Serum metabolomics analysis reveals amelioration effects of sea cucumber ether phospholipids on oxidative stress and inflammation in high-fat diet-fed mice

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Table S1. The predominant molecular species of the plasmanyl PC and plasmenyl PE subclasses in sea cucumber (*Cucumaria frondosa*).

Molecular species	Relative content (%)	Molecular species	Relative content (%)
PC(P-14:0/20:4)	0.3±0.0	PE(P-18:0/17:0)	0.1±0.0
PC(O-16:0/15:0)	1.9±0.2	PE(P-16:0/20:5)	0.1±0.0
PC(O-16:1/17:1)	0.2±0.0	PE(P-18:0/18:1)	0.2±0.1
PC(O-16:0/17:0)	10.4±0.2	PE(P-18:0/18:0)	5.0±0.4
PC(O-18:0/16:1)	0.2±0.0	PE(P-17:0/20:5)	0.2±0.1
PC(O-15:0/20:5)	0.3±0.0	PE(P-18:0/19:1)	0.1±0.0
PC(O-15:0/20:4)	0.2±0.0	PE(P-18:0/19:0)	0.5±0.1
PC(O-18:0/17:2)	0.2±0.0	PE(P-18:1/20:5)	0.1±0.0
PC(O-17:0/18:1)	0.7±0.0	PE(P-18:0/20:5)	69.1±0.2
PC(O-16:1/20:5)	0.7±0.2	PE(P-18:0/20:4)	13.8±0.4
PC(O-16:0/20:5)	9.3±0.4	PE(P-18:0/20:2)	0.1±0.1
PC(O-16:0/20:4)	1.2±0.2	PE(P-18:0/20:1)	0.5±0.1
PC(O-16:0/20:3)	0.2±0.0	PE(P-18:0/20:0)	1.5±0.3
PC(O-16:0/20:2)	0.2±0.0	PE(P-19:1/20:5)	0.1±0.0
PC(O-17:1/20:5)	0.3±0.1	PE(P-19:2/20:4)	0.1±0.0
PC(O-17:0/20:5)	2.8±0.3	PE(P-19:0/20:5)	2.9±0.1
PC(O-17:0/20:4)	0.5±0.0	PE(P-19:1/20:4)	0.2±0.0
PC(O-18:2/20:5)	0.2±0.0	PE(P-19:0/20:4)	1.0±0.3
PC(O-18:1/20:5)	36.4±0.1	PE(P-19:0/20:3)	0.1±0.0
PC(O-18:0/20:5)	21.5±0.1	PE(P-18:0/21:1)	0.2±0.1
PC(O-18:0/20:4)	2.0±0.2	PE(P-20:2/20:5)	0.1±0.0
PC(O-18:1/20:2)	0.2±0.0	PE(P-19:0/20:0)	0.1±0.0
PC(O-19:2/20:5)	0.5±0.0	PE(P-20:1/20:5)	0.5±0.2
PC(O-19:1/20:5)	2.0±0.1	PE(P-20:0/20:5)	0.2±0.0
PC(O-19:0/20:5)	0.3±0.0	PE(P-20:1/20:4)	1.0±0.2
PC(O-19:0/20:4)	0.3±0.0	PE(P-20:0/20:4)	0.5±0.0
PC(O-20:3/20:5)	4.1±0.1	PE(P-18:0/22:1)	0.2±0.0
PC(O-18:1/22:6)	0.2±0.0	PE(P-19:0/22:5)	0.1±0.1
PC(O-20:1/20:5)	1.7±0.2	PE(P-18:0/23:1)	0.3±0.1
PC(O-20:0/20:5)	0.5±0.0	PE(P-19:0/22:1)	0.1±0.1
PC(O-20:0/20:4)	0.2±0.0	PE(P-18:0/25:1)	0.2±0.1
PC(O-18:1/24:6)	0.5±0.0	PE(P-24:0/20:4)	0.2±0.1

Results are displayed as mean ± SD (n = 5).

Table S2. The differential metabolites identified by cross-comparisons of different groups (ND versus HFD) in mice serum samples.

Metabolites	HMDB ID	Formula	Obs *m/z*	FC	*p* value
11,12-EET	HMDB0004673	$C_{20}H_{32}O_3$	320.2351	2.8015	6.22E-06
12 -HPETE	HMDB0004243	$C_{20}H_{32}O_4$	336.2301	0.2588	1.79E-03
12,13-DiHOME	HMDB0004705	$C_{18}H_{34}O_4$	314.2457	0.0880	1.65E-04
12,13-EpODE	HMDB0010220	$C_{18}H_{30}O_3$	294.2195	0.1543	6.65E-02
12-HETE	HMDB0006111	$C_{20}H_{32}O_3$	320.2351	0.1253	2.79E-06
15(S)-HETE	HMDB03876	$C_{20}H_{32}O_3$	320.2347	0.4800	8.40E-04
2-hydroxybutyric acid	HMDB0000008	$C_4H_8O_3$	104.0473	0.1798	1.18E-03
9,10-DiHOME	HMDB0004704	$C_{18}H_{34}O_4$	314.2457	0.4314	4.63E-06
9-HODE	HMDB0062652	$C_{18}H_{32}O_3$	296.2351	0.2278	2.67E-04
Acetylcarnitine	HMDB0000201	$C_9H_{18}NO_4$	204.1236	0.5370	2.76E-03
Acetylcholine	HMDB0000895	$C_7H_{16}NO_2$	146.1181	0.4954	1.56E-02
Adenosine	HMDB0000050	$C_{10}H_{13}N_5O_4$	267.0968	0.4132	3.49E-06
Adenosine 5'-monophosphate	HMDB0000045	$C_{10}H_{14}N_5O_7P$	347.0631	0.2777	4.85E-06
Adipic acid	HMDB0000448	$C_6H_{10}O_4$	146.0579	0.4080	6.67E-03
Adrenic acid	HMDB02226	$C_{22}H_{36}O_2$	332.2711	0.3728	1.64E-04
Alpha-ketoglutarate	HMDB0000208	$C_5H_6O_5$	146.0215	0.2174	7.42E-03
Aminoadipic acid	HMDB0000510	$C_6H_{11}NO_4$	296.2351	0.2318	4.31E-05
Arachidonic acid	HMDB0001043	$C_{20}H_{32}O_2$	304.2402	0.0963	8.20E-03
Arginine	HMDB0000517	$C_6H_{14}N_4O_2$	174.1117	2.3020	4.11E-02
Carnitine	HMDB0000062	$C_7H_{16}NO_3$	162.1130	2.7424	3.66E-03
Cerulenin	HMDB0015168	$C_{12}H_{17}NO_3$	223.2683	0.4349	3.90E-04
Choline	HMDB0000097	$C_5H_{14}NO$	104.1075	2.4393	1.87E-04
Citrate	HMDB0000094	$C_6H_8O_7$	192.0270	0.1797	1.18E-03
Citrulline	HMDB0000904	$C_6H_{13}N_3O_3$	175.0957	0.4442	3.51E-04
Creatine	HMDB0000064	$C_4H_9N_3O_2$	131.0695	2.4053	6.65E-03
Creatinine	HMDB0000562	$C_4H_7N_3O$	113.0589	2.0389	2.61E-02
Cytidine	HMDB0000089	$C_9H_{13}N_3O_5$	243.0855	0.3030	4.60E-03
Cytosine	HMDB0000630	$C_4H_5N_3O$	111.0433	0.4294	2.72E-02
Deoxyglucose	HMDB0062477	$C_6H_{12}O_5$	164.0685	0.2742	6.29E-05
Docosahexaenoic Acid	HMDB02183	$C_{22}H_{32}O_2$	328.2402	5.6775	3.60E-03
Dodecanoylcarnitine	HMDB02250	$C_{19}H_{37}NO_4$	343.2721	0.2710	5.79E-06
Dodecenoic acid	HMDB0032248	$C_{12}H_{22}O_2$	198.1620	0.4724	2.23E-03
Eicosapentaenoic acid	HMDB01999	$C_{20}H_{30}O_2$	302.2241	4.4849	1.35E-05
Gluconic acid	HMDB0001316	$C_6H_{13}O_{10}P$	276.0246	0.3701	4.81E-02
Glucose	HMDB0000122	$C_6H_{12}O_6$	180.0634	0.6713	7.82E-04
Glutamate	HMDB0060475	$C_5H_9NO_4$	147.0532	3.0421	2.62E-03
Glutamine	HMDB0000641	$C_5H_{10}N_2O_3$	146.0691	2.1579	9.88E-02
Histamine	HMDB0000870	$C_5H_9N_3$	111.0796	0.4962	1.27E-05
Histidine	HMDB00177	$C_6H_9N_3O_2$	155.0695	0.4177	5.29E-05

Metabolites	HMDB ID	Formula	Obs *m/z*	FC	*P* value
Hydroxybutyrylcarnitine	HMDB13127	$C_{11}H_{21}NO_5$	247.1419	0.2736	3.96E-03
Hydroxyproline	HMDB0000725	$C_5H_9NO_3$	131.0582	0.1583	4.62E-02
Isoleucine	HMDB0000172	$C_6H_{13}NO_2$	131.0946	0.2060	7.26E-02
Leucine	HMDB00687	$C_6H_{13}NO_2$	131.0946	0.1197	7.08E-05
Linoleic Acid	HMDB0000673	$C_{18}H_{32}O_2$	280.2402	0.2710	5.79E-06
Linolenic acid	HMDB03073	$C_{18}H_{30}O_2$	278.2241	2.0042	2.30E-02
Linoleyl carnitine	HMDB0006469	$C_{25}H_{46}NO_4$	424.3421	0.1561	2.40E-04
Lysine	HMDB0000182	$C_6H_{14}N_2O_2$	146.1055	2.2475	2.14E-03
LysoPC (18:1)	HMDB0002815	$C_{26}H_{52}NO_7P$	521.3481	4.4162	9.89E-08
LysoPC (16:0)	HMDB0010382	$C_{24}H_{50}NO_7P$	495.3325	0.2736	3.16E-02
LysoPC (18:0)	HMDB0010384	$C_{26}H_{54}NO_7P$	523.3638	0.1197	7.08E-05
LysoPC (18:2)	HMDB10386	$C_{26}H_{50}NO_7P$	519.3326	4.4849	8.63E-04
LysoPE (16:0)	HMDB11473	$C_{21}H_{44}NO_7P$	453.2856	2.2969	3.42E-02
LysoPE (18:2)	HMDB11477	$C_{23}H_{44}NO_7P$	477.2855	2.4052	6.65E-03
Malic acid	HMDB0031518	$C_4H_6O_5$	134.0215	0.6870	4.94E-04
N-Acetylisoleucine	HMDB61684	$C_8H_{15}NO_3$	173.1051	0.7040	8.91E-05
N-Acetylleucine	HMDB11756	$C_8H_{15}NO_3$	173.1051	0.2616	5.72E-06
Nonadecanoic acid	HMDB00772	$C_{19}H_{38}O_2$	298.2867	0.4989	2.76E-03
Palmitic Acid	HMDB0000220	$C_{16}H_{32}O_2$	256.2402	0.3814	1.54E-03
Palmitoleic acid	HMDB03229	$C_{16}H_{30}O_2$	254.2243	2.6897	3.49E-03
Palmitoylcarnitine	HMDB0000222	$C_{23}H_{46}NO_4$	400.3421	0.1726	1.07E-05
Paullinic acid	HMDB35159	$C_{20}H_{38}O_2$	310.2867	0.3030	4.60E-03
PC (22:6)	HMDB08731	$C_{48}H_{78}NO_8P$	827.5440	2.2475	6.97E-05
Phenylalanine	HMDB0000159	$C_9H_{11}NO_2$	165.0790	3.5643	2.40E-03
Proline	HMDB0000162	$C_5H_9NO_2$	115.0633	2.6804	1.52E-02
Prostaglandin D2	HMDB0001403	$C_{20}H_{32}O_5$	352.2250	0.4939	8.02E-04
Prostaglandin E1	HMDB0001442	$C_{20}H_{34}O_5$	354.2406	0.4301	6.22E-03
Prostaglandin E2	HMDB0001220	$C_{20}H_{32}O_5$	352.2250	0.2315	7.84E-03
Prostaglandin F2	HMDB0004240	$C_{20}H_{32}O_5$	352.2250	0.4126	5.12E-05
Spermidine	HMDB0001257	$C_7H_{19}N_3$	145.1579	3.0421	9.29E-05
Spermine	HMDB0001256	$C_{10}H_{26}N_4$	202.2157	2.7791	4.55E-04
Sphingosine	HMDB0000252	$C_{18}H_{37}NO_2$	299.2824	2.4967	1.12E-04
Succinate	HMDB0000254	$C_4H_6O_4$	118.0266	0.3442	5.64E-03
Tetracosahexaenoic acid	HMDB02007	$C_{24}H_{36}O_2$	356.2710	0.4597	1.76E-02
Tryptophan	HMDB0000929	$C_{11}H_{12}N_2O_2$	204.0899	2.2783	3.16E-02
Ttradecanoylcarnitine	HMDB05066	$C_{21}H_{41}NO_4$	371.3035	0.2612	1.59E-05
Uric acid	HMDB0000289	$C_5H_4N_4O_3$	168.0283	2.4102	2.15E-05
Valine	HMDB0000883	$C_5H_{11}NO_2$	117.0790	0.1998	1.02E-04

Variable importance in the projection (VIP) was obtained from OPLS-DA with a threshold of 1.0. Human Metabolome Database ID (HMDB ID). observed *m/z* (Obs

m/z). Fold change (FC) was calculated from the arithmetic mean values between ND and HFD group. *P* value was calculated from WilcoxonMann U test.

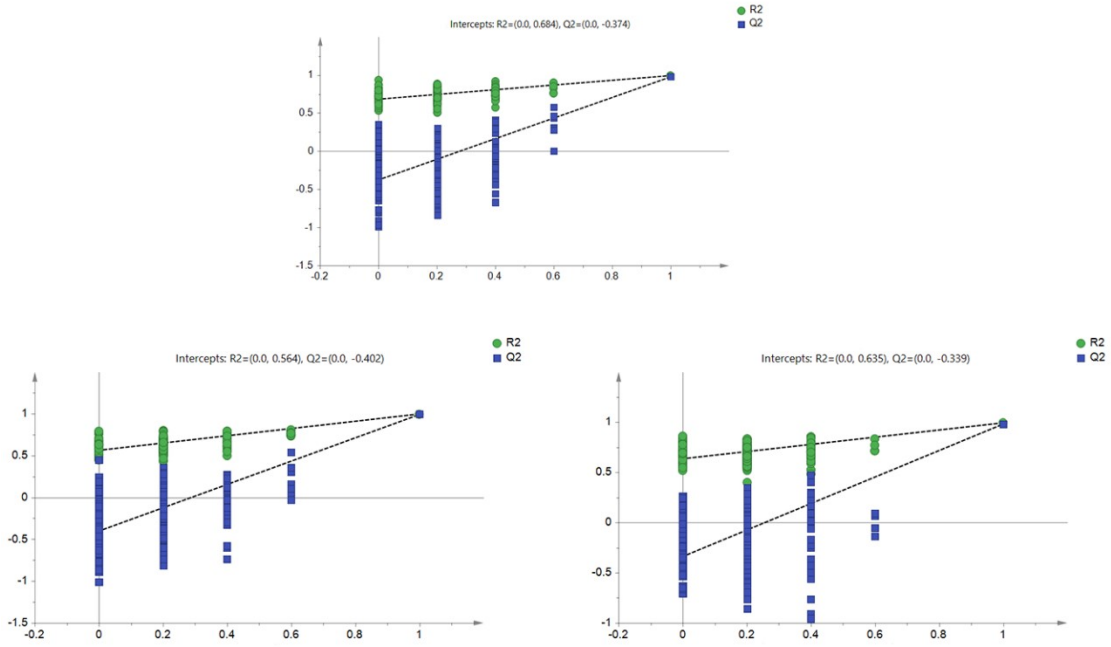

Figure S1. Permutation tests of the OPLS-DA model of ND vs. HFD, HFD vs. HFD+PC-O and HFD+PE-P groups.