Electronic Supplementary Material (ESI) for Toxicology Research.

Table S1 Identification of metabolites that were significantly differentiating plasma profiles of treated groups from controls in LC-MS analysis ($p < 0,05$)

Name	Formula	MW (DB)	RT (min)	DET	Mass error (ppm)	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE	MS/MS fragments
Phosphocholine*	$C_5H_{14}NO_4P$	183.0660	18.01	Pos	-0.22	12.99	-15.6	-	-23.1	184.0720, 124.9969, 86.0965, 60.0811
Oleic acid	$C_{18}H_{34}O_2$	282.2559	31.29	Neg	-0.35	19.99	-40.9	-	-	Putative
Sphingosine*	$C_{18}H_{37}NO_2$	299.2824	16.03	Pos	-1.04	18.63	-60.7	-	-	300.2809, 282.2757, 264.2645, 252.2713, 139.1139, 95.0819, 57.0678
Eicosapentaenoic acid	$C_{20}H_{30}O_2$	302.2246	25.48	Neg	-1.98	10.20	-48.8	-	-	Putative
Arachidonic Acid	$C_{20}H_{32}O_2$	304.2402	27.87	Neg	1.97	11.51	-46.3	-	-29.3	303.2315, 285.2254, 259.2400, 59.0135
Dihomo-ɣ-linoleic acid	$C_{20}H_{34}O_2$	306.2559	29.60	Neg	-3.26	16.99	-50.9	-	-39.7	Putative
15-deoxy-Δ12,14-Prostaglandin J2	$C_{20}H_{28}O_3$	316.2039	12.04	Neg	-2.53	11.71	-66.0	-	-	Putative
9-HETE	$C_{20}H_{32}O_3$	320.2351	20.24	Neg	-0.94	7.57	-85.4	-	-	319.2242, 301.2166, 257.2269, 179.1049, 135.1135, 107.0820, 81.0739, 69.0333
Anandamide*	$C_{20}H_{35}NO_2$	321.2668	27.79	Pos	-0.56	6.01	-25.5	-	-16.9	322.1735, 304.2363, 292.1269, 242.0940, 175.1356, 160.1376, 147.1134, 127.0886, 120.0558, 95.0914, 89.0652, 79.0628, 60.0782
Docosahexaenoic acid*	$C_{22}H_{32}O_2$	328.2402	28.05	Pos	3.03	20.15	-37.3	-	-23.2	329.2449, 311.2371, 293.2188, 207.1281, 173.1299, 109.0979, 93.0686, 81.0682, 67.0532
Docosahexaenoic acid	$C_{22}H_{32}O_2$	328.2402	29.03	Neg	0.91	12.53	-	-43.2	-28.9	327.2274, 283.2419, 229.1926, 177.1631, 121.1019, 59.0148
Docosapentaenoic acid	$C_{22}H_{34}O_2$	330.2559	29.55	Neg	-1.82	13.79	-41.2	-	-	Putative

Name	Formula	MW (DB)	RT (min)	DET	Mass error (ppm)	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE	MS/MS fragments
Docosatetranoic acid	$C_{22}H_{36}O_2$	332.2715	30.79	Neg	-3.01	18.50	-38.1	-	-	Putative
Dihydroxypregnenolone	$C_{21}H_{32}O_4$	348.2301	28.36	Neg	-8.62	6.80	-31.5	-	-	347.2316, 280.2365, 279.2316
C16 Sphingosine-1-phosphate*	$C_{16}H_{34}NO_5P$	351.2175	11.37	Pos	-0.48	2.52	-72.8	-	-	Putative
MG(18:3)*	$C_{21}H_{36}O_4$	352.2614	23.18	Pos	1.14	12.70	-	-	-74.9	Putative
MG(18:2)*	$C_{21}H_{38}O_4$	354.2770	25.80	Pos	2.82	17.67	-	-	-60.4	Putative
MG(18:1)*	$C_{21}H_{40}O_4$	356.2927	28.26	Pos	-3.36	16.01	-	-	-68.3	Putative
Calcitroic acid*	$C_{23}H_{36}O_3$	360.2664	19.43	Pos	-4.44	15.30	-	-	-72.0	Putative
Cortisol	$C_{21}H_{30}O_5$	362.2093	5.35	Neg	-2.21	7.58	-	-81.2	-	361.2014, 304.3312, 184.9345, 64.5371
Cholacalcioic acid*	$C_{24}H_{36}O_3$	372.2664	7.90	Pos	1.11	19.31	-	-86.3	-	Putative
PA(15:0)	$C_{18}H_{37}O_7P$	396.2277	27.28	Neg	-1.77	7.13	-39.1	-	-	395.2275, 327.2356, 283.2446, 59.0146
Asn Tyr Leu*	$C_{19}H_{28}N_4O_6$	408.2009	25.80	Pos	-7.59	15.21	-	-	-60.8	Putative
Dihydroxyvitamin D3*	$C_{27}H_{44}O_3$	416.3290	22.23	Pos	0.22	17.16	44.4	-31.2	-	Putative
PE(16:0)*	$C_{21}H_{44}NO_7P$	453.2855	18.58	Pos	1.12	15.80	-23.1	-	-	313.2730, 282.2744, 155.0075, 62.0605
PC(O-12:0/O-2:0)*	$C_{22}H_{48}NO_6P$	453.3219	16.50	Pos	-1.83	1.76	-34.6	-15.8	-	Putative
PC(14:0)*	$C_{22}H_{46}NO_7P$	467.3012	15.52	Pos	0.26	12.68	-34.8	-	-	468.3025, 184.0720, 104.1067, 86.0945
PC(O-14:0/O-1:0)	$C_{23}H_{50}NO_6P$	467.3376	24.77	Neg	-2.57	24.53	-35.1	-	-	466.3358, 405.2826, 140.0111, 78.9594
LPE(18:3)*	$C_{23}H_{42}NO_7P$	475.2699	15.78	Pos	5.90	24.80	-80.3	-	-	Putative

Name	Formula	MW (DB)	RT (min)	DET	Mass error (ppm)	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE	MS/MS fragments
LPE(18:2)	$C_{23}H_{44}NO_7P$	477.2856	1.88	Neg	0.84	9.46	-54.6	-	-46.7	476.2804, 279.2347, 196.0370, 140.0115, 78.9592
PE(18:1)	$C_{23}H_{46}NO_7P$	479.3011	20.38	Neg	-1.88	8.58	-	-36.9	-	478.3007, 281.2499, 255.2328, 196.0368, 140.0108, 78.95588
PE(18:1)*	$C_{23}H_{46}NO_7P$	479.3011	20.30	Pos	0.94	16.82	-35.2	-	-25.8	480.2823, 339.2898, 308.2969, 265.2477, 155.0085, 62.0601
PC(15:0)*	$C_{23}H_{48}NO_7P$	481.3168	17.57	Pos	-0.01	17.33	-33.8	-	-18.4	482.3301, 429.3081, 369.1566, 248.1679, 184.0703, 166.0630, 146.9808, 104.1029, 57.1029
PC(16:1)*	$C_{24}H_{48}NO_7P$	493.3168	17.72	Pos	-1.01	10.93	-	-	-53.6	Putative
PC(16:0)*	$C_{24}H_{50}NO_7P$	495.3325	18.82	Pos	5.68	18.01	-80.2	-	-	496.3369, 184.0736, 104.1067, 86.0964
LPE(20:5)*	$C_{25}H_{42}NO_7P$	499.2699	15.98	Pos	-1.40	19.61	-	-	-66.6	Putative
PE(20:4)	$C_{25}H_{44}NO_7P$	501.2856	17.95	Neg	1.00	7.71	-53.7	-	-33.7	500.2772, 303.2313, 279.2319, 259.2383, 196.0367, 78.9560
LPE(20:3)	$C_{25}H_{46}NO_7P$	503.3012	17.87	Pos/ Neg	0.44	17.97	-43.2	-	-50.6	Putative
LPE(20:2)	$C_{25}H_{48}NO_7P$	505.3168	17.41	Neg	-2.37	1.74	-	-	-24.0	Putative
PC(17:1)*	$C_{25}H_{50}NO_7P$	507.3325	18.58	Pos	-0.18	20.68	-32.4	-	-17.8	508.3303, 258.7617, 184.0708, 124.0633, 104.1073, 86.0932
PC(17:0)*	$C_{25}H_{52}NO_7P$	509.3481	20.87	Pos	0.00	13.43	-	-	-20.3	Putative
LPC (18:2)*	$C_{26}H_{50}NO_7P$	519.3325	17.37	Pos	4.78	14.90	-33.8	-	-23.3	520.3410, 502.3298, 443.2556, 337.2736, 258.1094, 184.0737, 124.9993, 104.1075, 86.0965, 60.0810

Name	Formula	MW (DB)	RT (min)	DET	Mass error	CV for QC (%)	FC (%)	FC (%)	FC (%)	MS/MS fragments

					(ppm)		A / C	NE / C	A / NE	
LPC(18:1)*	$C_{26}H_{52}NO_7P$	521.3481	20.56	Pos	5.48	15.65	-28.8	-		522.3549, 339.2872, 258.1082, 184.0733, 166.0612, 124.9995, 104.1073, 86.0969, 60.0813
LPE(22:6)	$C_{27}H_{44}NO_7P$	525.2855	17.89	Neg	0.76	7.66	-49.0	-	-34.1	524.2777, 327.2294, 283.2427, 196.0363, 140.0093, 78.9587
LPE(22:5)	$C_{27}H_{46}NO_7P$	527.3012	18.79	Neg	-0.02	18.14	-90.7	-	-61.1	Putative
PC(19:3)*	$C_{27}H_{50}NO_7P$	531.3325	20.92	Pos	2.97	8.52	-77.4	-	-	532.3370, 473.2613, 104.1065
PC(20:5)*	$C_{28}H_{48}NO_7P$	541.3168	16.14	Pos	-0.62	17.00	-40.7	-	-	542.322, 184.072, 104.096, 86.095
LPC(20:4)*	$C_{28}H_{50}NO_7P$	543.3325	17.50	Pos	3.46	15.10	-24.9	-	-	544.3387, 184.0734, 104.1073, 86.0962, 60.0812
PS(20:4)	$C_{26}H_{44}NO_9P$	545.2754	17.22	Neg	-7.34	6.60	-	-	-83.9	Putative
LPC(20:2)*	$C_{28}H_{54}NO_7P$	547.3638	21.61	Pos	-0.31	18.18	-29.4	-	-	548.3737, 184.0723, 104.1064, 86.0959
PS(20:0)	$C_{26}H_{52}NO_9P$	553.338	18.63	Neg	-4.70	8.80	-	-	-31.9	Putative
PS(22:6)	$C_{28}H_{44}NO_9P$	569.2754	17.95	Neg	-4.22	8.87	-47.5	-	-36.1	508.3307, 500.2690, 303.2319, 281.2358, 259.2420, 214.0511, 95.7203, 78.9568
PI (16:0)	$C_{25}H_{49}O_{12}P$	572.2961	22.17	Neg	-2.62	18.34	-39.5	-	-	571.2878, 391.2222, 315.0458, 255.2325, 241.0091, 152.9944, 78.9579
PC(16:0/5:0(CHO))	$C_{29}H_{56}NO_9P$	593.3693	17.89	Neg	-5.73	7.37	-	-	-38.6	Putative
PI(18:2)	$C_{27}H_{49}O_{12}P$	596.2961	18.93	Neg	-3.52	10.29	-	-	-69.9	Putative
PC(16:0/5:0(COOH))	$C_{29}H_{56}NO_{10}P$	609.3642	17.42	Neg	-3.61	12.46	-	-	-24.6	Putative
PI(20:4)	$C_{29}H_{49}O_{12}P$	620.2961	20.14	Neg	-1.128	4.25	-45.3	-	-	619.2872, 439.2218, 315.0489, 303.2318, 241.0113, 152.9946, 78.9599

Name	Formula	MW (DB)	RT (min)	DET	Mass error	CV for QC (%)	FC (%)	FC (%)	FC (%)	MS/MS fragments

					(ppm)		A / C	NE / C	A / NE	
PI(20:3)*	$C_{29}H_{51}O_{12}P$	622.3118	28.46	Pos	5.10	4.06	-	223.5	-	Putative
PA(P-16:0\16:1)	$C_{35}H_{67}O_7P$	630.4625	27.87	Neg	-4.92	17.73	-	-	-45.1	Putative
PI(22:6)	$C_{31}H_{49}O_{12}P$	644.2961	20.08	Neg	-2.95	8.10	-	-	-59.2	Putative
PS(P-16:0/13:0)*	$C_{35}H_{68}NO_9P$	677.4632	30.21	Pos	1.48	17.20	-	-90.4	-	Putative
PC(38:7)*	$C_{46}H_{78}NO_8P$	803.5465	30.72	Pos	-0.26	14.14	-33.1	-	-	Putative
PS(42:10)*	$C_{48}H_{74}NO_{10}P$	855.505	20.57	Pos	7.13	20.57	-	-	-32.1	Putative
Amphotericin B	$C_{47}H_{73}NO_{17}$	923.4879	8.63	Neg	-6.17	26.98	669.7	1123.0	-	Putative
TG(44:3)*	$C_{65}H_{114}O_6$	990.8615	19.58	Pos	0.40	3.34	-	-	-47.4	Putative
TG(65:2)*	$C_{68}H_{128}O_6$	1040.971	18.02	Pos	-3.27	15.03	-	-	-27.32	Putative

Note: A, C-AmB group; NE, AmB-loaded NE group; C, Control group; FC, fold change; FC was calculated as follows: (Average [Treated] – Average [Control])/Average[control] × 100); +/–, increase/decrease in treated when compared with controls; RT, retention time; CV, coefficient of variation
*Metabolites obtained from the LC positive, which the prediction capability (Q2:0.02) was low.

Table S2 Putative identification of metabolites that were significantly differentiating plasma profiles of treated groups from controls in CE-MS analysis ($p < 0,05$)

Name	Formula	MW (DB)	MT (min)	error (ppm)	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE
L-Pipecolate*	$C_6H_{11}NO_2$	129.0790	13.23	0.04	29.86	42.4	-	-
Methionine*	$C_5H_{11}NO_2S$	149.0510	13.85	0.03	4.36	-27.6	-	-
Gly Ala	$C_5H_{10}N_2O_3$	146.0691	13.24	1.11	12.66	-	138.8	-
L-Methionine S-oxide	$C_5H_{11}NO_3S$	165.0460	14.85	2.67	10.14	-12.9	-	-13.4
N8-Acetylspermidine	$C_9H_{21}N_3O$	187.1685	9.56	-4.29	13.76	-	47.2	-55.9
Ala Ile	$C_9H_{18}N_2O_3$	202.1317	13.11	-0.22	6.81	-	30.1	-
Deoxycytidine	$C_9H_{13}N_3O_4$	227.0906	12.59	1.29	8.54	-	11.1	-
Ile Pro	$C_{11}H_{20}N_2O_3$	228.1474	12.69	-2.63	14.49	-	26.6	-
Glu Ser	$C_8H_{14}N_2O_6$	234.0852	15.48	-7.65	28.58	76.5	-	-
Cytidine	$C_9H1_3N_3O_5$	243.0855	12.83	-0.52	6.07	43.2	-	-
L-Hexanoylcarnitine	$C_{13}H_{25}NO_4$	259.1783	13.07	-0.17	10.04	48.7	-	-
Phe Val	$C_{14}H_{20}N_2O_3$	264.1474	13.62	-7.19	10.78	95.9	97.1	-
Ile Ala Ala	$C_{12}H_{23}N_3O_4$	273.1689	13.84	4.34	4.48	27.8	46.4	-
Met Phe	$C_{14}H_{20}N_2O_3S$	296.1195	13.68	-3.30	8.76	-	-92.1	913.9
Val Trp	$C_{16}H_{21}N_3O_3$	303.1583	12.04	-9.89	7.43	-	-	-13.4
Ala Ile Leu	$C_{15}H_{29}N_3O_5$	315.2158	14.11	-0.70	9.98	-	55.6	-
Phe Ala Val	$C_{17}H_{25}N_3O_4$	335.1845	14.15	-0.33	7.34	-	64.4	-24.2
Ile Val Ile	$C_{17}H_{33}N_3O_4$	343.2471	14.33	-0.88	8.00	-	43.1	-
Ile Ala Phe	$C_{18}H_{27}N_3O_4$	349.2002	14.25	-0.76	9.71	-	27.0	-
Gly Phe Phe	$C_{20}H_{23}N_3O_4$	369.1689	14.12	0.40	15.38	-	146.7	-
Ile Ile Lys	$C_{18}H_{36}N_4O_4$	372.2737	11.38	1.74	4.74	-	91.5	-36.4
Ser Leu Arg	$C_{15}H_{30}N_6O_5$	374.2278	11.31	3.25	6.57	73.3	43.8	-
Leu Ile Tyr	$C_{21}H_{33}N_3O_5$	407.2420	14.65	-2.05	15.50	45.2	46.9	-
Arg Lys Lys	$C_{18}H_{38}N_8O_4$	430.3016	14.69	3.24	13.78	-	706.3	-
Glu Tyr Gln	$C_{19}H_{26}N_4O_8$	438.1751	14.64	0.05	11.03	326.4	223.3	-

Name	Formula	MW (DB)	RT (min)	error (ppm)	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE
Arg Arg Leu	$C_{18}H_{37}N_9O_4$	443.2968	16.24	5.31	9.58	-	143.0	-
Trp Lys Met	$C_{22}H_{33}N_5O_4S$	463.2253	14.90	4.96	10.98	-	-	820.9
N-(2'-(4-benzenesulfonamide)-ethyl) arachidonoyl amine	$C_{28}H_{42}N_2O_3S$	486.2916	11.80	0.42	5.66	-	54.4	-
Thyroxine	$C_{15}H_{11}I_4NO_4$	776.6867	13.14	5.27	9.91	-	40.5	-22.3

Note: A, C-AmB group; NE, AmB-loaded NE group; C, Control group; FC, fold change; FC was calculated as follows: (Average [Treated] – Average [Control])/Average [Control] × 100). +/–, increase/decrease in treated when compared with controls. MT, migration time. CV, coefficient of variation
* Compounds identified with standards

Table S3 Identification of metabolites that were significantly differentiating plasma profiles of treated groups from controls in GC-MS analysis ($p < 0,05$)

Name	T (target ion)	Q (qualifier ion)	RT (min)	*p*-value	CV for QC (%)	FC (%) A / C	FC (%) NE / C	FC (%) A / NE
2-hydroxybutyric acid	131	205, 147, 73	7.77	0.008	29.94	-100	-	-100
PYRANOSE (Glucose/Altrose/Galactose/Talose)	73	73, 319, 205, 147	17.55	0.019	29.14	-	-36.9	-
L-glutamic acid	156	156, 73, 147, 258	13.16	0.042	13.99	-	-	-100

Note: A, C-AmB group; NE, AmB-loaded NE group; C, Control group; FC, fold change; FC was calculated as follows: (Average [Treated] – Average [Control])/Average [Control] × 100). +/–, increase/decrease in treated when compared with controls. RT, retention time. CV, coefficient of variation