Authentic human data for C_6–C_5 metabolites in urine, plasma, ileal fluid and feces

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Introduction

This document is a compilation of published quantitative data obtained with authentic calibrants for the concentrations of C_6–C_5 metabolites (i.e. 5-phenylvaleric acids, 4-hydroxy-5-hydroxyphenylvaleric acids, phenylvalerolactones and the associated phase-2 conjugates) in human urine, plasma, ileal fluid and feces. The originating publications were identified by searching Web of Science, PubMed and Google Scholar up to May 2024.

Data originally reported on a mass/day or mass/volume basis have been converted to a molar basis to facilitate comparisons, but some published data were excluded from these tables:

(i) Data originally reported relative to creatinine, the standard clinical practice with spot plasma and urine samples, cannot be accurately converted to a molar basis because creatinine production varies with sex, age and protein intake.

(ii) Data produced by acid or enzymic hydrolysis of phase-2 conjugates have not been tabulated except for glycine or glutamine conjugates when β-glucuronidase and sulfatase hydrolysis has been used.

Similar compilations have been prepared for C_6–C_1 metabolites (benzoic acids), C_6–C_2 metabolites (phenylacetic acids) and C_6–C_3 metabolites (3-phenylpropanoic acids and cinnamic acids) and the metabolites have been identified using the nomenclature recommended by Kay *et al*. (Kay et al. 2020) and are numbered consecutively in a single series through the five documents.

Table 1. 5-(3′,5′-dihydroxyphenyl)valeric acid											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		2.4 ± 0.4 [a]							Mean ± s.e. *N*=6 men. Wheat bread 61 mg alkyl-resorcinols	(Zhu et al. 2014)	6
		1.2 ± 0.3 [a]							Mean ± s.e. *N*=6 women. Wheat bread 61 mg alkyl-resorcinols		6
										1	12

Notes: a) 32-hour urine collection

Table 2. 4*R/S*-hydroxy- 5-(3′,4′-dihydroxyphenyl)valeric acid											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		Ca 2 ± 1 [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										1	13

Notes: a) Read from published graph. 36-Hours urine collection

Table 3. 4*R/S*-5-(Phenyl)-γ-valerolactone-3′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	**nmol/24 hours**	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		1.7 ± 0.5 [a]							Mean ± s.e., *N*=2. Theaflavin extract (998 µmol)	(Pereira-Caro et al. 2017)	2
		1.01 ± 0.88							Mean ± s.e., *N*-10. Cranberry juice dose response 375 mg	(Favari et al. 2020)	10
		0.58 ± 0.33							Mean ± s.e., *N*-10. Cranberry juice dose response 716 mg		10
		1.69 ± 1.69							Mean ± s.e., *N*-10. Cranberry juice dose response 1131 mg		10
		0.87 ± 0.45							Mean ± s.e., *N*-10. Cranberry juice dose response 1396 mg		10
		0.88 ± 0.53							Mean ± s.e., *N*-10. Cranberry juice dose response 1741 mg		10
		11230 ± 15380 **(7020)**							Mean ± s.d., *N*=11. Apples 5.8 mmol flavanols and proanthocyanidins	(Anesi et al. 2019)	11
	0.069 ± 0.025	10370 ± 2200 [c]	Three days	traces	?				Red grape pomace (1.5 g total polyphenols) (Mean ± s.e., *N*=10)	(Castello et al. 2018)	10
	0.0004 ± 0.0002								Mean ± s.e., *N*=20 ??? Capsules prepared from 36 commodities	(Bresciani et al. 2017)	20
0.019 (0.006–0.321)									Mean (min–max) *N*=104 Free-living individuals	(Angelino et al. 2023)	104
0.008 (0.002–0.200)									Mean (min–max) *N*=114 Free-living individuals	(Angelino et al. 2023)	114
		100 ± 0 day 1 100 ± 0 at 1 month	2-day including	0.0014 ± 0.0008					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22

			over-night fast								
		200 ± 100 day 1 200 ± 100 at 1 month	2-day including over-night fast	0.0013 ± 0.0005					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
										7	356

Notes: a) 30-hours urine collection

b) Median calculated from published data. Pearson coefficient 0.82

c) Urine collection 48-hours

Table 4. 4*R/S*-5-(phenyl)-γ-valerolactone-4′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	**nmol/24 hours**	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		0.13 ± 0.09							Mean ± s.e., *N*-10. Cranberry juice dose response 375 mg	(Favari et al. 2020)	10
		0.42 ± 0.24							Mean ± s.e., *N*-10. Cranberry juice dose response 716 mg		10
		0.60 ± 0.43							Mean ± s.e., *N*-10. Cranberry juice dose response 1131 mg		10
		0.23 ± 0.12							Mean ± s.e., *N*-10. Cranberry juice dose response 1396 mg		10
		0.61 ± 0.24							Mean ± s.e., *N*-10. Cranberry juice dose response 1741 mg		10
0.003 (0.002–0.028)									Mean (min–max) *N*=259 Free-living individuals	(Angelino et al. 2023)	259
0.003 (0.002–0.028)									Mean (min–max) *N*=166 Free-living individuals	(Angelino et al. 2023)	166
										2	475

Table 5. 4*R/S*-5-(phenyl)-γ-valerolactone-3′-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	**nmol/24 hours**	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		0.62 ± 0.62							Mean ± s.e., *N*-10. Cranberry juice dose response 375 mg	(Favari et al. 2020)	10
		0.87 ± 0.45							Mean ± s.e., *N*-10. Cranberry juice dose response 716 mg		10
		2.16 ± 1.24							Mean ± s.e., *N*-10. Cranberry juice dose response 1131 mg		10
		2.61 ± 1.32							Mean ± s.e., *N*-10. Cranberry juice dose response 1396 mg		10
		2.84 ± 2.14							Mean ± s.e., *N*-10. Cranberry juice dose response 1741 mg		10
		3930 ± 7510 **(420)** [a]							Mean ± s.d., *N*=11. Apples 5.8 mmol flavanols and proanthocyanidins	(Anesi et al. 2019)	11
	0.088 ± 0.045	14280 ± 3520 [b]	Three days	traces	?				Red grape pomace (1.5 g total polyphenols) (Mean ± s.e., *N*=10)	(Castello et al. 2018)	10
0.037 (0.015–0.389)									Mean (min–max) *N*=104 Free-living individuals	(Angelino et al. 2023)	104
0.037 (0.015–0.224)									Mean (min–max) *N*=79 Free-living individuals	(Angelino et al. 2023)	79
		600 ± 200 day 1 200 ± 0 at 1 month	2-day including over-night fast	n.d.					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		600 ± 200 day 1 500 ± 100 at 1 month	2-day including over-night fast	n.d.					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
										5	299

Notes: a) Median calculated from published data. Pearson coefficient 1.40

b) Urine collection 48 hours

Table 6. 4*R/S*-5-(3',4'-dihydroxyphenyl)-γ-valerolactone											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		0.6, 0.3–1.1							140 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=40)	(Hollands et al. 2020)	40
		0.4, 0.2–0.6							70 mg flavanols and 65 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		0.1, 0–0.2							6.5 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		0, 0–0.1							Placebo (median and quartiles *N*=42)		42
	0.014 ± 0.003	0.66 ± 0.09 [a]	Three days	traces	?				Red grape pomace (1.5 g total polyphenols) (Mean ± s.e., *N*=10)	(Castello et al. 2018)	10
		Ca 1 ± 1 [b]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										3	189

Notes a) Urine collection 48 hours rather than 24 hours

b) read from published graph. Urine collection 36-hours.

Table 7. 4*R/S*-5-(4′-hydroxyphenyl)-γ-valerolactone-3′-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		36.0, 14.9–56.3							140 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=40)	(Hollands et al. 2020)	40
		14.4, 6.4–35.1							70 mg flavanols and 65 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		2.0, 0.8–3.4							6.5 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		0.3, 0.1–1.5							Placebo (median and quartiles *N*=42)		42
		Ca 90 ± 60 [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
	0.0004 ± 0.0001								Mean ± s.e., *N*=20 ??? Capsules prepared from 36 commodities	(Bresciani et al. 2017)	20
		5.7 ± 1.9 day 1 3.4 ± 0.9 at 1 month	2-day including over-night fast	0.0039 ± 0.0007					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		10.7 ± 3.5 day 1 6.8 ± 1.1 at 1 month	2-day including over-night fast	0.0101 ± 0.0034					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
										4	244

Notes: a) Read from published graph. 36-hours urine collection

Table 8. 4*R/S*-5-(3'-hydroxyphenyl)-γ-valerolactone-4'-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		16.0, 7.9–32.1							140 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=40)	(Hollands et al. 2020)	40
		7.6, 3.1–20.8							70 mg flavanols and 65 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		1.2, 0.4–3.6							6.5 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		0.3, 0.1–1.0							Placebo (median and quartiles *N*=42)		42
		Ca 18 ± 18 [b]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
		1.7 ± 0.6 day 1 1.1 ± 0.3 at 1 month	2-day including over-night fast	n.d.					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		2.9 ± 1.0 day 1 2.1 ± 0.4 at 1 month	2-day including over-night fast	n.d.					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
										3	224

Notes: a) 48-hour urine collection

b) Read from published graph. 36-Hours urine collection

Table 9. 4*R/S*-5-(3'-Hydroxyphenyl)-γ-valerolactone-4'-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
0.0620 <LOQ–0.0620 [b]		**11.47 7.28–12.88** [b]							*N*=10, median and IQR. Polyphenol-rich breakfast for 3 days [a]	(Domínguez-Fernández et al. 2021)	10
		96.92 ± 56.92 **(91.97)** [a]							Mean ± s.d., *N*=11. Apples 5.8 mmol flavanols and proanthocyanidins	(Anesi et al. 2019)	11
	0.189 ± 0.080		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	0.306 ± 0.060								Daily Cranberry juice (787 mg) (mean ± s.e., *N*=10).		10
	0.303 ± 0.053		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	0.430 ± 0.111		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	0.683 ± 0.203		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
		2.3 ± 0.37 day 1 3.15 ± 0.95 at 1 month	1-day including over-night fast	2.8 ± 1.3 2.6 ± 0.16 1.6 ± 0.6 1.1 ± 0.3					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano et al. 2016)	18
										4	89

Notes: a) Median calculated from published data. Pearson coefficient 0.26

b) The participants consumed for breakfast for 3 days milled flaxseed (30 g/day), freeze-dried raspberry powder (40 g/day), and soy milk (250 mL/day), providing 300 mg/ day of lignans (300 mg of secoisolariciresinol diglucoside), 150 mg/ day of ellagitannins (118 mg of sanguiin H6, 14.3 mg of lambertianin C, and other minor ellagitannins), and 22 mg of isoflavones/day (20.10 mg of daidzin and 1.8 mg of daidzein).

Table 10. 4*R/S*-5-(4′-Hydroxyphenyl)-γ-valerolactone-3′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
1.40 ± 1.49 **(1.08)**									Free-living individuals	(Le Sayec et al. 2023)	90
		38.4, 20.1–74.8							140 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=40)	(Hollands et al. 2020)	40
		25.1, 13.9–62.5							70 mg flavanols and 65 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		5.2, 1.7–16.3							6.5 mg flavanols and 130 mg proanthocyanidins daily for 28 days (median and quartiles *N*=42)		42
		1.3, 0.3–4.4							Placebo (median and quartiles *N*=42)		42
			Ca 12 hours	0.056 ± 0.067 **0.032, (0.002–0.228)**					Breast cancer patients, 3 capsules /day plant extracts (mean ± s.d., median and range)	(Avila-Galvez et al. 2019)	19
	0.272 ± 0.056	38.0 ± 4.7 [a]							Mean ± s.e., *N*=8 [2-^{14}C](−)-epicatechin 207 µmol	(Ottaviani et al. 2016)	8
	0.0017 ± 0.0020								Mean ± s.e., *N*=20 ??? Capsules prepared from 36 commodities	(Bresciani et al. 2017)	20
		Ca 104 ± 50 [b]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										6	316

Notes: a) 48-hour urine collection

b) Read from published graph. 36-Hour urine collection

Table 11. 4*R/S*-5-(3′,5′-dihydroxyphenyl)valeric-γ-valerolactone											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		0.29 ± 0.06 [a]	Three days	traces	?				Red grape pomace (1.5 g total polyphenols) (Mean ± s.e., *N*=10)	(Castello et al. 2018)	10
										1	10

Notes: a) 48-hours urine collection

Table 12. 4*R/S*-5-(5′-Hydroxyphenyl)valerolactone-3′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	**nmol/24 hours**	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		0.64 ± 0.38							Mean ± s.e., *N*-10. Cranberry juice dose response 375 mg	(Favari et al. 2020)	10
		0.08 ± 0.08							Mean ± s.e., *N*-10. Cranberry juice dose response 716 mg		10
		0 ± 0							Mean ± s.e., *N*-10. Cranberry juice dose response 1131 mg		10
		0.12 ± 0.12							Mean ± s.e., *N*-10. Cranberry juice dose response 1396 mg		10
		0 ± 0							Mean ± s.e., *N*-10. Cranberry juice dose response 1741 mg		10
		3620 ± 1030 [a]	Three days	traces	?				Red grape pomace (1.5 g total polyphenols) (Mean ± s.e., *N*=10)	(Castello et al. 2018)	10
0.063 (0.063–0.125)									Mean (min–max) *N*=?? Free-living individuals	(Angelino et al. 2023)	??
0.063 (0.063–0.125)									Mean (min–max) *N*=?? Free-living individuals	(Angelino et al. 2023)	??
										3	>60

Notes: a) 48 hour urine collection

Table 13. 4*R/S*-5-(5′-Hydroxyphenyl)valerolactone-3′-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	**nmol/24 hours**	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		3.24 ± 1.45							Mean ± s.e., *N*-10. Cranberry juice dose response 375 mg	(Favari et al. 2020)	10
		4.01 ± 1.39							Mean ± s.e., *N*-10. Cranberry juice dose response 716 mg		10
		1.42 ± 0.99							Mean ± s.e., *N*-10. Cranberry juice dose response 1131 mg		10
		4.80 ± 1.51							Mean ± s.e., *N*-10. Cranberry juice dose response 1396 mg		10
		2.10 ± 1.11							Mean ± s.e., *N*-10. Cranberry juice dose response 1741 mg		10
0.015 (0.003–0.159)									Mean (min–max) *N*=675 Free-living individuals	(Angelino et al. 2023)	675
0.009 (0.003–0.077)									Mean (min–max) *N*=280 Free-living individuals	(Angelino et al. 2023)	280
										2	1005

Notes a) 48-hour urine collection

Table 14. 4*R/S*-5-(3′-methoxyphenyl)valerolactone-4′-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		Ca 14 ± 6 [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13

Notes: a) Read from published graph. 36-Hours urine collection

Table 15. 4*R/S*-5-(4′-methoxyphenyl)valerolactone-3′-glucuronide											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		Traces [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										1	13

Notes: a) Read from published graph. 36-Hours urine collection

Table 16. 4*R/S*-5-(4′-methoxyphenyl)valerolactone-3′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		Traces [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										1	13

Notes: a) Read from published graph. 36-Hours urine collection

Table 17. 4*R/S*-5-(3′-methoxyphenyl)valerolactone-4′-sulfate											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	N
µmol/l	µmol/l	µmol/24 hours	Washout duration	Plasma spot conc^{n} µmol/l	Urine collection duration	Urine content µmol	µmol/l	µmol/l			
		Traces [a]							Cocoa flavanols (829 mg) (Mean ± s.d., *N*=13)	(Momma et al. 2023)	13
										1	13

Notes: a) Read from published graph. 36-Hours urine collection

References

Anesi, A., P. Mena, A. Bub, M. Ulaszewska, D. Del Rio, S. E. Kulling, and F. Mattivi. 2019. "Quantification of Urinary Phenyl-gamma-Valerolactones and Related Valeric Acids in Human Urine on Consumption of Apples." *Metabolites* 9 (11). doi: 10.3390/metabo9110254.

Angelino, D., A. Caffrey, H. McNulty, C. I. R. Gill, P. Mena, A. Rosi, K. Moore, L. Hoey, M. Clements, E. Laird, K. Boyd, B. Mullen, B. Pucci, H. Jarrett, C. Cunningham, M. Ward, J. J. Strain, K. McCarroll, A. J. Moore, A. M. Molloy, and D. Del Rio. 2023. "Association of dietary flavan-3-ol intakes with plasma phenyl-gamma-valerolactones: analysis from the TUDA cohort of healthy older adults." *American Journal of Clinical Nutrition* 118 (2):476-484. doi: 10.1016/j.ajcnut.2023.06.006.

Avila-Galvez, M. A., R. Garcia-Villalba, F. Martinez-Diaz, B. Ocana-Castillo, T. Monedero-Saiz, A. Torrecillas-Sanchez, B. Abellan, A. Gonzalez-Sarrias, and J. C. Espin. 2019. "Metabolic Profiling of Dietary Polyphenols and Methylxanthines in Normal and Malignant Mammary Tissues from Breast Cancer Patients." *Molecular Nutrition & Food Research* 63 (9). doi: 10.1002/mnfr.201801239.

Bresciani, Letizia, Daniela Martini, Pedro Mena, Michele Tassotti, Luca Calani, Giacomo Brigati, Furio Brighenti, Sandra Holasek, Daniela-Eugenia Malliga, Manfred Lamprecht, and Daniele Del Rio. 2017. "Absorption Profile of (Poly)Phenolic Compounds after Consumption of Three Food Supplements Containing 36 Different Fruits, Vegetables, and Berries." *Nutrients* 9 (3). doi: 10.3390/nu9030194.

Castello, F., G. Costabile, L. Bresciani, M. Tassotti, D. Naviglio, D. Luongo, P. Ciciola, M. Vitale, C. Vetrani, G. Galaverna, F. Brighenti, R. Giacco, D. Del Rio, and P. Mena. 2018. "Bioavailability and pharmacokinetic profile of grape pomace phenolic compounds in humans." *Archives of Biochemistry and Biophysics* 646:1-9. doi: 10.1016/j.abb.2018.03.021.

Domínguez-Fernández, Maite, Yifan Xu, Paul Young Tie Yang, Wafa Alotaibi, Rachel Gibson, Wendy L. Hall, Leon Barron, Iziar A. Ludwig, Concepción Cid, and Ana Rodriguez-Mateos. 2021. "Quantitative Assessment of Dietary (Poly)phenol Intake: A High-Throughput Targeted Metabolomics Method for Blood and Urine Samples." *Journal of Agricultural and Food Chemistry* 69 (1):537-554. doi: 10.1021/acs.jafc.0c07055.

Favari, C., P. Mena, C. Curti, G. Istas, C. Heiss, D. Del Rio, and A. Rodriguez-Mateos. 2020. "Kinetic profile and urinary excretion of phenyl-gamma-valerolactones upon consumption of cranberry: a dose-response relationship." *Food & Function* 11 (5):3975-3985. doi: 10.1039/d0fo00806k.

Feliciano, R. P., C. E. Mills, G. Istas, C. Heiss, and A. Rodriguez-Mateos. 2017. "Absorption, Metabolism and Excretion of Cranberry (Poly) phenols in Humans: A Dose Response Study and Assessment of Inter-Individual Variability." *Nutrients* 9 (3):268. doi: 10.3390/nu9030268.

Feliciano, R.P., G. Istas, C. Heiss, and A. Rodriguez-Mateos. 2016. "Plasma and urinary phenolic profiles after acute and repetitive intake of wild blueberry." *Molecules* 21 (9):1120. doi: https://doi.org/10.3390/molecules21091120

Heiss, Christian, Geoffrey Istas, Rodrigo P. Feliciano, Timon Weber, Brian Wang, Claudia Favari, Pedro Mena, Daniele Del Rio, and Ana Rodriguez-Mateos. 2022. "Daily consumption of cranberry improves endothelial function in healthy adults: a double blind randomized controlled trial." *Food & Function* 13 (7):3812-3824. doi: 10.1039/d2fo00080f.

Hollands, Wendy J, Mark Philo, Natalia Perez-Moral, Paul W Needs, George M Savva, and Paul A Kroon. 2020. "Monomeric Flavanols are More Efficient Substrates for gut Microbiota Conversion to Hydroxyphenyl- γ-Valerolactone Metabolites than Oligomeric Procyanidins: A Randomized, Placebo-Controlled Human Intervention Trial." *Molecular Nutrition & Food Research* 64 (10):e1901135. doi: 10.1002/mnfr.201901135.

Kay, C.D., M.N. Clifford, P. Mena, J.G. McDougall, C. Andres-Lacueva, A. Cassidy, D. Del Rio, N. Kuhnert, C. Manach, G. Pereira-Caro, A. Rodriguez-Mateos, A. Scalbert, F. Tomas-Barberan, G. Williamson, A. Crozier, and D.S. Wishart. 2020. "Special Article Recommendations for standardizing nomenclature for dietary (poly)phenol catabolites." *American Journal of Clinical Nutrition* 112:1051-1068. doi: https://doi.org/10.1093/ajcn/nqaa204.

Le Sayec, Melanie, Diogo Carregosa, Khadija Khalifa, Chiara de Lucia, Dag Aarsland, Cláudia N. Santos, and Ana Rodriguez-Mateos. 2023. "Identification and quantification of (poly)phenol and methylxanthine metabolites in human cerebrospinal fluid: evidence of their ability to cross the BBB." *Food & Function* 14 (19):8893-8902. doi: 10.1039/D3FO01913F.

Momma, T. Y., G. G. C. Kuhnle, R. Y. Fong, J. L. Ensunsa, A. Crozier, H. Schroeter, and J. I. Ottaviani. 2023. "5-(3',4'-Dihydroxyphenyl)-gamma-Valerolactone Is a Substrate for Human Paraoxonase: A Novel Pathway in Flavan-3-ol Metabolism." *Mol Nutr Food Res* 67 (17):e2300281. doi: 10.1002/mnfr.202300281.

Ottaviani, J.I., G. Borges, T.Y. Momma, J.P.E. Spencer, C.L. Keen, A. Crozier, and H. Schroeter. 2016. "The metabolome of [2-C-14] (–)-epicatechin in humans: implications for the assessment of efficacy, safety, and mechanisms of action of polyphenolic bioactives." *Scientific Reports* 6:29034. doi: https://doi.org/10.1038/srep29034.

Pereira-Caro, Gema, Jose-Manuel Moreno Rojas, Nicolettaa Brindani, Daniele Del Rio, Michael Lean, Yukihiko Hara, and Alan Crozier. 2017. "Bioavailability of Black Tea Theaflavins: Absorption, Metabolism and Colonic Catabolism." *Journal of Agricultural and Food Chemistry* 65 (26):5365-5374. doi: 10.1021/acs.jafc.7b01707.

Zhu, Y. D., K. L. Shurlknight, X. X. Chen, and S. M. Sang. 2014. "Identification and Pharmacokinetics of Novel Alkylresorcinol Metabolites in Human Urine, New Candidate Biomarkers for Whole-Grain Wheat and Rye Intake." *Journal of Nutrition* 144 (2):114-122. doi: 10.3945/jn.113.184663.