

Supplemental Table S1. Selected reaction monitoring (SRM) conditions used for the quantification of phloretin derivatives and its generated metabolites.

Phloretin derivatives	SRM Quantification		
	Transition	Cone Voltage (V)	Collision energy (eV)
Phloretin-2'-O-glucoside	435 > 273	40	15
Phloretin-O-xylosylglucoside	567 > 273	45	15
Hydroxyphloretin-O-xylosylglucoside	583 > 289	45	15
Phloretin-O-glucuronide	449 > 273	40	20
Phloretin-O-sulphate	353 > 273	40	20
Phloretin-O-sulphate-O-glucuronide	529 > 353	40	20

Supplemental Table S2. Phloretin composition and its concentration (mg and μmol) consumed in 80 g of low-PhA snack and 80 g of high-PhA snack by the volunteers. The results are expressed as the mean \pm standard deviation ($n=6$)

Phloretin derivatives	Low-PhA snack (mg/80 g snack)	High-PhA snack (mg/80 g snack)	High-PhA vs Low-PhA snacks
Phloretin-2'-O-glucoside	8.32 \pm 2.70	21.4 \pm 4.10	2.57
Phloretin-O-xylosylglucoside	10.8 \pm 0.91	29.4 \pm 5.82	2.72
Hydroxyphloretin-O-xylosylglucoside	0.80 \pm 0.14	1.24 \pm 0.19	1.55
<i>TOTAL (mg/80 g)</i>	<i>19.9 \pm 3.76</i>	<i>52.0 \pm 10.1</i>	<i>2.61</i>
<i>TOTAL ($\mu\text{mol}/80\text{ g}$)</i>	<i>39.5 \pm 8.03</i>	<i>103 \pm 20.0</i>	<i>2.49</i>

Supplemental Table S3. Dose of macronutrients and other phytochemicals consumed in 80 g of Low-PhA snack and High-PhA snack by the volunteers. The results are expressed as the mean \pm standard deviation ($n=6$)

<i>Macronutrients and other phytochemicals</i>	Low-PhA snack	High PhA snack
Energy (Kcal)	221 \pm 1.89	188 \pm 7.49
Protein (g)	2.10 \pm 0.00	2.40 \pm 0.00
Lipids (g)	0.66 \pm 0.01	0.69 \pm 0.04
Carbohydrates (g)	73.9 \pm 0.27	74.9 \pm 0.14
Sugars from carbohydrates (g)	51.4 \pm 0.66	43.0 \pm 1.85
Total fibre (g)	11.1 \pm 1.37	13.2 \pm 0.02
Organic acids (citric, malic) (g)	2.20 \pm 0.01	2.35 \pm 0.02
Triterpenes (mg)	26.2 \pm 1.27	21.8 \pm 3.61

Supplemental Table S4. Stratification of a) phloretin-O-glucuronide, b) phloretin-O-sulphate, and c) phloretin-O-sulphate-O-glucuronide after the sustained intake of high-PhA Snack. In addition to the sustained intake, the volunteers from H1 to H8 also participated in the two acute studies: days 0 and 42 before and after the sustained intake.

a) Phloretin-O-glucuronide

n°	Volunteer	Producers ($\mu\text{mol}/24\text{ h}$)			
		All	High	Medium	Low
1	34 (H1)	4.88	4.88		
2	35	2.27	2.27		
3	36	0.86		0.86	
4	37 (H2)	0.84		0.84	
5	38 (H3)	2.48	2.48		
6	39 (H4)	0.00			0.00
7	40	1.60		1.60	
8	41	3.22	3.22		
9	42 (H5)	3.28	3.28		
10	43	0.00			0.00
11	44	1.24		1.24	
12	45	0.00			0.00
13	46	0.76		0.76	
14	47	2.47	2.47		
15	48	0.00			0.00
16	49 (H6)	0.83		0.83	
17	50	0.00			0.00
18	51	2.15		2.15	
19	52	1.52		1.52	
20	53	2.76	2.76		
21	54 (H7)	2.90	2.90		
22	55	0.70			0.70
23	56	1.86		1.86	
24	57 (H8)	2.98	2.98		
25	58	0.58			0.58
26	59	2.16		2.16	
27	60	1.35		1.35	
28	61	0.00			0.00
29	62	0.21			0.21
	Mean	1.51 ^b	3.03 ^c	1.38 ^b	0.17 ^a
	SEM	0.24	0.26	0.16	0.09
	<i>n</i>	29	9	11	9

b) Phloretin-O-sulphate

n°	Volunteer	Producers (µmol/24 h)			
		All	High	Medium	Low
1	34 (H1)	0.84	0.84		
2	35	0.53	0.53		
3	36	0.15			0.15
4	37 (H2)	0.17		0.17	
5	38 (H3)	0.17		0.17	
6	39 (H4)	0.25		0.25	
7	40	0.13			0.13
8	41	0.24		0.24	
9	42 (H5)	0.51	0.51		
10	43	0.28		0.28	
11	44	0.25		0.25	
12	45	0.11			0.11
13	46	0.43	0.43		
14	47	0.52	0.52		
15	48	0.10			0.10
16	49 (H6)	0.12			0.12
17	50	0.30		0.30	
18	51	0.39	0.39		
19	52	0.50	0.50		
20	53	0.46	0.46		
21	54 (H7)	0.42	0.42		
22	55	0.19		0.19	
23	56	0.21		0.21	
24	57 (H8)	0.28		0.28	
25	58	0.09			0.09
26	59	0.24		0.24	
27	60	0.11			0.11
28	61	0.18		0.18	
29	62	0.08			0.08
	Mean	0.28 ^b	0.51 ^c	0.23 ^{a,b}	0.11 ^a
	SEM	0.03	0.04	0.01	0.01
	<i>n</i>	29	9	12	8

c) phloretin-*O*-sulphate-*O*-glucuronide

n°	Volunteer	Producers (µmol/24 h)			
		All	High	Medium	Low
1	34 (H1)	0.38	0.38		
2	35	0.52	0.52		
3	36	0.20		0.20	
4	37 (H2)	0.19		0.19	
5	38 (H3)	0.15		0.15	
6	39 (H4)	0.00			0.00
7	40	0.01			0.01
8	41	0.16		0.16	
9	42 (H5)	0.36	0.36		
10	43	0.00			0.00
11	44	0.16		0.16	
12	45	0.05			0.05
13	46	0.30	0.30		
14	47	0.14		0.14	
15	48	0.00			0.00
16	49 (H6)	0.11		0.11	
17	50	0.00			0.00
18	51	0.30	0.30		
19	52	0.29	0.29		
20	53	0.14		0.14	
21	54 (H7)	0.41	0.41		
22	55	0.00			0.00
23	56	0.25	0.25		
24	57 (H8)	0.25	0.25		
25	58	0.11		0.11	
26	59	0.20		0.20	
27	60	0.23		0.23	
28	61	0.00			0.00
29	62	0.07			0.07
	Mean	0.17 ^b	0.34 ^c	0.16 ^b	0.01 ^a
	SEM	0.03	0.03	0.01	0.01
	<i>n</i>	29	9	11	9

Supplemental Table S5. Stratification of a) phloretin-*O*-glucuronide, b) phloretin-*O*-sulphate, and c) phloretin-*O*-sulphate-*O*-glucuronide after the first acute intake of high-PhA Snack.

a) Phloretin-*O*-glucuronide

n°	Volunteer	Producers (µmol/24 h)		
		All	High	Low
1	H1	3.34		3.34
2	H2	2.11		2.11
3	H3	1.17		1.17
4	H4	5.86	5.86	
5	H5	3.08		3.08
6	H6	4.83	4.83	
7	H7	3.47	3.47	
8	H8	3.67	3.67	
	Mean	3.44 ^{a,b}	4.46 ^b	3.44 ^a
	SEM	0.52	0.56	0.52
	<i>n</i>	8	4	4

b) Phloretin-*O*-sulphate

n°	Volunteer	Producers (µmol/24 h)		
		All	High	Low
1	H1	1.17	1.17	
2	H2	0.08		0.08
3	H3	0.12		0.12
4	H4	0.74	0.74	
5	H5	1.06	1.06	
6	H6	0.92	0.92	
7	H7	0.69		0.69
8	H8	0.35		0.35
	Mean	0.64 ^{a,b}	0.97 ^b	0.31 ^a
	SEM	0.15	0.09	0.14
	<i>n</i>	8	4	4

c) Phloretin-*O*-sulphate-*O*-glucuronide

n°	Volunteer	Producers (µmol/24 h)		
		All	High	Low
1	H1	1.37	1.37	
2	H2	0.33		0.33
3	H3	0.15		0.15
4	H4	1.09	1.09	
5	H5	0.89	0.89	
6	H6	0.83	0.83	
7	H7	0.72		0.72
8	H8	0.30		0.30
	Mean	0.71 ^{a,b}	1.05 ^b	0.38 ^a
	SEM	0.15	0.12	0.12
	<i>n</i>	8	4	4

Supplemental Table S6. Percent absorption of the native phloretin-O-xylosylglucoside, phloretin-O-glucuronide, phloretin-O-sulphate, and phloretin-O-sulphate-O-glucuronide and its total phase-II conjugates after the sustained intake of low- and high-PhA snack. In addition to the sustained intake, the volunteers from L1 to L7 also participated in the two acute studies: days 0 and 42 before and after the sustained intake of low-PhA snack, and H1 to H8 after the sustained intake of high-PhA snack.

Volunteer	Excretion					Percent Absorption				
	µmol/24 h									
	PhXG	PhG	PhS	PhSG	Total	PhXG	PhG	PhS	PhSG	Total
Low-PhA snack										
<i>Low excretor</i>										
1	n.d.	n.d.	0.17	n.d.	0.17	0	0	0.43	0	0.43
2	n.d.	n.d.	0.73	0.23	0.96	0	0	1.85	0.58	2.43
11	n.d.	n.d.	0.08	0.08	0.16	0	0	0.20	0.20	0.41
15 (L5)	n.d.	n.d.	0.21	n.d.	0.21	0	0	0.53	0	0.53
21	n.d.	0.21	0.21	0.21	0.63	0	0.53	0.53	0.53	1.59
22	n.d.	n.d.	0.23	n.d.	0.23	0	0	0.58	0	0.58
24	n.d.	n.d.	0.12	n.d.	0.12	0	0	0.30	0	0.30
25	n.d.	0.18	0.07	n.d.	0.25	0	0.46	0.18	0	0.63
26	n.d.	n.d.	0.13	n.d.	0.13	0	0	0.33	0	0.33
29	n.d.	0.05	0.12	0.01	0.18	0	0.13	0.30	0.03	0.46
32	n.d.	n.d.	0.15	n.d.	0.15	0	0	0.38	0	0.38
<i>Medium excretor</i>										
6	n.d.	0.54	0.36	n.d.	0.90	0	1.37	0.91	0	2.28
8	n.d.	0.86	0.27	0.22	1.35	0	2.18	0.68	0.56	3.42
10 (L4)	n.d.	0.90	0.45	0.35	1.70	0	2.28	1.14	0.89	4.30
13	n.d.	0.62	0.34	0.17	1.13	0	1.57	0.86	0.43	2.86
16	n.d.	0.39	0.08	0.16	0.63	0	0.99	0.20	0.41	1.59
23	n.d.	0.42	0.10	n.d.	0.52	0	1.06	0.25	0	1.32
27	n.d.	0.26	0.25	0.02	0.53	0	0.66	0.63	0.05	1.34
28	n.d.	0.40	0.24	0.18	0.82	0	1.01	0.61	0.46	2.08
30	n.d.	0.69	0.38	0.08	1.15	0	1.75	0.96	0.20	2.91
31	n.d.	0.93	0.09	0.37	1.39	0	2.35	0.23	0.94	3.52
33	n.d.	0.22	0.17	0.07	0.46	0	0.56	0.43	0.18	1.16
<i>High excretor</i>										
3	n.d.	1.24	0.13	0.17	1.54	0	3.14	0.33	0.43	3.90
4 (L1)	n.d.	0.97	n.d.	0.18	1.15	0	2.46	0	0.46	2.91
5 (L2)	n.d.	1.15	0.15	0.16	1.46	0	2.91	0.38	0.41	3.70
7	n.d.	1.62	0.16	n.d.	1.78	0	4.10	0.41	0	4.51
9 (L3)	n.d.	1.28	0.26	0.19	1.73	0	3.24	0.66	0.48	4.38
12	n.d.	2.24	0.25	0.25	2.74	0	5.67	0.63	0.63	6.94
14	n.d.	0.95	n.d.	n.d.	0.95	0	2.41	0	0	2.41
17 (L6)	n.d.	1.26	0.16	n.d.	1.42	0	3.19	0.41	0	3.59
18	n.d.	1.45	0.24	0.19	1.88	0	3.67	0.61	0.48	4.76
19	n.d.	1.08	n.d.	0.14	1.22	0	2.73	0	0.35	3.09
20 (L7)	n.d.	1.62	0.10	0.13	1.85	0	4.10	0.25	0.33	4.68
High-PhA snack										
<i>Low excretor</i>										
39 (H4)	n.d.	n.d.	0.25	n.d.	0.25	0	0	0.24	0	0.24
43	n.d.	n.d.	0.28	n.d.	0.28	0	0	0.27	0	0.27
45	n.d.	n.d.	0.11	0.05	0.16	0	0	0.11	0.05	0.16
48	n.d.	n.d.	0.10	n.d.	0.10	0	0	0.10	0	0.10
50	n.d.	n.d.	0.30	n.d.	0.30	0	0	0.29	0	0.29
55	n.d.	0.70	0.19	n.d.	0.89	0	0.68	0.18	0	0.86
58	n.d.	0.58	0.09	0.11	0.78	0	0.56	0.09	0.11	0.76
61	n.d.	n.d.	0.18	n.d.	0.18	0	0	0.17	0	0.17
62	n.d.	0.21	0.08	0.07	0.36	0	0.20	0.08	0.07	0.35
<i>Medium excretor</i>										
36	0	0.86	0.15	0.20	1.21	0.00	0.83	0.15	0.19	1.17
37 (H2)	n.d.	0.84	0.17	0.19	1.20	0	0.82	0.17	0.18	1.17
40	n.d.	1.60	0.13	0.01	1.74	0	1.55	0.13	0.01	1.69
44	n.d.	1.24	0.25	0.16	1.65	0	1.20	0.24	0.16	1.60
46	0.01	0.76	0.43	0.30	1.50	0.01	0.74	0.42	0.29	1.46
49 (H6)	n.d.	0.83	0.12	0.11	1.06	0	0.81	0.12	0.11	1.03
51	0.01	2.15	0.39	0.30	2.85	0.01	2.09	0.38	0.29	2.77
52	0.01	1.52	0.50	0.29	2.32	0.01	1.48	0.49	0.28	2.25

56	0.02	1.86	0.21	0.25	2.34	0.02	1.81	0.20	0.24	2.27
59	0.02	2.16	0.24	0.20	2.62	0.02	2.10	0.23	0.19	2.54
60	n.d.	1.35	0.11	0.23	1.69	0	1.31	0.11	0.22	1.64
<i>High excretor</i>										
34 (H1)	0.02	4.88	0.84	0.38	6.12	0.02	4.74	0.82	0.37	5.94
35	0.01	2.27	0.53	0.52	3.33	0.01	2.20	0.51	0.50	3.23
38 (H3)	n.d.	2.48	0.17	0.15	2.80	0	2.41	0.17	0.15	2.72
41	n.d.	3.22	0.24	0.16	3.62	0	3.13	0.23	0.16	3.51
42 (H5)	n.d.	3.28	0.51	0.36	4.15	0	3.18	0.50	0.35	4.03
47	n.d.	2.47	0.52	0.14	3.13	0	2.40	0.50	0.14	3.04
53	n.d.	2.76	0.46	0.14	3.36	0	2.68	0.45	0.14	3.26
54 (H7)	0.004	2.90	0.42	0.41	3.73	0.00	2.82	0.41	0.40	3.63
57 (H8)	0.02	2.98	0.28	0.25	3.53	0.02	2.89	0.27	0.24	3.43
