

**Daily consumption of cranberry improves endothelial function in healthy adults: a double blind randomized controlled trial**

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2 **Supplemental Table S1:** Mean habitual baseline daily intake of total energy, macro-  
3 , and micronutrients.<sup>1</sup>

<b>Macro- &amp; micronutrients (/day)</b>	<b>Cranberry (n=22)</b>	<b>Control (n=22)</b>	<b>p<sup>2</sup></b>
Total energy, kJ	6,149 ± 1,648	7,238 ± 3,698	0.21
Carbohydrate, g	159 ± 43	191 ± 104	>0.99
Total sugars, g	77 ± 23	90 ± 41	>0.99
Dietary fibre, g	10 ± 3	13 ± 7	>0.99
Protein, g/Kg body weight	0.9 ± 0.3	1.0 ± 0.5	>0.99
Total fat, g	63 ± 22	72 ± 39	>0.99
Saturated fatty acids, g	25 ± 9	28 ± 16	>0.99
Monounsaturated fatty acids, g	22 ± 7	26 ± 14	>0.99
Polyunsaturated fatty acids, g	10 ± 4	11 ± 6	>0.99
Cholesterol, mg	263 ± 146	340 ± 160	>0.99
Alcohol, g	5.4 ± 4.7	5.1 ± 4.5	>0.99
Sodium, mg	1,846 ± 428	2,196 ± 1,483	>0.99
Potassium, mg	2,460 ± 515	3,075 ± 1,240	0.25
Chloride, mg	2,808 ± 623	3,316 ± 2,198	0.78
Calcium, mg	788 ± 304	892 ± 499	>0.99
Iron, mg	8 ± 2	9 ± 5	>0.99
Vitamin A, µg	449 ± 308	729 ± 1,035	>0.99
Vitamin C, mg	67 ± 29	81 ± 44	>0.99
Vitamin D, µg	2.4 ± 1.6	2.5 ± 1.8	>0.99
Vitamin E, mg	8.0 ± 2.6	9.5 ± 4.4	>0.99

4 <sup>1</sup>Values are mean ± SD; ND: not defined.

5 <sup>2</sup>Independent samples t-test

7 **Supplemental Table S2:** Baseline (poly)phenol intake of population. Results are  
 8 presented as mean  $\pm$  SD.

<b>(Poly)phenol (mg/d)</b>	<b>Cranberry (n=23)</b>	<b>Placebo (n=21)</b>	<b>p-value</b>
Total polyphenols	802 $\pm$ 549	1,278 $\pm$ 1,125	ns
Flavonoids	190 $\pm$ 211	165 $\pm$ 157	ns
Anthocyanins	4.22 $\pm$ 3.43	5.60 $\pm$ 9.93	ns
Chalcones	0.00 $\pm$ 0.00	0.00 $\pm$ 0.00	ns
Dihydrochalcones	0.26 $\pm$ 0.46	0.26 $\pm$ 0.31	ns
Dihydroflavonols	0.07 $\pm$ 0.07	0.04 $\pm$ 0.06	ns
Flavanols	87 $\pm$ 145	73 $\pm$ 106	ns
Flavanol monomers	61 $\pm$ 121	48 $\pm$ 89	ns
Proanthocyanidins	26 $\pm$ 27	25 $\pm$ 21	ns
Theaflavins	14 $\pm$ 30	11 $\pm$ 22	ns
Flavanones	19 $\pm$ 19	21 $\pm$ 21	ns
Flavones	14 $\pm$ 10	10 $\pm$ 7	ns
Flavonols	32 $\pm$ 31	34 $\pm$ 26	ns
Isoflavones	1.8 $\pm$ 3.8	0.6 $\pm$ 1.1	ns
Phenolic acids	590 $\pm$ 546	1,089 $\pm$ 1,030	ns
Hydroxybenzoic acids	26 $\pm$ 39	25 $\pm$ 29	ns
Hydroxycinnamic acids	564 $\pm$ 581	1020 $\pm$ 1085	ns
Hydroxyphenylacetic acids	0.08 $\pm$ 0.08	0.09 $\pm$ 0.08	ns
Hydroxyphenylpropanoic acids	0 $\pm$ 0	0 $\pm$ 0	ns

Lignans	21	±	11	23	±	20	ns
Stilbenes	0.1	±	0.1	0.1	±	0.1	ns
Alkylmethoxyphenols	2.0	±	2.1	3.6	±	3.8	ns
Catechols	0.01	±	0.01	0.01	±	0.01	ns
Hydroxybenzaldehydes	0.002	±	0.002	0.002	±	0.002	ns
Hydroxybenzoketones	0.08	±	0.07	0.08	±	0.08	ns
Hydroxycoumarins	0.27	±	0.30	0.50	±	0.56	ns
Methoxyphenols	0.63	±	0.68	0.54	±	0.55	ns
Pyrogallols	802	±	549	1278	±	1125	ns
Tyrosols	190	±	211	165	±	157	ns

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10 **Supplemental Table S3:** List of 137 (poly)phenols / metabolites analyzed in plasma  
 11 and urine. Green designates metabolites that were detected and analysed, red not  
 12 detected and not analysed and yellow detected but not analysed as only detected in  
 13 traces in individual samples.

	Plasma	Urine		Plasma	Urine
<b>Hippuric acids</b>			<b>Flavonols</b>		
Hippuric acid			Kaempferol		
2-(Benzoylamino)-2-hydroxyacetic acid (α-Hydroxyhippuric acid)			Quercetin		
2-Hydroxyhippuric acid			Kaempferol-3-O-β-D-glucuronide		
3'-Hydroxyhippuric acid			Quercetin-3-sulfate		
4'-Hydroxyhippuric acid			Quercetin-7-O-β-D-glucuronide		
<b>Benzoic acids</b>			<b>Phenyl-γ-valerolactones and phenylvaleric acids</b>		
Benzoic acid			5-(Phenyl)-γ-valerolactone-sulfate-glucuronide isomer (3',4')		
2,3-Dihydroxybenzoic acid			5-(Phenyl)-γ-valerolactone-4'-glucuronide		
2,5-Dihydroxybenzoic acid			5-(4'-Hydroxyphenyl)-γ-valerolactone-3'-glucuronide		
2-Hydroxybenzoic acid			5-(3'-Hydroxyphenyl)-γ-valerolactone-4'-glucuronide		
3-Hydroxybenzoic acid			5-(3',5'-Dihydroxyphenyl)-γ-valerolactone		
4-Hydroxybenzoic acid			5-(3',4'-Dihydroxyphenyl)-γ-valerolactone		
3,4-Dihydroxybenzoic acid (Protocatechuic acid)			5-(Phenyl)-γ-valerolactone-3'-glucuronide		
3-Methoxybenzoic acid-4-sulfate (Vanillic acid-4-O-sulfate)			5-(5'-Hydroxyphenyl)-γ-valerolactone-3'-sulfate		
3-Hydroxybenzoic acid-4-sulfate (Protocatechuic acid-4-O-sulfate)			5-(Hydroxyphenyl)-γ-valerolactone-sulfate (3',4' isomers)		
4-Hydroxybenzoic acid-3-sulfate (Protocatechuic acid-3-O-sulfate)			5-(Phenyl)-γ-valerolactone-4'-sulfate		
4-Hydroxy-3-methoxybenzoic acid (Vanillic acid)			5-(Phenyl)-γ-valerolactone-3'-sulfate		
3-Hydroxy-4-methoxybenzoic acid (Isovanillic acid)			5-(Methoxyphenyl)-γ-valerolactone-sulfate isomer (3',4')		
3,4,5-Trihydroxybenzoic acid (Gallic acid)			5-(Phenylvaleric acid-sulfate-glucuronide isomer		
4-Hydroxybenzoic acid-3-glucuronide (Protocatechuic acid-3-O-β-D-glucuronide)			5-(3'-Methoxyphenyl)-γ-valerolactone		
3-Hydroxy-4-methoxybenzoic acid-5-sulfate (4-Methylgallic acid-3-O-sulfate)			5-(4'-Methoxyphenyl)-γ-valerolactone		
4-Hydroxy-3,5-dimethoxybenzoic acid (Syringic acid)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone (3',4')		
<b>Cinnamic acids</b>			<b>5-(Hydroxy-methoxyphenyl)-γ-valerolactone-3'-glucuronide isomer (3',4')</b>		
4'-Hydroxy-3'-methoxycinnamic acid (Ferulic acid)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone (3',5')		
3'-Hydroxy-4'-methoxycinnamic acid (Isoferulic acid)			5-(Dihydroxy-methoxyphenyl)-γ-valerolactone (3',4',5')		
3',4'-Dihydroxycinnamic acid (Caffeic acid)			5-(Methoxyphenyl)-γ-valerolactone-sulfate (3',4') isomer 2		
5-O-Caffeoylquinic acid (Chlorogenic acid)			5-(Methoxyphenyl)-γ-valerolactone-sulfate (3',5') isomer 1		
4'-Hydroxycinnamic acid (p-Coumaric acid)			5-(Methoxyphenyl)-γ-valerolactone-sulfate (3',5') isomer 2		
2'-Hydroxycinnamic acid (o-Coumaric acid)			5-(Dihydroxyphenyl)-γ-valerolactone-sulfate (3',4',5')		
3'-Hydroxycinnamic acid (m-Coumaric acid)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone-sulfate (3',4',5') isomer 1		
3-Methoxycinnamic acid-4'-glucuronide (Ferulic acid 4-O-β-D-glucuronide)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone-sulfate (3',4',5') isomer 2		
3-Methoxycinnamic acid-4'-sulfate (Ferulic acid 4-O-sulfate)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone-sulfate (3',4',5') isomer 3		
4-Methoxycinnamic acid-3'-glucuronide (Isoferulic acid 3-O-β-D-glucuronide)			5-(5'-Hydroxyphenyl)-γ-valerolactone-3'-glucuronide		
4-Methoxycinnamic acid-3'-sulfate (Isoferulic acid 3-O-sulfate)			5-(Methoxyphenyl)-γ-valerolactone-glucuronide isomer (3',4')		
4-Hydroxycinnamic acid-3'-glucuronide (Caffeic acid 3-O-β-D-glucuronide)			5-(Methoxyphenyl)-γ-valerolactone-glucuronide isomer (3',5')		
3'-Hydroxycinnamic acid-4'-glucuronide (Caffeic acid 4-O-β-D-glucuronide)			5-(Dihydroxyphenyl)-γ-valerolactone-glucuronide (3',4',5')		
3'-Hydroxycinnamic acid-4'-sulfate (Caffeic acid 4-O-sulfate)			5-(Hydroxy-methoxyphenyl)-γ-valerolactone-glucuronide (3',4',5')		
Cinnamic acid-4'-glucuronide (p-Coumaric acid 4-O-β-D-glucuronide)			5-(Phenyl)-γ-valerolactone-sulfate-glucuronide isomer (3',4',5')		
4'-Hydroxy-3',5'-dimethoxycinnamic acid (Sinapic acid)			5-(Hydroxyphenyl)-γ-valerolactone-sulfate-glucuronide (3',4',5')		
<b>Phenylacetic acids</b>			<b>4-Hydroxy-5-(phenylvaleric acid</b>		
Phenylacetic acid			5-(Methoxyphenyl)valeric acid		
3'-Hydroxyphenylacetic acid			5-(3',4'-dihydroxyphenyl)valeric acid		
4'-Hydroxyphenylacetic acid			4-Hydroxy-5-(hydroxyphenyl)valeric acid		
3',4'-Dihydroxyphenylacetic acid			5-(Hydroxy-methoxyphenyl)valeric acid		
4'-Hydroxy-3'-methoxyphenylacetic acid (Homovanillic acid)			4-Hydroxy-5-(3',4'-dihydroxyphenyl)valeric acid		
3'-Methoxyphenylacetic acid-4'-sulfate (Homovanillic acid sulfate)			4-Hydroxy-5-(hydroxy-methoxyphenyl)valeric acid		
<b>Phenylpropanoic acids</b>			<b>4-Hydroxy-5-(3',4',5'-trihydroxyphenyl)valeric acid</b>		
3-(4'-Hydroxyphenyl)propanoic acid			4-Hydroxy-5-(dihydroxy-methoxyphenyl)valeric acid (3',4',5')		
3-(3'-Hydroxyphenyl)propanoic acid			5-(Phenylvaleric acid-sulfate		
2-(4'-Hydroxyphenoxy)propanoic acid			5-(Hydroxyphenyl)valeric acid-sulfate		
3-(4'-Hydroxy-3'-methoxyphenyl)propanoic acid (Dihydroferulic acid)			4-Hydroxy-5-(phenylvaleric acid-sulfate		
3-(3',4'-Dihydroxyphenyl)propanoic acid (Dihydrocaffeic acid)			5-(Methoxyphenyl)valeric acid-sulfate		
3-(3'-Methoxyphenyl)propanoic acid-4'-glucuronide (Dihydroferulic acid 4-O-β-D-glucuronide)			4-Hydroxy-5-(hydroxyphenyl)valeric acid-sulfate isomer (3',4')		
3-(4'-Methoxyphenyl)propanoic acid-3'-sulfate (Dihydro ferulic acid 3-O-sulfate)			4-Hydroxy-5-(hydroxyphenyl)valeric acid-sulfate isomer (3',5')		
3-(3'-Methoxyphenyl)propanoic acid-4'-sulfate (Dihydroferulic acid 4-O-sulfate)			4-Hydroxy-5-(methoxyphenyl)valeric acid-sulfate		
3-(4'-Methoxyphenyl)propanoic acid-3'-glucuronide (Dihydro isoferulic acid 3-O-β-D-glucuronide)			4-Hydroxy-5-(dihydroxyphenyl)valeric acid-sulfate (3',4',5')		
3-(4'-Hydroxyphenyl)propanoic acid-3'-sulfate (Dihydrocaffeic acid 3-O-sulfate)			4-Hydroxy-5-(hydroxy-methoxyphenyl)valeric acid-sulfate (3',4',5')		
3-(4'-Hydroxyphenyl)propanoic acid-3'-glucuronide (Dihydrocaffeic acid 3-O-β-D-glucuronide)			5-(Phenylvaleric acid-disulfate		
3-(3'-Hydroxy-4'-methoxyphenyl)propanoic acid (Dihydroisoferrulic acid)			5-(Phenylvaleric acid-glucuronide isomer 1		
<b>Benzaldehydes</b>			<b>5-(Phenylvaleric acid-glucuronide isomer 2</b>		
3-Hydroxybenzaldehyde			4-Hydroxy-5-(phenylvaleric acid-disulfate		
4-Hydroxybenzaldehyde			4-Hydroxy-5-(phenylvaleric acid-glucuronide		
3,4-Dihydroxybenzaldehyde			5-(Methoxyphenyl)valeric acid-glucuronide		
<b>Benzene diols and triols</b>			<b>4-Hydroxy-5-(hydroxyphenyl)valeric acid-glucuronide isomer (3',4')</b>		
2-Hydroxybenzene-1-sulfate (Catechol-O-sulfate)			4-Hydroxy-5-(hydroxyphenyl)valeric acid-glucuronide isomer (3',5')		
2-Hydroxybenzene-1-glucuronide (Catechol-O-1-glucuronide)			4-Hydroxy-5-(dihydroxyphenyl)valeric acid-disulfate (3',4',5')		
2-Hydroxy-4-methylbenzene-1-sulfate/2-Hydroxy-5-methylbenzene-1-sulfate (4-Methylcatechol-1-sulfate/4-Methylcatechol-2-sulfate)			4-Hydroxy-5-(dihydroxyphenyl)valeric acid-glucuronide		
5,6-Dihydroxybenzene-1-sulfate (Pyrogallol-1-O-sulfate)			4-Hydroxy-5-(dihydroxyphenyl)valeric acid-glucuronide (3',4',5')		
3-Hydroxy-2-methoxybenzene-1-sulfate (2-Methylpyrogallol-1-sulfate)			5-(Phenylvaleric acid-sulfate-glucuronide isomer 2		
2,6-Dihydroxybenzene-1-sulfate (Pyrogallol-2-O-sulfate)			4-Hydroxy-5-(phenylvaleric acid-sulfate-glucuronide		
2-Hydroxy-5-methoxybenzene-1-sulfate/3-Hydroxy-2-methoxybenzene-1-sulfate (1-Methylpyrogallol-2-sulfate/2-Methylpyrogallol-1-sulfate)			4-Hydroxy-5-(hydroxyphenyl)valeric acid-sulfate-glucuronide (3',4',5')		
			5-(Phenylvaleric acid-digluconide		
			4-Hydroxy-5-(phenylvaleric acid-digluconide		
Plasma Urine					
<b>Deleted and quantified</b>					
56 74					
<b>Deleted but not quantified as only present in traces in just few samples</b>					
8 5					
<b>Not detected and not quantified</b>					
71 58					
<b>Total analysed</b>					
137 137					

14

15



23 **Supplemental TABLE S5** Analysis of 74 (poly)phenol metabolites detected in 24 h urine samples after consumption of cranberry  
24 or placebo. Data are expressed as total  $\mu\text{mol}$  collected over 24 h, after adjusted for volume of urine excreted. Differences represent  
25 mean estimated effect of cranberry over control and 95% confidence intervals. Statistical analyses are based on repeated  
26 measurements analysis of covariance.



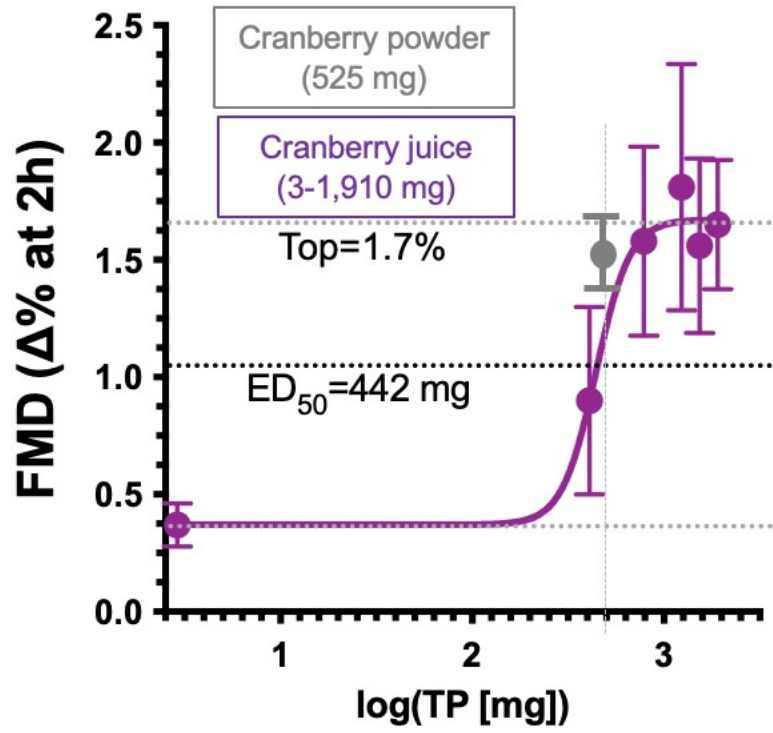


## 28 **SUPPLEMENTAL FIGURE LEGENDS**

29 **Supplemental Figure S1:** Dose-response between total cranberry polyphenols  
30 consumed with cranberry juice. The amount of total (poly)phenols (TP) to be  
31 consumed to achieve half-maximal effects ( $ED_{50}$ ) at 2 h after consumption was 442  
32 mg (based on data previously published in (18)). The grey dotted lines designate the  
33 top (1.7%) and bottom of the best fit curve. The grey symbol indicates 2h increase  
34 with cranberry powder in present study.

36

37 Supplemental FIGURE S1



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