (No. Bs-1044R) were purchased from Bioss Biotechnology Co., Ltd. (Beijing, China). 4,4'-Dihydroxy-2-methoxychalcone (D-2-MC, No. TC0022-231215), trans-cinnamaldehyde (t-CA, No. TC0824-230622), eburicoic acid (EA, No. TC1758-231120), alisol F 24-acetate (AF-24, No. TC0328-231129), cinnamic acid (CA, No. TC0822-230522), atractylenolide II (AT-II, No. TC0526-240325), betaine (Bet, No. TC1061-230325), liquiritigenin (Liq, No. TC0019-240325), and glycyrrhetinic acid (GA, No. TC0015-230325) were purchased from Sichuan Jingcui Tiancheng Pharmaceutical Technology Co., Ltd. (Chendu, China). Dehydrotrametenolic acid (DLA, No. QC90577), 16α-hydroxydehydrotrametenolic acid (16-HA, No. QC90790), 11-deoxyalisol A (11-DA, No. QC95661), 16,23-oxidoalisol B (16,23-OB, No. QC95650), 8beta-methoxyatractylenolide I (8-MA, No. QC89314), poricoic acid A (PA, No. QC92838), alisol F (AF, No. QC92402), 7-hydroxycoumarin (7-HC, No. QC97503), and 6-shogaol (6-SG, No. QC99531) were purchased from Shanghai Qincheng Biotechnology Co., Ltd. (Shanghai, China). 1-Dehydro-[10]-gingerdione (D10G, No. WP24050605) was purchased from Sichuan Vicky Biotechnology Co., Ltd (Chendu, China). All the other reagents were of analytical grade or higher. The PR, AR, AMR, CR, GRR, and CRR samples were purchased from Kunming Luosiwan Chinese Medicinal Materials Market (Kunming, China) and authenticated by Professor Xing-Xin Yang at the Yunnan University of Chinese Medicine.

Quality control of FZD extract

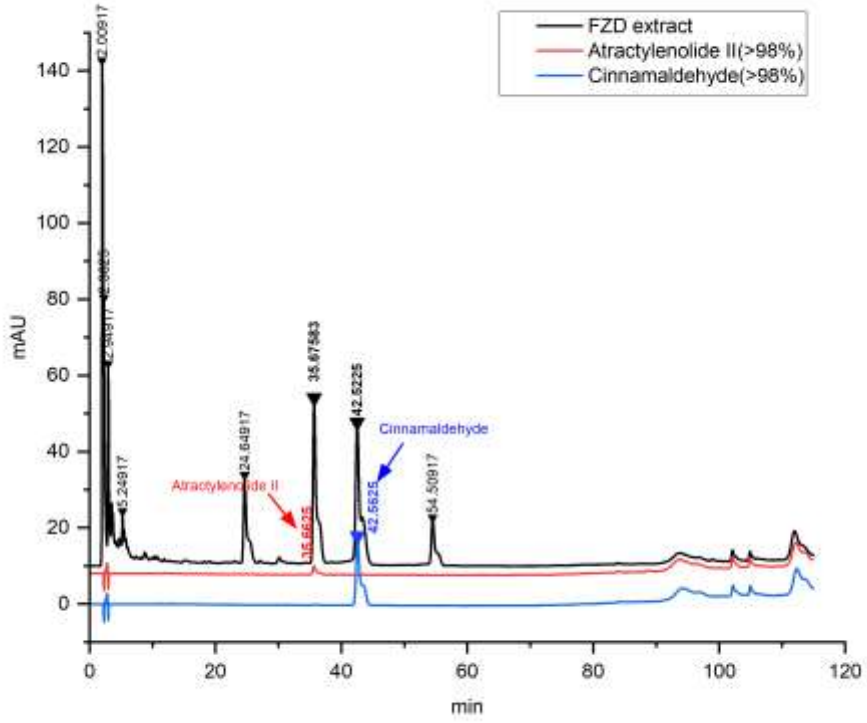
To ensure the quality control of FZD extract, the contents of atractylenolide II and cinnamaldehyde were quantified by means of an Agilent 1220 Infinity II UPLC system (Agilent Technologies, CA, USA). Precisely weighed atractylenolide II and cinnamaldehyde reference standards were each dissolved in methanol, with each prepared into a 10 μg/mL solution, while the

freeze-dried FZD extract powder was prepared into a 40 mg/mL solution. The prepared solutions underwent ultrasonic extraction for 30 minutes, followed by filtration via a 0.22 μm microporous membrane, and were subsequently subjected to UPLC analysis. Chromatographic separation was achieved on an Agilent ZORBAX SB-C18 column (4.6×250 mm, 5 μm; Agilent Technologies, CA, USA) with a constant flow rate of 1.0 mL/min, while the column temperature was maintained at 30°C. The injection volume was fixed at 10 μL, and the mobile phase comprised acetonitrile (phase A) and 0.1% phosphoric acid aqueous solution (phase B). The gradient elution program was detailed as below: 0-10.0 min, 19% A; 10.0-45.0 min, 30% A; 45.0-70.0 min, 45% A; 70.0-112.0 min, 70% A; 112.0-115.0 min, 70% A. The detection wavelength was set at 280 nm.

Metabolomic analysis

LC-MS analyses: LC-MS analysis was conducted using a Thermo UHPLC-Q Exactive system (Thermo Scientific, MA, USA) equipped with an ACQUITY HSS T3 column (1.8 μm, 100 mm × 2.1 mm, Waters, MA, USA). The mobile phase consisted of (A) 0.1 % formic acid in acetonitrile/isopropanol/water (47.5:47.5:5, v/v) and (B) 0.1 % formic acid in water/acetonitrile (95:5, v/v), and a gradient elution was performed as follows: 0-3 min, 5% A-20% A; 3-4.5 min, 20% A-35% A; 4.5-5 min, 35% A-100% A; 5-6.3 min, 100% A; 6.3-6.4min, 100% A-0% A; 6.4-8 min, 0% A. The injection volume was 3 μL, and the flow rate was 0.4 mL/min.

Mass spectrometric data were collected in both ionization modes (positive and negative) on the same instrument equipped with an ESI source, scanning from 70 to 1050 m/z. The spray voltages employed were 3500 V for positive ionization and 2800 V for negative ionization. The flow rates of sheath gas and auxiliary gas were set to 40 psi and 10 psi, respectively, while the collision energy was operated in a cyclic stepped mode (20, 40, and 60 V).



Supplementary Figure 1 Quantity control of FZD extract. A: FZD extract, atractylenolide II, and cinnamaldehyde. The content of corresponding substances in the FZD extract was indicated by calculating based on the positions and peak areas of the standards.

Supplementary Table 1 Differential metabolites in rat serum

NO.	t_R /min	Metabolite	M/Z	Formula	HMDB ID	MOD vs CON	FZD vs MOD
ESI$^+$							
1	0.3656	Ornithine	133.0972	$C_5H_{12}N_2O_2$	HMDB0000214	↓	↑
2	0.4744	5'-N-Ethylcarboxamidoadenosine	331.1109	$C_{12}H_{16}N_6O_4$	HMDB0255498	↑	↓
3	0.5206	Flavonol 3-O-D-glucoside	365.1052	$C_{21}H_{20}O_8$	HMDB0252295	↓	↑
4	0.8399	N(5)-Acetylornithine	157.0971	$C_7H_{14}N_2O_3$	HMDB0242109	↓	↑
5	2.3180	CDP-DG(18:3(9Z,12Z,15Z)/22:6(4Z,7Z,11E,13Z,15E,19Z)-2OH(10S,17))	540.7559	$C_{52}H_{79}N_3O_{17}P_2$	HMDB0291679	↑	↓
6	3.6745	6-Hydroxyoctanoylcarnitine	304.2116	$C_{15}H_{29}NO_5$	HMDB0241741	↑	↑

7	4.1240	Interleukin-1beta (163-171)	1037.4770	$C_{39}H_{64}N_{12}O_{19}$	HMDB0244321	↑	↓
8	4.4799	3,11,12-Trihydroxy-1(10)-spirovetiven-2-one	286.2010	$C_{15}H_{24}O_4$	HMDB0038154	↑	↓
9	5.1458	Indolophenanthridine	292.1805	$C_{19}H_{18}N_2$	HMDB0253475	↑	↓
10	5.2695	3-carboxy-4-methyl-5-pentyl-2-furanpropanoic acid	269.1357	$C_{14}H_{20}O_5$	HMDB0061643	↓	↑
11	5.2695	Epsilon-Caprolactone	229.1433	$C_6H_{10}O_2$	HMDB0060476	↓	↑
12	5.3930	3-Hydroxydodecanedioic acid	269.1358	$C_{12}H_{22}O_5$	HMDB0000413	↓	↑
13	5.5323	RHODAMINE 6G	443.2331	$C_{28}H_{30}N_2O_3$	HMDB0257199	↑	↓
14	5.7018	Hordatine A	584.3348	$C_{28}H_{38}N_8O_5$	HMDB0030461	↓	↑

15	5.8411	Eicosadienoic acid	331.2629	$C_{20}H_{36}O_2$	HMDB0005060	↓	↑
16	5.8722	Mifepristone	462.2977	$C_{29}H_{35}NO_2$	HMDB0014972	↓	↑
17	5.8722	PE(16:0/0:0)	454.2927	$C_{21}H_{44}NO_7P$	HMDB0011503	↓	↑
18	5.9182	1-hexadecyl-glycero-3-phosphate	438.2974	$C_{19}H_{41}O_6P$	HMDB0062325	↓	↑
19	5.9414	Mayzent	534.2953	$C_{29}H_{35}F_3N_2O_3$	HMDB0248844	↓	↑
20	5.9569	LysoPE(18:0/0:0)	482.3240	$C_{23}H_{48}NO_7P$	HMDB0011130	↓	↑
ESI-							
21	3.1719	Ferulic acid 4-O-sulfate	273.0077	$C_{10}H_{10}O_7S$	HMDB0029200	↓	↑
22	4.1216	3-Phenyllactic acid	165.0549	$C_9H_{10}O_3$	HMDB0000779	↓	↑

23	4.3136	Indolelactic acid	204.0662	$C_{11}H_{11}NO_3$	HMDB0000671	↓	↑
24	4.6097	Platyconic acid A	618.2763	$C_{57}H_{90}O_{29}$	HMDB0256635	↑	↓
25	5.6792	Isokobusone	267.1603	$C_{14}H_{22}O_2$	HMDB0036791	↑	↑
26	5.6952	(5Z)-7-[(1R,2E)-2-[(3S)-3-hydroxyoctylidene]-3-oxocyclopentyl]hept-5-enoylcarnitine	516.2743	$C_{27}H_{45}NO_6$	HMDB0241800	↓	↑
27	5.7032	2,2,2-Trifluoro-N-(2-nitrophenyl)acetamide	233.0187	$C_8H_5F_3N_2O_3$	HMDB0247856	↓	↑
28	5.7032	Xanthone	231.0216	$C_{13}H_8O_2$	HMDB0259922	↓	↑
29	5.7191	DG(i-12:0/0:0/20:4(6E,8Z,11Z,13E)-2OH(5S,15S))	637.4325	$C_{35}H_{60}O_7$	HMDB0298456	↓	↑
30	5.7591	10-HDoHE	343.2280	$C_{22}H_{32}O_3$	HMDB0060037	↓	↑

31	5.7989	2-Hydroxy-6-pentadecylbenzoic acid	347.2593	$C_{22}H_{36}O_3$	HMDB0029683	↓	↑
32	5.9268	Fenofibric acid	317.0587	$C_{17}H_{15}ClO_4$	HMDB0015173	↓	↑
33	6.9909	PC(22:2(13Z,16Z)/16:0)	858.5959	$C_{46}H_{88}NO_8P$	HMDB0008593	↑	↑

↑: The levels of metabolites were significantly upregulated; ↓: The levels of metabolites were significantly downregulated.

Supplementary Table 2 Differential metabolites in rat liver

NO.	t_R /min	Metabolite	M/Z	Formula	HMDB ID	MOD vs CON	FZD vs MOD
ESI⁺							
1	0.7380	4-Guanidinobutanoic acid	146.0924	$C_5H_{11}N_3O_2$	HMDB0003464	↓	↑
2	0.7457	Glutaminylvaline	263.1712	$C_{10}H_{19}N_3O_4$	HMDB0028810	↓	↑
3	0.9381	Ophthalmic Acid	290.1345	$C_{11}H_{19}N_3O_6$	HMDB0005765	↑	↑
4	1.8180	Asn Ile	246.1447	$C_{10}H_{19}N_3O_4$	-	↑	↑
5	2.0562	Trigonelline	138.0549	$C_7H_7NO_2$	HMDB0000875	↓	↑

6	3.3647	7-imidazo[1,2-a]pyridin-6-Ylisoquinolin-1-Amine	278.1419	$C_{16}H_{12}N_4$	-	↑	↓
7	3.4806	L-Prolinamide, 5-oxo-L-prolyl-L-norvalyl-	671.3430	$C_{15}H_{24}N_4O_4$	HMDB0253911	↑	↓
8	4.5733	Alanine lactate	195.0991	$C_6H_{11}NO_5$	HMDB0248104	↓	↓
9	6.3851	DG(20:2(11Z,14Z)/18:4(6Z,9Z,12Z,15Z)/0:0)	641.5111	$C_{41}H_{68}O_5$	HMDB0007425	↑	↑
10	6.5019	DG(PGE1/0:0/i-18:0)	659.5216	$C_{41}H_{74}O_8$	HMDB0299742	↑	↑
11	6.6650	1-Naphthylamine	144.0807	$C_{10}H_9N$	HMDB0243964	↑	↑
12	6.7893	Serotonin	159.0916	$C_{10}H_{12}N_2O$	HMDB0000259	↑	↑
13	7.1549	LysoPE(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	500.2748	$C_{25}H_{42}NO_7P$	HMDB0011519	↓	↓
14	7.9771	(2-Hydroxy-3-phosphonooxypropyl) octadec-9-enoate	478.2928	$C_{21}H_{41}O_7P$	HMDB0242470	↓	↓
ESI-							
15	0.9643	Prolyl-Gamma-glutamate	288.1204	$C_{10}H_{17}N_3O_4$	HMDB0029031	↑	↑
16	1.4996	Inosine pyruvate	319.0672	$C_{13}H_{14}N_4O_7$	HMDB0253490	↑	↑
17	1.6593	Leonurine	292.1307	$C_{14}H_{21}N_3O_5$	HMDB0254014	↑	↑
18	1.6593	Cycloheximide	302.1360	$C_{15}H_{23}NO_4$	HMDB0250657	↑	↑
19	2.1561	Asparaginyl-Leucine	244.13030	$C_{10}H_{19}N_3O_4$	HMDB0028735	↑	↑
20	2.6679	DL-Alanyl-DL-leucine	201.1241	$C_9H_{18}N_2O_3$	HMDB0251509	↑	↑

21	2.6999	Leucyl-Tyrosine	293.1510	$C_{15}H_{22}N_2O_4$	HMDB0028941	↑	↑
22	2.7319	1-Octanesulfonic acid	387.1890	$C_8H_{18}O_3S$	HMDB0243978	↑	↑
23	2.9239	Austalide G	517.2420	$C_{28}H_{38}O_9$	HMDB0030154	↑	↑
24	3.9000	Dialdehyde	389.1471	$C_{21}H_{24}N_2O_4$	HMDB0251125	↑	↑
25	5.4041	Rubiadin	253.0507	$C_{15}H_{10}O_4$	HMDB0257354	↓	↑

↑: The levels of metabolites were significantly upregulated; ↓: The levels of metabolites were significantly downregulated.

Supplementary Table 3 Differential metabolites in rat urine.

NO.	t_R /min	Metabolite	M/Z	Formula	HMDB ID	MOD vs CON	FZD vs MOD
ESI⁺							
1	0.3565	Alcophosphamide	261.0302	$C_7H_{17}Cl_2N_2O_3P$	HMDB0060432	↓	↑
2	0.4112	1-Methylhistidine	170.0923	$C_7H_{11}N_3O_2$	HMDB0000001	↑	↓
3	0.4269	Agmatine	131.1291	$C_5H_{14}N_4$	HMDB0001432	↓	↑
4	0.4731	Homarine	176.0106	$C_7H_7NO_2$	HMDB0253198	↓	↑
5	0.4731	L-Targinine	211.1163	$C_7H_{16}N_4O_2$	HMDB0029416	↓	↑
6	0.5107	Proline betaine	144.1018	$C_7H_{13}NO_2$	HMDB0004827	↑	↑

7	0.5644	Argininic acid	176.1028	$C_6H_{13}N_3O_3$	HMDB0003148	↓	↑
8	0.5950	Statine	158.1174	$C_8H_{17}NO_3$	HMDB0258487	↓	↑
9	0.6025	Pindolol	271.1397	$C_{14}H_{20}N_2O_2$	HMDB0015095	↓	↑
10	0.6025	Citrulline	158.0922	$C_6H_{13}N_3O_3$	HMDB0000904	↓	↑
11	0.6873	P-Aminobenzoic acid	138.0548	$C_7H_7NO_2$	HMDB0004992	↓	↑
12	0.8032	4-Guanidinobutanoic acid	146.0922	$C_5H_{11}N_3O_2$	HMDB0031842	↓	↑
13	1.0212	D-Citrulline	158.0923	$C_6H_{13}N_3O_3$	HMDB0250742	↓	↑
14	1.0833	N-Acetyl-L-glutamate 5-semialdehyde	138.0548	$C_7H_{11}NO_4$	HMDB0006488	↓	↑
15	1.1145	5'-O-beta-D-glucosylpyridoxine	332.1336	$C_{14}H_{21}NO_8$	HMDB0246884	↓	↑
16	1.1457	Gamma-glutamyl-beta-aminopropiononitrile	200.1028	$C_8H_{13}N_3O_3$	HMDB0060477	↓	↑
17	1.3717	4-Amino-1-[(2R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-methylpyrimidin-2-one	290.1341	$C_{10}H_{15}N_3O_5$	HMDB0257731	↓	↑
18	1.3951	Anabasine	163.1228	$C_{10}H_{14}N_2$	HMDB0004350	↓	↑
19	1.4105	2-(3-Carboxy-3-aminopropyl)-L-histidine	289.1501	$C_{10}H_{16}N_4O_4$	HMDB0011655	↓	↑
20	1.4183	Lysinoalanine	198.1235	$C_9H_{19}N_3O_4$	HMDB0029447	↑	↓
21	1.4418	Threoninyl-gamma-glutamate	230.1134	$C_9H_{17}N_3O_5$	HMDB0029075	↓	↑

22	1.4496	Ethinamate	150.0912	$C_9H_{13}NO_2$	HMDB0015165	↓	↑
23	1.7147	2,4-dichloro-N-(2-phenylimidazo[1,2-a]pyridin-3-yl)benzamide	382.0531	$C_{20}H_{13}Cl_2N_3O$	-	↓	↓
24	1.7773	Solerol	188.0916	$C_6H_{10}O_4$	HMDB0002173	↑	↓
25	1.7773	N-Acetyl-DL-homocysteine	178.0531	$C_6H_{11}NO_3S$	HMDB0255054	↑	↓
26	1.8008	4-Amino-1-[5-(hydroxymethyl)oxolan-2-yl]pyrimidin-2-one	253.1291	$C_9H_{13}N_3O_3$	HMDB0255802	↓	↑
27	2.0731	Lycopsamine	264.1591	$C_{15}H_{25}NO_5$	HMDB0301846	↓	↑
28	2.1196	1,4'-Bipiperidine-1'-carboxylic acid	235.1438	$C_{11}H_{20}N_2O_2$	HMDB0060336	↓	↑
29	2.2350	Valeric acid	144.1018	$C_5H_{10}O_2$	HMDB0000892	↑	↑
30	2.2811	Hymenoxon	300.1802	$C_{15}H_{22}O_5$	HMDB0253305	↑	↑
31	2.3276	N(2)-phenylacetyl-L-glutaminate	282.1443	$C_{13}H_{16}N_2O_4$	HMDB0062645	↓	↑
32	2.3354	Hydroxy-lacosamide	283.1285	$C_{13}H_{18}N_2O_5$	HMDB0061146	↓	↑
33	2.4284	Lysylproline	285.1917	$C_{11}H_{21}N_3O_3$	HMDB0028959	↓	↑
34	2.5137	3-(1-Hydroxymethyl-1-propenyl)pentanedioic acid	185.0807	$C_9H_{14}O_5$	HMDB0033092	↓	↑
35	2.5137	Fasoracetam	197.1282	$C_{10}H_{16}N_2O_2$	HMDB0252174	↓	↑
36	2.5293	N-Arachidonoyl glycine	358.1129	$C_{15}H_{19}NO_9$	HMDB0241918	↓	↑

37	2.6369	Vicine	287.0997	$C_{10}H_{16}N_4O_7$	HMDB0034073	↑	↓
38	2.6757	Epinephrine glucuronide	324.1073	$C_{15}H_{21}NO_9$	HMDB0010336	↑	↓
39	2.6757	2-Naphthylamine	144.0806	$C_{10}H_9N$	HMDB0041802	↓	↑
40	2.6835	L-1,2,3,4-Tetrahydro-beta-carboline-3-carboxylic acid	217.0970	$C_{12}H_{12}N_2O_2$	HMDB0035665	↓	↑
41	2.7609	2-Guanidinobutanoic acid	146.0922	$C_5H_{11}N_3O_2$	HMDB0245137	↓	↑
42	2.8076	Cytosine deoxyribonucleoside	455.1863	$C_9H_{13}N_3O_4$	HMDB0000014	↑	↑
43	2.8154	N-Benzyl-D-glucamine	335.1599	$C_{13}H_{21}NO_5$	HMDB0255091	↑	↑
44	2.8775	DL-O-tyrosine	182.0811	$C_9H_{11}NO_3$	HMDB0006050	↓	↑
45	2.8775	Aspartyl-tryptophan	284.1058	$C_{15}H_{17}N_3O_5$	HMDB0028764	↓	↑
46	2.9778	1,2-Naphthoquinone	159.0439	$C_{10}H_6O_2$	HMDB0244101	↓	↑
47	2.9854	Ephedrine	148.1119	$C_{10}H_{15}NO$	HMDB0015451	↓	↑
48	2.9931	Metyrosine	237.1230	$C_{10}H_{13}NO_3$	HMDB0247174	↓	↑
49	3.0088	Leucylleucine	245.1858	$C_{12}H_{24}N_2O_3$	HMDB0028933	↑	↓
50	3.1177	Cinnamaldehyde	133.0647	C_9H_8O	HMDB0245299	↑	↑
51	3.1410	(+)-Abscisic acid	265.1431	$C_{15}H_{20}O_4$	HMDB0035140	↓	↑
52	3.1721	Glutamyltryptophan	298.1214	$C_{16}H_{19}N_3O_5$	HMDB0028830	↓	↑
53	3.1955	Daidzein 4'-O-glucuronide	431.0968	$C_{21}H_{18}O_{10}$	HMDB0041717	↓	↑

54	3.1955	Daidzein	255.0648	$C_{15}H_{10}O_4$	HMDB0003312	↓	↑
55	3.2651	N-Acetyl-1-aspartylglutamic acid	322.1216	$C_{11}H_{16}N_2O_8$	HMDB0001067	↑	↓
56	3.3272	4-Hydroxybenzoic acid	121.0285	$C_7H_6O_3$	HMDB0000500	↓	↑
57	3.3272	Parthenin	263.1275	$C_{15}H_{18}O_4$	HMDB0253304	↑	↑
58	3.3816	P-Cresol glucuronide	302.1230	$C_{13}H_{16}O_7$	HMDB0011686	↑	↓
59	3.3816	2,4'-Dihydroxyacetophenone	322.1313	$C_8H_8O_3$	HMDB0029657	↑	↓
60	3.3972	Coumarin	147.0439	$C_9H_6O_2$	HMDB0001218	↓	↑
61	3.4050	3-Coumaric acid	165.0545	$C_9H_8O_3$	HMDB0001713	↓	↑
62	3.4206	Homocitrulline	379.2334	$C_7H_{15}N_3O_3$	HMDB0000679	↑	↓
63	3.4284	Hydroxyphenylacetylglycine	210.0759	$C_{10}H_{11}NO_4$	HMDB0000735	↓	↑
64	3.5607	Patulin	137.0232	$C_7H_6O_4$	HMDB0034299	↓	↑
65	3.6075	Carboxyibuprofen	219.1014	$C_{13}H_{16}O_4$	HMDB0060564	↓	↑
66	3.6309	Brassicanal A	178.0319	C_9H_7NOS	HMDB0038591	↓	↓
67	3.6309	Tyrosyl-Cysteine	307.0744	$C_{12}H_{16}N_2O_4S$	HMDB0029102	↓	↓
68	3.7555	Pinocembrin	257.0805	$C_{15}H_{12}O_4$	HMDB0030808	↓	↑
69	3.7555	Americanin B	493.1450	$C_{27}H_{24}O_9$	HMDB0037338	↓	↑
70	3.8334	D-Cathine	134.0963	$C_9H_{13}NO$	-	↓	↑

71	3.9267	Quinoline-4,8-diol	340.1320	$C_9H_7NO_2$	HMDB0060289	↑	↓
72	4.0358	Imidazolepropionic acid	158.0923	$C_6H_8N_2O_2$	HMDB0002271	↓	↑
73	4.0513	Chrysophanol	255.0652	$C_{15}H_{10}O_4$	HMDB0030670	↓	↑
74	4.0513	(S)-Pterosin P	252.1592	$C_{14}H_{18}O_3$	HMDB0036607	↓	↑
75	4.0669	Sulfobutyl ether	335.0216	$C_8H_{18}O_7S_2$	HMDB0258592	↓	↑
76	4.1759	(2S,3S,4S,5R)-6-[4-(5,7-Dihydroxy-4-oxo-2,3-dihydrochromen-2-yl)phenoxy]-3,4,5-trihydroxyoxane-2-carboxylic acid	449.1074	$C_{21}H_{20}O_{11}$	HMDB0257722	↓	↑
77	4.2228	Glycitein 4'-O-glucuronide	461.1073	$C_{22}H_{20}O_{11}$	HMDB0041740	↓	↑
78	4.2306	Prolyl-asparagine	271.1399	$C_9H_{15}N_3O_4$	HMDB0029012	↓	↑
79	4.4410	Hernandulcin	281.1490	$C_{15}H_{24}O_2$	HMDB0037906	↓	↑
80	4.4801	Dihydro-3-hydroxy-4,4-dimethyl-2(3H)-Furanone	278.1599	$C_6H_{10}O_3$	-	↓	↑
81	4.4957	Jubanine B	762.3870	$C_{43}H_{47}N_5O_6$	HMDB0030206	↑	↓
82	4.7296	Tetraxetan	422.2278	$C_{16}H_{28}N_4O_8$	HMDB0251592	↑	↓
83	4.8389	(R)-Oxypeucedanin	319.1178	$C_{16}H_{14}O_5$	HMDB0030622	↓	↑
84	4.9171	Stercobilin	595.3482	$C_{33}H_{46}N_4O_6$	HMDB0240259	↑	↓
85	4.9171	Isoliquiritigenin	257.0805	$C_{15}H_{12}O_4$	HMDB0037316	↓	↑

86	5.3226	Heliangin	345.1663	$C_{20}H_{26}O_6$	HMDB0036692	↓	↑
87	5.5255	Zeranol	345.1663	$C_{18}H_{26}O_5$	HMDB0041824	↓	↓
88	5.5568	5,6-Dihydroxyprostaglandin F1a	411.2349	$C_{20}H_{36}O_7$	HMDB0012109	↓	↑
89	5.5881	6-[2-(4-Carboxybut-2-en-1-yl)-3,5-dihydroxycyclopentyl]-4-oxohexanoate	311.1463	$C_{16}H_{24}O_7$	HMDB0256370	↓	↑
90	5.7433	Pregnan-20-one, 17-(acetyloxy)-3-hydroxy-6-methyl-, (3b,5b,6a)-	413.2656	$C_{24}H_{38}O_4$	-	↑	↓
91	7.1155	2,8-bis-Trifluoromethyl-4-quinoline carboxylic acid	292.0164	$C_{12}H_5F_6NO_2$	HMDB0060726	↓	↑
ESI-							
92	0.4813	D-Erythroascorbic acid 1'-a-D-xylopyranoside	315.0143	$C_{10}H_{14}O_9$	HMDB0033626	↑	↓
93	0.4892	Dl-Tartaric acid	149.0083	$C_4H_6O_6$	-	↑	↑
94	0.5210	Gluconolactone	223.0454	$C_6H_{10}O_6$	HMDB0000150	↓	↑
95	0.6001	Glycineamideribotide	285.0493	$C_7H_{15}N_2O_8P$	HMDB0002022	↑	↓
96	0.8920	Alpha-D-glucuronate 1-phosphate	540.961	$C_6H_8O_{10}P_{-3}$	HMDB0304535	↑	↑
97	1.0031	Thiobencarb	292.0360	$C_{12}H_{16}ClNOS$	HMDB0248966	↓	↑
98	1.0031	Glucosamine 6-phosphate	258.0385	$C_6H_{14}NO_8P$	HMDB0001254	↑	↓
99	1.3684	(4-Hydroxybenzoyl)choline	269.1257	$C_{12}H_{18}NO_3$	HMDB0029559	↓	↑

100	1.8392	Pyrogallol-2-O-glucuronide	301.0567	$C_{12}H_{14}O_9$	HMDB0060017	↓	↑
101	2.0698	2-Methyl-5-(methylthio)furan	301.0566	C_6H_8OS	HMDB0041566	↓	↑
102	2.0698	3,4-Dihydroxymandelic acid	183.0292	$C_8H_8O_5$	HMDB0001866	↓	↑
103	2.0777	1,3-Diethyl-6-hydroxy-2-sulfanylidenepyrimidin-4-one	245.0601	$C_8H_{12}N_2O_2S$	HMDB0246707	↓	↑
104	2.0856	D-Tartaric Acid	149.0082	$C_4H_6O_6$	HMDB0029878	↑	↑
105	2.1015	L-2,3-Dihydrodipicolinate	168.0294	$C_7H_7NO_4$	HMDB0012247	↓	↑
106	2.1335	Protocatechuic acid 3-O-sulfate	232.9760	$C_7H_6O_7S$	HMDB0124993	↓	↑
107	2.1335	4-Hydroxybenzoyl glucose	345.0829	$C_{13}H_{16}O_8$	HMDB0303022	↓	↑
108	2.1655	Pyrocatechol sulfate	188.9857	$C_6H_6O_5S$	HMDB0059724	↓	↑
109	2.1655	Osmundalactone	109.0284	$C_6H_8O_3$	HMDB0031303	↓	↑
110	2.2131	Vinclozolin M2	304.0134	$C_{11}H_{11}Cl_2NO_2$	HMDB0259812	↓	↑
111	2.2848	Sumiki's acid	329.0517	$C_6H_6O_4$	HMDB0002432	↓	↑
112	2.2848	10,11-Dihydroxycarbamazepine	307.0495	$C_{15}H_{14}N_2O_3$	HMDB0060568	↓	↑
113	2.3166	Chakanoside I	343.1036	$C_{14}H_{18}O_7$	HMDB0302044	↓	↑
114	2.3485	Benzoyl glucuronide (Benzoic acid)	343.0674	$C_{13}H_{14}O_8$	HMDB0010324	↓	↑
115	2.4123	4-Hydroxyphenylacetic acid sulfate	277.0024	$C_8H_8O_6S$	HMDB0304906	↓	↑

116	2.4123	Syringic acid	197.0450	$C_9H_{10}O_5$	HMDB0002085	↓	↑
117	2.4680	8-Hydroxythioguanine	203.9968	$C_5H_5N_5OS$	HMDB0060804	↓	↑
118	2.4760	3-dehydroshikimate	152.0106	$C_7H_7O_5$	HMDB0304122	↓	↑
119	2.4838	4-methoxy-3-(sulfooxy)benzoic acid	246.9917	$C_8H_8O_7S$	HMDB0140929	↓	↑
120	2.4918	3,4-Dihydroxyphenylacetic acid	167.0341	$C_8H_8O_4$	HMDB0001336	↓	↑
121	2.5549	Mycophenolic acid O-acyl-glucuronide	495.1512	$C_{23}H_{28}O_{12}$	HMDB0060491	↑	↑
122	2.6025	Cis,cis-Muconic acid	343.0673	$C_6H_6O_4$	HMDB0006331	↓	↑
123	2.6817	2-Phenylethanol glucuronide	343.1036	$C_{14}H_{18}O_7$	HMDB0010350	↓	↑
124	2.7611	1-O-Feruloyl-beta-D-glucose	401.1090	$C_{16}H_{20}O_9$	HMDB0301952	↓	↑
125	2.7929	Vanillylmandelic acid	197.0449	$C_9H_{10}O_5$	HMDB0304531	↓	↑
126	2.8483	Citrazinic acid	154.0137	$C_6H_5NO_4$	-	↓	↑
127	2.8720	Homovanillic acid sulfate	261.0075	$C_9H_{10}O_7S$	HMDB0011719	↓	↑
128	2.8799	Cefcapene	498.0714	$C_{17}H_{19}N_5O_6S_2$	HMDB0249757	↓	↑
129	2.9354	1-(3-Methyl-2-butenoyl)-6-apiosylglucose	415.1226	$C_{16}H_{26}O_{11}$	HMDB0039952	↓	↑
130	2.9512	4-Methylbenzoic acid	135.0441	$C_8H_8O_2$	HMDB0029635	↓	↑
131	2.9672	5-Dihydroxyhept-6-enoic acid	205.0714	$C_7H_{12}O_4$	HMDB0246781	↓	↑
132	3.0068	Carbamazepine-O-quinone	303.0180	$C_{15}H_{10}N_2O_3$	HMDB0060566	↓	↑

133	3.0068	Gentisic acid	153.0184	$C_7H_6O_4$	HMDB0059999	↓	↑
134	3.0544	2H-1-Benzopyran-2-one, 7-(sulfooxy)-	240.9811	$C_9H_6O_6S$	HMDB0242135	↓	↑
135	3.0703	4-Vinylphenol	119.0491	C_8H_8O	HMDB0004072	↓	↑
136	3.0703	2-Hydroxycinnamic acid	163.0393	$C_9H_8O_3$	HMDB0002641	↓	↑
137	3.0783	P-Coumaric acid sulfate	242.9968	$C_9H_8O_6S$	HMDB0125166	↓	↑
138	3.0783	Indole-3-acetyl-methionine	340.0674	$C_{15}H_{17}N_2O_3S$-	HMDB0304384	↓	↓
139	3.0783	5-Caffeoylquinic acid	399.0931	$C_{16}H_{18}O_9$	HMDB0240477	↓	↑
140	3.1177	Cyclo-dopa 5-O-glucoside	356.0988	$C_{15}H_{19}NO_9$	HMDB0304310	↓	↑
141	3.1408	Ferulic acid 4-O-sulfate	273.0076	$C_{10}H_{10}O_7S$	HMDB0029200	↓	↑
142	3.1408	Methyl 2-hydroxybenzoate	133.0284	$C_8H_8O_3$	HMDB0034172	↓	↑
143	3.1566	Bms-378806	443.1131	$C_{22}H_{22}N_4O_4$	HMDB0249317	↑	↓
144	3.1641	Caffeoyl C1-glucuronide	355.0673	$C_{15}H_{16}O_{10}$	HMDB0041709	↓	↑
145	3.1717	8-Hydroxyquinoline-5-sulfonic acid	270.0079	$C_9H_7NO_4S$	HMDB0247444	↓	↓
146	3.1797	Hippuric acid sulfate	239.9971	$C_9H_9NO_6S$	HMDB0304910	↓	↓
147	3.1876	4-Hydroxy-3-(2-hydroxyethyl)acetophenone 4-glucoside	323.1168	$C_{16}H_{22}O_8$	HMDB0037552	↓	↑
148	3.2268	Paeoniflorin	515.1308	$C_{23}H_{28}O_{11}$	HMDB0256075	↓	↓

149	3.2348	Cimoxatone	375.0757	$C_{19}H_{18}N_2O_4$	HMDB0250256	↓	↑
150	3.3062	[(2S,3S,4S,5S,6R)-4,5-Dihydroxy-2,6-dimethyloxan-3-yl] hydrogen sulfate	263.0231	$C_7H_{14}O_7S$	HMDB0252508	↓	↑
151	3.3300	Oxazepam	331.0495	$C_{15}H_{11}ClN_2O_2$	HMDB0014980	↓	↑
152	3.3931	5-(3-Pyridyl)-2-hydroxytetrahydrofuran	210.0768	$C_9H_{11}NO_2$	HMDB0062407	↓	↑
153	3.4011	5-(2-Chloroethyl)-2'-deoxyuridine	271.0473	$C_{11}H_{15}ClN_2O_5$	HMDB0246718	↑	↑
154	3.4011	Caffeic acid 4-O-glucuronide	355.0674	$C_{15}H_{16}O_{10}$	HMDB0041707	↓	↑
155	3.4249	Protocatechuic acid	153.0184	$C_7H_6O_4$	HMDB0001856	↓	↑
156	3.4722	Dantrolene	313.0567	$C_{14}H_{10}N_4O_5$	HMDB0015350	↓	↑
157	3.4961	D-Erythroascorbic acid 1'-a-D-glucoside	675.1681	$C_{11}H_{16}O_{10}$	HMDB0033627	↓	↓
158	3.5038	Ethyl 2-furanacrylate	211.0608	$C_9H_{10}O_3$	HMDB0041611	↓	↑
159	3.5196	Mascaroside	561.1761	$C_{26}H_{36}O_{11}$	HMDB0035603	↓	↓
160	3.5591	Dihydroferulic acid 4-O-sulfate	275.0232	$C_{10}H_{12}O_7S$	HMDB0041724	↓	↑
161	3.6221	Terephthalic acid	165.0185	$C_8H_6O_4$	HMDB0002428	↓	↑
162	3.6299	2-Hydroxycarbamazepine	289.0389	$C_{15}H_{12}N_2O_2$	HMDB0060651	↓	↑
163	3.6537	4-(4-Hydroxyphenyl)-2-butanone glucoside	371.1340	$C_{16}H_{22}O_7$	HMDB0034863	↓	↑
164	3.7090	3-Indole carboxylic acid glucuronide	336.0727	$C_{15}H_{15}NO_8$	HMDB0013189	↓	↓

165	3.7566	7,4'-Dihydroxyflavone	253.0506	$C_{15}H_{10}O_4$	HMDB0247290	↓	↑
166	3.7566	Chrysin-7-O-glucuronide	429.0828	$C_{21}H_{18}O_{10}$	-	↓	↑
167	3.7801	CMPF	239.0923	$C_{12}H_{16}O_5$	HMDB0061112	↓	↑
168	3.8118	Propofol glucuronide	399.1662	$C_{18}H_{26}O_7$	HMDB0060933	↓	↑
169	3.8593	Salicyluric acid	194.0453	$C_9H_9NO_4$	HMDB0000840	↓	↑
170	3.8751	2-Polyprenyl-6-methoxy-1,4-benzoquinone	295.1298	$C_{17}H_{22}O_3$	HMDB0060354	↓	↑
171	3.8831	17-Beta-estradiol 3-sulfate-17-(beta-D-glucuronide)	263.0778	$C_{24}H_{32}O_{11}S$	HMDB0010358	↑	↓
172	3.9228	Methyl (Z)-5-(1-propynyl)-2-thienylacrylate	471.0967	$C_{11}H_{10}O_2S$	HMDB0034858	↑	↓
173	4.0651	Diacetone alcohol	115.0753	$C_6H_{12}O_2$	HMDB0031511	↓	↑
174	4.1286	M-Coumaric acid	163.0393	$C_9H_8O_3$	HMDB0001713	↓	↑
175	4.1603	Dihydrodeoxy-8-epiaustdiol	267.0875	$C_{12}H_{14}O_4$	HMDB0031668	↑	↓
176	4.1920	Imazamethabenz-methyl	325.0938	$C_{16}H_{20}N_2O_3$	HMDB0034913	↓	↑
177	4.2237	Methotrexate	489.1405	$C_{20}H_{22}N_8O_5$	HMDB0014703	↓	↑
178	4.2317	3-Hydroxycarbamazepine	289.0389	$C_{15}H_{12}N_2O_2$	HMDB0060653	↓	↑
179	4.2395	Acuminoside	429.2131	$C_{21}H_{36}O_{10}$	HMDB0029347	↑	↑
180	4.3189	Abacavir	307.1303	$C_{14}H_{18}N_6O$	HMDB0015182	↓	↑
181	4.3189	Indole-3-propionic acid	234.0770	$C_{11}H_{11}NO_2$	HMDB0002302	↓	↑

182	4.4062	Garbanzol	253.0505	$C_{15}H_{12}O_5$	HMDB0037254	↓	↑
183	4.4141	3-Hydroxyoctanoic acid	205.1076	$C_8H_{16}O_3$	HMDB0001954	↓	↑
184	4.4537	6-Thioinosine-5'-monophosphate	363.0182	$C_{10}H_{13}N_4O_7PS$	HMDB0060416	↓	↑
185	4.4777	Phenylethyl primeveroside	415.1613	$C_{19}H_{28}O_{10}$	HMDB0041274	↓	↑
186	4.4856	1-[[4-(Dimethylamino)-3-methylphenyl]methyl]-5-(2,2-diphenylacetyl)-6,7-dihydro-4H-imidazo[4,5-c]pyridine-6-carboxylic acid	489.2280	$C_{31}H_{32}N_4O_3$	HMDB0243806	↑	↓
187	4.5173	2-Anthraquinonesulfonic acid	333.0077	$C_{14}H_8O_5S$	HMDB0245031	↓	↑
188	4.6202	Naringenin-7-O-beta-D-glucuronide	447.0936	$C_{21}H_{20}O_{11}$	-	↓	↑
189	4.6282	Isovaleraldehyde glyceryl acetal	205.1077	$C_8H_{16}O_3$	HMDB0303245	↓	↑
190	4.6362	Prostaglandin C1	381.2284	$C_{20}H_{32}O_4$	HMDB0060104	↑	↓
191	4.6362	Ifetroban	477.1769	$C_{25}H_{32}N_2O_5$	HMDB0247885	↓	↑
192	4.6521	Wogonoside	459.0936	$C_{22}H_{20}O_{11}$	HMDB0259901	↓	↑
193	4.6916	Musabalbisiane A	477.1450	$C_{23}H_{28}O_{12}$	HMDB0038680	↑	↓
194	4.7470	Naringenin 4'-O-glucuronide	447.0936	$C_{21}H_{20}O_{11}$	HMDB0041759	↓	↑
195	4.7629	Combretastatin A4	315.1241	$C_{18}H_{20}O_5$	HMDB0253622	↑	↑
196	4.8104	Fluticasone 17beta-carboxylic acid	441.1768	$C_{21}H_{26}F_2O_5$	HMDB0061092	↑	↑

197	4.8104	L-Linalool 3-[xylosyl-(1->6)-glucoside]	429.213	$C_{21}H_{36}O_{10}$	HMDB0030421	↑	↑
198	4.8896	4R,5R,6S-Trihydroxy-2-hydroxymethyl-2-cyclohexen-1-one 6-(2-hydroxy-6-methylbenzoate)	353.088	$C_{15}H_{16}O_7$	HMDB0040692	↑	↑
199	4.9212	Nivalenol	311.1142	$C_{15}H_{20}O_7$	HMDB0004304	↑	↑
200	4.9292	Alpha-Hydroxytamoxifen	422.1856	$C_{26}H_{29}NO_2$	HMDB0060585	↓	↑
201	4.9451	3alpha-Hydroxyoreadone	297.1343	$C_{14}H_{20}O_4$	HMDB0036047	↑	↑
202	4.9609	Melleolide B	469.1659	$C_{24}H_{32}O_7$	HMDB0038787	↓	↑
203	4.9766	(-)-Wikstromol	419.1358	$C_{20}H_{22}O_7$	HMDB0030598	↓	↑
204	4.9925	Phenylpyruvic acid	163.0392	$C_9H_8O_3$	HMDB0304081	↓	↑
205	5.1509	Secologanin	369.1193	$C_{17}H_{24}O_{10}$	HMDB0304482	↓	↑
206	5.1589	3-O-alpha-D-Glucopyranuronosyl-D-xylose	371.0814	$C_{11}H_{18}O_{11}$	HMDB0039723	↓	↑
207	5.2146	Tavulin	263.1290	$C_{15}H_{20}O_4$	HMDB0036773	↓	↑
208	5.3574	Liquiritin rhamnoside	255.0663	$C_{15}H_{12}O_4$	HMDB0303602	↓	↑
209	5.3654	N-Acetylmuramate	631.2247	$C_{11}H_{19}NO_8$	HMDB0060493	↓	↑
210	5.3654	Anisatin	327.1087	$C_{15}H_{20}O_8$	HMDB0302686	↓	↑
211	5.3891	Benazeprilat	433.1147	$C_{22}H_{24}N_2O_5$	HMDB0060582	↓	↑
212	5.4445	2-(4-Methoxyphenyl)ethyl hydrogen sulfate	231.0330	$C_9H_{12}O_5S$	HMDB0304915	↓	↑

213	5.4525	2-Hydroxynevirapine	327.1086	$C_{15}H_{14}N_4O_2$	HMDB0013912	↓	↑
214	5.4921	11b-Hydroxyprogesterone	377.1968	$C_{20}H_{28}O_4$	HMDB0004031	↑	↓
215	5.5078	Melledonal A	413.1648	$C_{23}H_{28}O_8$	HMDB0035865	↑	↓
216	5.5394	Hexahydrophthalic anhydride	353.1245	$C_8H_{10}O_3$	HMDB0253140	↓	↑
217	5.9191	2-Methoxyhydroquinone sulfate	218.9965	$C_7H_8O_6S$	HMDB0304923	↓	↑
218	6.0935	(1R,6R)-6-Hydroxy-2-succinylcyclohexa-2,4-diene-1-carboxylate	285.0618	$C_{11}H_{12}O_6$	HMDB0303951	↓	↑
219	6.9954	(-)-Naringenin	253.0507	$C_{15}H_{12}O_5$	HMDB0002670	↓	↑
220	7.6736	2-Methylhippuric acid	385.1405	$C_{10}H_{11}NO_3$	HMDB0011723	↑	↓
221	7.7932	Alginic acid	379.0915	$C_{14}H_{22}O_{13}$	HMDB0029940	↓	↑

↑: The levels of metabolites were significantly upregulated; ↓: The levels of metabolites were significantly downregulated.