

Supplementary Materials: Influence of Vegetarian Dietary Intervention on Urinary Paraben Concentrations: A Pilot Study with ‘Temple Stay’ Participants

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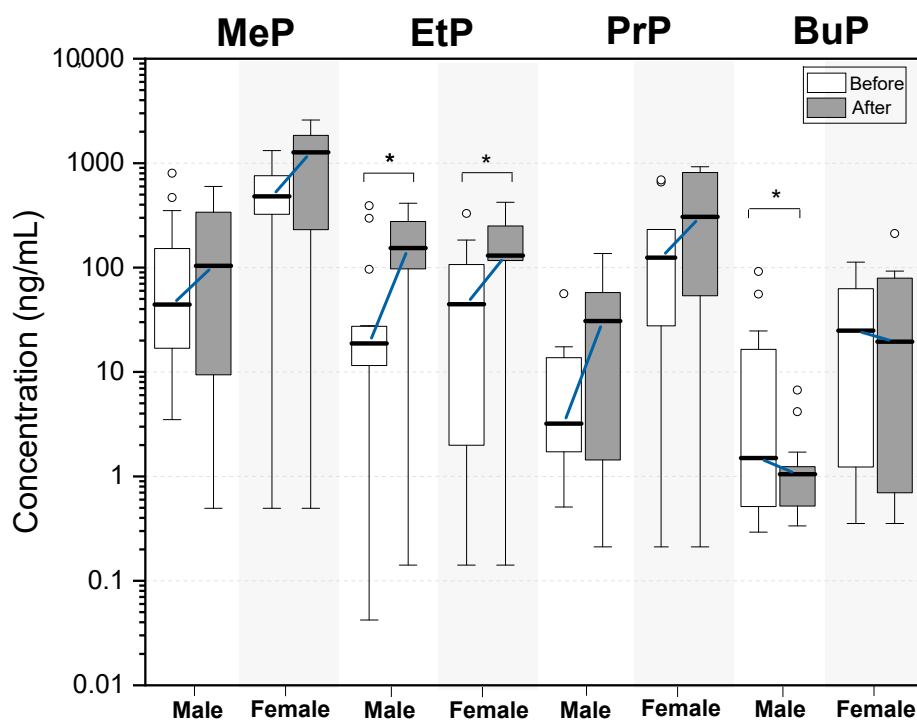


Figure S1. Distribution of urinary parabens among the temple stay participants (unadjusted, $n = 25$). Bottom and top of a box indicates the first and third quartiles of the distribution, respectively. The black bands inside the boxes show the median. The whiskers represent the 5th and 95th percentiles. * difference between intervention as determined by p -value (<0.05) for non-parametric method (paired-Wilcoxon signed-rank test).

Table S1. Characteristics of study population.

Characteristic	<i>n</i> (%)
Age (years)	
10 to 19	3 (12)
20 to 39	11 (44)
40 to <60	9 (36)
≥60	2 (8)
Gender	
Male	16 (64)
Female	9 (36)
Body mass index (kg/m ²)	
<18.5	0 (0)
18.5 to 22.9	16 (64)
>23	9 (36)
Urinary creatinine (mg/dL) ^a	
Pre-intervention	
<118.6	5 (20)
>118.6	20 (80)
Post-intervention	
<118.6	2 (8)
>118.6	23 (92)

^a Creatinine data are classified by the median (118.6 mg/dL) reported in [1] for a 1988–1994 sample of 22,245 individuals (6–90 years of age).

Table S2. Tap water (mL/day) and food (servings per day) intake information of study participants before the temple stay (*n* = 25).

Type	Gender	Median	95th
Tap water	Male	1000.0	3600
	Female	1360.0	1780
Beef	Male	0.30	2.00
	Female	0.15	1.50
Pork	Male	0.40	2.50
	Female	0.45	5.00
Chicken	Male	0.62	1.00
	Female	0.85	2.00
Dairy products	Male	2.25	5.00
	Female	2.00	5.50
Other meats	Male	0.00	0.50
	Female	0.00	0.50
Raw fish (sashimi)	Male	0.00	1.00
	Female	0.00	1.00

None of the subjects indicated the consumption of mutton, goat meat, duck, or turkey during the surveyed period. Source : [2].

Table S3. HPLC condition for analysis of urinary chemicals.

Parameter	Condition
Column	Synergi 4 μ Fusian-RP 75 $\times$ 2 mm 4 μ m
Mobile phase	A: 0.1% acetic acid in water B: 0.1% acetic acid in ACN
flow rate	400 μ L/min (gradient)
Injection volume	5 μ L
Ionization mode	ESI negative/positive ^a
Curtain gas	10 psi
Column temperature	40 $^{\circ}$ C
Ion spray voltage	−4500 V/5500 V ^a
Ion source gas 1	40 psi/30 psi ^a
Ion source gas 2	60 psi/10 psi ^a
Collision gas	5

^aHPLC condition of benzophenone-3.

Quality control and quality assurance

The accuracy of analysis was tested at three different concentrations of spiked samples, i.e., low (2 μ g/L), medium (10 μ g/L), and high (50 μ g/L). For each concentration of the spiked samples, five replicates were prepared and were measured. Percent recovery was then calculated as a measure of accuracy. Precision of the analytical procedure was measured as the coefficient of variation (CV) divided by the mean of the measured concentrations at a given concentration (Table S4).

Table S4. Mass spectrometer conditions for analysis of urinary chemicals.

Compound	Q1 Mass	Q3 Mass	DP	EP	CE	CXP
¹³ C ₆ -Methylparaben	157	98	−75	−10	−30	−1
¹³ C ₆ -Ethylparaben	171	98	−65	−10	−26	−5
¹³ C ₆ -Propylparaben	185	98	−60	−10	−32	−17
¹³ C ₆ -Butylparaben	199	98	−80	−10	−28	−19
¹³ C ₆ -Benzophenone-1	219	135	−95	−10	−26	−7
Benzophenone-d ₁₀	193	110	76	10	25	10
Methylparaben	151	92	−50	−10	−26	−17
Ethylparaben	165	92	−55	−10	−30	−17
Propylparaben	179	92	−60	−10	−30	−17
Butylparaben	193	92	−65	−10	−30	−17
Benzophenone-1	213	135	−100	−10	−22	−23
Benzophenone-3	229	105	61	10	29	10

Abbreviations: DP, Declustering Potential, V; CE, Collision Energy, V; CXP, Collision Cell Exit Potential, V; Q1, Precursor ion mass, m/z; Q3, Daughter ion mass, m/z. EP, Entrance Potential.

Table S5. Recoveries and precisions of benzophenones and parabens in urine samples.

Compound	Spiking Concentration (µg/L)	Recovery		Precision (CV ^a , %)	
		Intra-day (n = 5)	Inter-day (n = 5)	Intra-day (n = 5)	Inter-day (n = 5)
Methylparaben	2	108.0	100.8	8.6	7.4
	10	113.6	100.2	12.4	8.6
	50	109.4	104.3	3.4	3.8
Ethylparaben	2	107.7	97.7	5.6	4.7
	10	97.9	95.7	3.8	4.1
	50	99.5	98.2	1.8	2.5
Propylparaben	2	85.5	84.5	16.7	14.5
	10	91.8	92.7	7.2	5.2
	50	100.1	98.5	5.1	4.2
Butylparaben	2	97.6	101.5	18.8	11.7
	10	91.7	93.1	6.9	6.4
	50	95.4	94.7	2.1	2.1
Benzophenone-1	2	97.6	85.6	8.7	4.9
	10	106.1	109.6	6.4	3.4
	50	99.8	101.0	4.9	6.0
Benzophenone-3	2	108.8	99.4	6.2	7.1
	10	101.9	98.3	2.6	3.0
	50	99.8	98.8	4.8	5.4

^aCoefficient of variation.**Table S6.** Comparison of urinary levels of test chemicals by gender and following the temple stay, based on the mixed effects model.

Analyte	Male vs. Female			Pre vs. Post Temple Stay		
	Slope ^a	95% CI for Slope Estimate	p	Slope ^b	95% CI for Slope Estimate	p
MeP	1.93	0.07 to 3.80	0.04*	0.09	−0.66 to 0.85	0.80
EtP	−0.01	−1.70 to 1.68	0.99	1.91	0.76 to 3.07	0.00**
PrP	2.85	1.10 to 4.60	0.00**	0.44	−0.48 to 1.37	0.33
BuP	1.68	0.34 to 3.01	0.02*	−1.08	−2.06 to −0.10	0.03*
BP-1	0.85	−0.30 to 2.01	0.14	0.06	−0.43 to 0.54	0.81
BP-3	0.36	−0.54 to 1.26	0.42	−0.36	−0.90 to 0.17	0.18

Abbreviation: CI, Confidence interval; Pre, Pre-intervention, Post, Post-intervention. ^aSlope between gender. ^bSlope between the temple stay. Adjusted for age and log creatinine concentration in the urine. * $p < 0.05$, ** $p < 0.01$.

Table S7. Mixed-effects model results from multilevel spline model.

Analyte	Gender	Percent Change (%) ^a	95% CI for Slope Estimate	<i>p</i> -value
MeP	Male	−28.02 (51.21 vs. 53.74)	−1.70 to 1.04	0.627
	Female	36.34 (208.33 vs. 384.3)	−2.45 to 3.08	0.811
EtP	Male	561.28 (14.70 vs. 121.78)	0.35 to 3.43	0.018*
	Female	425.93 (12.93 vs. 81.34)	−1.05 to 4.37	0.210
PrP	Male	12.42 (4.28 vs. 7.46)	−1.23 to 1.47	0.860
	Female	70.65 (58.89 vs. 133.15)	−2.23 to 3.30	0.685
BuP	Male	−75.66 (3.60 vs. 1.03)	−2.52 to −0.31	0.014*
	Female	−34.16 (7.57 vs. 7.11)	−2.83 to 1.99	0.715
BP-1	Male	7.38 (2.60 vs. 3.78)	−0.53 to 0.67	0.811
	Female	2.33 (9.34 vs. 12.06)	−2.09 to 2.14	0.981
BP-3	Male	−16.36 (5.38 vs. 6.19)	−0.87 to 0.52	0.603
	Female	−52.29 (13.57 vs. 6.99)	−2.29 to 0.80	0.318

Abbreviation: CI, Confidence interval; Pre, Pre-intervention, Post, Post-intervention. ^aPercent change in the GM between the two time periods, with GMs of the two time periods shown in parentheses.

Adjusted for age and log creatinine concentrations. **p* < 0.05.

Table S8. Concentrations (µg/L) of parabens in the human urines reported worldwide.

Country	Sampling Year	N	Population	Age (Years)	Median (µg/L) (95 th Percentile)				Reference
					MeP	EtP	PrP	BuP	
Korea	2007	16	Males	14–64	44.2 (551)	20.1 (320.5)	3.3 (27.1)	3.9 (64.7)	This study
		16		14–64	104 (579.5)	175.5 (399.8)	20.9 (127)	1.1 (4.8)	
		9	Females	13–47	481 (1248)	42.9 (240.2)	120 (677.8)	20.4 (93.92)	
		9		13–47	1270 (2350)	130 (378.8)	359 (893.2)	15 (164.2)	
		25	All	13–64	103 (1072)	21.3 (154)	9.8 (572.8)	6.4 (86.34)	
		25		13–64	231 (1962)	154 (410.2)	51.2 (837.6)	1.1 (89.84)	
	2015	108	Males	27.5–36.4	9.10 (31.6) ^a	32.6 (80) ^a	<LOD (2.7) ^a	<LOD (<LOD) ^a	[3]
		108		27.5–36.4	11.1 (48.2) ^a	19.4 (67.1) ^a	0.8 (5.9) ^a	<LOD (<LOD) ^a	
		153	Females	27.5–36.4	11.6 (52.1) ^a	31.4 (90.1) ^a	0.9 (10.7) ^a	<LOD (1.4) ^a	
		153		27.5–36.4	19.2 (69.5) ^a	19.2 (56.8) ^a	1.8 (11) ^a	<LOD (<LOD) ^a	
		261	All	27.5–36.4	9.9 (39.8) ^a	32.4 (82.8) ^a	0.6 (6.2) ^a	<LOD (<LOD) ^a	
		261		27.5–36.4	15.8 (62) ^a	19.2 (62.5) ^a	1.5 (8.8) ^a	<LOD (<LOD) ^a	
	2009–2010	1167	Males	3–69	123 (-)	37.9 (-)	5 (-)	0.33 (-)	[4]
		1374	Females	3–69	233 (-)	29.2 (-)	37.8 (-)	1.48 (-)	
		2541	All	3–69	166 (1145)	32.8 (467)	15.5 (300)	0.51 (57.4)	
China	2006–2007	26	All	30	112 (1440)	32.7 (113)	47.4 (421)	4.30 (46.7)	[5]
	2010–2012	47	All	2–67	10.1 (883)	2.74 (67.1)	9.91 (357)	<LOQ (1.59)	
India	2010–2012	41	All	24–75	6.28 (96.4)	0.25 (11.1)	0.39 (44.4)	<LOQ (0.9)	[6]
Japan	2012–2013	128	Females	19–22	273 (4107) ^b	4.04 (166) ^b	8.39 (441) ^b	0.634 (73.7) ^b	
Kuwait	2010–2012	36	All	2–59	8.65 (298)	0.52 (98.5)	0.13 (98.3)	<LOQ (18.7)	[5]
	2010–2012	40	All	6–73	4.03 (137)	0.68 (47.6)	1.24 (50)	<LOQ (37.1)	
Saudi Arabia	2012	30	All	3–87	6.80 (99.3)	0.19 (4.5)	0.58 (30.4)	<LOQ (0.78)	[7]
Vietnam	2010–2012	19	All	19–83	2.92 (72.8)	0.26 (1.31)	0.07 (35.6)	-	
Belgium	2013	123	Males	1–85	7.70 (223.4)	1.30 (41.4)	0.50 (20.2)	<LOD (4.9)	[7]
		138	Females	1–85	32.4 (630.6)	1.9 (83.1)	3.30 (116.5)	0.50 (11.1)	
Denmark	2006	261	All	1–85	16.1 (462.6)	1.7 (67.7)	1.2 (78.8)	<LOD (8)	[8]
		60	Males	19.7	17.7 (64.6) ^a	1.98 (5.35) ^a	3.60 (14) ^a	0.19 (1.01) ^a	

Country	Sampling Year	N	Population	Age (Years)	Median (µg/L) (95 th Percentile)				Reference
					MeP	EtP	PrP	BuP	
Denmark	2007	65	Males	5–20	4.65 (64.4)	0.58 (13.8)	0.67 (20.2)	-(2.4)	[9]
		64	Females	5–20	10.4 (555)	0.52 (40.2)	1.85 (84.8)	-(20.6)	
		129	All	5–20	7.7 (251)	0.58 (13.8)	1.02 (46.2)	-(5.24)	
	2007–2009	130	Males	18.9	12.7 (383)	1.35 (37.6)	2.72 (127)	0.22 (27.1)	[10]
	1995–2012	660	Males	20–30	23.2 (224)	1.2 (17.7)	1.5 (46)	<LOQ (5.4)	[11]
Germany	1995–2012	330	Females	20–30	57.2 (388)	4.1 (51.5)	9.5 (122)	0.9 (12.7)	[11]
		330	All	20–30	39.8 (319)	2.1 (39.1)	4.8 (74)	<LOQ (10.7)	
	2010–2011	39	Males	18–64	20.7 (231)	1.3 (47.1)	0.8 (25.8)	<LOQ (17.7)	[12]
Greece	2007–2009	59	Females	29–48	51.4 (609)	4.2 (44)	3.9 (79.4)	0.6 (16.9)	[12]
		30	All	23–75	4.01 (208)	0.76 (24.5)	0.37 (112)	<LOQ (5.54)	
	2012	34	Females	≥18	34.94 (80.91) ^a	1.77 (9.90) ^a	3.06 (12.54) ^a	<LOD (5.15) ^a	[13]
U.S.A.	2010–2012	31	All	11–66	4.23 (123)	0.30 (12.6)	0.69 (24.8)	<LOQ (3.88)	[5]
	2004–2015	383	Males	18–55	23.2 (80.4) ^a	-	2.30 (12.1) ^a	<LOD (0.30) ^a	[14]
	2011	30	All	-	8 (240) ^b	0.58 (23.5) ^b	-	-	[15]
	2004–2010	245	Male	23.9–56.8	29 (96.7) ^a	-	3.10 (16.80) ^a	<LOD (0.50) ^a	[16]
		408	Females	20.9–46.7	155 (422) ^a	-	34.3 (118) ^a	1.20 (7.65) ^a	
		653	All	20.9–56.8	112 (354) ^a	-	24.2 (90.2) ^a	0.70 (5.40) ^a	
	2005–2007	143	Females	18–44	59 (552.7)	1.1 (49.4)	15.1 (202.4)	0.5 (17.9)	[17]
	2003–2005	100	All	-	43.9 (680)	1.0 (47.5)	9.1 (279)	0.5 (29.5)	[18]
NHANE S ^c	2011–2012	1,699	All	>30	48.80 (188) ^a	0.71 (7.10) ^a	6.2 (35.5) ^a	0.14 (0.4) ^a	[19]
	2009–2010	1,830	All	>30	59.20 (241) ^a	1.30 (8.7) ^a	7.70 (49.9) ^a	0.14 (0.8) ^a	[19]
	2009–2010	415	Females	18–40	119 (1,269)	-	24.8 (434)	0.4 (22.1)	[20]
	2007–2008	365	Females	18–40	146 (1,444)	-	33.6 (410)	0.7 (33.6)	[20]

Abbreviations: LOD, Limit of detection; LOQ, Limit of quantification; -, not available. ^a 75th percentiles. ^b max. ^c NHANES, National Health and Nutrition Survey conducted by the U.S. Centers for Disease Control and Prevention (CDC).

Table S9. Maximum levels of parabens allowed in food, cosmetics and personal care products in several countries worldwide.

Country	Category	Chemicals	Type	Criteria	Reference
Korea	Food	MeP and EtP	Capsule and jam	1.0 g/kg	[21]
			Mango chutney and soy sauce	0.25 g/kg	
			Vinegar and beverage	1.0 g/L	
			Sauces	0.2 g/kg	
			Fruit and vegetable peel	0.012 g/kg	
	Cosmetic product	Single ester and mixture		0.4%, 0.8%	
	Quasi-drugs	MeP and PrP	Toothpaste	<0.2%	
			Oral pharmaceutical liquid	<0.01%	
			Oral cleansing wipes	<0.01%	
Japan	Cosmetic product	<i>p</i> -hydroxybenzoic acid ester		1.00%	[22]
EU	Food	Single ester and mixture (MeP, EtP, PrP, BuP)	Snacks - Potato, cereal, flour or starch-based and processed nuts (including coated nuts and nut mixtures)	0.3 g/kg	[23]
			Confectionery (excluding chocolate)	0.3 g/kg	
			Liquid dietary food supplements	2 g/kg	
			Jelly coatings of meat products (cooked, cured or dried)	1 g/kg	
				0.3–2 g/kg	
	Cosmetic product	MeP and EtP		Prohibited	[24]
		Other parabens			
		Single ester and mixture		0.4%, 0.8%	
	Baby product	PrP and BuP	Products of diaper wearing area of infant (<3 years old)	Prohibited	[25]
Danish	Personal care product	PrP, BuP and their isoforms and salts	Products (<3 years old)	Prohibited	[26]
U.S.	Food	MeP and PrP		< 0.1%	[27]

Table S10. Concentrations of parabens reported in condiment and other foodstuff in several Asian countries.

Country	Food Groups	Analyte	Food Type	N	DR (%)	Concentration (mg/kg)	Reference
Korea	Beverage	MeP, EtP, PrP, BuP	Functional beverage, green tea, black tea, red ginseng	61	9.8	2.7	[28,29]
	Condiments	EtP, BuP	Soy sauce	46	43.5	29.7	
		BuP	Gochujang	12	8.3	2.9	
		BuP, isoBuP, isoPrP	Sauces	19	31.6	22.4	
	Kimchi, pickles	BuP	Pickle	80	6.3	1.9	[30]
	Condiments		Soy sauce	75	68	54.6	
			Seasoning	18	0	-	
			Vinegar	69	0	-	
	Beverage	BuP, iso-BuP, EtP, PrP, iso-PrP	Mixed beverage	42	0	-	
	Beverage		Ginseng	6	0	-	
	Beverage		Red ginseng	9	0	-	
	Beverage		Fruit and vegetable juice (except unheated juice)	75	0	-	
	Liquors			12	25	20.7	
	Vegetable		Surface of vegetable	42	0	-	
	Beverage		Nonalcoholic beverages	1592	14	27	
	Condiments		Soy sauce	1260	49.8	69	
	Condiments		Fruit sauce	148	16.9	86	
	Condiments		Vinegar	31	9.7	45	
	Condiments		Syrup	24	37.5	63	
Japan	Fruits and vegetables	EtP, PrP, iso-PrP, BuP, n-BuP		46	0	0	[31]
	Non-permissible foods*		Non-permissible foods	6775	0.2	39	
	Breakdown of non-permissible foods		Preserved foods boiled down in soy sauce, "Tsukudani"	270	0.7	25	
	Condiments		Condensed seasoned soy sauce, "Tare"	369	0.8	23	
	Condiments		Soy sauce-pickled foods, "Shoyu-zuke"	42	11.9	56	
	Condiments	EtP, PrP, iso-PrP, BuP, n-BuP	Sauce other than fruit sauce	20	5	20	
	Condiments		Processed soy sauce, "Shoyu-kakouhin"	3	100	30	
	Beverage		Latic acid bacteria beverages	48	2.1	20	
	Condiments	EtP	A grate soy sauce	10	10	86.4 ^a	
Taiwan	Condiments	EtP	A grate soy sauce	10	10	86.4 ^a	[32]

Country	Food Groups	Analyte	Food Type	N	DR (%)	Concentration (mg/kg)	Reference
Taiwan	Condiments	PrP	A grate soy sauce	10	10	54.2 ^a	[32]
	Condiments	BuP	A grate soy sauce	10	60	33.4–142.4 ^a	
	Condiments	EtP	Fish sauce	4	25	97.1 ^a	
	Condiments	BuP	Fish sauce	4	25	32.4 ^a	
China	Condiments	EtP	High salt constant temperature fermentation	-	-	12.1	[33]
	Condiments	MeP	Soy sauce (10), vinegar (9), cooking wine (3), ketchup	47	100	0.02	[34]
		EtP	(2), bean paste (7), starch (3), aniseed (3), chili		87	0.043	
		PrP	powder (3),		79	0.012	
		BuP	dried soup materials (4), honey (1), oyster sauce (1), sugar (1)		57	0.0002	

* non-permissible foods: foods in which preservatives are not permitted to be used in Japan [31].

Table S11. Estimated daily intake amount of each paraben among the study participants.

Chemical	Gender	UC (µg/L)	F _{ue}	EDI (µg/kg bw-d)					
				Median	SD	Min	25 th	75 th	Max
MeP	Male	104	0.174	17.46	35.89	0.08	2.40	55.29	109.29
	Female	1270		224.58	187.21	0.10	53.10	386.62	476.53
EtP	Male	175.5	0.137	37.17	27.84	0.03	25.12	58.99	95.93
	Female	130		39.54	24.96	0.04	30.41	66.62	78.98
PrP	Male	20.9	0.102	6.09	11.96	0.05	0.45	16.50	38.10
	Female	359		108.30	145.74	0.07	21.10	300.89	378.27
BuP	Male	1.1	0.056	0.52	0.88	0.13	0.39	0.74	3.15
	Female	15		9.74	50.89	0.23	0.47	42.35	157.74

Estimated daily intake (EDI) of each paraben was calculated following Moos, *et al.* [20]): $EDI = UC \times UV_{24h} / F_{ue} \times bw$. UC: urinary concentration (µg/L). EDI was calculated using urinary concentration of each participant after the temple stay. F_{ue}: urinary excretion fraction. UV_{24h}: the total volume of urine in 24 h (assumed 2 L). BW: body weight of each participant of the present study.

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