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Evaluation of estrogenic chemicals in capsule and French press coffee using ultra-performance liquid chromatography with tandem mass spectrometry

Junichi R. Sakaki [a], Melissa M. Melough [a], Anthony A. Provatas [b], Christopher Perkins [b], Ock K. Chun [a,*]

[a] Department of Nutritional Sciences, University of Connecticut, 27 Manter Rd., Unit 4017, Storrs, CT 06269, USA
[b] Center for Environmental Sciences and Engineering, University of Connecticut, 3107 Horsebarn Hill Rd., Storrs, CT 06269, USA

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ABSTRACT

The objective of this study was to examine exposure to estrogenic chemicals (ECs) via capsule coffee. Twenty-two brands of capsule coffee and 15 brands of French press coffee for comparison were brewed, and their contents of ECs were identified and quantified using ultra-performance liquid chromatography with tandem mass spectrometry. Exposure to ECs in coffee were compared to tolerable daily intake guidelines to assess potential hazard to health. Benzophenone was the most frequently detected EC in capsule coffee (mean concentration ± SD: 20.37 ± 47.07 ng/mL, n = 6), followed by bisphenol A (BPA, 0.31 ± 0.71, n = 4), dibutyl phthalate (1.41 ± 3.58, n = 3), 4-nonylphenol (0.67 ± 1.82, n = 3) and bisphenol F (BPF, 0.49 ± 1.54, n = 2). BPA and BPF were each detected in 3 French press coffee samples (0.29 ± 0.58 and 0.85 ± 1.75 ng/mL, respectively). Two French press coffee brands purchased as ground coffee rather than whole bean were positive for ECs (BPA in one and BPF in both). Hazard indexes were below 1.0 for each EC for both coffee types. These results indicate that there is EC contamination in capsule and French press coffee, but the quantities of ECs are low relative to established safety guidelines.

1. Introduction

Coffee is a popular beverage in the US, with 49 % of US adults consuming coffee daily [1]. While the most common method of brewing coffee in the US is drip coffee, single-serve coffee makers utilizing a pre-packed capsule or pod (capsule coffee) have recently become popular. Indeed, 28 % of US adults reported drinking coffee prepared from a single-serve coffee maker compared to 50 % from a drip coffee maker [2].

Capsule coffee is popular because it is quick to prepare and convenient; however, the brewing process requires high temperature and pressure which can cause harmful endocrine disruptors to leach from the plastic in the capsules and machine into the coffee [3]. Endocrine disruptors interfere with the hormonal system by inhibiting or mimicking certain hormones such as the sex hormones estrogen and androgens, causing deleterious health effects [4]. Xenoestrogens, estrogenic chemicals (ECs) that mimic the effects of estrogen, can pass from mothers' breast milk to infants, potentially causing developmental issues such as shorter gestation, low birth weight, low rate of weight gain, and shorter head and abdominal circumferences [5]. In men, EC exposure can reduce fertility and sperm count and increase the incidence of congenital malformations [6,7].

Due to their utility in improving qualities of plastic compounds, certain types of ECs are highly prevalent in everyday items. For example, phthalates, with demonstrated capacity to disrupt sex hormones [8–11], enhance the properties of polyvinyl chloride, a synthetic substance commonly used in food packaging. Similarly, bisphenol A (BPA) is used in the production of many plastic-based items such as water bottles, food containers and epoxy resins, and has been rigorously studied as a xenoestrogen [12]. Consequently, there have been calls to reduce its usage and production. However, bisphenol analogues such as bisphenol S (BPS) and bisphenol F (BPF), which impose similar health risks, are still

Abbreviations: -, not detected; 4-NP, 4-nonyphenol; BP, benzophenone; BPA, bisphenol A; BPF, bisphenol F; BPS, bisphenol S; DBP, dibutyl phthalate; DEHP, di(2-ethylhexyl) phthalate; DMTP, dimethyl terephthalate; EC, estrogenic chemical; EDI, estimated daily intake; HI, hazard index; HPLC, high-performance liquid chromatography; MDL, method detection limit; MQL, method quantification limit; SD, standard deviation; TDI, tolerable daily intake; UPLC-MS/MS, ultra-performance liquid chromatography with tandem mass spectrometry.

* Corresponding author.
E-mail address: ock.chun@uconn.edu (O.K. Chun).

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frequently used as BPA replacements [12,13].

Given the popularity of capsule coffee and its potential to increase exposure to ECs over traditional coffee brewing methods, it is critical to examine the level of EC exposure associated with capsule coffee consumption. The current evidence regarding EC contents of capsule coffee is fairly limited. Two studies reported the EC contents of coffee brewed from Italian espresso capsules [4,14], although espressos are less common in the US. Therefore, the objective of this study was to identify and quantify EC concentrations in popular US capsule coffees and evaluate the exposure in relation to established safety guidelines.

2. Methods

2.1. Coffee brewing equipment and samples

Twenty-two popular brands of plastic capsule coffee were selected, which were each designed to be brewed in one of four different capsule coffee brewing machines. Additionally, a stainless-steel French press coffee maker (Model SFP-34DS, Secura Inc., Brookfield, WI) and coffee grinder (Model BCG111OB, KitchenAid, St. Joseph, MI) were purchased and used to brew French press coffees, which were used for comparison to capsule coffees. French press coffees were selected to match the capsule coffee brands. Of the 22 capsule coffee brands, 15 were available as either whole bean (13 brands) or ground coffee (2 brands) and were used in the French press. Whole bean coffees were selected over ground whenever available as the lower surface area was believed to limit contamination from packaging. When whole bean coffees were unavailable, ground varieties were purchased in the largest available package sizes in order to minimize contact with packaging. All coffee brewing equipment and samples were purchased and analyzed in 2019 between January and July (Fig. 1).

2.2. Coffee preparation

Capsule coffee samples were prepared as follows: first, high-performance liquid chromatography (HPLC)-grade water (Fisher Scientific, Fair Lawn, NJ) was run through the capsule coffee machine (without inserting a capsule) on the smallest volume setting to rinse out any residue. Then, three capsules were brewed with HPLC-grade water, each time replacing the capsule, on the smallest volume setting (dispensed approximately 160−240 mL). The samples were combined and mixed, and 110 mL were saved and used for analysis. These steps were repeated for each brand of capsule coffee, with rinsing between each capsule coffee brand.

French press coffee samples were prepared as follows: first, the coffee grinder was filled to the 4-cup fill line with whole beans and ground for 14 s to achieve a coarse grind. Then, 11 g of coffee was transferred to the French press coffee maker. Then, 500 mL of hot (but not boiling) HPLC-grade water was poured into the French press and brewed for four minutes. Finally, the coffee was poured out and mixed, and 110 mL was subsequently saved and used for analysis. These steps were repeated for each French press coffee brand, rinsing in between brands. For the two coffee brands that were purchased as ground, the first step was skipped and 11 g were directly added to the French press. All glassware and equipment used for coffee preparation were washed and rinsed in distilled water then autoclaved for 45 min at 150 °C. Extra care was taken to avoid any contact with plastic throughout the preparation and handling processes.

2.3. Extraction of ECs from coffee samples

The extraction of ECs from capsule and French press coffee samples was performed with liquid-liquid extraction. Twenty-five mL of coffee was spiked with 50 µL of the surrogate 4-hydroxy-biphenyl-d9 to a final concentration of 125 ng/mL. Meanwhile, the lab control sample and matrix spike sample were spiked with the target ECs to a final concentration of 500 ng/mL for each EC. Twenty mL of ethyl acetate was added to each sample and the mixture was centrifuged (2500 rpm for 5 min), removing the top ethyl acetate layer with a pipette. The remaining emulsion was then evaporated in an EZ-2 Genevac evaporator (Genevac Ltd, Ispswich, UK) at the low boiling point setting for 60 min. Then, 950 µL methanol was added followed by 50 µL of the internal standard 1-naphthol-d3 to a final concentration of 500 ng/mL. Glass equipment including syringes, vials and pipettes were used in order to avoid contact with plastic.

2.4. Identification and quantification of ECs

EC contents of capsule and French press coffee samples were identified and quantified using ultra-performance liquid chromatography with tandem mass spectrometry (UPLC-MS/MS). LC–MS/MS methods are highly selective and sensitive, demonstrating a limit of detection of 0.4 ng/mL for BPA [15]. They are also advantageous compared to gas chromatography-mass spectrometry methods because they utilize a simple sample preparation without the need for derivatization [16]. Identification and characterization of unknown ECs were conducted based on retention time and *m/z* values of compounds/fragments or signature ion fragments of a peak generated by EC standards. Nine ECs

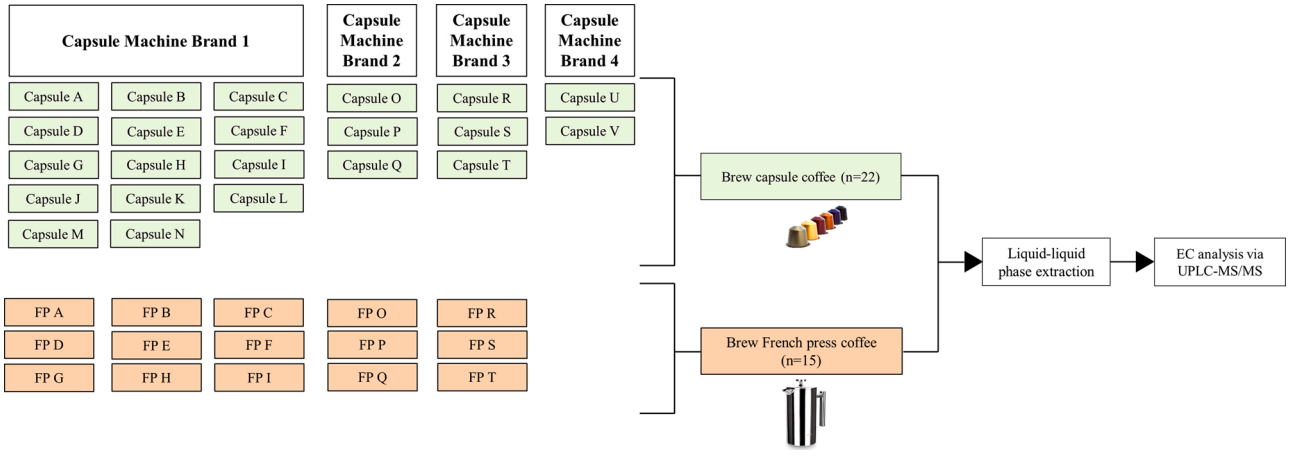

Fig. 1. Study design. Four brands of capsule coffee machines were selected (brands 1-4) and 22 capsule coffee brands (capsules A-V) were brewed using these machines. Fifteen whole bean or ground coffee brands were available and brewed using a French press (FP A-T). All coffee samples were then assessed to identify and quantify ECs using UPLC-MS/MS. Abbreviations: EC, estrogenic chemical; FP, French press; UPLC-MS/MS, ultra-performance liquid chromatography with tandem mass spectrometry.

were selected for target analysis: caprolactam, BPA, BPS, BPF, benzophenone (BP), 4-nonylphenol (4-NP), dimethyl terephthalate (DMTP), dibutyl phthalate (DBP) and di(2-ethylhexyl) phthalate (DEHP).

2.5. UPLC and mass spectrometric conditions

Quality control and coffee samples were analyzed using a Waters Acquity™ UPLC® coupled with an Acquity™ TQD™ tandem mass spectrometer (Waters Co., Milford, MA). Analytic conditions were modified from Langer et al. [17] and are outlined in Table 1. The detection and quantification of analytes, surrogate, and internal standard compounds were performed in negative ESI-MS/MS mode (MRM) using the Waters, Inc. IntelliStart™ software for analyte signal optimization. Statistical analysis for obtaining calibration and quantification results for all compounds were performed using Waters QuanLynx™, which was included in the MassLynx software v.4.2. Parameters for the mass spectrometer were set as follows: capillary voltage, 3.2 kV; variable cone voltage and collision energy; desolvation temperature, 350 °C; source temperature, 145 °C; desolvation gas flow, 600 L/h; collision gas flow, 0.2 mL/min.

2.6. Method validation

The UPLC-MS/MS analytic method was first validated to demonstrate the accuracy, precision, method detection limit (MDL) and method quantification limit (MQL) for each EC, according to Environmental Protection Agency guidelines [18]. Briefly, accuracy was calculated as the mean calculated concentration of the analyte relative to the nominal concentration of the spike while precision was calculated as the relative standard deviation. MDL was determined as 3.143 (the Student's *t*-value for a single-tailed 99th percentile for seven replicates) times the standard deviation (SD) of the replicate analysis. MQL was determined as 10 times the SD.

2.7. Data analysis

In order to succinctly present the results, the EC concentrations in coffee samples were averaged (mean ± SD) for each brewing method. The range of ECs detected and the number (%) of positive coffee samples were also presented. To evaluate exposure to ECs from consuming coffee, the estimated daily intake (EDI) and hazard index (HI) for each EC was calculated [19]. EDI was determined by multiplying the average amount of coffee consumed by US adult coffee consumers (417 mL) [1] by the mean (expected estimate of EDI) or highest (least conservative estimate of EDI) EC concentration and standardizing by the weight of an adult (70 kg). The HI for each EC was calculated by dividing the EDI by its tolerable daily intake (TDI), established by external guidelines and references [8,12,20–22].

3. Results

3.1. Method validation

The UPLC-MS/MS analytic method for determining EC content was highly accurate and precise, with an overall recovery of 94.9 % (range: 80–105 %) and precision of 2.0 % (range: 0.7–3.8 %) for the nine measured ECs (Table 2). This method was also highly sensitive, as indicated by the low MDLs and MQLs of the ECs. The high accuracy, precision and sensitivity for detecting ECs make this method suitable for identifying and quantifying ECs in coffee samples.

MDL and MQL were determined using a 2 ng/mL spike of the estrogenic chemical mixture. MDL = 3.14*SD. MQL = 10*SD. Abbreviations: 4-NP, 4-nonylphenol; BP, benzophenone; BPA, bisphenol A; BPF, bisphenol F; BPS, bisphenol S; DBP, dibutyl phthalate; DEHP, di(2-ethylhexyl) phthalate; DMTP, dimethyl terephthalate; EC, estrogenic chemical; MDL, method detection limit; MQL, method quantification limit; SD, standard deviation.

Table 1
UPLC-MS/MS column conditions, solvent compositions and gradient profile.

Column	Acquity™ UPLC CSH Phenyl-Hexyl (1.7 μm, 2.1 × 100 mm)				
Column temp. (°C)	55				
Solvent A	2 mM ammonium acetate in 95 % water/5 % methanol				
Solvent B	2 mM ammonium acetate in 100 % methanol				
Time (min)	0	0.2	6	7.8	8.8
Solvent A (%)	50	50	0	0	50
Total run time (min)	9				
Injection volume (μL)	5				
Flow rate (mL/min)	0.2				

Abbreviation: UPLC-MS/MS, ultra-performance liquid chromatography with tandem mass spectrometry.

3.2. EC concentration in capsule and French press coffee

Of the nine ECs targeted, five were detected in capsule coffee. BP was the most prevalent, detected in six of the 22 capsule coffee samples, followed by BPA (four), 4-NP (three), DBP (three), and BPF (two) (Table 3). There was wide variation in the concentrations of BP in the samples, ranging from 0 to 149 ng/mL. BPA and BPF were the only ECs found in French press coffee (detected in three of 15 samples for each). Notably, for the two French press coffee brands purchased as ground coffee, one was positive for BPA and both were positive for BPF. This suggests that French press coffee prepared from pre-packed ground coffee may contain more ECs than French press coffee prepared from freshly ground whole beans. BP, 4-NP and DBP were not detected in any French press coffee, and DMTP, BPS, and caprolactam were not detected in either type of coffee. Trace amounts of DEHP were detected (in amounts below the MDL) in one capsule and three French press coffee samples. There were no ECs detected in sample blanks for each capsule machine and the French press, suggesting no detectable contamination was introduced through the brewing machines, equipment, or analytical procedures. Due to the low number of positive samples (especially in the French press coffee), it was not possible to meaningfully compare the average EC concentrations between capsule and French press coffee.

3.3. Estimated daily intake and hazard indexes of ECs

EDIs of ECs were calculated using mean and highest EC concentration in coffee samples, and then used to calculate HI (Table 4). Overall, for both capsule and French press coffee, the HI for each EC using the mean concentration was very low (BP, the highest estimate: 4×10^{-3}), suggesting minimal exposure. Estimates using the highest concentration increased HIs approximately ten-fold in all samples but HIs remained low. In capsule coffee samples, the HIs for BPA, BPF, 4-NP and DBP were comparable to one another, while the HI for BP was approximately ten-fold higher.

None of the samples had detectable amounts of DMTP, BPS, or caprolactam. DEHP was detected in quantities below the method detection limit in one capsule and three French press samples. EDI was calculated by multiplying the concentration of the chemical by 417 mL,

Table 2
Accuracy, precision, MDL and MQL of the UPLC-MS/MS analytic method for detecting ECs in coffee samples.

EC	Recovery (%)	Precision (%)	MDL (ng/mL)	MQL (ng/mL)
Caprolactam	80.3	2.1	0.19	0.6
BPA	81.5	3.1	0.34	1.1
BPS	100.0	1.0	0.23	0.7
BPF	90.6	1.5	0.35	1.1
BP	100.6	0.7	0.25	0.8
4-NP	96.4	2.0	0.18	0.6
DMTP	96.6	3.8	0.67	2.1
DBP	105.1	1.1	0.26	0.8
DEHP	102.8	2.7	0.29	0.9

Table 3
Concentration of ECs in coffee brewed from capsules and French press (ng/mL).

Samples	BPA	BPF	BP	4-NP	DBP
Capsules (n = 22)					
Positive sample, n (%)	4 (18.2 %)	2 (9.1 %)	6 (27.3 %)	3 (13.6 %)	3 (13.6 %)
Mean ± SD	0.31 ± 0.71	0.49 ± 1.54	20.37 ± 47.07	0.67 ± 1.82	1.41 ± 3.58
Range	0–2.42	0–5.57	0–149.0	0–7.39	0–12.34
French press (n = 15)					
Positive sample, n (%)	3 (20.0 %)	3 (20.0 %)	0	0	0
Mean ± SD	0.29 ± 0.58	0.85 ± 1.75	n.d.	n.d.	n.d.
Range	0–1.70	0–5.24	n.d.	n.d.	n.d.

None of the samples had detectable amounts of DMTP, BPS, or caprolactam. DEHP was detected in quantities below the method detection limit in one capsule and three whole bean samples. Abbreviations: 4-NP, 4-nonylphenol; BPA, bisphenol A; BPF, bisphenol F; BP, benzophenone; DPB, dibutyl phthalate; n.d., not detected; SD, standard deviation.

Table 4
Estimated daily intakes (ng/kg body weight) and hazard indexes of estrogenic chemicals from coffee prepared from capsules and French press.

Coffee samples	BPA		BPF		BP		4-NP		DBP	
	EDI	HI	EDI	HI	EDI	HI	EDI	HI	EDI	HI
Mean concentration										
Capsule	1.85	5×10^{-4}	2.92	3×10^{-4}	121.35	4×10^{-3}	3.99	8×10^{-4}	8.40	8×10^{-4}
French press	1.73	4×10^{-4}	5.06	5×10^{-4}	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Highest concentration										
Capsule	14.42	4×10^{-3}	33.18	3×10^{-3}	887.61	3×10^{-2}	44.02	9×10^{-3}	73.51	7×10^{-3}
French press	10.13	3×10^{-3}	31.22	3×10^{-3}	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.

the average daily coffee consumption of US adults ≥20 years old [1], and dividing by 70 kg, the assumed weight of an adult. HI was calculated by dividing EDI by TDI, obtained from references: BPA: TDI = 4×10^3ng/kg BW [12], BPF: TDI = 1.1×10^4ng/kg BW [20], BP: TDI = 3×10^4ng/kg BW [21], 4-NP: TDI = 5×10^3ng/kg BW [8], DBP: TDI = 1×10^4ng/kg BW [22]. EDIs and HIs were calculated using the mean and highest concentrations of estrogenic chemicals detected in coffee extract solutions. Abbreviations: 4-NP, 4-nonylphenol; BPA, bisphenol A; BPF, bisphenol F; BP, benzophenone; DPB, dibutyl phthalate; EDI, estimated daily intake; HI, hazard index; n.d., not detected; TDI, tolerable daily intake.

4. Discussion

The purpose of this study was to determine the content of ECs in capsule coffee and assess the degree of exposure to these chemicals from typical consumption. This first required validation of an analytic method that, to our knowledge, has not yet been used to measure ECs in coffee. The UPLC-MS/MS method was suitable for this type of analysis given its high degree of accuracy, precision and sensitivity for these ECs in our samples. BPA, BPF, BP, 4-NP and DBP were detected in capsule coffee, while only BPA and BPF were detected in French press coffee. BP was the most frequently detected EC in capsule coffee samples and had the highest HI, which was still considerably low. While we were unable to make statistical inferences comparing the EC content of capsule coffee to French press coffee, it is evident that ECs may be prevalent in minor, yet detectable concentrations in both types of coffee.

A few studies have similarly evaluated the content of plasticizers and phthalates in different types of coffee. DEHP and DBP have been identified in instant black coffee, with higher concentrations in coffee prepared in plastic compared to coffee prepared in glass [23]. DEHP as well as other phthalates have also been found in Italian espresso [4,14], with higher concentrations when brewed in a plastic capsule versus by a moka pot (plastic-free) 14]. Furthermore, plasticizers including BP were evident in plastic capsule coffee [24], which is consistent with the results of our study. In our study, neither DBP nor BP were detected in French press coffee, suggesting that the content of ECs in coffee may be contingent on the types of material making contact with the coffee. Plasticizers can leach from food packing, particularly from plastic containers [25] including polyvinyl chloride film (food wrap) and polypropylene capsules [24]. However, even non-plastic food containers such as paper and cardboard can leach ECs [26] which may explain the BPA and BPF detected in the few French press coffee samples. There is thus some suggestion that the packaging material may play an integral role in the EC contamination of coffee, but further studies are required for confirmation.

Estimated EC exposure from consuming a typical amount of capsule coffee was below established safety limits [8,12,20–22] for the identified compounds, and therefore unlikely to cause health concerns. Even using the least conservative estimate, HIs remained low. While there were only two studies that evaluated the HIs for ECs in coffee, they reported low HIs for DBP and DEHP, both when prepared in plastic and in metal [4,14]. Comparatively, in our study the HI for DBP was in the same order of magnitude for capsule coffee, and DEHP was not detected in either type of coffee. However, while the HIs for each EC were low, it is important to consider the aggregate effects of EC mixtures found in coffee and other sources, including dietary and non-dietary sources. ECs are ubiquitous and abundant in other commercial food and food products [27–29]. The scope of this study was restricted to assessing the exposure to ECs from two different types of coffee and therefore we are unable to evaluate the contribution of EC from coffee relative to total EC exposure. Based on current evidence, food safety organizations have reported that typical low-level exposure to phthalates 22,30], BPA 12] and BP [21] pose little health risk to most individuals, but warn that certain populations may be more vulnerable, including occupationally exposed workers, women of reproductive age, and children 30]. Studies using biological samples to assess exposure to estrogenic chemicals confirm that exposure is ubiquitous, which may have harmful effects especially in these vulnerable populations. Analyses on hair samples have indicated that children have greater exposure to BPA compared to adults, likely due to the ubiquity of BPA in toys and food products and the fact that children consume more food per body weight than adults [31]. Additionally, women of childbearing age were found to have BPA, phthalates and 4-NP detected in urine, and those with recurrent spontaneous abortion had higher concentrations of some of these estrogenic chemicals [32]. Furthermore, while the typical exposure to ECs from coffee appears to be minimal, coffee consumption is often habitual and typically involves several drinks daily for years or decades. The effects of

long term bio-accumulation of estrogenic chemicals on health is not well understood and deserve further investigation.

There were several strengths of this study. First, the UPLC-MS/MS analytical method was validated to identify and quantify the EC content of coffee for this study. Additionally, the analysis spanned over 37 brands of coffee and four brands of capsule coffee machines, giving these results a relatively large degree of representation and generalizability to the current US market. There are, however, some limitations. First, the low number of positive samples in capsule and French press coffee precluded the use of meaningful statistical testing and therefore the data are merely descriptive. Second, despite using strict procedures to avoid using plastic throughout our entire analytic process, the coffee may have been contaminated with ECs during the manufacturing, packaging, storing, or transportation processes, all of which may differentially affect the EC content by brand.

In conclusion, BPA, BPF, BP, 4-NP and DBP were detected in capsule coffee and BPA and BPF were detected in French press coffee. However, the level of exposure to these ECs from coffee is minimal and the potential risk to health is likely to be low relative to established safety guidelines. Future studies should extend these findings by determining the estrogenic activity of the ECs present in coffee in vitro as well as evaluate the health risk of EC exposure from chronic coffee consumption.

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CRediT authorship contribution statement

Junichi R. Sakaki: Formal analysis, Writing - original draft. **Melissa M. Melough:** Investigation, Writing - review & editing. **Anthony A. Provatas:** Validation, Data curation, Investigation, Methodology, Writing - review & editing. **Christopher Perkins:** Validation, Methodology. **Ock K. Chun:** Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Visualization, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] E. Loftfield, N.D. Freedman, K.W. Dodd, et al., Coffee drinking is widespread in the United States, but usual intake varies by key demographic and lifestyle factors, J. Nutr. 146 (9) (2016) 1762–1768, https://doi.org/10.3945/jn.116.233940.
[2] National Coffee Association USA. U.S. Coffee Consumption Trends, 2016. BILL MURRAY.pdf. Published. Accessed January 14, 2020, http://www.ico.org/documents/cy2015-16/Presentations/4.0NCA.
[3] E. Fasano, F. Bono-Blay, T. Cirillo, P. Montuori, S. Lacorte, Migration of phthalates, alkylphenols, bisphenol A and di(2-ethylhexyl)adipate from food packaging, Food Control 27 (1) (2012) 132–138, https://doi.org/10.1016/j.foodcont.2012.03.005.
[4] L. De Toni, F. Tisato, R. Seraglia, et al., Phthalates and heavy metals as endocrine disruptors in food: a study on pre-packed coffee products, Toxicol. Rep. 4 (May) (2017) 234–239, https://doi.org/10.1016/j.toxrep.2017.05.004.
[5] I. Katsikantami, S. Sifakis, M.N. Tzatzarakis, et al., A global assessment of phthalates burden and related links to health effects, Environ. Int. 97 (2016) 212–236, https://doi.org/10.1016/j.envint.2016.09.013.
[6] L. Nordkap, U.N. Joensen, M. Blomberg Jensen, N. Jørgensen, Regional differences and temporal trends in male reproductive health disorders: semen quality may be a sensitive marker of environmental exposures, Mol. Cell. Endocrinol. 355 (2) (2012) 221–230, https://doi.org/10.1016/j.mce.2011.05.048.
[7] A. Thankamony, V. Pasterski, K.K. Ong, C.L. Acerini, I.A. Hughes, Anogenital distance as a marker of androgen exposure in humans, Andrology 4 (4) (2016) 616–625, https://doi.org/10.1111/andr.12156.
[8] E. Nielsen, G. Ostergaard, I. Thorup, O. Ladefoged, J. Jelnes, Toxicological Evaluation and Limit Values for Nonylphenol, Nonylphenol Ethoxylates, Tricresyl Phosphates and Benzoic Acid, Danish Environmental Project No. 512, Miljoprojekt, 2000, https://www2.mst.dk/Udgiv/publications/1999/87-7909-566-6/pdf/87-7909-565-8.pdf.
[9] J. Nevoral, Y. Kolinko, J. Moravec, et al., Long-term exposure to very low doses of bisphenol S affects female reproduction, Reproduction 156 (1) (2018) 47–57, https://doi.org/10.1530/REP-18-0092.
[10] M. Castillo, D. Barceló, Analysis of industrial effluents to determine endocrine-disrupting chemicals, Trends Analyt. Chem. 16 (10) (1997) 574–583, https://doi.org/10.1016/S0165-9936(97)00090-3.
[11] M. Shelby, NTP-CERHR monograph on the potential human reproductive and developmental effects of di (2-ethylhexyl) phthalate (DEHP), NTP CERHR MON 18 (2006) v, vii-7, II-iii-xiii passim, https://www.ncbi.nlm.nih.gov/pubmed/19407857.
[12] European Food Safety Authority, Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs: executive summary, EFSA J. 13 (1) (2015) 3978, https://doi.org/10.2903/j.efsa.2015.3978.
[13] S. Eladak, T. Grisin, D. Moison, et al., A new chapter in the bisphenol a story: bisphenol S and bisphenol F are not safe alternatives to this compound, Fertil. Steril. 103 (1) (2015) 11–21, https://doi.org/10.1016/j.fertnstert.2014.11.005.
[14] G. Di Bella, A.G. Potortì, V. Lo Turco, M. Saitta, G. Dugo, Plasticizer residues by HRGC-MS in espresso coffees from capsules, pods and moka pots, Food Control 41 (1) (2014) 185–192, https://doi.org/10.1016/j.foodcont.2014.01.026.
[15] X. Ye, Z. Kuklenyik, L.L. Needham, A.M. Calafat, Automated on-line column-switching HPLC-MS/MS method with peak focusing for the determination of nine environmental phenols in urine, Anal. Chem. 77 (16) (2005) 5407–5413, https://doi.org/10.1021/ac050390d.
[16] A. Khedr, Optimized extraction method for LC-MS determination of bisphenol A, melamine and di(2-ethylhexyl) phthalate in selected soft drinks, syringes, and milk powder, J. Chromatogr. B Anal. Technol. Biomed. Life. Sci. 930 (2013) 98–103, https://doi.org/10.1016/j.jchromb.2013.04.040.
[17] S. Langer, G. Bekö, C.J. Weschler, et al., Phthalate metabolites in urine samples from Danish children and correlations with phthalates in dust samples from their homes and daycare centers, Int. J. Hyg. Environ. Health 217 (1) (2014) 78–87, https://doi.org/10.1016/j.ijheh.2013.03.014.
[18] USEPA, Definition and Procedure for the Determination of the Method Detection Limit, Revision 2, Doc. No. EPA 821-R-16-006., United States Environmental Protection Agency, Office of Water, 2016 https://www.epa.gov/sites/production/files/2016-12/documents/mdl-procedure_rev2_12-13-2016.pdf.
[19] D.Y. Bang, M. Kyung, M.J. Kim, et al., Human risk assessment of endocrine-disrupting chemicals derived from plastic food containers, Compr. Rev. Food Sci. Food Saf. 11 (2012), https://doi.org/10.1111/j.1541-4337.2012.00197.x.
[20] O. Zoller, B.J. Brüschweiler, R. Magnin, et al., Natural occurrence of bisphenol F in mustard, Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess. 33 (1) (2016) 137–146, https://doi.org/10.1080/19440049.2015.1110623.
[21] European Food Safety Authority, Safety of benzophenone to be used as flavouring, EFSA J. 15 (11) (2017) 5013.
[22] European Food Safety Authority, Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Material in Contact with Food (AFC) on a request from the Commission related to Di-Butylphthalate (DBP) for use in food contact materials, EFSA J. (2005) 1–17.
[23] M.A. Mohamed, A.S. Ammar, Quantitative analysis of phthalates plasticizers in traditional egyptian foods (Koushary and foul medams), black tea, instant coffee and bottled waters by solid phase extraction-capillary gas chromatography-mass spectroscopy, Am. J. Food. Technol. 3 (5) (2008) 341–346, https://doi.org/10.3923/ajft.2008.341.346.
[24] L. Rubio, L. Valverde-Som, L.A. Sarabia, M.C. Ortiz, The behaviour of Tenax as food simulant in the migration of polymer additives from food contact materials by means of gas chromatography/mass spectrometry and PARAFAC, J. Chromatogr. A 1589 (2019) 18–29, https://doi.org/10.1016/j.chroma.2018.12.054.
[25] C.Z. Yang, S.I. Yaniger, V.C. Jordan, D.J. Klein, G.D. Bittner, Most plastic products release estrogenic chemicals: a potential health problem that can be solved, Environ. Health Perspect. 119 (7) (2011) 989–996, https://doi.org/10.1289/ehp.1003220.
[26] N.A. Suciu, F. Tiberto, S. Vasileiadis, L. Lamastra, M. Trevisan, Recycled paper-paperboard for food contact materials: contaminants suspected and migration into foods and food simulant, Food Chem. 141 (4) (2013) 4146–4151, https://doi.org/10.1016/j.foodchem.2013.07.014.
[27] M. Skinner, Epigenetic transgenerational inheritance, Nat. Rev. Endorcinol. 12 (2) (2016) 68–70, https://doi.org/10.1038/nrendo.2015.206.
[28] J. Thomas, M. Thomas, S. Gangolli, Biological effects of DI-(2-Ethylhexyl) phthalate and other phthalic acid esters, Crit. Rev. Toxicol. 13 (4) (1984) 283–317, https://doi.org/10.3109/10408448409023761.
[29] H.J. Lehmler, B. Liu, M. Gadogbe, W. Bao, Exposure to bisphenol a, bisphenol F, and bisphenol S in U.S. Adults and children: the national health and nutrition examination survey 2013-2014, ACS Omega 3 (6) (2018) 6523–6532, https://doi.org/10.1021/acsomega.8b00824.
[30] U.S. Environmental Protection Agency, Proposed Designation of Di-ethylhexyl Phthalate (DEHP) (1,2-Benzene- Dicarboxylic Acid, 1,2-bis (2-ethylhexyl) Ester) (CASRN 117-81-7) As a High-priority Substance for Risk Evaluation, 2019. Published. Accessed January 9, 2020, https://www.epa.gov/sites/production/files/2019-08/documents/di-ethylhexyl_phthalate_117-81-7_proposeddesignation_082219.pdf.
[31] V. Karzi, M.N. Tzatzarakis, E. Vakonaki, et al., Biomonitoring of bisphenol A, triclosan and perfluorooctanoic acid in hair samples of children and adults, J. Appl. Toxicol. 38 (8) (2018) 1144–1152, https://doi.org/10.1002/jat.3627.
[32] F. Peng, W. Ji, F. Zhu, et al., A study on phthalate metabolites, bisphenol A and nonylphenol in the urine of Chinese women with unexplained recurrent spontaneous abortion, Environ. Res. 150 (2016) 622–628, https://doi.org/10.1016/j.envres.2016.04.003.