Authentic human data for phenylacetic acid (C_6–C_2) 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_2 metabolites (i.e. phenylacetic acids 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_3 metabolites (3-phenylpropanoic acids and cinnamic acids) and C_6–C_5 metabolites (5-phenylvaleric acids, 4-hydroxy-5-hydroxyphenylvaleric acids and phenylvalerolactones) 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 64. Phenylacetic acid and phenylacetyl-glutamine											
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			
47.2 ± 5.9 58.9 ± 3.8 50.3 ± 5.0 48.5 ± 3.8 51.6 ± 6.1									Healthy free-living adults (mean ± s.d., *N*=12). Data from HMDB supplementary data attached to the journal no longer available. **ENZYME HYDROLYSED (NOT AMINO ACID CONJUGATES)**	(Loke et al. 2009)	12
1.41 (0.37, 14.61)									Healthy free-living adults (**Median**, min, max, *N*=72)	(Beloborodova et al. 2015)	72
38.1 ± 73.0 (**11.2** and 13.3)									Free-living volunteers (*N*=90, mean ± s.d.) (**median** and IQR)	(Le Sayec et al. 2023)	90
0.79 ± 0.45 free acid 1.17 ± 0.63 glutamine conjugate									Free-living fasting individuals (*N*=28, mean ± s.d.) **BEFORE AND AFTER ACID HYDROLYSIS**	(Davis, Durden, and Boulton 1982)	28
1.14 ± 0.61 free acid 0.86 ± 0.50 glutamine conjugate									Free-living non-fasting individuals (*N*=10, mean ± s.d.) **BEFORE AND AFTER ACID HYDROLYSIS**		14
0.343 **0.243–0.453** [e]		**<LOQ** [e]							*N*=10, median and IQR. Polyphenol-rich breakfast for 3 days [a]	(Domínguez-Fernández et al. 2021)	10
		18 ± 4	—						Placebo 7 days (mean ± s.e., *N*=20)	(Olthof et al. 2003)	20
		20 ± 4							5-CQA 5.5 mmol/day, 7 days (mean ± s.e., *N*=20)		
		22 ± 4							660 µmol rutin/day, 7 days (mean ± s.e., *N*=20)		

		21 ± 5							4.3 mmol/d black tea solids, 7 days (mean ± s.e., 4*N*=20). **No significant differences**		
	8.3 ± 1.9	14.7 ± 6.2	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	8.11 ± 2.45		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	7.90 ± 2.00		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	8.05 ± 2.11		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	10.35 ± 3.76		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, Istas, et al. 2016)	18
		0.8 ± 0.2 [d]	Two days		12 hours	0.7 ± 0.4 [d]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		1.5 ± 0.4 [d]	Two days		12 hours	0.4 ± 0.2 [d]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
		46.7 ± 10.5 day 1 64.1 ± 17.4 at 1 month	2-day including over-night fast	13.3 ± 1.5					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		97.5 ± 18.7 day 1 37.3 ± 10.9 at 1 month	2-day including over-night fast	12.9 ± 1.5					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e., *N*=23)		23
	19.21 ± 1.28 20.32 ± 1.20	42.77 ± 5.51 49.30 ± 7.77	overnight fast						Skimmed milk (mean ± s.e., *N*=42) Cocoa (248 mg) with skimmed milk (mean ± s.e., *N*=42) **ENZYME HYDROLYSED (NOT AMINO ACID CONJUGATES)**	(Urpi-Sarda et al. 2009)	42
			—				188 ± 70		Free-living volunteers (mean ± s.e., *N*=5)	(Karlsson et al. 2005)	5

			—				479 ± 391		Free-living volunteers (*N*=5) (mean ± s.d.). No increase on hydrolysis	(Jenner, Rafter, and Halliwell 2005)	5
			—				1116 826 400 677		One free-living volunteer over four consecutive days. No increase on hydrolysis		
			—				4923 ± 1765 [c] 998 ± 758 [c] 4246 ± 1100 [c] 7150 ± 3376 [c]		(*N*=5, mean ± s.e.) Italy (*N*=5, mean ± s.e.) Germany (*N*=5, mean ± s.e.) Spain (*N*=5, mean ± s.e.) Denmark	(Knust et al. 2006)	20
			Two weeks				499 ± 288 [b] 690 ± 439 [b]		Low (poly)phenol diet four weeks Zero time (mean ± s.d., *N*=8) Four weeks (mean ± s.d., *N*=8)	(Munoz-Gonzalez et al. 2013)	41
			Two weeks				1184 ± 1037 [b] 1346 ± 1279 [b]		Red wine (*ca* 112 mg/250 ml) daily for four weeks Zero time (mean ± s.d., *N*=33) Four weeks (mean ± s.d., *N*=32)		
										16	472

Notes: a) described as fecal matrix and unclear precisely how it compares with fecal water as used by Jenner *et al*. and Karlsson *et al*.

b) µmol/g rather than µmol/l but authors do not indicate whether this is wet weight or dry weight

c) described as fecal matrix and unclear precisely how it compares with fecal water as used by Jenner *et al*. and Karlsson *et al*.

d) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

e) 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 65. 2'-Hydroxyphenylacetic 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			
	0.186 ± 0.029								Watermelon, Overweight / obese individuals (*N*=6, mean ± s.e.)	(Fan et al. 2020)	6
		8.4 ± 0.5	—						Placebo 7 days (mean ± s.e., *N*=20)	(Olthof et al. 2003)	20
		8.0 ± 0.6							5-CQA 5.5 mmol/day, 7 days (mean ± s.e., *N*=20)		
		8.2 ± 0.6							660 µmol rutin/day, 7 days (mean ± s.e., *N*=20)		
		6.5 ± 0.6							4.3 mmol/d black tea solids, 7 days (mean ± s.e., 4*N*=20). **No significant differences**		
										2	26

Table 66. 3'-Hydroxyphenylacetic 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			
0.058 (0.002, 0.236) **									Healthy controls (*N*=809, **median** 5 and 95% C.I.) Hydrolysed	(Murphy et al. 2018)	809
0.055 (0.002, 0.239) **									Cancer patients (*N*=809, **median** 5 and 95% C.I.) Hydrolysed		809
16.8 ± 13.7 (**12.1** and 9.7)									Free-living volunteers (*N*=90, mean ± s.d.) (**median** and IQR)	(Le Sayec et al. 2023)	90
<LOQ [e]		**31.80 18.34–50.00** [e]							*N*=10, median and IQR. Polyphenol-rich breakfast for 3 days [a]	(Domínguez-Fernández et al. 2021)	10
		5 and 5							Healthy individuals (*N*=17, median and IQR) low flavonol diet 3 days	(Combet et al. 2011)	17
		38 and 24							Healthy individuals (*N*=17, median and IQR) high flavonol diet 3 days		
									Mangoes (500 µmol) (*N*=8, mean ± s.e.)	Crozier	8
		9 ± 3							Mangoes (500 µmol) Ileostomists (*N*=10, mean ± s.e.)		10
		21 ± 3	—						Placebo 7 days (mean ± s.e., *N*=20)	(Olthof et al. 2003)	20
		18 ± 2							5-CQA 5.5 mmol/day, 7 days (mean ± s.e., *N*=20)		
		259 ± 51							660 µmol rutin/day, 7 days (mean ± s.e., *N*=20)		
		68 ± 6							4.3 mmol/d black tea solids, 7 days (mean ± s.e., 4*N*=20). **No significant differences**		
		1332 ± 336 day 1 417 ± 118 at 1 month	2-day including over-night fast	3.6 ± 1.4					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22

		625 ± 148 day 1 508 ± 101 at 1 month	2-day including over-night fast	1.43 ± 0.43					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e., *N*=23)		23
	0.62 ± 0.36	4.4 ± 0.9	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	0.69 ± 0.25		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	0.46 ± 0.12		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	0.33 ± 0.07		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	0.49 ± 0.13		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
		5.9 ± 0.86 day 1 8.1 ±1.2 µmol at 1 month	1-day including over-night fast	0.14 ± 0.03 0.10 ± 0.025 0.17 ± 0.03 0.15 ± 0.03					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano, Istas, et al. 2016)	18
		2.24 ± 0.6	Three days		2 hours	0.26 ± 0.05			Maté (1118 µmol) (mean ± s.d., *N*=12)	(Gomez-Juaristi et al. 2018)	12
		n.d. 7.3 ± 3.0 3.9 ± 2.6	2 days						Control (*N*=5, mean ± s.e.) Orange juice (180 µmol) (*N*=5, mean ± s.e.) Orange juice (180 µmol) and Yoghurt (*N*=5, mean ± s.e.)	(Roowi et al. 2009)	5
		0.37 ± 0.04 [c]	2 days						Orange juice (368 µmol) (*N*=9, mean ± s.e.)	(Pereira-Caro et al. 2023)	9
		0.86 ± 0.05 [c]	2 days						Orange juice (368) plus oat bran (58 µmol) (*N*=9, mean ± s.e.)		
	0.034 ± 0.002		Over-night	0.017 ± 0.005					Orange juice (398 µmol) (*N*=10, mean ± s.e.) Trained athletes	(Pereira-Caro et al. 2020)	10
		<LOQ [c]	Two days		12 hours	0.3 ± 0.1 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		1.7 ± 0.6 [c]	Two days		12 hours	0.3 ± 0.3 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
		9.2 (6.0, 14.0) 6.8 (4.2, 11.0)	Partial						Zero time (*N*=69, mean and 95% C.I.)	(Ward et al. 2004)	69

									Placebo for 6 weeks (*N*=69, mean and 95% C.I.)		
		7.8 (5.5, 11.0) 11.3 (7.3, 17.6)	Partial						Zero time (*N*=69, mean and 95% C.I.) Daily grape seed phenols (1 g) for 6 weeks (*N*=69, mean and 95% C.I.) Statistically significant increase		
	1.2 ± 0.7	4 ± 2	3 days including over-night fast		2 hours	0.16 ± 0.06			Rosemary tea (1055 µmol rosmarinic acid equivalent) (mean ± s.d., *N*=12)	(Achour et al. 2021)	12
	0.2 ± 0.07 zero time	12 ± 3 zero time	Two days						Green coffee extract (600 mg) (*N*=9, mean ± s.e.) zero time	(Angel Seguido et al. 2022)	9
	0.15 ± 0.05 8 weeks	9 ± 2 at 8 weeks	Two days						Green coffee extract (600 mg) (*N*=9, mean ± s.e.) 8 weeks		
	0.21 ± 0.06 zero time	8.0 ± 2.0 zero time	Two days		?	3.0 ± 1.0			Green coffee extract (600 mg) and oat β-glucan day 1 (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers	(Seguido et al. 2022)	9
	0.15 ± 0.04 at 8 weeks	7.0 ± 2.0 at 8 weeks	Two days		?	2.2 ± 0.5			Green coffee extract (600 mg) and oat β-glucan 8 weeks (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers		
0.068 ± 0.007 0.074 ± 0.006			—						Placebo daily for 12 weeks Zero time (mean ± s.e., *N*= 31) Twelve weeks (mean ± s.e., *N*= 31)	(Tosi et al. 2023)	60
0.078 ± 0.009	0.087 ± 0.009		—						Cranberries (588 mg) daily for 12 weeks Zero time (mean ± s.e., *N*= 29) Twelve weeks (mean ± s.e., *N*= 29)		
			—				110 ± 50		(*N*=5) (mean ± s.e.)	(Karlsson et al. 2005)	5
			—				479 ± 46		Free-living volunteers. (*N*=5) (mean ± s.d.). No increase on hydrolysis	(Jenner, Rafter, and Halliwell 2005)	5
			—				395 105 62 76		One free-living volunteer over four consecutive days. No increase on hydrolysis		

			—				49 ± 24 [a] 52 ± 24 [a] 63 ± 32 [a] 30 ± 12		(*N*=5, mean ± s.e.) Italy (*N*=5, mean ± s.e.) Germany (*N*=5, mean ± s.e.) Spain (*N*=5, mean ± s.e.) Denmark	(Knust et al. 2006)	20
			Two weeks				14 ± 80 [b] 33 ± 38 [b]		Low (poly)phenol diet four weeks Zero time (mean ± s.d., *N*=7) Four weeks (mean ± s.d., *N*=8)	(Munoz-Gonzalez et al. 2013)	41
			Two weeks				60 ± 54 [b] 122 ± 132 [b]		Red wine (*ca* 112 mg/250 ml) daily for four weeks Zero time (mean ± s.d., *N*=29) Four weeks (mean ± s.d., *N*=33)		
										23	549

Notes: a) described as fecal matrix and unclear precisely how it compares with fecal water as used by Jenner *et al*. and Karlsson *et al*.

b) µmol/g rather than µmol/l but authors do not indicate whether this is wet weight or dry weight

c) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

e) 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 67. 4′-Hydroxyphenylacetic 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			
0.98 (0.26, 3.00)									Healthy free-living adults (**median**, min, max, *N*=72)	(Beloborodova et al. 2015)	72
0.324 (0.185, 0.888) **									Healthy controls (*N*=809, **median**, 5 and 95% C.I.) Hydrolysed	(Murphy et al. 2018)	809
0.315 (0.194, 0.888) **									Cancer patients (*N*=809, **median**, 5 and 95% C.I.) Hydrolysed		809
0.36 ± 0.22 free acid 0.43 ± 0.27 total after hydrolysis									Free-living fasting individuals (*N*=28, mean ± s.d.) **BEFORE AND AFTER ACID HYDROLYSIS**	(Davis, Durden, and Boulton 1982)	28
0.45 ± 0.18 free acid 0.47 ± 0.19 total after hydrolysis									Free-living non-fasting individuals (*N*=10, mean ± s.d.) **BEFORE AND AFTER ACID HYDROLYSIS**		14
		160 ± 20	—						Placebo 7 days (mean ± s.e., *N*=20)	(Olthof et al. 2003)	20
		160 ± 10							5-CQA 5.5 mmol/day, 7 days (mean ± s.e., *N*=20)		
		150 ± 20							660 µmol rutin/day, 7 days (mean ± s.e., *N*=20)		
		170 ± 20							4.3 mmol/d black tea solids, 7 days (mean ± s.e., 4*N*=20). **No significant differences**		
		653 ± 130 day 1 662 ± 148 at 1 month	2-day including over-night fast	8.2 ± 0.98					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		381 ± 73 day 1	2-day including	9.8 ± 1.3					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23)		23

		697 ± 137 at 1 month	over-night fast						Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		
	1.85 ± 0.72	10.2 ± 3.2	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	1.79 ± 0.73		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	2.61 ± 1.41		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	1.70 ± 0.66		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	3.83 ± 2.59		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
	0.65 ± 0.34 0.78 ± 0.45		2 Days						Cranberry juice (189 mg) (*N*=10, mean s.d.) T_{max} 1.5 ± 1.3 hours and 7.8 ± 2.5 hours. AUC 2.30 ± 2.29 mmol.h/l	(McKay et al. 2015)	10
		12.6 ± 1.9 at day 1 10.5 ± 1.3 at day 30	1 day including over-night fast	0.33 ± 0.05 0.22 ± 0.03 0.29 ± 0.06 0.23 ± 0.05					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano, Istas, et al. 2016)	18
		87 ± 7	60 hours including 12 hour fast		24 hours	65 ± 12			Raspberries (344 µmol) (mean ± s.e., *N*=8). No increase on hydrolysis.	(Gonzalez-Barrio, Edwards, and Crozier 2011)	8
	0.151 ± 0.012		Over-night	0.002 ± 0.001					Orange juice (398 µmol) (*N*=10, mean ± s.e.) Trained athletes	(Pereira-Caro et al. 2020)	10
		104 ± 24 [c]	Two days		12 hours	6 ± 2 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		122 ± 38 [c]	Two days		12 hours	3 ± 1 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
		610 ± 451	—						White-fleshed apple (mean ± s.e., *N*=8) (197 mg)	(Macià et al. 2022)	29
		213 ± 52	—						Red-fleshed apple (mean ± s.e., *N*=12) (193 mg)		
		289 ± 43	—						Aronia infusion (mean ± s.e., *N*=9) (99 mg)		

	ca 1.15 [a] *ca* 0.86 [a]		1 day	*ca* 0.3 [a]					Free acid Zero time (*N*=10, mean) Beer (10 mg) 30 minutes post-consumption (*N*=10, mean) Beer (10 mg) 60 minutes post-consumption (*N*=10, mean)	(Nardini et al. 2006)	10
		16 ± 3	3 days including over-night fast	traces	2 hours	1.5 ± 0.1			Rosemary tea (1055 µmol rosmarinic acid equivalent) (mean ± s.d., *N*=12)	(Achour et al. 2021)	12
	2 ± 1 zero time	?							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) zero time	(Angel Seguido et al. 2022)	9
	7 ± 3 at 8 weeks	?							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) 8 weeks		
			—				18.54 ± 9.54		Free-living volunteers (mean ± s.e., *N*=5). No increase on hydrolysis	(Jenner, Rafter, and Halliwell 2005)	5
			—				32.7, 41.0, 39.5, 81.0		One free-living volunteer over four consecutive days. No increase on hydrolysis		
			—				41 ± 17 [a] 221 ± 85 [a] 75 ± 45 [a] 29 ± 8 [a]		(*N*=5, mean ± s.e.) Italy (*N*=5, mean ± s.e.) Germany (*N*=5, mean ± s.e.) Spain (*N*=5, mean ± s.e.) Denmark	(Knust et al. 2006)	20
			Two weeks				63 ± 89 [b] 24 ± 22 [b]		Low (poly)phenol diet four weeks Zero time (mean ± s.d., *N*=6) Four weeks (mean ± s.d., *N*=7)	(Munoz-Gonzalez et al. 2013)	37
			Two weeks				31 ± 50 [b] 27 ± 33 [b]		Red wine (*ca* 112 mg/250 ml) daily for four weeks Zero time (mean ± s.d., *N*=31) Four weeks (mean ± s.d., *N*=31)		
										18	407

Notes: a) values were read from a graph and are approximate.

b) µmol/g rather than µmol/l but authors do not indicate whether this is wet weight or dry weight

c) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

Table 68. 3′,4′-Dihydroxyphenylacetic acid (DOPAC)											
Free-living Plasma spot value	Feeding Study Plasma C_{max}	Feeding Study Urine	Washout				Fecal water	Ileal fluid	Notes	Reference	
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			N
0.015 ± 0.005 0.014 ± 0.004 0.013 ± 0.005									MetMet COMT genotype (*N*=45, mean ± s.d.) ValMet COMT genotype (*N*=110, mean ± s.d.) ValVal COMT genotype (*N*=42, mean ± s.d.)	(Zumarraga et al. 2010)	197
0.016 ± 0.005									Low MAOA activity MetMet COMT genotype (*N*=12, mean ± s.d.)		
0.015 ± 0.004									Low MAOA activity ValMet COMT genotype (*N*=22, mean ± s.d.)		
0.012 ± 0.004									Low MAOA activity ValVal COMT genotype (*N*=10, mean ± s.d.)		
0.015 ± 0.005									High MAOA activity MetMet COMT genotype (*N*=23, mean ± s.d.)		
0.014 ± 0.004									High MAOA activity ValMet COMT genotype (*N*=58, mean ± s.d.)		
0.014 ± 0.006									High MAOA activity ValVal COMT genotype (*N*=24, mean ± s.d.)		
0.041 (0.024, 0.077) **									Healthy controls (*N*=809, **median**, 5 and 95% C.I.) Hydrolysed	(Murphy et al. 2018)	809
0.040 (0.024, 0.078) **									Cancer patients (*N*=809, **median**, 5 and 95% C.I.) Hydrolysed		809
1.44 ± 0.62 (**1.37** and 0.92)									Free-living volunteers (*N*=90, mean ± s.d.) (**Median** and IQR)	(Le Sayec et al. 2023)	90
0.019 ± 0.0007									Free-living volunteers (*N*=5, mean ± s.d.)	(Mitchell and Coscia 1978)	5
0.022 **0.016–0.040** [f]		**4.28** **2.60–6.80** [f]							*N*=10, median and IQR. Polyphenol-rich breakfast for 3 days [a]	(Domínguez-Fernández et al. 2021)	10
		3 and 1							Healthy individuals (*N*=17, median and IQR) low flavonol diet 3 days	(Combet et al. 2011)	17
		6 and 6							Healthy individuals (*N*=17, median and IQR) high flavonol diet 3 days		

		0.376 ± 0.118	Three days		2 hours	0.097 ± 0.017			Maté (1118 µmol) (mean ± s.d., *N*=12)	(Gomez-Juaristi et al. 2018)	12
		1.5 ± 0.97	Three days		2 hours	0.094 ± 0.032			Cocoa (68 µmol) (mean ± s.d., *N*=13), UNHYDROLYSED	(Gomez-Juaristi et al. 2019)	13
		2.15 ± 0.40	Three days		2 hours	0.109 ± 0.015			Cocoa (235 µmol) (mean ± s.d., *N*=13), UNHYDROLYSED		
0.017 ± 0.005 zero time 0.013 ± 0.005 at 6 hours									Normal diet (*N*=10, mean ± s.e.) caffeinated coffee	(Goldstein et al. 2021)	10
0.014 ± 0.005 zero time 0.015 ± 0.005 at 6 hours									Normal diet (*N*=10, mean ± s.e.) decaffeinated coffee		
		1.2 ± 0.2 zero time							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) zero time	(Angel Seguido et al. 2022)	9
		1.3 ± 0.2 at 8 weeks							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) 8 weeks		
	n.d.	1.3 ± 0.3	Two days		?	0.5 ± 0.2			Green coffee extract (600 mg) and oat β-glucan day 1 (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers	(Seguido et al. 2022)	9
	n.d.	1.6 ± 0.3	Two days		?	0.7 ± 0.2.			Green coffee extract (600 mg) and oat β-glucan 8 weeks (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers		
		1.1 ± 0.4 [c]	Two days		12 hours	0.2 ± 0.1 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		0.7 ± 0.3 [c]	Two days		12 hours	0.4 ± 0.4 [c]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
		2.9 ± 1.3 [a]	Two days		2 hours	0.4 ± 0.2			Raspberries (553 µmol) (*N*=9, mean ± s.e.)	(Ludwig et al. 2015)	9
		3.4 ± 0.3	60 hours including 12 hour fast		24 hours	2.0 ± 0.6			Raspberries (344 µmol) (mean ± s.e., *N*=8). No increase on hydrolysis.	(Gonzalez-Barrio, Edwards, and Crozier 2011)	8

		49.3 ± 7.8 day 1 27.5 ± 3.7 at 1 month	2-day including over-night fast	0.47 ± 0.26					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		38.5 ± 7.3 day 1 30.3 ± 6.0 at 1 month	2-day including over-night fast	0.69 ± 0.42					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
	0.48 ± 0.14	1.6 ± 0.3	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	0.30 ± 0.09		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	0.58 ± 0.20		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	0.64 ± 0.17		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	0.82 ± 0.31		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
		1.3 ± 0.23 day 1 1.0 ± 0.17 at 1 month	1 day including over-night fast	0.09 ± 0.01 0.08 ± 0.01 0.09 ± 0.01 0.09 ± 0.01					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano, Istas, et al. 2016)	18
		16 ± 3	Two days		2 hours	n.d.			Tomato juice (176 µmol) (*N*=6, mean ± s.e.) Intact colon	(Jaganath et al. 2006)	6
		n.d.	Two days		2 hours	n.d.			Tomato juice (176 µmol) (*N*=6, mean ± s.e.) Ileostomists		
		0.60 ± 0.09 [c]	2 days						Orange juice (368 µmol) (*N*=9, mean ± s.e.)	(Pereira-Caro et al. 2023)	9
		2.1 ± 0.03 [c]	2 days						Orange juice (368 µmol) plus oat bran (58 µmol) (*N*=9, mean ± s.e.)		
	0.025 (0.013, 0.064)	8.5 (5.2, 16.0)	24 hours	0.018 ± 0.005	spot	5.08 ± 0.57			Artichoke (5727 µmol) (*N*= 8, mean) (min, max)	(Dominguez-Fernandez et al. 2022)	8
	0.03 ± 0.01	(0.11 ± 0.024)10^{-3}	Two days and Over-night fast		2 hours	(0.011 ± 0.007)10^{-3}			Hydroxy-tyrosol enriched biscuits (5.25 mg) (*N*=13, mean ± s.d.). T_{max} = 36 ± 13 min. AUC 132 ± 48 µmol.h.l^{-1} Quantified with free acid	(Mateos et al. 2016)	13

	n.d.	(0.032 ± 0.005)10^{-3}	Two days and Over-night fast		2 hours	(0.007 ± 0.004)10^{-3}			Control biscuits (*N*=13, mean ± s.d.). Quantified with free acid		
	0.30 ± 0.13	44.3 ± 17.5 [b]	—						Hydroxy-tyrosol-rich supplement 1 (11 g) (*N*=12, mean ± s.e.) T_{max} = 30 min	(Bender, Strassmann, and Golz 2023)	13
	0.47 ± 0.15	59.7 ± 3.0 [b]	—						Hydroxy-tyrosol-rich supplement 2 (10 g)(*N*=13, mean ± s.e.) T_{max} = 30 min		
			?	0.012 ± 0.02					Intravenous dopamine infusion (*N*=7, mean ± s.e.)	(Claustre et al. 1990)	7
			—				6.98 ± 7.34		Free-living volunteers (mean ± s.e., *N*=5). No increase on hydrolysis	(Jenner, Rafter, and Halliwell 2005)	5
			—				1.54, 1.54, 69.19 7.42		One free-living volunteer over four consecutive days. No increase on hydrolysis		
			—				37 ± 30 [e] 14 ± 7 [e] 9 ± 6 [e] 1 ± 0.1 [e]		(*N*=5, mean ± s.e.) Italy (*N*=5, mean ± s.e.) Germany (*N*=5, mean ± s.e.) Spain (*N*=5, mean ± s.e.) Denmark	(Knust et al. 2006)	20
			Two weeks				28 ± 21 [d] 14 [d]		Low (poly)phenol diet four weeks Zero time (mean ± s.d.?, *N*=2) Four weeks (single value, *N*=1)	(Munoz-Gonzalez et al. 2013)	9
			Two weeks				41 ± 60 [d] 40 ± 49 [d]		Red wine (*ca* 112 mg/250 ml) daily for four weeks Zero time (mean ± s.d., *N*=5) Four weeks (mean ± s.d., *N*=7)		
			—				64 ± 50		(*N*=5) (mean ± s.e.)	(Karlsson et al. 2005)	5
										26	600

Notes: a) collection of urine 48 hours rather than 24

b) collection of urine 12 hours rather than 24

c) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

d) µmol/g rather than µmol/l but authors do not indicate whether this is wet weight or dry weight

e) described as fecal matrix and unclear precisely how it compares with fecal water as used by Jenner *et al*. and Karlsson *et al*.

f) 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 69. 4′-Hydroxy-3′-methoxyphenylacetic acid (Homovanillic acid, HVA)											
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			
0.073 ± 0.022 0.080 ± 0.041 0.087 ± 0.031									MetMet COMT genotype (*N*=47, mean ± s.d.) ValMet COMT genotype (*N*=116, mean ± s.d.) ValVal COMT genotype (*N*=44, mean ± s.d.)	(Zumarraga et al. 2010)	207
0.071 ± 0.017									Low MAOA activity MetMet COMT genotype (*N*=45, mean ± s.d.)		
0.078 ± 0.034									Low MAOA activity ValMet COMT genotype (*N*=22, mean ± s.d.)		
0.071 ± 0.018									Low MAOA activity ValVal COMT genotype (*N*=10, mean ± s.d.)		
0.071 ± 0.021									High MAOA activity MetMet COMT genotype (*N*=23, mean ± s.d.)		
0.082 ± 0.043									High MAOA activity ValMet COMT genotype (*N*=58, mean ± s.d.)		
0.094 ± 0.030									High MAOA activity ValVal COMT genotype (*N*=24, mean ± s.d.)		
0.076 ± 0.033 Zero time 0.078 ± 0.033 at 8 days		$(0.159 \pm 0.047)10^{-3}$ zero time $(0.141 \pm 0.053)10^{-3}$ at 8 days	—						Healthy free-living volunteers (mean ± s.d., *N*=18) on two occasions one week apart	(Veselinovic et al. 2018)	18
0.088 (0.051, 0.182) **									Healthy controls (*N*=809, **median,** 5% and 95% C.I.) Hydrolysed	(Murphy et al. 2018)	809
0.084 (0.051, 0.172) **									Cancer patients (*N*=809, **median**, 5% and 95% C.I.) Hydrolysed		809
		32.1, 15.5–40.9							Free-living healthy volunteers (mean and range, *N*=5)	(Chauhan and Darbre 1980)	5
0.051 ± 0.005									Free-living volunteers (*N*=5, mean ± s.d.)	(Mitchell and Coscia 1978)	5

		12 and 7							Healthy individuals (*N*=17, median and IQR) low flavonol diet 3 days	(Combet et al. 2011)	17
		17 and 8							Healthy individuals (*N*=17, median and IQR) high flavonol diet 3 days		
		15 ± 4							Mangoes (500 µmol) (*N*=8, mean ± s.e.)	Crozier	8
									Mangoes (500 µmol) Ileostomists (*N*=10, mean ± s.e.)		10
	0.14 ± 0.06 zero time	13.2 ± 0.9 zero time							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) zero time	(Angel Seguido et al. 2022)	9
	0.12 ± 0.05 at 8 weeks	12.0 ± 1.0 at 8 weeks							Green coffee extract (600 mg) (*N*=9, mean ± s.e.) 8 weeks		
	0.3 ± 0.1 zero time	15.0 ± 2.0	Two days		?	6.0 ± 1.0			Green coffee extract (600 mg) and oat β-glucan day 1 (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers	(Seguido et al. 2022)	9
	0.3 ± 0.04 at 8 weeks	14.0 ± 2.0	Two days		?	7.0 ± 2.0			Green coffee extract (600 mg) and oat β-glucan 8 weeks (*N*=9, mean ± s.e.) Free-living overweight / obese volunteers		
	0.9 ± 0.7	3 ± 1	3 days including over-night fast		2 hours	0.3 ± 0.1			Rosemary tea (1055 µmol rosmarinic acid equivalent) (mean ± s.d., *N*=12)	(Achour et al. 2021)	12
		0.2 ± 0.2 [a]	Two days		2 hours	n.d.			Raspberries (553 µmol) (*N*=9, mean ± s.e.)	(Ludwig et al. 2015)	9
		17 ± 2	60 hours including 12 hour fast		24 hours	18 ± 2			Raspberries (344 µmol) (mean ± s.e., *N*=8). No increase on hydrolysis.	(Gonzalez-Barrio, Edwards, and Crozier 2011)	8
		15.8 ± 2.7 day 1 18.2 ± 2.6 at 1 month	2-day including over-night fast	0.87 ± 0.07					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		18.5 ± 2.5 day 1	2-day including	0.77 ± 0.07					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23)		23

		15.6 ± 2.5 at 1 month	over-night fast						Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		
	0.51 ± 0.17	6.6 ± 1.5	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	0.49 ± 0.17		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	0.80 ± 0.35		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	0.68 ± 0.23		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	1.76 ± 1.00		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
		3.58 ± 0.67 day 1 3.59 ± 0.55 at 1 month	1 day including over-night fast	0.07 ± 0.007 0.05 ± 0.003 0.09 ± 0.014 0.07 ± 0.011					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano, Istas, et al. 2016)	18
		0.07 ± 0.01 [a]	2 days						Orange juice (368 µmol) (*N*=9, mean ± s.e.)	(Pereira-Caro et al. 2023)	9
		0.15 ± 0.01 [a]	2 days						Orange juice (368 µmol) plus oat bran (58 µmol) (*N*=9, mean ± s.e.)		
		19 ± 6	Two days		2 hours	n.d.			Tomato juice (176 µmol) (*N*=6, mean ± s.e.) Intact colon	(Jaganath et al. 2006)	6
		n.d.	Two days		2 hours	n.d.			Tomato juice (176 µmol) (*N*=6, mean ± s.e.) Ileostomists		
		0.7 ± 0.2 [d]	Two days		12 hours	0.8 ± 0.2 [d]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		1.1 ± 0.1 [d]	Two days		12 hours	0.6 ± 0.2 [d]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
	0.10 ± 0.02	$(1.65 \pm 0.26)10^{-3}$	Two days and Over-night fast		2 hours	$(0.21 \pm 0.12)10^{-3}$			Hydroxy-tyrosol enriched biscuits (5.25 mg) (*N*=13, mean ± s.d.). T_{max} = 53 ± 24 min. AUC 900 ± 180 µmol.h.l^{-1} Quantified with free acid	(Mateos et al. 2016)	13
0.04 ± 0.01		$(0.86 \pm 0.09)10^{-3}$	Two days and Over-night fast		2 hours	$(0.20 \pm 0.08)10^{-3}$			Control biscuits (*N*=13, mean ± s.d.). T_{max} = 88 ± 100 min. AUC 600 ± 120 µmol.h.l^{-1} Quantified with free acid		

	0.87 ± 0.11	36.0 ± 20.0 [c]	—						Hydroxy-tyrosol-rich supplement 1 (10 g) (*N*=12, mean ± s.e.) T_{max} = 30 min	(Bender, Strassmann, and Golz 2023)	5
	0.95 ± 0.16	46.2 ± 5.4 [c]	—						Hydroxy-tyrosol-rich supplement 2 (11 g) (*N*=13, mean ± s.e.) T_{max} = 30 min		
			—				0.60 ± 0.66		Free-living volunteers (mean ± s.e., *N*=5). No increase on hydrolysis	(Jenner, Rafter, and Halliwell 2005)	5
			—				0.83, 0.25, 0.77, 0.27		One free-living volunteer over four consecutive days. No increase on hydrolysis		
			Two weeks				2 [b] n.d.		Low (poly)phenol diet four weeks Zero time (single value *N*=1) Four weeks	(Munoz-Gonzalez et al. 2013)	5
			Two weeks				25 ± 32 [b] 35 ± 55 [b]		Red wine (*ca* 112 mg/250 ml) daily for four weeks Zero time (mean ± s.d., *N*=4) Four weeks (mean ± s.d., *N*=3)		
										22	483

Notes: a) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

b) µmol/g rather than µmol/l but authors do not indicate whether this is wet weight or dry weight

c) collection of urine 12 hours rather than 24

d) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

n.d.= not detected

Table 70. 3′-Methoxy-phenylacetic acid-4′-sulfate											
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			
0.42 ± 0.235 (**0.38** and 0.22)									Free-living volunteers (*N*=90, mean ± s.d.) (**Median** and IQR)	(Le Sayec et al. 2023)	90
0.031 **0.021–0.061** [b]		**0.230** **0.053–0.399** [b]							*N*=10, median and IQR. Polyphenol-rich breakfast for 3 days [a]	(Domínguez-Fernández et al. 2021)	10
		10.0 ± 1.4 day 1 6.4 ± 1.0 at 1 month	2-day including over-night fast	0.18 ± 0.02					Day 1 placebo (mean ± s.e., *N*=22) Placebo after 1 month (mean ± s.e., *N*=22)	(Heiss et al. 2022)	22
		6.9 ± 1.0 day 1 7.2 ± 1.2 at 1 month	2-day including over-night fast	0.2 ± 0.02					Day 1 cranberries (525 mg) (mean ± s.e., *N*=23) Cranberries (525 mg) after 1 month (mean ± s.e.), *N*=23)		23
	0.030 ± 0.010	0.21 ± 0.04	Three days						Daily Cranberry juice (787 mg) for 1 month (mean ± s.e., *N*=10).	(Feliciano, Boeres, et al. 2016)	10
	0.033 ± 0.014		Three days						Daily Cranberry juice (476 mg) (mean ± s.e., *N*=10).	(Feliciano et al. 2017)	10
	0.034 ± 0.010		Three days						Daily Cranberry juice (1238 mg) for (mean ± s.e., *N*=10).		10
	0.038 ± 0.012		Three days						Daily Cranberry juice (1534 mg (mean ± s.e., *N*=10).		10
	0.052 ± 0.015		Three days						Daily Cranberry juice (1910 mg) (mean ± s.e., *N*=10).		10
		0.14 ± 0.03 day 1 0.18 ± 0.04 at 1 month	1 day including over-night fast	0.004 ± 0.001 0.004 ± 0.001 0.006 ± 0.001 0.004 ± 0.001					Daily Wild blueberries (726 mg) for 1 month (mean ± s.e., *N*=18).	(Feliciano, Istas, et al. 2016)	18
	0.006 (0.001, 0.013)	0.2 (0.04, 0.4)	24 hours	0.002 ± 0.001	spot	0.096 ± 0.012			Artichoke (5727 µmol) (*N*= 8, mean) (min, max)	(Dominguez-Fernandez et al. 2022)	8
										7	221

Notes: a) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

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).

n.d. = not detected

Table 71. 2*R/S*-hydroxy-2-(4'-Hydroxy-3'-methoxyphenyl)acetic acid (Vanillylmandelic acid, VMA)											
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			
		$(0.102 \pm 0.034)10^{-3}$ zero time $(0.098 \pm 0.041)10^{-3}$ at 8 weeks	—						Healthy free-living volunteers (mean ± s.d., *N*=18) on two occasions one week apart	(Veselinovic et al. 2018)	18
		15 ± 1	60 hours including 12 hour fast		24 hours	13 ± 2			Raspberries (344 µmol) (mean ± s.e., *N*=8). No increase on hydrolysis.	(Gonzalez-Barrio, Edwards, and Crozier 2011)	8
	trace		Over-night	$(0.4 \pm 0.1)10^{-3}$					Orange juice (398 µmol) (*N*=10, mean ± s.e.) Trained athletes	(Pereira-Caro et al. 2020)	10
		0.35 ± 0.1 [b]	Two days		12 hours	0.7 ± 0.2 [b]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		0.9 ± 0.1 [b]	Two days		12 hours	0.4 ± 0.1 [b]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		
		11.8, 5.28–15.3							Free-living healthy volunteers (mean and range, *N*=5)	(Chauhan and Darbre 1980)	5
										5	51

Notes

b) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

Table 72. 2*R/S*-hydroxy-2-(4′-Hydroxyphenyl)acetic acid (4′-hydroxy-mandelic acid)											
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			
		15 ± 1	60 hours including 12 hour fast		24 hours	10 ± 2			Raspberries (344 µmol) (mean ± s.e., *N*=8). No increase on hydrolysis.	(Gonzalez-Barrio, Edwards, and Crozier 2011)	8
	$(11 \pm 0.6)10^{-3}$		Over-night	$(1.2 \pm 0.3)10^{-3}$					Orange juice (398 µmol) (*N*=10, mean ± s.e.) Trained athletes. T_{max} = 1.9 ± 0.1 hours	(Pereira-Caro et al. 2020)	10
		1.8 ± 0.6 [b]	Two days		12 hours	0.6 ± 0.2 [b]			Orange juice (398 µmol) (mean ± s.e., *N*=10 trained)	(Pereira-Caro et al. 2017)	10
		2.4 ± 0.1 [b]	Two days		12 hours	0.3 ± 0.07 [b]			Orange juice (398 µmol) (mean ± s.e., *N*=10 detrained)		10
										3	38

Notes: b) Phenolic content of baseline urine collected 12 h before orange juice intake used, on an excretion-per-hour basis, to subtract from excretion values in trained and detrained states obtained 0–24 h after supplementation to estimate increases in the phenolic content attributable to orange juice intake.

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			
		0.71, 0.44–1.01							Free-living healthy volunteers (mean and range, *N*=5)	(Chauhan and Darbre 1980)	5
									Mangoes (500 µmol) (*N*=8, mean ± s.e.)	Crozier	8
		8 ± 5							Mangoes (500 µmol) Ileostomists (*N*=10, mean ± s.e.)		10
										2	23

References

Achour, Mariem, Laura Bravo, Beatriz Sarria, Maha Ben Fredj, Manel Nouira, Ali Mtiraoui, Saad Saguem, and Raquel Mateos. 2021. "Bioavailability and nutrikinetics of rosemary tea phenolic compounds in humans." *Food Research International* 139. doi: 10.1016/j.foodres.2020.109815.

Angel Seguido, Miguel, Rosa Maria Tarradas, Susana Gonzalez-Ramila, Joaquin Garcia-Cordero, Beatriz Sarria, Laura Bravo-Clemente, and Raquel Mateos. 2022. "Sustained Consumption of a Decaffeinated Green Coffee Nutraceutical Has Limited Effects on Phenolic Metabolism and Bioavailability in Overweight/Obese Subjects." *Nutrients* 14 (12). doi: 10.3390/nu14122445.

Beloborodova, N. V., V. V. Moroz, A. A. Osipov, A. Y. Bedova, A. Y. Olenin, M. L. Getsina, O. V. Karpova, and E. G. Olenina. 2015. "Normal level of sepsis-associated phenylcarboxylic acids in human serum." *Biochemistry-Moscow* 80 (3):374-378. doi: 10.1134/s0006297915030128.

Bender, C., S. Strassmann, and C. Golz. 2023. "Oral Bioavailability and Metabolism of Hydroxytyrosol from Food Supplements." *Nutrients* 15 (2). doi: 10.3390/nu15020325.

Chauhan, J., and A. Darbre. 1980. "Determination of homovanillic, isohomovanillic and vanillylmandelic acids in human-urine by means of glass-capillary gas-liquid-chromatography with temperature-programmed electron-capture detection." *Journal of Chromatography* 183 (4):391-401. doi: 10.1016/s0378-4347(00)81581-9.

Claustre, J., J. M. Pequignot, B. Buixuan, R. Muchada, R. M. Cottetemard, and L. Peyrin. 1990. "Conjugation and deamination of circulating dopamine - relationship between sulfated and free dopamine in man." *Journal of the Autonomic Nervous System* 29 (2):175-182. doi: 10.1016/0165-1838(90)90183-j.

Combet, E., M.E. Lean, J.G. Boyle, A. Crozier, and D.F. Davidson. 2011. "Dietary flavonols contribute to false-positive elevation of homovanillic acid, a marker of catecholamine-secreting tumors." *Clin. Chim. Acta* 412 (1-2):165-169.

Davis, B. A., D. A. Durden, and A. A. Boulton. 1982. "Plasma-concentrations of *para*-hydroxyphenylacetic and *meta*-hydroxyphenylacetic acid and phenylacetic acid in humans - gas-chromatographic high-resolution mass-spectrometric analysis." *Journal of Chromatography* 230 (2):219-230. doi: 10.1016/s0378-4347(00)80473-9.

Dominguez-Fernandez, M., P. Young Tie Yang, I. A. Ludwig, M. N. Clifford, C. Cid, and A. Rodriguez-Mateos. 2022. "*In vivo* study of the bioavailability and metabolic profile of (poly)phenols after sous-vide artichoke consumption." *Food Chem* 367:130620. doi: 10.1016/j.foodchem.2021.130620.

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.

Fan, Jiayi, Eunyoung Park, Liyun Zhang, Indika Edirisinghe, Britt Burton-Freeman, and Amandeep K. Sandhu. 2020. "Pharmacokinetic Parameters of Watermelon (Rind, Flesh, and Seeds) Bioactive Components in Human Plasma: A Pilot Study to Investigate the Relationship to Endothelial Function." *Journal of Agricultural and Food Chemistry* 68 (28):7393-7403. doi: 10.1021/acs.jafc.0c02756.

Feliciano, R. P., A. Boeres, L. Massacessi, G. Istas, M. R. Ventura, C. N. dos Santos, C. Heiss, and A. Rodriguez-Mateos. 2016. "Identification and quantification of novel cranberry-derived plasma and urinary (poly)phenols." *Archives of Biochemistry and Biophysics* 599:31-41. doi: 10.1016/j.abb.2016.01.014.

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

Goldstein, David S., Patti Sullivan, Abraham Corrales, Risa Isonaka, Janna Gelsomino, Jamie Cherup, Genessis Castillo, and Courtney Holmes. 2021. "Multiple catechols in human plasma after drinking caffeinated or decaffeinated coffee." *Journal of Chromatography B*:122988. doi: https://doi.org/10.1016/j.jchromb.2021.122988.

Gomez-Juaristi, M., S. Martinez-Lopez, B. Sarria, L. Bravo, and R. Mateos. 2018. "Absorption and metabolism of yerba maté phenolic compounds in humans." *Food Chemistry* 240:1028-1038. doi: 10.1016/j.foodchem.2017.08.003.

Gomez-Juaristi, M., B. Sarria, S. Martinez-Lopez, L. Bravo Clemente, and R. Mateos. 2019. "Flavanol Bioavailability in Two Cocoa Products with Different Phenolic Content. A Comparative Study in Humans." *Nutrients* 11 (7):1441. doi: 10.3390/nu11071441.

Gonzalez-Barrio, R., C.A. Edwards, and A. Crozier. 2011. "Colonic catabolism of ellagitannins, ellagic acid, and raspberry anthocyanins: *in vivo* and *in vitro* studies." *Drug Metab Disp* 39 (9):1680-1688.

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.

Jaganath, I.B., W. Mullen, C.A. Edwards, and A. Crozier. 2006. "The relative contribution of the small and large intestine to the absorption and metabolism of rutin in man." *Free Radic. Res* 40 (10):1035-1046.

Jenner, A.M., J. Rafter, and B. Halliwell. 2005. "Human fecal water content of phenolics: the extent of colonic exposure to aromatic compounds." *Free Radical Biology & Medicine* 38 (6):763-772. doi: 10.1016/j.freeradbiomed.2004.11.020.

Karlsson, P.C., U. Huss, A. Jenner, B. Halliwell, L. Bohlin, and J.J. Rafter. 2005. "Human fecal water inhibits COX-2 in colonic HT-29 cells: Role of phenolic compounds." *J. Nutr* 135 (10):2343-2349.

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.

Knust, U., G. Erben, B. Spiegelhalder, H. Bartsch, and R.W. Owen. 2006. "Identification and quantitation of phenolic compounds in faecal matrix by capillary gas chromatography and nano-electrospray mass spectrometry." *Rapid Communications in Mass Spectrometry* 20 (20):3119-3129. doi: 10.1002/rcm.2702.

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.

Loke, W.M., A.M. Jenner, J.M. Proudfoot, A.J. McKinley, J.M. Hodgson, B. Halliwell, and K.D. Croft. 2009. "A metabolite profiling approach to identify biomarkers of flavonoid intake in humans." *J. Nutr* 139 (12):2309-2314.

Ludwig, Iziar A., Pedro Mena, Luca Calani, Gina Borges, Gema Pereira-Caro, Letizia Bresciani, Daniele Del Rio, Michael E. Lean, and Alan Crozier. 2015. "New insights into the bioavailability of red raspberry anthocyanins and ellagitannins." *Free Radical Biology and Medicine* 89:758-769. doi: 10.1016/j.freeradbiomed.2015.10.400.

Macià, Alba, Maria-Paz Romero, Silvia Yuste, Iziar Ludwig, Anna Pedret, Rosa Maria Valls, Patricia Salamanca, Rosa Solà, Maria José Motilva, and Laura Rubió. 2022. "Phenol metabolic fingerprint and selection of intake biomarkers after acute and sustained consumption of red-fleshed apple versus common apple in humans. The AppleCOR study." *Food Chemistry* 384:132612. doi: https://doi.org/10.1016/j.foodchem.2022.132612.

Mateos, Raquel, Sara Martinez-Lopez, Gema Baeza Arevalo, Miryam Amigo-Benavent, Beatriz Sarria, and Laura Bravo-Clemente. 2016. "Hydroxytyrosol in functional hydroxytyrosol-enriched biscuits is highly bioavailable and decreases oxidised low density lipoprotein levels in humans." *Food Chemistry* 205:248-256. doi: 10.1016/j.foodchem.2016.03.011.

McKay, D. L., C. Y. O. Chen, C. A. Zampariello, and J. B. Blumberg. 2015. "Flavonoids and phenolic acids from cranberry juice are bioavailable and bioactive in healthy older adults." *Food Chemistry* 168:233-240. doi: 10.1016/j.foodchem.2014.07.062.

Mitchell, J., and C. J. Coscia. 1978. "Application of paired-ion high-pressure liquid column chromatography to analysis of L-3,4-dihydroxyphenylalanine metabolites." *Journal of Chromatography* 145 (2):295-301. doi: 10.1016/s0378-4347(00)81351-1.

Munoz-Gonzalez, I., A. Jimenez-Giron, P.J. Martin-Alvarez, B. Bartolome, and M.V. Moreno-Arribas. 2013. "Profiling of microbial-derived phenolic metabolites in human feces after moderate red wine intake." *J Agric. Food Chem* 61 (39):9470-9. doi: 10.1021/jf4025135.

Murphy, N., D. Achaintre, R. Zamora-Ros, M. Jenab, M. C. Boutron-Ruault, F. Carbonnel, I. Savoye, R. Kaaks, T. Kühn, H. Boeing, K. Aleksandrova, A. Tjønneland, C. Kyrø, K. Overvad, J. R. Quirós, M. J. Sánchez, J. M. Altzibar, J. María Huerta, A. Barricarte, K. T. Khaw, K. E. Bradbury, A. Perez-Cornago, A. Trichopoulou, A. Karakatsani, E. Peppa, D. Palli, S. Grioni, R. Tumino, C. Sacerdote, S. Panico, H. B. A. Bueno-de-Mesquita, P. H. Peeters, M. Rutegård, I. Johansson, H. Freisling, H. Noh, A. J. Cross, P. Vineis, K. Tsilidis, M. J. Gunter, and A. Scalbert. 2018. "A prospective evaluation of plasma polyphenol levels and colon cancer risk." *Int J Cancer* 143 (7):1620-1631. doi: 10.1002/ijc.31563.

Nardini, M., F. Natella, C. Scaccini, and A. Ghiselli. 2006. "Phenolic acids from beer are absorbed and extensively metabolized in humans." *Journal of Nutritional Biochemistry* 17 (1):14-22.

Olthof, M.R., P.C. Hollman, M.N. Buijsman, J.M. van Amelsvoort, and M.B. Katan. 2003. "Chlorogenic acid, quercetin-3-rutinoside and black tea phenols are extensively metabolized in humans." *Journal of Nutrition* 133 (6):1806-1814.

Pereira-Caro, G., T. Polyviou, I. A. Ludwig, A. M. Nastase, J. M. Moreno-Rojas, A. L. Garcia, D. Malkova, and A. Crozier. 2017. "Bioavailability of orange juice (poly) phenols: the impact of short-term cessation of training by male endurance athletes." *American Journal of Clinical Nutrition* 106 (3):791-800. doi: 10.3945/ajcn.116.149898.

Pereira-Caro, Gema, Tahani M. Almutairi, Salud Cáceres-Jiménez, José Manuel Moreno-Rojas, Dalia Malkova, Ada L. García, and Alan Crozier. 2023. "Bioavailability of orange juice (poly)phenols: β-glucan-rich oat bran decreases urinary excretion of flavanone phase II metabolites and enhances excretion of microbiota-derived phenolic catabolites." *Free Radical Biology and Medicine*. doi: https://doi.org/10.1016/j.freeradbiomed.2023.02.002.

Pereira-Caro, Gema, Michael N. Clifford, Thelma Polyviou, Iziar A. Ludwig, Hani Alfheeaid, José Manuel Moreno-Rojas, Ada L. Garcia, Dalia Malkova, and Alan Crozier. 2020. "Plasma pharmacokinetics of (poly)phenol metabolites and catabolites after ingestion of orange juice by endurance trained men." *Free Radical Biology and Medicine* 160:784-795. doi: https://doi.org/10.1016/j.freeradbiomed.2020.09.007.

Roowi, S., W. Mullen, C.A. Edwards, and A. Crozier. 2009. "Yoghurt impacts on the excretion of phenolic acids derived from colonic breakdown of orange juice flavanones in humans." *Mol. Nutr. Food Res* 53 Suppl 1:S68-S75.

Seguido, Miguel Ángel, Rosa María Tarradas, Susana González-Rámila, Joaquín García-Cordero, Beatriz Sarriá, Laura Bravo-Clemente, and Raquel Mateos. 2022. "Influence of 8-week daily consumption of a new product combining green coffee hydroxycinnamates and beta-glucans on polyphenol bioavailability in subjects with overweight and obesity." *Food & Function* 13:1133-1152. doi: 10.1039/D1FO03327A.

Tosi, Nicole, Claudia Favari, Letizia Bresciani, Emma Flanagan, Michael Hornberger, Arjan Narbad, Daniele Del Rio, David Vauzour, and Pedro Mena. 2023. "Unravelling phenolic metabotypes in the frame of the COMBAT study, a randomized, controlled trial with cranberry supplementation." *Food Research International* 172. doi: 10.1016/j.foodres.2023.113187.

Urpi-Sarda, M., M. Monagas, N. Khan, R. Llorach, R.M. Lamuela-Raventos, O. Jauregui, R. Estruch, M. Izquierdo-Pulido, and C. Andres-Lacueva. 2009. "Targeted metabolic profiling of phenolics in urine and plasma after regular consumption of cocoa by liquid chromatography-tandem mass spectrometry." *J. Chromatogr. A* 1216 (43):7258-7267.

Veselinovic, T., H. Schorn, M. Paulzen, I. Vernaleken, and G. Gruender. 2018. "Effects of antidopaminergic intervention on catecholamine metabolites in plasma and urine in healthy volunteers." *International Journal of Neuropsychopharmacology* 14:1125-1138.

Ward, N.C., K.D. Croft, I.B. Puddey, and J.M. Hodgson. 2004. "Supplementation with grape seed polyphenols results in increased urinary excretion of 3-hydroxyphenylpropionic acid, an important metabolite of proanthocyanidins in humans." *J. Agric. Food Chem* 52 (17):5545-5549.

Zumarraga, M., R. Davila, N. Basterreche, A. Arrue, B. Goienetxea, M. I. Zamalloa, L. Erkoreka, S. Bustamante, L. Inchausti, M. A. Gonzalez-Torres, and J. Guimon. 2010. "Catechol *O*-methyltransferase and monoamine oxidase A genotypes, and plasma catecholamine metabolites in bipolar and schizophrenic patients." *Neurochemistry International* 56 (6-7):774-779. doi: 10.1016/j.neuint.2010.02.015.