Supporting information

Association between exposure to benzophenones and dietary pattern and health risk among the general population in Taiwan

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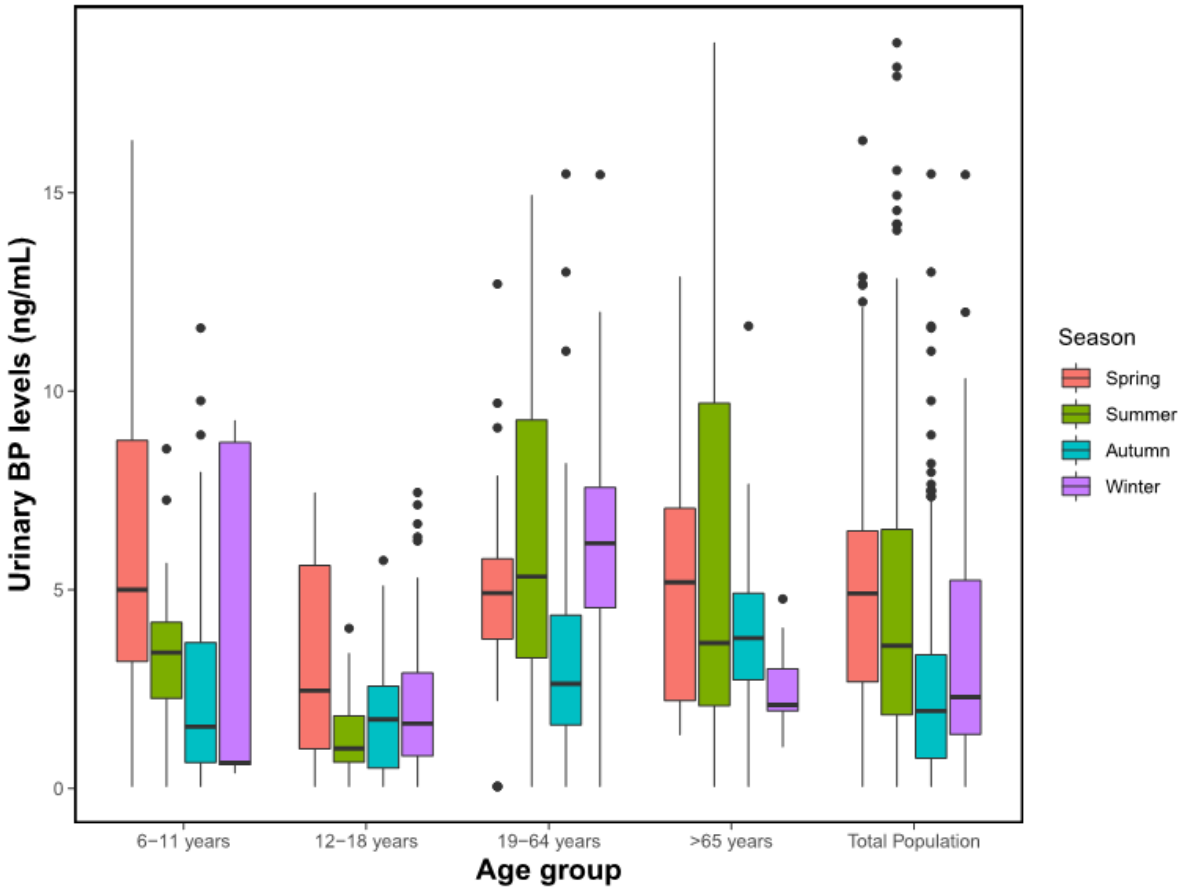

Figure S1. Box plot comparison of BP exposure levels of various age groups of the general population in Taiwan stratified by season.

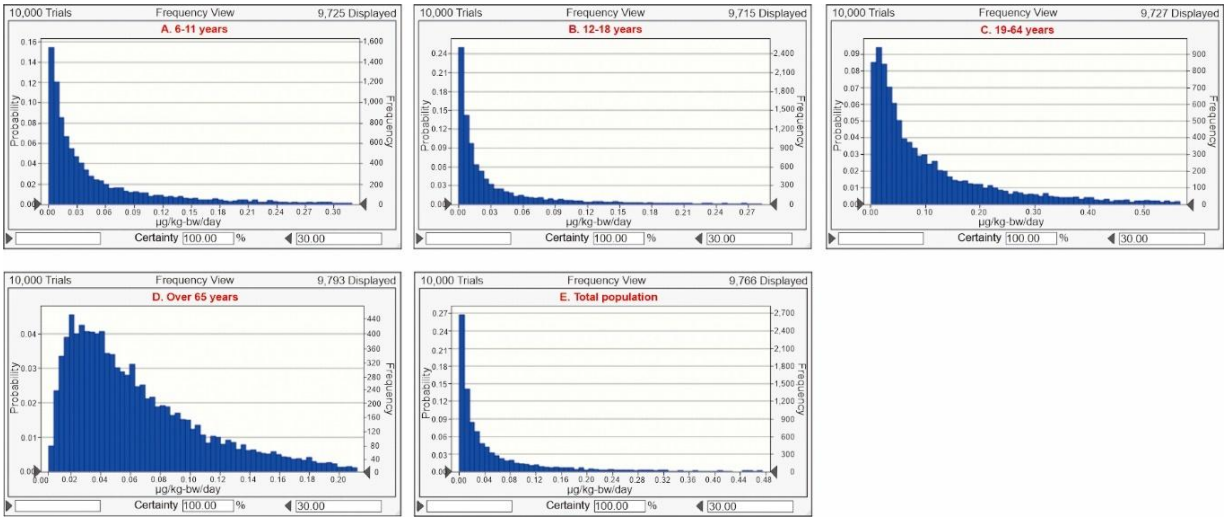

Figure S2. Monte Carlo simulation of daily intake of BP estimated from urinary BP concentrations of various age groups of general population in Taiwan (Unit: µg/kg-bw/day).

Table S1. Mass spectrometric parameters used for the urinary analysis of BPs.

Analyte	RT (time)	Precursor ion (m/z)	Product ion (m/z)
BP	6.60	183.00	105.05
d_5-BP	6.66	188.10	105.10
BP-1	6.48	214.90	137.00
d_5-BP1	6.46	220.10	137.00
BP-2	5.59	245.00	135.00
d_5-BP2	5.45	249.00	137.00
BP-3	7.33	229.00	151.05
d_5-BP3	7.30	234.10	151.00
BP-4	6.09	307.00	197.00
BP-8	6.64	245.00	121.00
d_3-BP8	6.69	248.10	121.10
4-OH-BP	6.09	199.00	121.05
d_4-4-OHBP	6.07	203.10	125.15

Table S2. Limit of detection and limit of quantitation of BPs (n=706).

BPs	LOD (ng/mL)	LOQ (ng/mL)
BP	0.1	0.3
BP-1	0.03	0.1
BP-2	0.004	.0.01
BP-3	0.003	0.01
BP-4	0.333	1
BP-8	0.053	0.16
4-OH-BP	0.001	0.002

Table S3. Food groups and food items of the eating frequency questionnaire

Food groups	Food items
Rice and noodle products	Rice, rice porridge, noodles, Chinese wheat product, filled buns (salty), filled buns (sweet), dumplings, sticky rice products, sticky rice dessert, whole–wheat rice
Grains and bread	Breakfast cereals, breads, whole–wheat bread
Eggs	Eggs, duck eggs, quail eggs, other eggs, processed eggs
Milk, yogurt, cheese	Whole and skim milk, flavored milk, yogurt, cottage cheese, fresh white cheese, cream cheese, white and yellow processed cheese
Vegetables	Light green leafy vegetables, dark green leafy vegetables, root and stem vegetables, mushrooms, bamboo shoots, cucurbits, legumes, marine vegetables, pickled vegetables, seasoned vegetables
Soybean products	Soybean milk, fried soybean products, fermented soybean curd, other soybean products
Nuts and seeds	Peanuts, peanut products, peanut butter, melon seeds, walnuts, cashews, pistachio, almond nuts
Fresh fruits	Fruit, 100% fruit juices
Seafood	Abyssal fishes, freshwater fishes, fish with edible bones, crab, prawn, oyster, shellfish, marine products, processed seafood
Meat	Poultry, red meat, liver (beef, pork, chicken, goose), haslet, blood (pork, duck), meat products
Sweetened beverages	Sugar vegetable juice, lactic acid drink, carbonated beverages, sports drink, milk tea, instant powdered drinks, packaged drink, sugared beverages,
coffee	Caffeinated coffee
Ice products	Ice cream, sundae, popsicle, sorbet, shaved ice
Fried snacks	Oily snack foods, cookies, instant noodles
Sweetened snacks	Canned fruit, pickled fruit, preserved fruits, jam, jelly, pudding
Cake	Cakes, pastries
Candy, chocolate	Chocolate drink, chocolates
Fried foods	Fried food, fast food

Table S4. Distribution of unadjusted urinary BPs levels among the general Taiwanese population (ng/mL).

	Detection frequency (%)	Total population (N= 706) Median (range)	6-11 years (n = 189) Median (range)	12-18 years (n = 189) Median (range)	19-64 years (n= 137) Median (range)	≥ 65 years (n= 150) Median (range)
BP	90.37	3.18 (ND – 18.77)	2.76 (ND-16.31)	1.6 (ND-7.45)	5.15 (ND-15.47)	3.73 (ND-18.77)
BP-1	8.92	21.46 (ND – 1007.1)	4.20 (ND-30.23)	28.42 (ND-1007.10)	49.02 (ND-550.90)	11.98 (ND-427.15)
BP-3	21.39	23.69 (ND – 8455.8)	7.47 (ND-118.70)	35.39 (ND-8455.80)	59.93 (ND-5992.00)	13.79 (ND-4552.05)
BP-8	0.14	-	-	-	-	-
4-OHBP	1.56	8.80 (ND – 34.33)	0.08 (ND-2.00)	5.52 (ND-8.80)	20.07 (ND-23.99)	24.02 (ND-34.33)

Table S5. Urinary BP concentrations (μg/g cre.) and dietary intake frequency stratified by median level.

Food groups (fg) (times/week)	**N (%)**	**6-11 years (n= 189)**	**p-value [a]**	**Food groups (times/week)**	**N (%)**	**12-18 years (n= 230)**	***p*-value [a]**
Rice and noodle products (fg1_1)				**Rice and noodle products (fg1_1)**			
<median (<0.03)	111	4.36	0.43	<median	223	1.96	0.94[a]
≥median (≥0.03)	78	3.88		≥median (≥0)	7	2.23	
Grains and bread (fg1_2)				**Grains and bread (fg1_2)**			
<median	152	4.26	0.94	<median	226	1.85	0.09[a]
≥median (≥0)	37	3.76		≥median (≥0)	4	8.19	
Eggs (fg2)				**Eggs (fg2)**			
<median	146	4.35	0.60	<median	141	2.07	0.55
≥median (≥1.00)	43	3.52		≥median (≥1.00)	89	1.80	
Milk, yogurt, cheese (fg3)				**Milk, yogurt, cheese (fg3)**			
<median		4.15	0.61	<median	122	1.998	0.98
≥median (≥1.47)		4.17		≥median (≥1.23)	108	1.924	
Vegetables (fg4)				**Vegetables (fg4)**			
<median	13	4.11	0.89[a]	<median	115	1.95	0.22
≥median (≥7.00)	176	4.16		≥median (≥14.35)	115	1.97	
Soybean products (fg5)				**Soybean products (fg5)**			
≤median	127	4.49	0.28	≤median	117	1.85	0.62
>median (≥1.23)	62	3.48		>median (≥1.70)	113	2.08	
Nuts and seeds (fg6)				**Nuts and seeds (fg6)**			
≤media				≤median	141	1.97	0.96
>median				>median (≥0.23)	89	1.95	
Fresh fruits (fg7)				**Fresh fruits (fg7)**			
≤median	107	4.17	0.24	≤median	129	1.91	0.35
>median (≥2.00)	82	4.15		>median (≥1.23)	101	2.03	
Seafood (fg8)				**Seafood (fg8)**			
≤median	115	4.22	0.35	≤median	122	2.16	0.78
>median (≥1.23)	74	4.07		>median (≥2.70)	108	1.74	

Meat (fg9)				**Meat** (fg9)			
≤median	148	3.9964	0.13	≤median	115	1.77	0.34
>median (≥7.00)	41	4.7473		>median (≥4.70)	114	2.16	
Sweetened beverages (fg10)				**Sweetened beverages (fg10)**			
≤median	112	4.3783	0.82	≤median	115	2.28	0.25
>median (≥1.23)	77	3.8406		>median (≥3.08)	115	1.65	
Coffee (fg11)				**Coffee (fg11)**			
≤median				≤median	197	1.99	0.50
>median				>median (>0)	33	1.82	
Ice products (fg12)				**Ice products (fg12)**			
≤media	118	4.2659	0.24	≤median	193	2.11	**0.03**
>median (≥0.23)	71	3.9820		>median (≥0)	37	1.21	
Fried snacks (fg13_1)				**Fried snacks (fg13_1)**			
≤median	113	3.9806	0.74	≤median	206	2.03	0.73[a]
>median (≥1.23)	76	4.4249		>median (≥1.00)	24	1.42	
Sweetened snacks (fg13_2)				**Sweetened snacks (fg13_2)**			
≤median				≤median	115	2.30	0.18
>median				>median (≥0.58)	115	1.62	
Cake (fg14)				**Cake (fg14)**			
≤median	179	4.1464	0.93[a]	≤median	115	2.23	0.06
>median (≥1.00)	10	4.3900		>median (≥0.12)	115	1.69	
Candy, chocolate (fg15)				**Candy, chocolate (fg15)**			
≤median	95	4.0981	0.89	≤median	169	2.03	0.85
>median (≥0.23)	94	4.2211		>median (≥1.00)	61	1.77	
Fried foods (fg16)				**Fried foods (fg16)**			
≤median	115	4.3674	0.42	≤median	130	2.03	0.66
>median (≥0.23)	74	3.8358		>median (≥0.47)	100	1.88	

Independent t-test **p< 0.05; [a] Mann-Whitney U test was applied. **p< 0.05.

Food groups (times/week)	N (%)	19-64 years (n= 137)	p-value[a]	Food groups (times/week)	N (%)	>64 years (n= 150)	*p*-value [a]
Rice and noodle products (fg1_1)				**Rice and noodle products (fg1_1)**			
<median	62	5.46	0.85	<median	74	8.00	0.93
≥median (≥8.70)	75	6.15		≥median (≥9.17)	74	8.76	
Grains and bread (fg1_2)				**Grains and bread (fg1_2)**			
<median	72	4.66	**0.02**	<median	80	8.87	0.71
≥median (≥1.23)	65	7.14		≥median (≥1.00)	70	7.89	
Eggs (fg2)				**Eggs (fg2)**			
<median	110	6.04	0.33[a]	<median	131	8.64	0.35
≥median (≥1.00)	27	5.00		≥median (≥1.00)	19	6.87	
Milk, yogurt, cheese (fg3)				**Milk, yogurt, cheese (fg3)**			
<median	82	4.96	**0.04**	<median	75	8.26	0.94
≥median (≥1.00)	55	7.15		≥median (≥0.35)	75	8.57	
Vegetables (fg4)				**Vegetables (fg4)**			
<median	70	6.10	0.50	<median	75	9.47	**0.02**
≥median (≥15.47)	67	5.57		≥median (≥17.23)	75	7.36	
Soybean products (fg5)				**Soybean products (fg5)**			
≤median	76	5.51	0.99	≤median	81	9.01	0.30
>median (≥1.47)	61	6.25		>median (≥1.23)	69	7.71	
Nuts and seeds (fg6)				**Nuts and seeds (fg6)**			
≤median	84	6.4065	0.26	≤median	93	8.85	0.06
>median (≥0.23)	53	4.9394		>median (≥0.23)	57	7.70	
Fresh fruits (fg7)				**Fresh fruits (fg7)**			
≤median	118	5.75	0.99[a]	≤median	128	8.66	0.30
>median (≥7.00)	19	6.40		>median (≥7.00)	22	6.99	
Seafood (fg8)				**Seafood (fg8)**			
≤median	70	5.89	0.45	≤median	77	8.75	0.44
>median (≥3.00)	67	5.79		>median (≥3.00)	73	8.06	
Meat (fg9)				**Meat (fg9)**			

≤median	71	6.15	0.44	≤median	77	9.30	0.33
>median (≥3.47)	66	5.51		>median (≥2.93)	73	7.48	
Sweetened beverages (fg10)				**Sweetened beverages (fg10)**			
≤median	69	5.74	0.36	≤median	82	8.89	0.22
>median (≥2.23)	68	5.94		>median (≥1.00)	68	7.84	
Coffee (fg11)				**Coffee (fg11)**			
≤median	93	6.21	0.052	≤median	141	8.64	0.07[a]
>median (>0.23)	44	5.06		>median (>0)	9	4.87	
Ice products (fg12)				**Ice products (fg12)**			
≤median	124	5.98	0.24	≤median	147	8.49	0.23[a]
>median (≥0)	13	4.54		>median (≥0)	3	4.61	
Fried snacks (fg13_1)				**Fried snacks (fg13_1)**			
≤median	77	5.66	0.39	≤median	91	8.77	0.57
>median (≥0.23)	60	6.07		>median (≥0.23)	59	7.86	
Sweetened snacks (fg13_2)				**Sweetened snacks (fg13_2)**			
≤median	95	6.04	0.09	≤median	136	8.58	0.82
>median (≥0.23)	42	5.39		>median (≥0)	14	6.83	
Cake (fg14)				**Cake (fg14)**			
≤median	122	5.80	0.24	≤median	140	8.51	0.50[a]
>median (≥0)	15	6.14		>median (≥0)	10	7.13	
Candy, chocolate (fg15)				**Candy, chocolate (fg15)**			
≤median	123	5.50	0.46	≤median	140	8.52	0.73[a]
>median (≥0)	14	8.77		>median (≥0)	10	6.89	
Fried foods (fg16)				**Fried foods (fg16)**			
≤median				≤median			
>median				>median			

Independent t-test **p< 0.05; [a] Mann-Whitney U test was applied. **p< 0.05.

Table S6. Monte Carlo simulation of estimated daily BP intake and health risk.

Percentiles	6-11 years		12-18 years		19-64 years		>65 years		Total	
	EDI	HQ[a]	EDI	HQ[a]	EDI	HQ[a]	EDI	HQ[a]	EDI	HQ[a]
5th	0.00	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.00	0.00
25th	0.01	0.00	0.00	0.00	0.03	0.00	0.03	0.00	0.01	0.00
50th	0.03	0.00	0.02	0.00	0.07	0.00	0.05	0.00	0.02	0.00
75th	0.08	0.00	0.05	0.00	0.17	0.01	0.09	0.00	0.08	0.00
90th	0.17	0.01	0.12	0.00	0.33	0.01	0.14	0.00	0.21	0.01
95th	0.25	0.01	0.21	0.01	0.47	0.02	0.17	0.01	0.34	0.01
99th	0.40	0.01	0.41	0.01	0.75	0.02	0.23	0.01	0.75	0.03

EDI: Estimated daily intake (µg/kg-bw/day)

HQ: Hazard quotient = EDI/TDI

[a]TDI = 30 µg/kg-bw/day (EFSA, 2009)

Table S7. Concentration a of benzophenones in various food items and general population of Taiwan.

	Detection rate (%)						Mean					
	Freshwater fish (n=30)	Saltwater fish (n=80)	Bread (n=56)	Whole milk (n=37)	Low-fat milk (n=14)	Urine (n=706)	Freshwater fish (ng/g)	Saltwater fish (ng/g)	Bread (ng/g)	Whole milk (ng/mL)	Low-fat milk (ng/mL)	Urine (ng/mL)
BP	100	100	95	100	100	90.37	13.34	8.56	15.112	8.07	10.02	1.99
BP-1	7	6	5	X	X	8.92	0.15	0.06	1.31	X	X	<LOQ
BP-2	X	X	X	21	11	X	X	X	X	4.24	2.64	X
BP-3	70	89	11	7	X	21.39	0.18	0.18	19.91	X	X	0.01
BP-4	X	X	X	X	X	X	X	X	X	X	X	X
BP-8	X	X	5	X	X	0.14	X	X	0.52	X	X	X
2-OHBP	100	100	75	14	X	X	15.8	20.57	26.74	X	X	X
4-OHBP	73	93	13	7	14	1.56	0.63	0.88	3.94	9.86	X	<LOQ
4-DHB	X	X	X	X	X	X	X	X	X	X	X	X
M2BB	57	15	X	93	100	X	0.44	0.29	X	0.29	0.26	X
PBZ	70	70	X	79	57	X	X	0.09	X	1.56	1.39	X
4-MBP	93	9	57	50	30	X	1.07	0.58	33.34	27.56	25.31	X

X: Not detected

Table S8. Urinary concentrations of BP (ng/mL) in various countries.

Country	N	Year of Study	Age (year)	%>LOD	Median	Range	Reference
Taiwan	706	2005-2012	All	90.3	2.72	ND – 18.77	This study
	189		6 - 11		2.76	ND – 16.31	
	230		12 - 18		1.6	ND – 7.45	
	137		19 - 64		5.15	ND – 15.47	
	150		>65		3.73	ND – 18.77	
China	208	2019	8-11, 21-64	48	7.60	ND – 74.45	(Wang et al., 2021)
Denmark	36	2013[a]	3-5	38.9	<LOD	ND – 15.8	(Krause et al., 2017)
	49	2013[b]	3-5	22.4	<LOD	ND – 9.09	(Krause et al., 2017)
Denmark	200	2012-2014	>18[c]	27	<LOD	ND – 74.5	(Krause et al., 2018)
Denmark	195	1996-2010	18–29[d]	10.7	<LOD	ND – 17.6	(Joensen et al., 2018)
Denmark	309	2013	18–29[d]	41.1	<LOD	ND – 13.6	(Frederiksen et al., 2021)
Spain	20	-	-	25	<LOD	ND – 3.1	(Vela-Soria et al., 2014)
Japan	10	-	-	10	<LOD	ND – 0.38	(Kawaguchi et al., 2009)

[a] Summer, [b] Winter, [c] Pregnant women, [d] Young men

Table S9. Body weight and creatinine excretion rate among all age groups in Taiwan.

Age group	Body weight (Kg) (Mean)	Creatinine excretion rate (g cre/day) (GM)
6-11 years	32.09	0.59
12-18 years	54.91	1.05
19-64 years	64.38	1.02
>65 years	59.76	0.64

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