Isobavachalcone ameliorates cognitive deficits, Aβ and tau pathologies in triple-transgenic mice of Alzheimer's disease

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Table S1. Summary of the 176 differential metabolites.

Index	Compounds	VIP	p_value	Fold_Change	Log2FC	Type
MEDN010	L-Citrulline	1.2430	0.0304	0.7830	-0.3528	Down
MEDN018	L-Serine	1.3809	0.0181	0.6899	-0.5355	down
MEDN030	5-Hydroxy-L-Tryptophan	1.1118	0.0489	0.7621	-0.3920	down
MEDN061	N-Phenylacetylglycine	1.5973	0.0004	0.2966	-1.7534	down
MEDN068	S-(5-Adenosy)-L-Homocysteine	1.2060	0.0400	0.7135	-0.4871	down
MEDN092	3,4-Dihydroxybenzeneacetic Acid	1.7485	0.0041	0.4429	-1.1748	down
MEDN097	P–Hydroxyphenyl Acetic Acid	1.2529	0.0469	0.6564	-0.6074	down
MEDN105	Taurocholic Acid	1.3291	0.0151	0.2811	-1.8310	down
MEDN112	Glycocholic Acid	1.4557	0.0037	0.1013	-3.3034	down
MEDN120	Dulcitol	1.3069	0.0111	1.4373	0.5234	up

MEDN153	Adenosine 5'-Monophosphate	1.4268	0.0006	0.5274	-0.9230	down
MEDN159	Flavin Adenine Dinucleotide	1.6266	0.0014	0.6023	-0.7315	down
MEDN165	Inosine 5'-Monophosphate	1.3115	0.0017	0.5303	-0.9151	down
MEDN200	L-Malic Acid	1.3956	0.0038	0.5572	-0.8438	down
MEDN201	Succinic Acid	1.7027	0.0222	0.3658	-1.4510	down
MEDN213	D-Sorbitol	1.3329	0.0082	1.4585	0.5445	up
MEDN240	L-Gulonic-Γ-Lactone	1.3444	0.0265	0.6907	-0.5338	down
MEDN285	2-Methylsuccinic Acid	1.3602	0.0467	0.6238	-0.6809	down
MEDN297	4-Hydroxy-2-Oxoglutaric Acid	1.5734	0.0018	0.6046	-0.7259	down
MEDN305	Creatine	1.4376	0.0235	0.6845	-0.5468	down
MEDN314	Glutaric Acid	1.6092	0.0112	0.5825	-0.7797	down
MEDN321	Kinic Acid	1.3270	0.0266	0.8254	-0.2769	down
MEDN325	L-Lactic Acid	1.3256	0.0333	0.7155	-0.4829	down
MEDN334	Mandelic Acid	1.3976	0.0136	0.5939	-0.7518	down
MEDN335	Methylmalonic Acid	1.6837	0.0270	0.3631	-1.4617	down
MEDN336	N'-Formylkynurenine	1.5949	0.0006	0.5261	-0.9265	down
MEDN343	Shikimic Acid	1.5182	0.0045	0.3612	-1.4689	down
MEDN348	TXB2 [9α,11,15S-trihydroxythromba-5Z,13E-dien-1-oic acid]	1.3744	0.0016	0.4138	-1.2730	down
MEDN352	O-Phosphorylethanolamine	1.3378	0.0196	0.6859	-0.5440	down
MEDN375	13-HOTrE [13S-hydroxy-9Z,11E,15Z-octadecatrienoic acid]	1.5463	0.0193	1.7439	0.8023	up
MEDN376	9,10-DiHOME [(±)9,10-dihydroxy-12Z-octadecenoic acid]	1.2836	0.0209	1.1277	0.1733	up
MEDN378	γ-Linolenic Acid(C18:3N6)	1.6529	0.0135	3.6309	1.8603	up
MEDN379	Tridecanoic Acid	1.4656	0.0046	1.6518	0.7241	up

MEDN380	Palmitoleic Acid (C16:1)	1.6220	0.0088	3.8642	1.9502	up
MEDN381	Hexadecanoic Acid (C16:0)	1.3382	0.0035	1.7473	0.8051	up
MEDN383	Linoleic Acid (C18:2N6C)	1.4638	0.0011	2.2386	1.1626	up
MEDN385	Dodecanoic Acid(C12:0)	1.5675	0.0122	1.5439	0.6266	up
MEDN388	Elaidic Acid (C18:1N9T)	1.5836	0.0008	2.3655	1.2422	up
MEDN390	EPA [5Z,8Z,11Z,14Z,17Z-eicosapentaenoic acid]	1.1876	0.0472	1.7910	0.8408	up
MEDN391	DHA [4Z,7Z,10Z,13Z,16Z,19Z-docosahexaenoic acid]	1.2911	0.0107	1.8404	0.8801	up
MEDN400	A-Linolenic Acid(C18:3N3)	1.6612	0.0114	3.5885	1.8434	up
MEDN419	Uridine 5-Monophosphate	1.3491	0.0285	0.5821	-0.7808	down
MEDN421	Cyclic Amp	1.3526	0.0163	0.6381	-0.6481	down
MEDN478	Aminomalonic Acid	1.6956	0.0196	0.3753	-1.4138	down
MEDN478	Aminomalonic Acid	1.6956	0.0196	0.3753	-1.4138	down
MEDN491	9-HOTrE [9S-hydroxy-10E,12Z,15Z-octadecatrienoic acid]	1.3183	0.0134	1.1501	0.2018	up
MEDN494	8,15-Dihete	1.6342	0.0034	3.9363	1.9769	up
MEDN496	N-Acetylmethionine	1.6274	0.0017	0.5309	-0.9134	down
MEDN533	Xanthosine	1.2152	0.0393	0.6106	-0.7118	down
MEDN536	estrone 3-sulfate	1.2956	0.0205	0.3955	-1.3381	down
MEDN561	N-Acetylaspartylglutamic acid	1.3143	0.0135	0.6415	-0.6405	down
MEDN568	2-Methylguanosine	1.4427	0.0067	0.7579	-0.3999	down
MEDN579	N-lactoyl-phenylalanine	1.6637	0.0015	0.4114	-1.2815	down
MEDN593	D-(+)-Malic acid	1.3587	0.0099	0.6416	-0.6403	down
MEDN594	m-Coumaric acid	1.0089	0.0458	0.2803	-1.8348	down
MEDN602	deoxyguanosine 5'-monophosphate (dGMP)	1.5722	0.0001	0.4869	-1.0384	down

MEDN622	Porphobilinogen	1.7179	0.0002	1.3935	0.4787	up
MEDN623	Salicyluric acid	1.3666	0.0220	0.4873	-1.0372	down
MEDN632	N-Oleoyl Glycine	1.1519	0.0240	1.5718	0.6524	up
MEDN651	Succinic anhydride	1.2463	0.0340	1.1961	0.2583	up
MEDN673	Isopropyl myristate	1.3504	0.0095	1.3062	0.3854	up
MEDN675	Methylstearate	1.2912	0.0098	1.3884	0.4735	up
MEDN678	Ethylsalicylate	1.6678	0.0003	1.3857	0.4706	up
MEDN719	2-n-Pentylfuran	1.2314	0.0318	0.6763	-0.5642	down
MEDN720	N-(2-Methylbenzoyl)glycine	1.6089	0.0003	0.2936	-1.7683	down
MEDN733	PHENYL-BETA-D-GLUCOPYRANOSIDE	1.3612	0.0029	1.7741	0.8271	up
MEDN736	2-(Methylthio)ethanol	1.3598	0.0062	1.2960	0.3740	up
MEDN748	Methylparaben	1.2594	0.0131	1.2212	0.2884	up
MEDN754	(±)17-HDHA [(±)17-hydroxy-4Z,7Z,10Z,13Z,15E,19Z-docosahexaenoic acid]	1.3841	0.0389	3.1198	1.6414	up
MEDN756	(±)18-HEPE [(±)-18-hydroxy-5Z,8Z,11Z,14Z,16E-eicosapentaenoic acid]	1.3734	0.0482	5.2494	2.3921	up
MEDN768	13-oxoODE [13-oxo-9Z,11E-octadecadienoic acid]	1.1230	0.0406	1.1627	0.2174	up
MEDN769	14(S)-HDHA [14S-hydroxy-4Z,7Z,10Z,12E,16Z,19Z-docosahexaenoic acid]	1.4336	0.0383	5.1804	2.3731	up
MEDN783	9,10-EpOME [(±)9,10-epoxy-12Z-octadecenoic acid]	1.2559	0.0210	1.1450	0.1954	up
MEDN807	Myristic acid	1.4700	0.0479	2.0652	1.0463	up
MEDN809	Taurodeoxycholic acid sodium salt	1.4559	0.0178	0.3244	-1.6242	down
MEDN816	4-Hydroxyhippurate	1.5242	0.0093	0.4309	-1.2146	down
MEDN818	N-acetyl-beta-alanine	1.2093	0.0266	0.7895	-0.3410	down

MEDN824	7-ketodeoxycholic acid	1.5819	0.0099	0.1679	-2.5743	down
MEDP002	D-Homocysteine	1.3262	0.0306	0.7953	-0.3304	down
MEDP009	L-Tyrosine	1.5356	0.0067	0.7009	-0.5127	down
MEDP020	L-Methionine	1.5488	0.0035	0.7693	-0.3784	down
MEDP022	L-Proline	1.5721	0.0027	0.7242	-0.4656	down
MEDP032	3-Hydroxy-3-Methylpentane-1,5-Dioic Acid	1.2711	0.0155	0.9331	-0.0999	down
MEDP039	Betaine	1.7206	0.0003	0.6423	-0.6387	down
MEDP043	Glutathione Oxidized	1.5417	0.0016	0.5197	-0.9444	down
MEDP061	N,N-Dimethylglycine	1.5560	0.0029	0.7816	-0.3555	down
MEDP062	N6-Acetyl-L-Lysine	1.6370	0.0009	0.7490	-0.4170	down
MEDP077	Phenylacetyl-L-Glutamine	1.5478	0.0034	0.2975	-1.7489	down
MEDP081	Serotonin	1.1463	0.0264	1.9870	0.9906	up
MEDP087	L-Alanyl-L-Lysine	1.6521	0.0020	0.4093	-1.2888	down
MEDP101	P-Coumaric Acid	1.5321	0.0063	0.6700	-0.5777	down
MEDP102	Syringic Acid	1.3219	0.0373	0.3853	-1.3760	down
MEDP111	3-(4-Hydroxyphenyl)-Propionic Acid	1.2065	0.0489	0.7666	-0.3835	down
MEDP114	Phthalic Acid	1.4284	0.0076	0.9411	-0.0875	down
MEDP118	4-Pyridoxic Acid	1.4474	0.0171	0.5585	-0.8404	down
MEDP125	Choline	1.3616	0.0147	0.8218	-0.2832	down
MEDP128	Diethanolamine	1.8373	0.0009	0.4849	-1.0442	down
MEDP129	Phenethylamine	1.4611	0.0052	0.9580	-0.0619	down
MEDP152	3'-Aenylic Acid	1.5547	0.0001	0.4629	-1.1111	down
MEDP154	5,6-Dihydro-5-Methyluracil	1.4671	0.0055	0.8277	-0.2728	down
MEDP156	5-Methyluridine	1.4499	0.0331	0.6600	-0.5994	down
MEDP159	Adenine	1.5097	0.0054	0.6775	-0.5617	down
MEDP160	Adenosine	1.5343	0.0004	0.6036	-0.7284	down

MEDP165	Cytosine	1.3189	0.0353	0.8402	-0.2512	down
MEDP168	Guanosine 3',5'-Cyclic Monophosphate	1.7484	0.0002	0.5852	-0.7730	down
MEDP169	Guanosine Monophosphate	1.5274	0.0013	0.3882	-1.3650	down
MEDP174	Purine	1.6154	0.0009	0.8588	-0.2197	down
MEDP177	Thymine	1.4826	0.0096	0.4553	-1.1351	down
MEDP178	Uracil	1.6937	0.0346	0.3047	-1.7146	down
MEDP184	3,3',5-Triiodo-L-Thyronine	1.2940	0.0337	0.6633	-0.5923	down
MEDP212	N-Acetyl-5-Hydroxytryptamine	1.3788	0.0107	0.6342	-0.6569	down
MEDP230	Maltose	1.1856	0.0223	0.8145	-0.2959	down
MEDP244	All-Trans-13,14-Dihydroretinol	1.5741	0.0020	0.8352	-0.2599	down
MEDP246	Nicotinic Acid	1.3683	0.0154	0.8265	-0.2749	down
MEDP250	Riboflavin	1.2535	0.0230	0.8056	-0.3118	down
MEDP274	Indole-2-Carboxylic Acid	1.7091	0.0002	0.5757	-0.7967	down
MEDP275	Indole-3-Acetic Acid	1.3605	0.0041	0.5880	-0.7661	down
MEDP295	4-Acetamidobutyric Acid	1.3111	0.0132	0.6996	-0.5153	down
MEDP297	5-Aminovaleric Acid	1.4376	0.0246	0.3537	-1.4996	down
MEDP303	Chlorogenic Acid	1.4031	0.0248	0.0880	-3.5058	down
MEDP316	Homovanillic Acid	1.4712	0.0131	0.6768	-0.5632	down
MEDP321	L-Dihydroorotic Acid	1.1534	0.0402	0.9583	-0.0615	down
MEDP325	Maleic Acid	1.4671	0.0043	0.7173	-0.4794	down
MEDP332	Cinnamic Acid	1.5749	0.0036	0.7310	-0.4520	down
MEDP333	Uric Acid	1.7459	0.0017	0.4284	-1.2230	down
MEDP346	Lysopc 18:2	1.6120	0.0004	1.1383	0.1868	up
MEDP361	4-Hydroxybenzaldehyde	1.3392	0.0339	0.7020	-0.5104	down
MEDP368	Taurocholic Acid Sodium Salt Hydrate	1.4075	0.0053	0.8792	-0.1858	down
MEDP370	2-(Formylamino)Benzoic Acid	1.5574	0.0025	0.7575	-0.4008	down

MEDP373	N-Acetylglycine	1.8377	0.0003	0.6010	-0.7346	down
MEDP379	3-Hydroxyhippuric Acid	1.5217	0.0052	0.4737	-1.0781	down
MEDP380	2-(Dimethylamino)Guanosine	1.4025	0.0431	0.5102	-0.9710	down
MEDP381	7-Methylguanine	1.5774	0.0026	0.7423	-0.4299	down
MEDP389	Pantetheine	1.6752	0.0012	0.8412	-0.2494	down
MEDP410	Trans-Citridic Acid	1.3804	0.0101	0.8949	-0.1602	down
MEDP416	6-Phosphogluconic Acid Trisodium Salt	1.5102	0.0060	0.6146	-0.7023	down
MEDP431	Hordenine	1.3772	0.0210	0.7667	-0.3832	down
MEDP435	6-Methylmercaptopurine	1.3522	0.0134	0.9494	-0.0749	down
MEDP438	N-Formylmethionine	1.1296	0.0379	2.1615	1.1120	up
MEDP453	Indole	1.1322	0.0318	0.7865	-0.3464	down
MEDP454	Isoquinoline	1.3991	0.0019	0.6804	-0.5556	down
MEDP455	Dihydrojasmone	1.5038	0.0042	0.6361	-0.6526	down
MEDP507	2-Hydroxycinnamic acid	1.5235	0.0081	0.6744	-0.5683	down
MEDP509	trans-3-Indoleacrylic acid	1.0916	0.0427	0.8005	-0.3210	down
MEDP519	L-Norleucine	1.1324	0.0308	0.7784	-0.3615	down
MEDP546	Oxindole	1.1465	0.0367	0.5873	-0.7678	down
MEDP578	alpha-Cadinene	1.3062	0.0200	0.8768	-0.1897	down
MEDP583	Asp-Phe methyl ester	1.1718	0.0325	0.7518	-0.4115	down
MEDP586	N-Acetylphenylalanine	1.4623	0.0085	0.6889	-0.5376	down
MEDP601	Spermidine	1.4540	0.0141	0.6149	-0.7016	down
MEDP603	Cuminaldehyde	1.5293	0.0041	0.7398	-0.4348	down
MEDP606	2-(3,4-dimethoxyphenyl)ethanamine	1.5476	0.0052	0.6817	-0.5527	down
MEDP653	Benzylcinnamate	1.1786	0.0239	0.8336	-0.2625	down
MEDP676	Butyl 3-methylbutanoate	1.2250	0.0251	0.9352	-0.0967	down
MEDP681	2,2,2-Trichloroethanol	1.4522	0.0110	0.7806	-0.3574	down

MEDP682	Hydroxyacetone	1.2950	0.0182	0.8338	-0.2623	down
MEDP685	Methylcysteine	1.5675	0.0045	0.6683	-0.5814	down
MEDP686	2-Acetylfuran	1.2351	0.0189	0.9262	-0.1106	down
MEDP707	2-Pentadecanone	1.8084	0.0000	0.8851	-0.1760	down
MEDP709	Methyl dihydrojasmonate	1.7005	0.0001	0.8991	-0.1535	down
MEDP736	1,3-diisopropylbenzene	1.1946	0.0394	0.9026	-0.1479	down
MEDP759	Glycyrrhetinic acid	1.4548	0.0060	0.6254	-0.6771	down
MEDP781	2-Undecanone	1.1538	0.0371	0.8976	-0.1558	down
MEDP784	Undecanal	1.3927	0.0146	0.8884	-0.1708	down
MEDP789	2-Pentyl-3-phenyl-2-propenal	1.6645	0.0030	0.8750	-0.1927	down
MEDP792	PYRROLIDINE	1.4429	0.0057	0.7795	-0.3593	down
MEDP796	Pyrene	1.4223	0.0085	0.9153	-0.1277	down
MEDP817	PROPYL HEXANOATE	1.2594	0.0171	0.9206	-0.1193	down
MEDP828	2-Methyl-1-propanol	1.4566	0.0073	0.7071	-0.5001	down
MEDP844	FURFURYL ALCOHOL	1.3271	0.0139	0.9399	-0.0895	down
MEDP853	Choline chloride	1.2027	0.0259	0.8383	-0.2544	down
MEDP855	caprate (10:0)	1.3211	0.0079	0.9239	-0.1142	down
MEDP856	Isobutyl decanoate	1.3176	0.0194	0.9085	-0.1384	down
MEDP863	proline betaine	1.8685	0.0000	0.6194	-0.6911	down
MEDP868	N-methylalanine	1.5298	0.0018	0.7674	-0.3820	down
MEDP871	sphinganine	1.1689	0.0462	0.9470	-0.0785	down
MEDP891	L-Tryptophanamide	1.2864	0.0122	0.5681	-0.8158	down

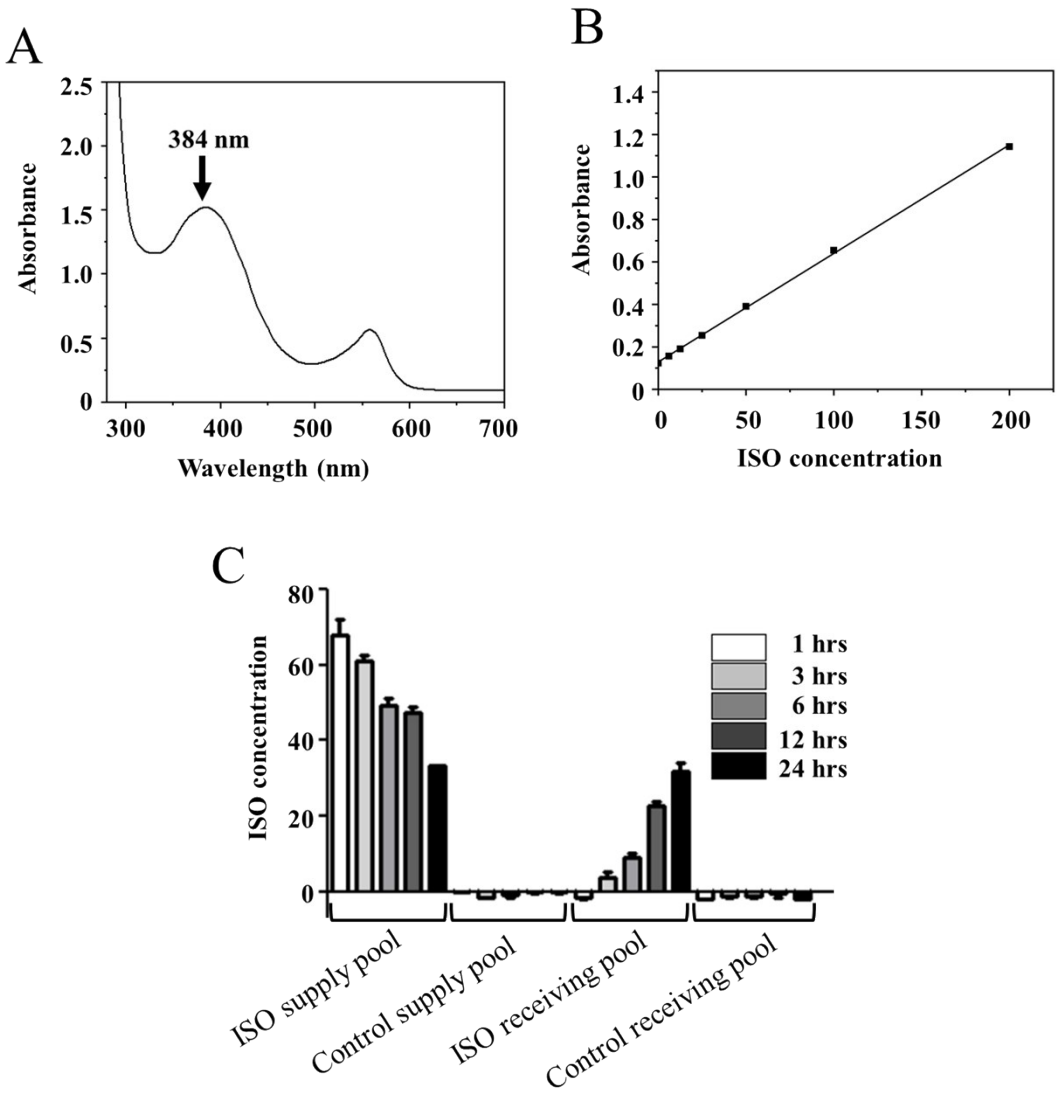

Figure S1. (A). Optical absorption spectrum of ISO. (B). The standard curve of the absorbance at 384 nm as a function of compound concentration. (C). The histogram of the ISO concentration in each pool at different time.

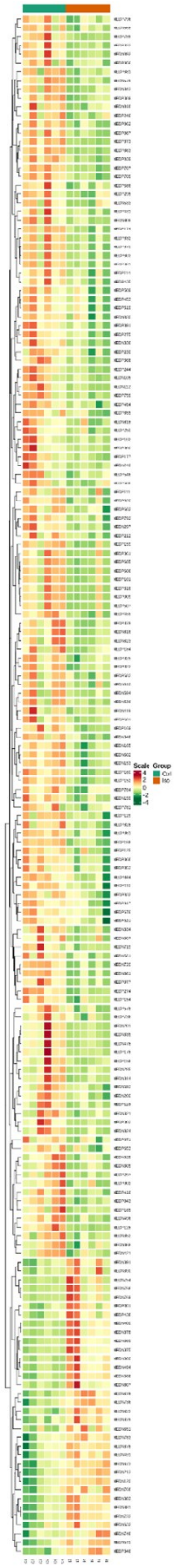

Figure S2. The heat map of the levels of 176 differential metabolites. Color represents the content of the metabolite, with red meaning a high content and green low.