

Online Supplemental Material

Supplemental Table: Additional Metabolites with Significant Changes Identified via Internet Databases by Supplement Groups*

Metabolite (Mass, PubChem Compound ID)	Time	Placebo (n=37)		Q-500 (n=32)		Q-1000 (n=31)		P [†]	Descriptor
		Peak Area [†]		Peak Area [†]		Peak Area [†]			
		Mean	95% CI	Mean	95% CI	Mean	95% CI		
Caffeine (mw=195.09, 2519)	0-mo	372	(264, 524)	404	(277, 588)	554	(378, 812)	3.35E-03	Central nervous system stimulant
	1-mo	377	(264, 539)	680	(460, 1006)	364	(244, 542)		
	3-mo	452	(315, 648)	526	(354, 781)	502	(336, 751)		
N-(4-Aminobutyl)-L-histidine (mw=253.13, Not available)	0-mo	69.5	(54.0, 89.4)	44.6	(33.8, 58.8)	54.3	(41.0, 71.9)	4.32E-03	Dipeptide found in brain and muscle of mammals; function unknown
	1-mo	51.7	(41.6, 64.2)	60.0	(47.3, 76.2)	74.1	(58.1, 94.4)		
	3-mo	51.2	(39.4, 66.6)	52.0	(39.0, 69.3)	73.2	(54.6, 98.1)		
Ubiquinone-2 (mw=319.19, 5280346)	0-mo	650	(608, 695)	532	(494, 573)	556	(515, 599)	5.10E-03	Enzyme involved in ubiquinone biosynthesis
	1-mo	595	(555, 638)	567	(525, 612)	613	(567, 663)		
	3-mo	592	(555, 632)	547	(510, 588)	615	(572, 662)		
Phosphatidylcholine(18:1n7/18:3n6) (mw=766.57, Not available)	0-mo	134	(110, 163)	133	(107, 164)	148	(119, 183)	5.83E-03	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	191	(161, 226)	152	(126, 183)	99	(82, 120)		
	3-mo	161	(134, 193)	168	(138, 206)	98	(80, 121)		
Phosphatidylcholine(14:0/20:2n6) (mw=758.57, Not available)	0-mo	129	(108, 153)	173	(143, 209)	176	(145, 214)	6.57E-03	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	163	(138, 193)	173	(144, 208)	124	(103, 149)		
	3-mo	185	(157, 218)	167	(140, 200)	108	(90, 129)		
Calcidiol (mw=399.33, 5283731)	0-mo	139	(116, 166)	95.6	(78.7, 116)	107	(88.3, 131)	7.25E-03	Inactive form of Vitamin D, indicative of body's stores of Vitamin D
	1-mo	108	(91.2, 128)	94.8	(78.8, 114)	117	(97.0, 141)		
	3-mo	117	(97.6, 141)	90.8	(74.3, 111)	113	(92.3, 139)		
Phosphatidylcholine(14:0/22:4n6) (mw=758.57, Not available)	0-mo	85.3	(68.8, 106)	112	(88.5, 142)	127	(100, 161)	8.27E-03	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	101	(83.0, 123)	166	(133, 206)	90.3	(72.5, 112)		
	3-mo	114	(93.9, 139)	137	(110, 170)	72.5	(58.2, 90.3)		
Phosphatidylcholine(20:3n9/18:1n7) (mw=794.61, Not available)	0-mo	87.4	(68.0, 112)	148	(112, 195)	124	(94.0, 164)	8.61E-03	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	107	(82.6, 138)	189	(143, 250)	80.7	(60.6, 107)		
	3-mo	156	(121, 200)	164	(125, 216)	80.2	(60.8, 106)		
Phosphatidylcholine(16:1n7/18:1n7) (mw=742.61, Not available)	0-mo	126	(94.3, 170)	247	(179, 340)	190	(137, 264)	1.16E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	153	(111, 212)	284	(199, 406)	153	(106, 220)		
	3-mo	244	(177, 337)	249	(175, 354)	108	(75.5, 155)		
N,N-dimethylmethanamine (mw=60.08, 1146)	0-mo	75.6	(69.8, 81.9)	85.8	(78.6, 93.8)	83.4	(76.2, 91.2)	1.27E-02	Amine; function unknown
	1-mo	75.0	(68.9, 81.6)	84.7	(77.1, 92.9)	74.7	(67.9, 82.1)		
	3-mo	80.1	(73.8, 86.8)	85.3	(78.0, 93.2)	69.5	(63.5, 76.1)		
4-methylsulfanyl-2-oxo-butanoic acid (mw=149.02, 473)	0-mo	220	(179, 271)	133	(106, 167)	133	(106, 168)	1.56E-02	Involved in cell apoptosis and proliferation; Methionine metabolite
	1-mo	132	(109, 159)	119	(96.9, 146)	176	(143, 217)		
	3-mo	141	(118, 168)	121	(100, 146)	190	(156, 231)		
Phosphatidylcholine(16:1n7/22:6n3) (mw=804.55, Not available)	0-mo	748	(491, 1140)	1452	(916, 2302)	966	(604, 1543)	1.70E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	1983	(1416, 2778)	1381	(960, 1987)	472	(326, 684)		
	3-mo	1383	(936, 2043)	1273	(830, 1952)	512	(332, 791)		

Metabolite (Mass, PubChem Compound ID)	Time	Placebo (n=37)		Q-500 (n=32)		Q-1000 (n=31)		P [†]	Descriptor
		Peak Area [†]		Peak Area [†]		Peak Area [†]			
		Mean	95% CI	Mean	95% CI	Mean	95% CI		
Phosphatidylcholine(14:0/20:3n9) (mw=756.55, Not available)	0-mo	945	(639, 1398)	1768	(1152, 2714)	1835	(1187, 2837)	1.73E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	2194	(1528, 3149)	1615	(1087, 2399)	820	(548, 1226)		
	3-mo	1738	(1219, 2478)	1273	(1393, 3028)	743	(501, 1103)		
Phosphatidylcholine(14:0/22:4n6) (mw=782.57, Not available)	0-mo	59.5	(49.5, 71.5)	80.7	(66.0, 98.7)	83.4	(68.0, 102)	1.81E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	69.3	(58.0, 82.9)	82.3	(67.6, 100)	72.4	(59.3, 88.5)		
	3-mo	87.6	(73.1, 105)	82.5	(67.6, 101)	54.8	(44.8, 67.0)		
Phosphatidylcholine(18:3n6/22:6n3) (mw=828.55, Not available)	0-mo	298	(211, 421)	782	(535, 1144)	648	(440, 953)	1.91E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	550	(377, 802)	834	(551, 1261)	501	(329, 763)		
	3-mo	691	(472, 1013)	626	(412, 952)	318	(207, 487)		
4-methylphenol (mw=107.05, 2879)	0-mo	578	(431, 725)	739	(570, 959)	709	(547, 919)	2.27E-02	Protein catabolism metabolite
	1-mo	522	(412, 661)	884	(675, 1157)	1126	(866, 1464)		
	3-mo	507	(391, 657)	991	(738, 1330)	843	(632, 1124)		
Phosphatidylcholine(18:2n6/18:1n7) (mw=768.58, not available)	0-mo	169	(117, 245)	300	(200, 449)	272	(180, 410)	2.27E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	236	(163, 341)	376	(251, 565)	145	(96.1, 219)		
	3-mo	380	(267, 541)	369	(251, 544)	118	(79.6, 175)		
Phosphatidylcholine(18:0/22:6n3) (mw=834.60, Not available)	0-mo	128	(90.5, 180)	162	(111, 237)	169	(115, 247)	2.32E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	199	(145, 271)	134	(95.2, 189)	111	(78.4, 157)		
	3-mo	204	(148, 282)	195	(137, 279)	87.5	(60.9, 126)		
Phosphatidylcholine(18:3n3/18:2n6) (mw=780.55, Not available)	0-mo	17711	(10261, 30570)	35383	(19470, 64299)	26030	(14182, 47775)	2.38E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	63627	(39481, 102542)	42293	(25266, 70796)	8699	(5152, 14687)		
	3-mo	40689	(24486, 67614)	33651	(19301, 58671)	8979	(5102, 15800)		
Phosphatidylcholine(20:3n9/18:1n7) (mw=794.60, Not available)	0-mo	94.7	(75.0, 120)	150	(116, 194)	116	(89.3, 151)	2.47E-02	Glycerolphospholipid involved in cell signaling and energy metabolism
	1-mo	113	(87.4, 145)	175	(132, 231)	98.8	(74.4, 131)		
	3-mo	166	(133, 206)	141	(110, 179)	81.1	(63.4, 104)		
(3R)-3-hydroxyoctadecanoic acid (mw=299.26, Not available)	0-mo	268	(239, 300)	226	(200, 256)	228	(201, 259)	2.60E-02	Fatty acid biosynthesis intermediate
	1-mo	226	(204, 251)	226	(202, 254)	236	(210, 265)		
	3-mo	255	(232, 280)	219	(197, 242)	239	(215, 265)		
Diacylglycerol(15:0/18:4n3) (mw=573.45, Not available)	0-mo	396	(331, 474)	302	(248, 367)	331	(271, 404)	2.95E-02	Diglyceride involved in cell signaling and energy metabolism
	1-mo	300	(256, 353)	292	(245, 349)	365	(304, 438)		
	3-mo	329	(275, 393)	298	(245, 361)	425	(349, 518)		
3-oxooctadecanoic acid (mw=297.24, Not available)	0-mo	112	(91.5, 137)	88.6	(71.5, 110)	105	(84.1, 131)	3.12E-02	Fatty acid biosynthesis intermediate
	1-mo	94.6	(78.8, 113)	129	(106, 158)	104	(84.5, 127)		
	3-mo	105	(85.0, 131)	111	(87.2, 141)	73.9	(58.1, 93.9)		
3a,7a-Dihydroxycoprostanic acid (mw=433.33, 440384)	0-mo	84.7	(60.7, 118)	46.1	(32.0, 66.4)	54.9	(37.9, 79.6)	3.47E-02	Bile acid
	1-mo	55.3	(40.0, 76.3)	39.7	(27.9, 56.7)	68.6	(47.8, 98.4)		
	3-mo	58.9	(43.6, 79.7)	39.3	(28.2, 54.8)	86.7	(62.0, 121)		
N,N-dimethylmethanamine (mw=60.08, 1146)	0-mo	80.0	(68.5, 93.4)	93.7	(79.0, 111)	84.2	(70.8, 100)	3.55E-02	Amine; function unknown
	1-mo	74.8	(64.3, 87.1)	95.3	(80.7, 112)	78.1	(66.0, 92.5)		
	3-mo	85.4	(73.5, 99.1)	85.9	(72.8, 101)	70.1	(59.3, 82.9)		

Metabolite (Mass, PubChem Compound ID)	Time	Placebo (n=37)		Q-500 (n=32)		Q-1000 (n=31)		P [‡]	Descriptor
		Peak Area [†]		Peak Area [†]		Peak Area [†]			
		Mean	95% CI	Mean	95% CI	Mean	95% CI		
Diacylglycerol(15:0/18:3n6) (mw=575.47, Not available)	0-mo	223	(183, 273)	173	(139, 215)	186	(148, 232)	3.96E-02	Diglyceride involved in cell signaling and energy metabolism
	1-mo	162	(132, 198)	163	(130, 203)	192	(153, 241)		
	3-mo	181	(146, 224)	163	(129, 206)	233	(183, 295)		
Ubiquinone-2 (mw=319.20, 5280346)	0-mo	69.5	(60.7, 79.7)	98.3	(84.7, 114)	94.6	(81.2, 110)	4.18E-02	Enzyme involved in ubiquinone biosynthesis
	1-mo	81.1	(70.2, 93.7)	102	(87.2, 120)	83.3	(70.9, 97.8)		
	3-mo	89.1	(77.8, 102)	95.8	(82.5, 111)	73.2	(62.9, 85.2)		

*Participants were randomly assigned to one of three supplement groups: placebo (0-mg/d of quercetin supplementation), Q-500 (500 mg/d of quercetin supplementation), or Q-1000 (1,000 mg/d of quercetin supplementation). These metabolites were characterized using ultra-performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UPLC-QTOFMS) and identified using on-line databases such as the Human Metabolome Database (<http://www.hmdb.ca/>).

[†]Peak area was adjusted for age, BMI, and sex.

[‡]Significance test was based on linear mixed model with repeated measures adjusting for age, sex, BMI, and subject effect (random). Metabolite concentration was the response variable, and supplement groups (placebo, Q-500, and Q-1000) and time (0-mo, 1-mo, and 3-mo) were the predictor variables. The Benjamini-Hochberg method for false discovery rate correction was used.