Endocrine-disrupting chemicals used as common plastic additives: levels, profiles, and human dietary exposure from the Indian food basket

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Abstract

Endocrine-disrupting chemicals such as phthalic acid esters (PAEs) and bisphenol-A (BPA) are the most widely used plastic additives in polymeric materials. Hence, twelve PAEs and BPA were investigated in twenty-five food types and drinking water (supply and packaged) from the metropolitan city, Delhi, and the peri-urban areas of a non-metropolitan city, Dehradun. PAEs and BPA in all the food types were significantly higher in Delhi over Dehradun ($p < 0.01$). Highest mean $\sum_{12}$PAEs (665 ng/g and BPA (73 ng/g) were observed in cottage cheese and potatoes, respectively followed by fish (PAEs - 477 ng/g, BPA - 16 ng/g). Supply water from the west zone of Delhi was found to contain the highest concentration of BPA (309 ng/L) and $\sum_{12}$PAEs (5688 ng/L) with the dominance of diethyl phthalate (DEP). Based on the compositional profile and compound-wise principal component analysis, environmental contamination and food processing were attributed as significant sources of most priority PAEs in food samples. Di-ethyl hexyl phthalate (DEHP) was over 100-fold higher in the bottled water from local brands than composite bottled water samples. Packaging material was identified as a source for di-n-butyl phthalate (DnBP) in packaged food. This study observed the highest estimated dietary intake (EDI) in the high-fat-containing food products viz., cottage cheese and fish from north Delhi. High bioaccumulation of BPA can be a possible reason for elevated EDI in vegetables and local fish of Delhi. Unlike Dehradun, EDI for $\sum_{12}$PAEs and BPA was slightly higher for the non-vegetarian adult when compared to the vegetarian adult. DEHP and DnBP exhibited the highest estimated estrogenic potential for bottled water from local brands. Dietary exposure due to six priority PAEs contamination in food stuffs was two to four-fold higher in Delhi than Dehradun for non-vegetarian adults.

Key words: PAEs, BPA, food, estimated dietary intake (EDI)

1. Introduction

Organic plastic additives such as phthalic acid esters (PAEs) and bisphenol A (BPA) have been extensively used to increase the durability and plasticity of synthetic polymers. PAEs, commonly referred to as phthalates, are organic lipophilic compounds mainly used as plasticizers for several consumer products, including food packaging. Plasticizers contribute up to 30% weight in food packaging films alone. On the other hand, BPA is a monomer for polycarbonate plastics and is found in epoxy resins commonly used in can linings and hard polycarbonate plastics, such as bottles, microwaveable food storage containers. Both PAEs and BPA are extensively produced and used in large volumes. Among the most common plastic materials utilized by the food industries, polyethylene terephthalate (PET) and high-density polyethylene (HDPE) are frequently used in food-contact materials. The migration and leakage of these high-volume industrial chemicals into food and drinks have been evidenced worldwide. Consequently, dietary intake is the primary exposure source of both PAEs and BPA for consumers.

Indian food and grocery markets hold the sixth position globally and account for 4% of the global food packaging market (IBEF). In India, food packaging alone contributes 38% of the flexible packaging segment for industrial applications. Polymers such as polyethylene (PE, 59%) followed by polypropylene (PP, 31%) and PET (10%) are the major constituents in the flexible packaging sector.

PAEs and BPA belong to a group of substances known as endocrine-disrupting chemicals (EDCs) as they can interfere with the human hormonal system and impact human health by affecting reproductive, developmental, immunological, and neurological functions. Human exposure studies have shown that PAEs and BPA can induce endocrine-disrupting effects and adversely impact children's growth. Due to their possible harmful effects, environmental monitoring of these plastic additives and human exposure assessment studies has gained momentum. The United States Environmental Protection Agency (USEPA) enlisted six

plasticizers viz., dimethyl phthalate (DMP), diethyl phthalate (DEP), di-n-butyl phthalate (DnBP), butyl benzyl phthalate (BBzP), diethyl hexyl phthalate (DEHP), and di-n-octyl phthalate (DnOP) as priority pollutants due to their effects on specific endocrine systems (USEPA, 2014). Several studies reported food as a major exposure pathway for PAEs and BPA. Reports (including from India) have also shown these EDCs can be released to the environment from open burning and acid baths (Chakraborty et al., 2019). Elevated PAEs have been reported in cooked food from south Delhi (Das et al., 2014). BPA was ubiquitously found in canned and un-canned foods worldwide (Cao et al., 2011, Sajiki et al., 2007).

A recent study detected a wide range of persistent organic pollutants (POPs), of which several have been identified as EDCs, in Indian food staples (Sharma et al., 2021). Like POPs, the foodstuffs available in local markets can provide the exposure pathway for PAEs (Guo et al., 2012). This study is the first attempt to investigate the occurrence and levels of a range of plastic additives (twelve PAEs and BPA) in 25 food types and drinking water (supply and packaged water) from a prime metropolitan (Delhi) and non-metropolitan environment in the state of Uttarakhand (Dehradun) in northern India. Delhi is an important food hub where food produced and processed from all parts of India is sold. Moreover, the Delhi population is representative of the social, ethnic, and cultural diversity of India. Hence, Delhi's food market is considered a good case study representative of the general Indian context (Sharma et al., 2021). The samples were collected from peri-urban areas of Dehradun and analyzed to contrast the assumptions made for the choice of Delhi as a broad representative market. In Dehradun, we mostly have locally produced food, often with a low level of processing (Sharma et al., 2021). The major objectives of this study were to: a. provide a pilot assessment of the levels of PAEs and BPA in the Indian food basket and water samples and compare results with other studies; b. elucidate the possible sources of PAEs and BPA in analyzed food products using multivariate principal component analysis and compositional profiles; c. assess (i) potential

risk estimated from the daily dietary intake of PAEs and BPA based on the ingestion rate of different food types by vegetarian and non-vegetarian inhabitants (ii) non-cancer risk of detected PAEs and BPA and cancer risk of carcinogenic PAEs, and (iii) potential estrogenic risk via drinking water using yeast assay by Cespedes et al. (2004) and human cell line assay by Chakraborty et al. (2021).

2. Materials and methods

2.1.Sample collection

Delhi houses a population of 31 million (2021 census), covering an area of 1,484 km^2. Delhi is the biggest trading centre and the largest centre for small industries in northern India, thereby attracting migrants from neighbouring states and other parts of the country. Among all the metropolitan cities in India, Delhi has the second-highest interstate migrants, suggesting the population can represent the entire country. Dehradun, a non-metropolitan city,, houses a population of close to 10 million, covering 196 km^2. Altogether 157 samples in 25 food types and drinking water were collected during 2018-2019 from four zones of Delhi and Dehradun (Figure 1 and Table S1), based on a survey given elsewhere (Sharma et al., 2021). The food basket consisted of five major types of produce: cereals (wheat, rice, green gram, red lentil, and yellow lentil); vegetables (tomato, potato, onion, ladies finger, spinach, cauliflower, and cabbage); fruits (mango, apple, banana, watermelon, and orange); dairy products (cottage cheese, yoghurt, and packaged milk); animal-based food products (eggs, fish, mutton, and chicken) and drinking water (supply water, composite bottled water, bottled water-local brands, bottled water-international brands, and water sachets). Composite bottled water included three international brands of PET bottles, one local brand in equal portions. Separately each of those international and local brands were also analysed. Water sachets contained water in plastic packets made of low-density polyethylene (LDPE). One set of locally cultured fish and locally

126 available unpacked milk samples were also sampled from Delhi. A composite sample of each
127 food type was prepared using a homogenizer by mixing an equal proportion of each food type
128 from supermarkets and local vendors. Composite samples of each food type were then stored
129 at -20 °C until extraction, as described in detail elsewhere (Sharma et al., 2021).
130
131 **2.2. Standards and Solvents**
132 Analytical mixed standard of PAEs containing dimethyl phthalate (DMP), diethyl phthalate
133 (DEP), diisobutyl phthalate (DiBP), di-n-butyl phthalate (DnBP), dimethoxy ethyl phthalate
134 (DMEP), bis(4-methyl-2-pentyl) phthalate (BMPP), dipentyl phthalate (DPP), dihexyl
135 phthalate (DHXP), butyl benzyl phthalate (BBzP), diethylhexyl phthalate (DEHP), di-n-octyl
136 phthalate (DnOP), and di-nonyl phthalate (DINP) with a purity of 98–99% was purchased from
137 Restek (Bellefonte, PA, USA). Analytical grade benzyl benzoate (purity >98 %) used as an
138 internal standard was procured from Sigma Aldrich, USA. BPA standard (99.99% purity) was
139 purchased from Sigma Aldrich. N-methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) of
140 purity >98.5 % was acquired from Sigma Aldrich, USA to use as a derivatizing agent for BPA
141 analysis in gas chromatography mass spectrometry (GC-MS). Isotope labelled ($^{13}C_{12}$-DEHP,
142 $^{13}C_{12}$-BPA) and deuterated standards (DMP-d_4, DnBP-d_4) were obtained from Cambridge
143 Isotope laboratories. All solvents, including dichloromethane, n-hexane, methanol, acetone,
144 and other chemicals, were 99% purity grade.
145
146 **2.3.Extraction**
147 *2.3.1 Food samples*
148 Pior to extraction, all the food samples were spiked with surrogate standards ($^{13}C_{12}$-DEHP,
149 $^{13}C_{12}$-BPA, DMP-d_4, DnBP-d_4). Solid food and dairy samples were analysed by the method
150 given elsewhere (Guo et al., 2012) with slight modifications. Briefly, 10 g of samples were

151 homogenized and extracted three times with n-hexane: acetone (1:1 v/v, 25 mL) in an orbital
152 shaker for 30 mins each time. After shaking, the samples were centrifuged at 4500 rpm for 10
153 mins, followed by decantation of the solvent. The pooled extracts were concentrated to 3 mL
154 using a rotary evaporator. The concentrated extracts were transferred into a glass separating
155 funnel containing 40 mL of n-hexane-saturated acetonitrile and shaken for 15 mins. After
156 vigorous shaking, the n-hexane layer containing lipids was discarded. Further, 3 mL of n-
157 hexane was added to the separating funnel, and the protocol was repeated twice to remove
158 lipids. The lipid-free sample extracts were then concentrated to 5 mL and transferred into glass
159 vessels containing 25 mL of >99% pure water. PAEs and BPA were extracted three times from
160 the solution with 7 mL of n-hexane by shaking for 30 mins in the orbital shaker. After
161 centrifugation for 10 min, the n-hexane layer was combined, concentrated using nitrogen
162 blowdown, and then transferred into a GC vial. The extracts were further subjected to a clean-
163 up procedure in a glass column filled with 3 cm silica gel (bottom) and 1 cm anhydrous sodium
164 sulfate (top). The final solution was reduced to 1 mL using rotary evaporator. In the case of
165 BPA analysis, the final extracts were derivatized using MSTFA prior to instrumental analysis.
166 *2.3.2 Water samples*
167 All water samples were subjected to solid-phase extraction (SPE) using the method given
168 elsewhere (Chakraborty et al., 2021). Briefly, 500 mL of water samples spiked with surrogates
169 ($^{13}C_{12}$-DEHP and $^{13}C_{12}$-BPA) were extracted using C18 cartridges (BondElut, Agilent
170 Technologies). The cartridges were pre-conditioned with 6 mL methanol followed by 2 x 3.5
171 mL of ultrapure water. Forelution, 4 x 2 mL of dichloromethane: n-hexane (4:1, v/v) was used.
172 Moisture content was then removed using a sodium sulphate column.
173 *2.3.3 Packaging material*
174 Packaging materials for packaged food items were extracted using method given elsewhere
175 (Shen 2005). Briefly, samples were finely grated (~2 mm^2). Each sample was then added with

20 ng of DMP-d_4 and DnBP-d_4. First, 1 g of each sample was soaked in n-hexane (10 mL) for 30 mins and then by ultrasonicated for 10 mins. This process was repeated three times, and the pooled extracts were reduced to 1 mL and further subjected to column-clean up.

2.4 Instrumental Analysis

Twelve PAEs and BPA were detected and quantified using an Agilent 7890B gas chromatograph coupled with a 5977A mass spectrometer with a DB-35MS column (30 m x 0.25 mm x 0.25 μm) in the selected ion monitoring (SIM) mode. The carrier gas flow rate (He, 99.999% purity) was kept constant at 1.2 mL/min. The column temperature for PAEs was set at 60°C for 2 mins, increased to 220°C at the rate of 20°C/min and held for 1 min, then increased to 250°C at the rate of 5°C/min and held for 5 mins and finally increased to 280°C at the rate of 6°C/min and held for 3 mins. In GC-MS, 1 μL of column cleaned extracts were injected in split-less mode with an inlet temperature of 280°C. The mass spectrometer was run in electron ionization (EI) mode (70 eV). The initial column temperature for BPA was 100°C for 1 min, increased to 180°C at the rate of 20°C/min and finally increased to 280°C at the rate of 10°C/min and held for 3 mins. 1 μL of extracts were injected into the GC in split-less mode at injector temperature of 250°C. The transfer line temperatures in analysis of both PAEs and BPA were maintained at 280°C.

2.5 Quality assurance and quality control

To minimize any contamination from lab wares, mostly glass wares were used. Before the experiments, all the glass wares were cleaned with soap and MilliQ water. For every batchof 5 samples, one blank sample with solvent alone was extracted and analyzed in the similar manner as the samples. Along with procedural blanks, instrumental blanks and spiked procedural blanks were run with a set of every 10 samples. Limit of detection (LOD), %RSD, R^2 and retention times are given in Table S2. LODs were determined as the lowest concentration of each analyte in a sample that gave rise to a peak with a signal-to-noise ratio (S/N) > 3:1.

Surrogate recovery for $^{13}C_{12}$-BPA and $^{13}C_{12}$-DEHP from the water was 82–117% and 87–109%, respectively. For DMP-d_4, DnBP-d_4 recovery percentage ranged between 82–113%. PAEs and BPA were found in trace levels in instrumental blank samples, with negligible influence on the quantification. All samples were blank corrected and reported in ng/g wet weight basis for food and ng/L for water samples.

2.6 Human exposure assessment

2.6.1 Dietary exposure

We have estimated the daily dietary intake of each PAE and BPA for the entire food basket as well as for individual food categories and different drinking water types based on the following equation given elsewhere (Guo et al., 2012, Cheng et al., 2016, Clark et al., 2011).

$$EDI = \frac{\sum C_i Q_i}{BW} r_i \ldots. \qquad (1)$$

where, *EDI* (ng/kg-bw/d) is the estimated daily intake from diet, C_i (ng/g) is the concentration of PAE or BPA in food products (for water, C_i is expressed in ng/L), Q_i (g/d) is the average amount of daily intake of food *i*, r_i is the gastrointestinal uptake factor for food *i*, and *BW* (kg) is the body weight. Generally, for *BW*, 60 kg and 55 kg are average values for an adult man and an adult woman, respectively. The weight of 18 kg is used as an average value for child (4–6 yr); for r_i, a value of 100% was assumed, and for Q_i, the intake values of various goods reported per capita for Delhi and Uttarakhand published by National Sample Survey Office (NSSO), Ministry of Statistics and Programme Implementation, Government of India, were used (NSSO 2014). The intake rates were expressed as per consumption unit (CU) per day (d), developed by ICMR for different age groups, sex, and physical activity (Singh et al., 2015). Thus, CU is considered as 1 for adults (man), 0.8 for adults (woman) and 0.6 for children (4–6 yr).

2.6.2. Non-cancer and cancer risk assessment

Contamination of detected plastic additives in food samples can pose carcinogenic and non-carcinogenic risks due to prolonged exposure. Since DMP, DEP, DnBP, DnOP and BPA were recognized as non-cancer compounds for human health, the non-cancer risk was evaluated using the Hazard Quotient method (HQ) as given in equation nos. (2 and 3). Reference doses (R_fD) used were 20, 100, 200, 800 µg/kg.d, and 50 µg/kg.d, for DEHP, DnBP, BBzP, DEP, BPA, respectively as suggested by the USEPA for adults (USEPA 1987a, b, c, 1989). The carcinogenic risk was assessed for BBzP & DEHP in all the food samples according to equation no. (4) using the USEPA Regional Screening Level 2021 cancer slope factors (Wang et al., 2015, Niu et al., 2014).. Briefly, the formulae used were

$$\mathrm{ADD} = \frac{\mathrm{C} \times \mathrm{I} \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{BW} \times \mathrm{AT}} \times 10^{-6} \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

$$\mathrm{HQ} = \mathrm{ADD}/RfD \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$\mathrm{CR} = \mathrm{ADD} \times \mathrm{CSF} \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

where, CR = carcinogenic risk (unitless), ADD = average daily dose via dietary intake (mg/kg.d), CSF = carcinogenic slope factor (mg/kg.d) [BBzP = 0.0019; DEHP = 0.0140], C = mean concentration of carcinogenic phthalates (BBzP, DEHP) in food (mg/kg), I = daily intake rate of food (mg/d), EF = exposure frequency (d/yr) [365 days – year long exposure], ED = exposure duration in years [72 yr], BW = body weight (kg) [60 for man, 55 for woman], AT = average lifetime exposure [72 × 365 d]

2.6.3 Estrogenicity

Water is consumed at regular intervals by people with varied dietary patterns. Hence the relative estrogenicity was calculated for water samples based on data available for estradiol equivalent for PAEs and BPA from yeast assay (Céspedes et al., 2004) and human mammary cell line (Chakraborty et al., 2021) using the following formula,

$$\mathbf{EEQ_y\ (pg/L) = C_i \times E2_{equiv}} \text{.....(5)}$$

$$\mathbf{EEQ_b\ (pg/L) = C_i \times \textit{Bio}E2Eqs} \text{ .....(6)}$$

C_i is the concentration detected for each compound. $E2_{equiv}$ and *Bio*E2Eqs are the relative estrogenicity factor obtainedfrom yeast assay (Céspedes et al., 2004) and bioassay (Chakraborty et al., 2021), respectively. EEQ_y and EEQ_b are the estradiol quotients calculated as Ci and estroenic factor products obtained from yeast assay (Céspedes et al., 2004) and bioassay (Chakraborty et al., 2021), respectively.

2.7 Statistical analysis

Statistical analyses were carried out using SPSS version 22, and it included linear regression analysis, one-way ANOVA including Latin square design (LSD), Tukey test at 95% confidence intervals, and principal component analysis (PCA).

3. Results and discussion

3.1 Levels and comparison with other studies

Ranges of PAEs and BPA in five broad food types from Delhi and Dehradun have been given in Table 1, Table S3, and S4. Concentrations of PAEs and BPA in packaging materials are given in Figure S1. Comparison between concentrations of each type of PAE and BPA with those determined in other worldwide studies is given in Table S5 and S6, respectively. Both the sum of six priority PAEs ($\sum_6$PAEs) and twelve PAEs ($\sum_{12}$PAEs) in all the food types, except vegetables, were significantly higher in Delhi than Dehradun ($p < 0.05$). A detailed description and discussion of these observed differences is provided in the following sections for each group of food items. In general, a trend observed in terms of maximum geomean for

273 $\sum_{12}$PAEs was cottage cheese (450 ng/g) > rice (279.9 ng/g) > local fish (212.7 ng/g) > wheat
274 (182.6 ng/g) > fish (171.5 ng/g) > mutton (136.7 ng/g). The geomean concentration of BPA
275 was highest in fish (10.9 ng/g) followed by mutton (10.8 ng/g), potato (10.4 ng/g), egg (5 ng/g),
276 and cottage cheese (4.8 ng/g). In water samples, the highest geomean concentration for
277 $\sum_{12}$PAEs was seen in composite bottled water (1043.8 ng/L) followed by bottled water-local
278 (926 ng/L), supply water (922 ng/L), and bottled water-international (269.9 ng/L). BPA
279 geomean concentration was highest in supply water (87 ng/L), followed by composite bottled
280 water (68.9 ng/L). $\sum_{6}$PAEs in water seems to be slightly higher than other studies reported
281 worldwide. However, BPA levels in this study were lower than in other studies.
282 $\sum_{12}$PAEs concentrations in packaging material varied between 6.06 µg/g to 96 µg/g (31 ± 43,
283 mean ± SD). The highest concentration of $\sum_{12}$PAEs was seen in the packaging material for
284 pulses, followed by cottage cheese, wheat, and milk, respectively. In packaging material, about
285 90% of $\sum_{12}$PAEs was contributed by DnBP, and BPA was not detected.
286
287 ***3.1.1 Cereals***
288 Range of $\sum_{12}$PAEs concentration in cereals was 12.3 ng/g (yellow lentil)–669 ng/g (rice) in
289 Delhi and 1.57 ng/g (yellow lentil) –27.1 ng/g (red lentil) in Dehradun. The highest mean of
290 $\sum_{12}$PAEs was observed in rice (372.2 ng/g) followed by wheat (186.6 ng/g), red lentil (97.5
291 ng/g), green gram (92.4 ng/g), and yellow lentil (55.4 ng/g) in Delhi. Maximum BPA
292 contribution in Delhi cereals was from green gram (mean, 2.6 ng/g) and yellow lentil (mean,
293 2.58 ng/g). In Dehradun, BPA was detected only in yellow lentils (18 ng/g).
294 In Delhi, the mean $\sum_{6}$PAEs in rice (15.7 ng/g) was tenfold lower than raw rice from Belgium
295 (107.3 ng/g) (Fierens et al., 2012) and about four-fold lower than a composite rice sample from
296 Quebec City, Canada (≈40 ng/g) (Cao et al., 2015). Further, average $\sum_{6}$PAEs were much lower
297 than rice samples from China and Serbia (Škrbić et al., 2017). DMP, DEP, DHXP, BBzP, and

298 DnOP concentrations in rice in this study were comparable to those of another study from
299 China (Guo et al., 2012). However, the maximum DiBP, DnBP, and DEHP concentrations
300 were much lower than that study. The average BPA in the wheat sample (1.2 ng/g) was three-
301 fold higher than the wheat flour from the Canadian total diet study (TDS) in Quebec City (0.4
302 ng/g) (Cao et al., 2011).
303
304 ***3.1.2 Vegetables***
305 Range of $\sum_{12}$PAEs concentrations in vegetables was 0.1 ng/g (cabbage)–105 ng/g (onion) in
306 Delhi and 0.6 ng/g (potato) –127.6 ng/g (cabbage) in Dehradun. The highest mean $\sum_{12}$PAEs
307 was in onion (33.6 ng/g) followed by spinach (23.3 ng/g), cauliflower (17.3 ng/g), ladies finger
308 (9.5 ng/g), tomato (6.8 ng/g), potato (3.7 ng/g), and cabbage (3.5 ng/g). However, mean BPA
309 was maximum in potato (72.9 ng/g) followed by onion (3.2 ng/g), ladies finger (3 ng/g), and
310 tomato (2.5 ng/g). DiBP (24%) and DMP (20%) were the dominant PAEs detected in
311 vegetables from Delhi. Higher DiBP concentration in cabbage (109 ng/g) led to a greater mean
312 concentration of $\sum_{12}$PAEs in vegetables from Dehradun. Excluding this value, the $\sum_{12}$PAEs in
313 Dehradun ranged from non-detectable (ND) to 23.6 ng/g. Except for DEHP, the levels of other
314 priority PAEs and DiBP in potato from Delhi were comparable to Belgian potato (Fierens et
315 al., 2012). $\sum_{6}$PAEs in cauliflower from the 2013 Canadian study was approximately 100-fold
316 higher than Delhi samples (Cao et al., 2015). Maximum values of BPA (7.2 ng/g) were lower
317 than canned tomatoes from New Zealand and tomatoes from the Japanese market (Thomson
318 and Grounds 2005; Martine et al., 2013). Average BPA concentration in un-canned tomatoes
319 from Delhi was comparable to the composite sample of canned tomatoes and nine-fold lower
320 than the canned peeled tomatoes from the Belgian market (Geens et al., 2010a).
321
322 ***3.1.3 Fruits***

323 The range of $\sum_{12}$PAEs concentrations in fruits was ND (orange)–101 ng/g (banana) in Delhi
324 and 1.2 ng/g (mango)-188.9 ng/g (orange) in Dehradun. The highest mean $\sum_{12}$PAEs was in
325 banana (49.1 ng/g) followed by watermelon (31 ng/g), mango (18.3 ng/g), orange (13.7 ng/g),
326 and apple (12.5 ng/g). DiBP (27%) and BMPP (15%) dominated the PAE profile in fruits.
327 Higher mean $\sum_{12}$PAEs in Dehradun was contributed by extreme DiBP concentration (186 ng/g)
328 observed in oranges. $\sum_{6}$PAEs in apples (≈600 ng/g) and bananas (≈390 ng/g) from the
329 Canadian study (Cao et al., 2015) were close to hundred-fold and thirty nine-fold higher than
330 the corresponding levels in apples and bananas of Delhi, respectively. Like Dehradun, BPA
331 was not detected in composite banana and apple samples from Canada (Cao et al., 2011).
332
333 ***3.1.4 Dairy products***
334 The range of $\sum_{12}$PAEs concentrations in dairy products was 0.4 ng/g (packaged milk)–864.3
335 ng/g (cottage cheese) in Delhi and 14 ng/g (packaged milk)–19 ng/g (yoghurt) in Dehradun.
336 The highest mean $\sum_{12}$PAEs was in cottage cheese (614 ng/g) followed by yoghurt (116.3 ng/g),
337 and packaged milk (38.1 ng/g), respectively. Similarly, the highest mean BPA was in cottage
338 cheese (6.1 ng/g) followed by yoghurt (3.3 ng/g), and packaged milk (2.5 ng/g). DMEP
339 contributed to 60% of $\sum_{12}$PAEs in dairy. Among all the quantified phthalates, DMEP (55%),
340 and BMPP (33%) were dominant in cottage cheese and yoghurt. Among all the food samples,
341 the highest mean concentration of priority PAEs stemmed from cottage cheese (31 ng/g) with
342 upto 50% contribution from DEHP. Mean DnBP and DEHP concentrations in yoghurt were
343 much lower than in a Mexican study, whereas DEP was comparable (García-Fabila et al.,
344 2020). Mean priority PAEs in the milk of Delhi was three-fold lower than Norway (Sakhi et
345 al., 2014) and thirteen-fold lower than New York (Schecter et al., 2013). Unlike mean
346 concentrations of DEHP and BBzP, the mean concentration of DnBP in milk was much higher

than in Tunisia (Beltifa et al., 2017). BPA concentration in cottage cheese (≈2 ng/g) from Quebec City, Canada, was three-fold lower than Delhi (Cao et al., 2011).

3.1.5 Animal-based food products

The range of $\sum_{12}$PAEs concentrations in animal-based food products was 1.8 ng/g (chicken)–1089 ng/g (fish) in Delhi and 0.2 ng/g (egg) - 1.95 ng/g (chicken) in Dehradun. Mean $\sum_{12}$PAEs in Delhi was maximum in local fish (455.7ng/g) followed by composite fish samples (360.4 ng/g), mutton (280.2 ng/g), egg (58.8 ng/g), and chicken (33.3 ng/g). $\sum_{12}$PAEs was maximum in chicken (1.9 ng/g) and fish (1.23 ng/g) in Dehradun, with 100% contribution from DEHP. $\sum_{6}$PAEs in Norwegian chicken fillets (≈2 ng/g) were comparable to those in chicken from this study (2.4 ng/g) (Sakhi et al., 2014). $\sum_{6}$PAEs in eggs (30 ng/g) from a Chinese study was approximately two times higher than from Delhi. Although the average concentration of DnBP and DEHP was much higher in egg samples from China than in the present study, DEP and DMP were up to two-fold higher in the present study (Yang et al., 2018). Further, the mean level of DnBP in eggs was threefold higher in the present study, DEHP and DEP levels were up to a hundred-fold lower when compared with the Mexican diet study (García-Fabila et al., 2020). $\sum_{6}$PAEs in chicken samples (≈21 ng/g) from New York (Schecter et al., 2013) were close to 10 times higher than Delhi.

Composite fish samples from Delhi had a higher mean level of BPA (16.4 ng/g) followed by local fish (14.1 ng/g), mutton (12.3 ng/g), egg (5.7 ng/g), and chicken (3.5 ng/g). Mean BPA concentration in Delhi chicken samples (3.5 ng/g) was five-fold higher than that in the poultry (liver plate) (≈0.7 ng/g) from Canada (Cao et al., 2011). In eggs, the mean BPA from Delhi was almost thrice (~6 ng/g) than that of China (~2 ng/g) (Liao and Kannan 2014). However, the mean BPA in chicken from Delhi was comparable to canned chicken in Japan (4 ng/g) (Sajiki et al., 2007).

372 ***3.1.6 Supply and Packaged water***

373 Plastic additives were ubiquitously present in all the types of drinking water from Delhi. Mean
374 $\sum_{12}$PAEs was highest in supply water of Delhi (1868.4 ng/L) followed by composite bottled
375 water (1441.5 ng/L), bottled water from local brands (1103 ng/L), bottled water from
376 international brands (274.6 ng/L), and water sachets (43.7 ng/L). $\sum_{12}$PAEs in supply and
377 packaged water from Dehradun varied between ND–11 ng/L and ND–20 ng/L, respectively. In
378 contrast to local brands, BPA was not detected, in bottled water from international brands of
379 Delhi. In both Delhi and Dehradun, 75% of the composite bottled water samples were from
380 the same international brands. The remaining one part of the composite bottled water samples
381 was from local brands from each zone of Delhi and Dehradun. Local bottled water in Delhi
382 showed a maximum level up to 2460 ng/L for $\sum_{6}$PAEs. Hence we suspect that the elevated
383 levels of these EDCs in composite bottled water of Delhi were mainly contributed by the low-
384 cost local brands using recycled plastic (PET) bottles and localized contaminated water
385 sources.

386 Among the priority PAEs, maximum contribution stemmed from DEP (58%), followed by
387 DnBP (26%) and DEHP (14%) in water samples from Delhi.

388 $\sum_{6}$PAEs concentrations in the supply water, composite bottled water, and water sachets and
389 packaged water of Delhi ranged from 35.5–4887.2 ng/L (1306 ± 2389 ng/L), 48.4-1343.9
390 (820.9 ± 55.7 ng/L) and 3.4–231.7 ng/L (32.8 ± 64.1 ng/L), respectively. BPA in supply water
391 and composite bottled water varied between 43.4-309.3 ng/L (121.4 ± 126 ng/L) and 8.7-264
392 (118.1 ± 106.8 ng/L), respectively. Such sachets are made of LDPE packaged and therefore
393 have higher leaching capacity for phthalates (Paluselli et al., 2018). However, we found very
394 low levels of PAEs from the water sachets from Delhi. This can be reasoned with the fact that
395 all of these water sachets were stored in refrigerated conditions.

396 $\sum_6$PAEs in Dehradun water samples ranged from 2.5–12 ng/g (8.6 ± 5.3 ng/g), while BPA was
397 not detected. Among bottled water, $\sum_6$PAEs in PET bottles was higher in local brands and
398 ranged between 332.1 1787.2 ng/L (806.1 ± 581 ng/L). In PET bottled water samples, we
399 found the highest contribution from DEP (up to 64%) followed by DiBP. Mean $\sum_6$PAEs in
400 Delhi composite bottled water from our study was almost double than the past study on
401 drinking water samples from ~~Jawaharlal Nehru University's~~ south Delhi (390 ng/L); however,
402 the levels were twofold lower than those from the industrial belt of Okhla, south Delhi (3389
403 ng/L) (Das et al., 2014).
404 Maximum levels in supply water samples from Delhi were nearly 40, 15500, and 220-fold
405 higher for DMP, DEP, and DnBP, respectively, compared with samples from public water
406 supply taps in Nigeria (Dada and Ikeh 2018). Mean $\sum_6$PAEs in Delhi composite bottled water
407 (820 ng/L) was much higher than the bottled water (≈0.6 ng/L) from Norway (Sakhi et al.,
408 2014) and China (≈0.25 ng/L) (Guo et al., 2012). Maximum DiBP (≈828 ng/L) and DnBP
409 (≈454 ng/L) levels in bottled water from Delhi were approximately two and sevenfold lower
410 than those in bottled water from Portugal (Santana et al., 2014). Maximum concentrations of
411 DMP and DEP in supply water of Delhi were about 1.5 and 12 times higher, respectively than
412 the tap water from Spain (Domínguez-Morueco et al., 2014). Mean BPA was highest in supply
413 water (121 ng/L) followed by composite bottled water (118 ng/L) and bottled water from local
414 brands (4.9 ng/L). DEP (39%), DiBP (24%), and DEHP (10%) were the significant contributors
415 to PAEs in water samples from Delhi.
416 The average BPA level in bottled water of Delhi was ≈118 ng/L, whereas BPA was below the
417 detection limit in mineral water from Belgium (Geens et al., 2010a). Average BPA
418 concentration in composite bottled water samples from Delhi (118 ng/L) displayed several
419 folds higher levels than Malaysia (3.3 ng/L) and Belgium (BDL) (Santhi et al., 2012, Geens et
420 al., 2010b).The average BPA in supply water of Delhi (≈121 ng/L) was 9-fold higher than the

tap water samples from Malaysia (≈14 ng/L) (Santhi et al., 2012); however, it was slightly lower than that of tap water from Brazil (160 ng/L) (Sodré et al., 2010). Maximum BPA concentrations in Delhi supply water (≈309 ng/L) and composite bottled water samples (≈264 ng/L) were comparable to those in tap (324 ng/L) and bottled water samples (317 ng/L) from Guangzhou, China (Li et al., 2010).

3.2. Compositional profiles and source apportionment

Multiple source factors can influence the concentration of different PAEs in different food matrices. Hence the entire dataset, excluding water samples, was subjected to compound-wise multivariate analysis using principal component analysis (PCA). PC-1, PC-2 and PC-3 contributed 30%, 12% and 9% of the total variance respectively. Compounds loaded in each component were attributed to different targeted plastic additives in different food matrices.

PC-1 was loaded with DMEP, BMPP, DiBP, BBzP, DPP, DEP and DHXP which contributed to more than three-fourth of $\sum_{12}$PAEs from food samples in this study (Figure 2). Nearly 50% of food matrices on average showed about 344 ng/g of these compounds. Up to 55% DMEP, DEP, BMPP, and DiBP stemmed from plant-based products (cereals, vegetables and fruits) and were significantly different than other food matrices (LSD, $p < 0.05$), suggesting a specific source type. Besides using sewage sludge as manure for agricultural lands, in India, plasticulture has become a booming innovative technique to reduce water consumption. Low molecular weight PAEs, such as DEP and DiBP have been seen abundantly in surface water and wastewater from India (Chakraborty et al., 2021) and other global studies (Saini et al., 2016). In addition, water samples from Delhi also had a higher contribution of DEP and DiBP when compared with other PAEs. Similar to DEP and DiBP, the dominance of BMPP and DMEP might have resulted from their entry via wastewater irrigation or use in fertilizers and insecticides coupled with their release from plastic mulching (Li et al., 2016). Elevated levels of BMPP and DMEP in food grains, particularly wheat, can be reasoned with more significant

446 transpiration rate-driven accumulation in vascular plants (Tan et al., 2016). Furthermore, it may
447 as well be related to the different crop cultivars planted, as PAEs concentration during different
448 growth stages are significantly different (Cai et al., 2017, Cai et al., 2015). It is noteworthy that
449 all the compounds in PC-1, were significantly higher (Tukey-test, $p < 0.01$) in lipid-based
450 products (animal and dairy products) than water-based products (fruits and vegetables). In
451 addition, more than half of PAEs in PC-1 were found in fish samples and were substantially
452 different from other animal products (LSD, $p < 0.01$). Contamination of commercial fishes in
453 aquaculture ponds can be reasoned for the bioaccumulation of plastic additives in fish samples,
454 potentially by untreated sewage discharge, disintegration of aquaculture liners and dumped
455 plastic waste (Cheng et al., 2019). Hence, we postulate that the aforementioned specific PAEs
456 in fish can be attributed to the contamination in aquaculture ponds and cereals due to
457 plasticulture.
458 PC-2 was loaded with relatively heavier PAEs viz., DEHP, DINP and DnOP (Figure 2). It is
459 to be noted that among these three compounds, DEHP was ubiquitously present in all the food
460 matrices and drinking water samples and was dominant in vegetables, fruits, and cottage
461 cheese. Abundance of heavier PAEs molecules such as DEHP and DnOP mostly in vegetables
462 and fruits may originate from soil contamination due to the combustion of dumped plastic
463 waste and wastewater irrigation (Chakraborty et al., 2019). DINP was detected in most food
464 samples, with elevated levels in vegetables and fruits. Most likely these resulted from
465 environmental contamination since it is used as a substitute plasticizer for priority PAEs
466 (Nagorka and Koschorreck 2020). Hence, the dominance of the above PAEs in fruits and
467 vegetables can be attributed to bioaccumulation from contaminated abiotic matrices. It is
468 noteworthy, among food samples, maximum DEHP among all the target PAEs was observed
469 in cottage cheese. Further DEHP level in cottage cheese was significantly different from other
470 food samples (Tukey test, $p < 0.01$). Elevated levels of DEHP in cottage cheese most likely

resulted from the heat facilitated (pasteurization) augmentation during the production of such high fat-containing products (Fierens et al., 2013). Hence, PAEs loaded in this component might have impacted food samples due to food processing and process-related environmental contamination.

PC-3 was loaded with DnBP with mean levels around 77 ng/g (Figure 2). More than 70% of DnBP stemmed from products mostly stored in plastic packets such as cereals and dairy products. Furthermore, DnBP in cottage cheese and yoghurt packed in polymeric material were significantly different from other unpacked dairy products such as milk (LSD, $p < 0.01$). Each of the analysed packing materials showed the dominance of DnBP (Figure S1) DnBP is used as a printing ink in polyethylene packaging materials (Cao et al., 2011). Furthermore, DnBP has maximum migration potential from LDPE packaging material under various environmental conditions (Paluselli et al., 2018). Apart from the packaged materials, composite food samples such as mutton, chicken, and fish showed a significant level of DnBP. We suggest this could be because these materials are stored in similar polymeric materials in supermarkets. Therefore, this component can be associated with the processing and usage of polymeric material during the packaging of different food products.

3.4 Human exposure and risk assessment

Estimates of exposure of EDCs due to the use of consumer products are confounded by minimal information concerning the concentrations of PAEs in the products, their intake rates, and absorption factors. The intake rates depend on the country, region, socio-economic group, age, sex, and weather. The European Food Safety Authority (EFSA) recommended that the daily intake limits of DnBP, BBzP, and DEHP are 10, 500, and 50 µg/kg-bw/d, respectively (Lovekamp-Swan and Davis 2003). The daily dietary exposure of the PAEs mentioned above for the Delhi adult population was lower than the EFSA recommended limit, even when their

maximum concentrations were considered for EDI estimation (Figure 3). Overall EDI for $\sum_6$PAEs in children (4–6 yrs) was nearly ten-fold higher than adults (Figure 3). Aggregated EDI values for all the foodstuffs, except for BBzP in seafood, milk, and dairy products, were lower than similar foodstuffs from China (Guo et al., 2012). Based on the food types, the mean EDI values for each priority PAEs, except for DMP in vegetables (Table S7), were lower than those for all the composite food samples from New York (Schecter et al., 2013). EDI for supply water in Delhi is much higher than water from Tianjin, China, and bottled water from Greece (Amiridou and Voutsa 2011). In contrast, EDI for BPA was almost comparable with bottled water from Greece (Amiridou and Voutsa 2011). Highest EDI for BPA in PET bottles (22 ng/kg-bw.d-composite bottled water) was approximately one-seventh of Turkey (163 ng/kg-bw/d) and Iran (157 ng/kg-bw/d) (Karayaka et al., 2019, Mohammadnezhad et al., 2019). Although the highest EDI for BPA in PET bottles was comparable to Malaysia (36 ng/kg-bw/d) (Rozaini et al., 2017), it was higher than that observed in various studies from China (Chang et al., 2017, Wu et al., 2019, Zhou et al., 2019). Maximum EDI in Delhi was due to cereals, mainly wheat and rice, forming a significant portion of the staple diet. Human exposure to the targeted PAEs seems to be dominant via dietary intake, mainly through fish consumption, primarily cultured in aquaculture farms. This observation is consistent with a study from China (Cheng et al., 2013).

We did not find any non-carcinogenic risk for any of the priority PAEs in this study (Table S8A). Excluding high (10^{-3}-10^{-1}) risk due to BPA inpotatoes from the west zone of Delhi, the rest of the zone exhibited very low to moderate risk ($<10^{-6}$-10^{-3}) for the rest of the food types (Table S8B). Furthermore, low carcinogenic risk was observed for DEHP intake from dairy products of north zone of Delhi (2.96×10^{-6}) (Table S9). However, all other food groups from all the zones for intakes of BBzP & DEHP posed "very low" carcinogenic risk ($< 10^{-6}$).

520 Overall range of EEQ_b and EEQ_y in Delhi varied between 0.129.1 pg/L E2Eq (Mean ± SD, 4.4
521 ± 7.1) and ND84.3 pg/L E2Eq (13.7 ± 21), respectively (Table S10). In Dehradun, EEQ_b and
522 EEQ_y ranged between 0.0010.003 pg/L and 0.040.21 pg/L, respectively. Mean EEQ_y and EEQ_b
523 in all the bottled water samples for DEHP and DnBP were much lower than EEQ levels
524 exhibited by water samples from Thailand, Saudi Arabia, Mexico, and Pakistan (Luo et al.,
525 2018). However, EEQ_y and EEQ_b for DEP were comparable to Thailand (6 pg/L) and Pakistan
526 (11 pg/L) (Luo et al., 2018).
527
528 **3.4.1 Metropolitan environment**
529 **Delhi:** Based on a balanced diet for a sedentary man and woman, maximum EDI for all the
530 priority PAEs in this study was observed in food basket of north Delhi (Figure 3). The
531 maximum EDI for ∑6PAEs was 412 and 433 ng/kg-bw/d for vegetarian adult males and
532 females, respectively. Maximum EDIs for $\sum_6$PAEs in non-vegetarian adult males and females
533 were 423.2 and 445.2 ng/kg-bw/d, respectively. It is noteworthy that in Delhi, non-vegetarian
534 adult has slightly higher EDI over the vegetarian adult.
535 Among the different food types, the highest EDI for $\sum_6$PAEs from the north zone was due to
536 the wheat sample (30.2 ng/kg-bw/d) with a significant contribution from priority PAEs viz.,
537 DnBP, and DEP. Interestingly, the EDI of both PAEs and BPA for wheat was significantly
538 different ($p < 0.01$) in the north than in other zones of Delhi. Among priority PAEs, DEHP
539 contributed close to 80% of $\sum_{12}$PAEs in cottage cheese from north Delhi and was significantly
540 different than other zones ($p<0.01$). It has been reported that people in this zone consume a
541 high frequency of wheat pancakes and cottage cheese (Ji et al., 2014). Hence, we can expect
542 ,more significant exposure potential of these ortho PAEs, among north Delhi residents.
543 We found DiBP concentration was dominant in onion while DMP was dominant in spinach,
544 and their maximum levels were from the east zone. About 50% of the respondents in this zone

consume tomatoes most frequently, indicating higher DEHP exposure since it was the major contributor of EDI in tomatoes. Likewise, we found the highest EDI due to BPA in potatoes (281 ng/kg-bw/d) because of the extreme BPA concentration from the west zone. More than 50% of the respondents in west zone consumed potatoes with medium and high frequency (Ji et al., 2014). Hence we suggest that elevated EDI due to BPA in potatoes may lead to relatively higher exposure to the residents in the west zone.

EDI was primarily contributed by DEP in supply water (i.e., 95%) (Figure 4). The highest EEQ_b and EEQ_y were observed in the supply water samples from the west zone among all the zones. EEQ_b (59 pg/L), and EEQ_y (29.08 pg/L) were mainly due to high DEP concentration in the supply water. The South zone exhibited the lowest EDI and estrogenic potential for drinking water, among other zones of Delhi.

3.4.2 Non metropolitan environment

Dehradun: Unlike Delhi, we found higher EDI in vegetarian adult (110 ng/kg-bw/d) than non-vegetarian adult (105 ng/kg-bw/d) in Dehradun for PAEs (Table S11). Except yellow lentils, BPA was not detected in any of the water and food samples. EDI in green gram was 2.07 ng/kg-bw/d and 12.44 ng/kg-bw/d for adult and children, respectively.

EDI in bottled water, for $\sum_{12}$PAEs was higher in composite bottled water (2.12 ng/kg-bw/d-adult; 12.7 ng/kg-bw/d-children) than supply water (0.7 ng/kg-bw/d-adult; 4.48 ng/kg-bw/d-children).

Conclusion

Commonly used plastic additives viz., twelve PAEs, and BPA were analysed in twenty-five different food and drinking water samples from the national capital territory of Delhi and the

570 peri-urban area of Dehradun in Uttarakhand, India, as a term of comparison of a metropolitan
571 city with a non-metropolitan area. Among the six priority PAEs, DnBP and DEHP were
572 dominant in food samples, whereas DEP was seen dominant in water samples. Our results show
573 that high fat-containing products such as cottage cheese and fish are sources of PAEs and BPA
574 in the metropolitan city (Delhi) compared to a non-metropolitan city (Dehradun) in India. In
575 Delhi, priority PAEs were maximum in bottled water from local brands, unlike supply water,
576 thereby exhibiting higher estrogenicity. Whereas the highest mean concentration of BPA was
577 seen in supply water. In general, EDI in Delhi was higher than in Dehradun for both PAEs and
578 BPA in food and water samples.
579 In contrast to Dehradun, non-vegetarian adults showed slightly higher EDI for the detected
580 EDCs from Delhi. This is due to elevated levels of targeted EDCs in both composite and local
581 fish samples from Delhi, although cottage cheese showed the maximum level of EDCs in both
582 the cities. Unlike food, water samples analysed in this study were generally higher in terms of
583 these EDCs than in other parts of the world, indicating a marginal improvement in the quality
584 of drinking water supplied in India. However, the EDI for foodstuffs and drinking water for
585 adults residing in the two Indian cities did not exceed the EFSA and USEPA recommended
586 limits.
587 Environmental contamination at the source of cultivation, production processes, and packaging
588 materials were eminent sources for PAEs in food samples. In particular, food packaging was
589 identified as a source of DnBP. This study showcases the need for implementing a wide range
590 of measures to eliminate or atleast reduce input of these EDCs from such sources. This includes
591 avoiding recycled material contaminated with PAEs and BPA, enhancing raw material
592 transparency in the plastic supply chain, and modernizing wastewater treatment systems.
593 Hence, packaging materials like recycled plastic water bottles and high-temperature storage
594 conditions should be avoided for packaged food items, especially those with higher shelf-lives,

as it can facilitate the leaching of plasticizers. However, further research is required to explore the leaching capacity of polymeric materials in Indian food to implement control measures effectively. It is of fundamental importance to identify advanced processing technologies and select packaging material to minimize chemical migration and contamination of food and water.

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