Supplementary materials

Suppl. Table S1

Potential biomarkers related to SCM, CY, Ade, Arb and All.

Mode	No.	Compound	Formula	t_R (min)	Determined *m/z*
ES^{I+}	1	L-Homocysteine [a,b]	$C_4H_9NO_2S$	15.2	90.5073
	2	Betaine [b,*]	$C_5H_{11}NO_2$	1.5	100.0758
	3	Neurine [a]	$C_5H_{13}NO$	0.8	104.1070
	4	L-Proline [a,b,*]	$C_5H_9NO_2$	1.2	116.0705
	5	5-Aminopentanoic acid [a,b]	$C_5H_{11}NO_2$	0.8	118.0862
	6	Phenylethylamine [a,b]	$C_8H_{11}N$	14.5	122.0966
	7	D-Leucine [b]	$C_6H_{13}NO_2$	1.2	132.1020
	8	L-Adrenaline [a,b]	$C_9H_{13}NO_3$	1.5	166.0862
	9	L-Tyrosine [b,*]	$C_9H_{11}NO_3$	1.2	182.0811
	10	L-Tryptophan [a,b,*]	$C_{11}H_{12}N_2O_2$	3.2	205.0970
	11	L-Kynurenine [a,b]	$C_{10}H_{12}N_2O_3$	6.8	250.1181
	12	Sphingosine [a,b]	$C_{18}H_{37}NO_2$	10.8	282.2790
	13	Dihydrosphingosine [a,b]	$C_{18}H_{39}NO_2$	12.2	284.2946
	14	Adenosine [b,*]	$C_{10}H_{13}N5O_4$	6.5	309.1306
	15	N,N-Dimethylsphingosine [a]	$C_{20}H_{41}NO_2$	12.2	310.3103
	16	Thromboxane A2 [a,b]	$C_{20}H_{40}O$	13.2	338.3417
	17	Cholic acid [a,b,*]	$C_{24}H_{40}O_5$	6.2	373.2735
	18	Cholesteryl acetate [a,b]	$C_{29}H_{48}O_2$	13.5	429.3728
	19	LysoPC (15:0) [a]	$C_{23}H_{48}NO_7P$	8.5	464.3132
	20	7-a,27-Dihydroxycholesterol [b]	$C_{27}H_{46}O_3$	8.5	482.3604
	21	LysoPC (16:1(9Z)) [a]	$C_{24}H_{48}NO_7P$	7.2	494.3242
	22	LysoPC (16:0) [a,b]	$C_{24}H_{50}NO_7P$	7.8	496.3408
	23	LysoPC (18:0) [b]	$C_{26}H_{54}NO_6P$	8.8	508.3762
	24	LysoPE (0:0/20:0) [a,b]	$C_{25}H_{52}NO_7P$	8.8	510.3557
	25	LysoPC (18:2 (9Z,12Z)) [a,b]	$C_{26}H_{50}NO_7P$	7.5	520.3407
	26	LysoPC (0:0/18:0) [a,b]	$C_{26}H_{52}NO_7P$	9.5	524.3718
	27	LysoPE (0:0/22:0) [a]	$C_{27}H_{56}NO_7P$	10.8	538.3870
	28	LysoPC (20:4(5Z,8Z,11Z,14Z)) [a,b]	$C_{28}H_{50}NO_7P$	7.5	544.3407
	29	LysoPC (22:6(4Z,7Z,10Z,13Z,16Z,19Z)) [b]	$C_{30}H_{50}NO_7P$	7.2	568.3394
	30	Ceramide 1-phosphate (d18:1/16:0) [a,b]	$C_{34}H_{68}NO_6P$	14.2	681.4953
	31	Cardiolipin (16:1(9Z)/18:1(9Z)/16:0/16:0) [a,b]	$C_{75}H_{142}O_{17}P_2$	12.2	689.4939

	32	Cardiolipin (16:1(9Z)/18:0/16:1(9Z)/18:0) [b]	$C_{77}H_{146}O_{17}P_2$	14.2	703.5082
	33	Sphingomyelin (d18:0/14:1(9Z)(OH)) [a,b]	$C_{37}H_{73}N_2O_7P$	12.2	711.5068
	34	PA (P-18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z)) [b]	$C_{43}H_{73}O_7P$	12.2	733.5188
	35	PE (14:0/20:3(8z,11z,14z)) [b]	$C_{39}H_{72}NO_8P$	11.8	755.5323
	36	PA (20:2(11Z,14Z)/22:4(7Z,10Z,13Z,16Z)) [b]	$C_{45}H_{77}O_8P$	11.8	777.5454
	37	PC (20:4(5Z,8Z,11Z,14Z)/16:0) [b]	$C_{44}H_{80}NO_8P$	9.8	782.5704
ESI^-	1	(R)-3-Hydroxybutyric acid [b]	$C_4H_8O_3$	1.1	103.0402
	2	Ketoleucine [b]	$C_6H_{10}O_3$	4.5	129.0557
	3	Uric acid [a,b,*]	$C_5H_4N_4O_3$	1.1	167.0210
	4	D-Glucose [a,b,*]	$C_6H_{12}O_6$	1.1	201.0383
	5	Hexadecanoic acid [a]	$C_{16}H_{32}O_2$	11.8	255.2332
	6	Linoleic acid [a,b,*]	$C_{18}H_{32}O_2$	10.8	279.2335
	7	Oleic acid [a,b,*]	$C_{18}H_{34}O_2$	11.8	281.2486
	8	*p*-Cresol glucuronide [a]	$C_{13}H_{16}O_7$	5.1	283.0823
	9	Arachidonic acid [a,b,*]	$C_{20}H_{32}O_2$	10.5	303.2337
	10	5,6-Dihydroxy-8Z,11Z,14Z-eicosatrienoate [a,b]	$C_{20}H_{32}O_3$	8.1	319.2283
	11	Docosahexaenoic acid [a]	$C_{22}H_{32}O_2$	10.1	327.2338
	12	Cholesterol sulfate [b]	$C_{27}H_{46}O_4S$	14.1	465.3043
	13	LysoPC (14:0) [a]	$C_{22}H_{46}NO_7P$	7.1	512.2998
	14	Taurocholic acid [b]	$C_{26}H_{45}NO_7S$	5.8	514.2845
	15	LysoPC (P-18:0) [b]	$C_{26}H_{54}NO_6P$	8.8	552.3671
	16	LysoPC (18:1(9Z)) [a,b]	$C_{26}H_{52}NO_7P$	8.5	566.3473
	17	PA (13:0/18:4(6Z,9Z,12Z,15Z)) [b]	$C_{34}H_{59}O_8P$	9.8	607.3735

[a] Metabolites obtained from SCM *vs.* C.

[b] Metabolites obtained from SCM *vs.* CY/Ade/Arb/All.

[*] Metabolites identified by standards.

PA: Phosphatidate; PC: Phosphatidylcholine; PE: Phosphatidylethanolamine; LysoPC: Lysophosphatidylcholine; LysoPE: Lysophosphatidylethanolamine.

Suppl. Table S2

RSDs and change trends for potential biomarkers.

Mode	No.	Compound	RSDs of retention times	RSDs of peak areas	SCM *vs.* C	CY *vs.* SCM	Ade *vs.* SCM	Arb *vs.* SCM	All *vs.* SCM
ESI^{I+}	1	L-Homocysteine [a,b]	0.01	4.30	↑	↑	↑	↑	↑
	2	Betaine [b,*]	1.42	26.96	↑	↓		↓	↓
	3	Neurine [a]	0.05	15.06	↓	↑	↑	↑	↑
	4	L-Proline [a,b,*]	0.73	12.08	↑	↓			
	5	5-Aminopentanoic acid [a,b]	1.00	12.78	↓			↑	
	6	Phenylethylamine [a,b]	0.07	3.89	↓	↓	↓	↓	↓
	7	D-Leucine [b]	0.43	7.14	↓	↑	↑	↑	↑
	8	L-Adrenaline [a,b]	0.58	5.24	↓		↑	↑	
	9	L-Tyrosine [b,*]	0.45	12.77	↓		↑		
	10	L-Tryptophan [a,b,*]	0.58	21.54	↓	↑	↑	↑	↑
	11	L-Kynurenine [a,b]	0.08	30.58	↑	↓	↓	↓	↓
	12	Sphingosine [a,b]	0.09	14.81	↓	↑	↑	↑	↑
	13	Dihydrosphingosine [a,b]	0.06	2.96	↑	↑	↑	↑	↑
	14	Adenosine [b,*]	0.08	33.84	↓			↑	↑
	15	N,N-Dimethylsphingosine [a]	0.08	11.00	↑	↓	↓	↓	↓
	16	Thromboxane A2 [a,b]	0.04	9.92	↑	↓	↓	↓	↓
	17	Cholic acid [a,b,*]	0.09	38.46	↑		↑		↑
	18	Cholesteryl acetate [a,b]	0.09	40.84	↑	↑	↑	↑	↑
	19	LysoPC (15:0) [a]	0.08	10.76	↓	↑	↑	↑	↓
	20	7-a,27-Dihydroxycholesterol [b]	0.09	15.26	↓		↑		↓
	21	LysoPC (16:1(9Z)) [a]	0.08	14.90	↓	↑	↑	↑	↓
	22	LysoPC (16:0) [a,b]	0.07	8.95	↓	↑	↑	↑	↓
	23	LysoPC (18:0) [b]	0.08	14.33	↓		↑		↓
	24	LysoPE (0:0/20:0) [a,b]	0.08	18.66	↓		↑	↑	
	25	LysoPC (18:2 (9Z,12Z)) [a,b]	0.10	14.83	↓		↑	↑	↓
	26	LysoPC (0:0/18:0) [a,b]	0.07	13.42	↓	↑	↑	↑	↓
	27	LysoPE (0:0/22:0) [a]	0.12	8.61	↓	↑	↑	↑	↓
	28	LysoPC (20:4(5Z,8Z,11Z,14Z)) [a,b]	0.08	8.68	↓	↑	↑	↑	
	29	LysoPC (22:6(4Z,7Z,10Z,13Z,16Z,19Z)) [b]	0.05	20.21	↓	↑	↑		↓
	30	Ceramide 1-phosphate (d18:1/16:0) [a,b]	0.13	9.42	↓	↓	↓	↓	↓
	31	Cardiolipin (16:1(9Z)/18:1(9Z)/16:0/16:0) [a,b]	0.12	10.34	↓	↓	↓	↓	↓
	32	Cardiolipin (16:1(9Z)/18:0/16:1(9Z)/18:0) [b]	0.16	10.29	↓	↓	↓	↓	↓

	33	Sphingomyelin (d18:0/14:1(9Z)(OH)) [a,b]	0.12	6.83	↓	↓	↓	↓	↓
	34	PA (P-18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z)) [b]	0.07	10.34	↓	↓	↓	↓	↓
	35	PE (14:0/20:3(8z,11z,14z)) [b]	0.04	7.49	↓	↓	↓	↓	↓
	36	PA (20:2(11Z,14Z)/22:4(7Z,10Z,13Z,16Z)) [b]	0.06	5.16	↓	↓	↓	↓	↓
	37	PC (20:4(5Z,8Z,11Z,14Z)/16:0) [b]	0.09	16.46	↑	↓	↓		
ESI-	1	(R)-3-Hydroxybutyric acid [b]	0.23	17.18	↓			↑	
	2	Ketoleucine [b]	0.20	17.97	↓	↑			
	3	Uric acid [a,b,*]	0.34	16.35	↓	↓	↓	↓	↓
	4	D-Glucose [a,b,*]	0.29	8.88	↑	↓	↓	↓	↓
	5	Hexadecanoic acid [a]	0.07	18.75	↓	↓	↓	↓	↓
	6	Linoleic acid [a,b,*]	0.04	14.45	↓	↓	↓	↓	↓
	7	Oleic acid [a,b,*]	0.05	17.20	↓			↓	↓
	8	*p*-Cresol glucuronide [a]	0.03	15.87	↑	↓	↓	↓	↓
	9	Arachidonic acid [a,b,*]	0.03	12.03	↓			↓	
	10	5,6-Dihydroxy-8Z,11Z,14Z-eicosatrienoate [a,b]	0.04	23.27	↓	↓		↓	
	11	Docosahexaenoic acid [a]	0.04	19.55	↓	↑	↑	↑	↑
	12	Cholesterol sulfate [b]	0.22	44.18	↑	↓	↓	↓	↓
	13	LysoPC (14:0) [a]	0.11	23.92	↓	↑	↑	↑	↓
	14	Taurocholic acid [b]	0.90	24.88	↑	↓			
	15	LysoPC (P-18:0) [b]	0.08	13.70	↓				↓
	16	LysoPC (18:1(9Z)) [a,b]	0.04	10.68	↓	↑	↑	↑	↓
	17	PA (13:0/18:4(6Z,9Z,12Z,15Z)) [b]	0.09	7.47	↓			↓	↓

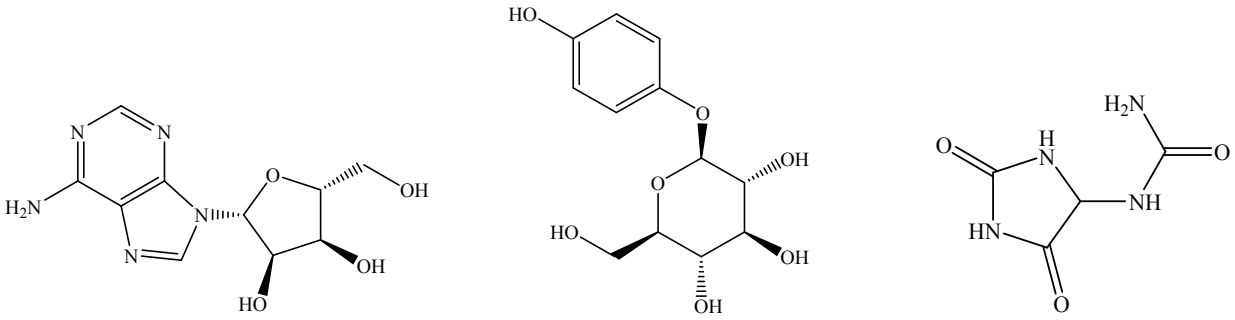
[a] Metabolites obtained from SCM *vs.* C.

[b] Metabolites obtained from SCM *vs.* CY/Ade/Arb/All.

[*] Metabolites identified by standards.

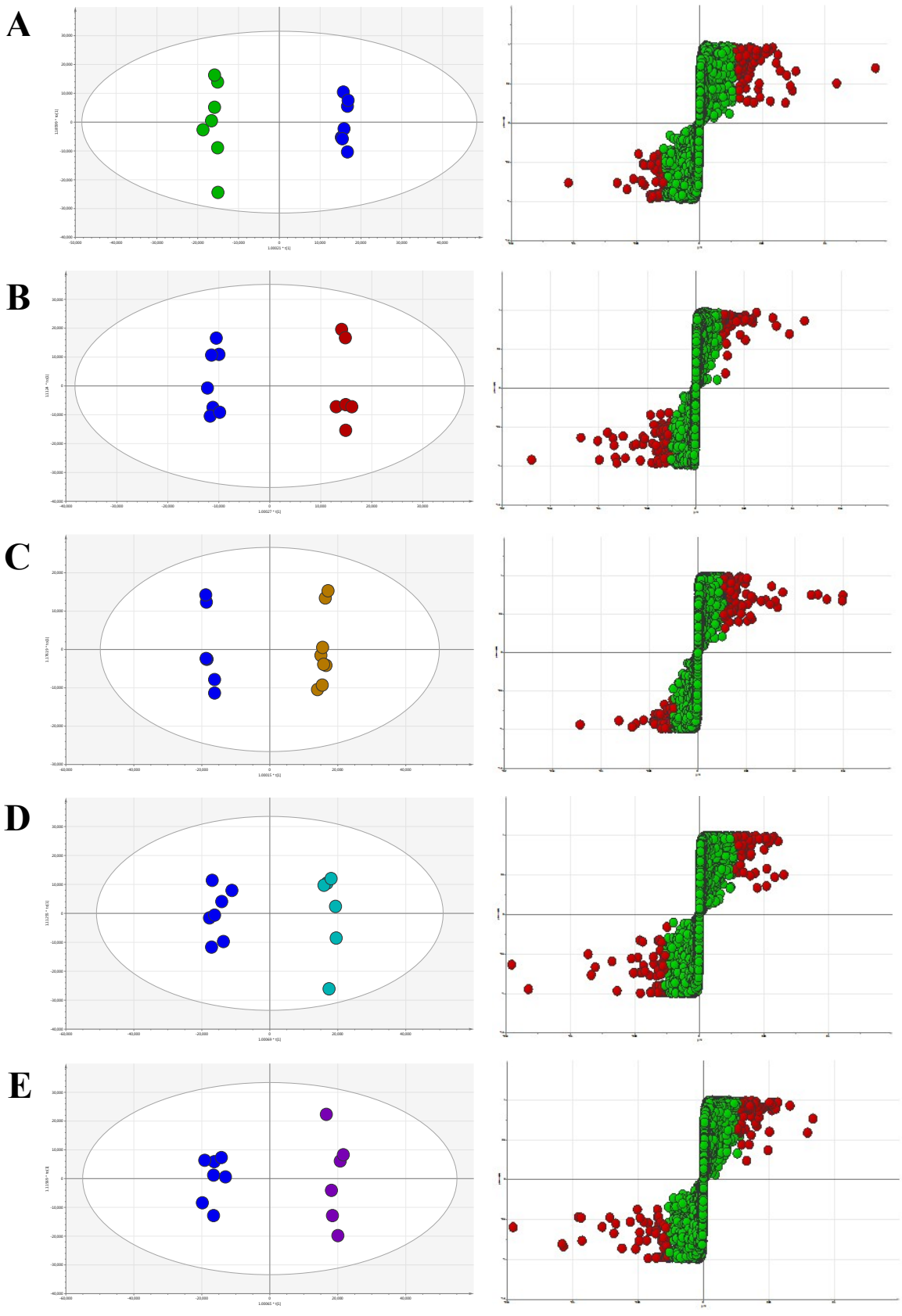
↑ up-regulated

↓ down-regulated



Adenosine **Arbutin** **Allantoin**

Suppl. Fig. S1. Chemical structures of adenosine, arbutin and allantoin.



● C group, ● SCM group, ● CY group, ● Ade group, ● Arb group, ● All group.

Suppl. Fig. S2. OPLS-DA score scatter plots and S-plots obtained from SCM and control/treatment

groups. C *vs.* SCM group (A), SCM *vs.* CY/Ade/Arb/All group (B-E).