Food Thermal Labels are a Source of Dietary Exposure to Bisphenol S and Other Color Developers

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ABSTRACT

To test the hypothesis that migration from the thermal labels on plastic film packaging is a major source of exposure to bisphenols and alternative color developers in food, we analyzed 140 packaging materials from packaged fresh food purchased in North America. No bisphenol A (BPA) was detected in either the packaging samples or thermal labels. However, significant amounts of bisphenol S (BPS) and alternative color developers (up to 214 μg/cm^2) were present in thermal labels; their relative occurrence varied among stores. In a controlled experiment, we wrapped fish in film with a thermal label for five days at 4°C. The fish in contact with the label contained BPS (≤ 1140 ng/g wet weight [ww]), 4-hydroxyphenyl 4-isoprooxyphenylsulfone (D-8) (≤ 230 ng/g ww), bis(2-chloroethyl)ether-4,400-dihydroxydiphenyl sulfone monomer (D-90) (≤ 3.41 ng/g ww), and Pergafast-201 (≤ 1.87 ng/g ww). This study provides evidence, for the first time, that BPS and alternative thermal label color developers migrate from packaging materials into food. Further, BPS migration significantly exceeded the European Union Specific Migration Limit (50 ng/g ww), suggesting that further risk assessment studies are warranted.

Keywords: Bisphenol analogues; Endocrine disrupting chemicals; Food contact material; Thermal labels; Food packaging.

Synopsis: This study demonstrates that migration from thermal labels on plastic film packaging is a major source of exposure to bisphenols and alternative color developers in food.

1. INTRODUCTION

Bisphenols are commonly used in the production of polycarbonate plastics, as epoxy resins in the lining of food and beverage cans and as color developers in thermal papers [1]. Exposure to bisphenol A (BPA), an endocrine disrupting chemical, has been associated with adverse effects on the reproductive, immune and nervous systems [2]. The Canadian Government prohibited the import and sale of BPA-containing polycarbonate baby bottles in 2010 based on potential health concerns related to exposure during neurodevelopment [3].

In addition to its functions as a monomer, BPA acts as a proton donor in thermal reactions and was used for decades as a color developer in thermal papers [4]. The European Union (EU) prohibited the use of BPA in thermal paper at concentrations ≥0.02% by weight as of January 2020 [5]. In 2015, the US Environmental Protection Agency (EPA) established a list of 19 BPA alternatives for use as color developers in thermal paper [6]; these included bisphenol S (BPS), 4-hydroxyphenyl 4-isoprooxyphenylsulfone (D-8), bis(2-chloroethyl)ether-4,400-dihydroxydiphenyl sulfone copolymer (D-90), bis-(3-allyl-4-hydroxyphenyl) sulfone (TGSA) and [3-[(4-methylphenyl)sulfonylcarbamoylamino]phenyl] 4-methylbenzenesulfonate (Pergafast 201 or PF-201).

BPS was the most frequently reported substitute for BPA in thermal papers in the past decade [7-9]. However, there is evidence that BPS may have adverse health effects that are similar to BPA [10]. Additional studies to determine the potential health implications of exposure to other BPA alternatives, especially those with structural similarities, should be a priority. To date, the role of food labels as a possible source of dietary exposure to those compounds has not been assessed although some studies have evaluated the effects of dermal exposure to bisphenol analogues in thermal paper in an occupational setting [9, 11, 12]. The specific migration limit (SML) for BPS is

presently 0.05 µg/g ww in food [13], the same as BPA [14]. In its recent updated assessment of BPS, the European Food Safety Agency (EFSA) recommended the collection of data on the use of BPS in plastic food contact materials (FCMs) and on its occurrence and migration into food [15].

In a recent Canadian Total Diet Study, BPS was detected in all 84 of the individual raw meat and meat products assessed [16, 17]. Based on significant variations in BPS levels in individual samples within the same food category collected from different stores, Cao et al. [17] concluded that packaging was unlikely to be the source for BPS in meat. However, in a previous study from our research group [18], BPS was detected in packaged fresh food (notably fish) purchased in Canada more frequently than in their non-packaged equivalents.

Here, we have tested the hypothesis that chemical migration from the thermal labels pasted on the cling wrapper films used for packaging fresh food are a major dietary source of BPS and other color developers. The specific objectives were to: (i) assess the occurrence of bisphenols and alternatives used as color developers in thermal labels and other food packaging materials from an assortment of packaged fresh food in Montreal, Canada; and (ii) conduct a specific controlled laboratory study on fish bought from stores in Canada and the USA, in order to compare the migration of these color developers into fish samples wrapped with cling films with or without thermal labels. We combined several approaches to assess chemical migration (direction extraction, food extraction, migration cells) and used liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QToF-MS) analyses to detect the bisphenols and their alternatives.

2. MATERIALS AND METHODS

2.1. Chemicals and reagents

Ammonium acetate (LC/MS grade), HPLC-grade solvents (water, methanol, acetonitrile,

and ethanol) were obtained from Fisher Scientific (Hampton, USA). Ultra-pure water was obtained from a Milli-Q® Reference Water Purification System (Millipore, Bedform, MA, USA). Analytical standards of BPA (purity ≥ 99%, CAS number: 80-05-7) and BPS (purity ≥ 98%, CAS number: 80-09-1) were purchased from Sigma-Aldrich (St. Louis, USA). D-8 (purity ≥ 95%, CAS number: 95235-30-6), TGSA (purity ≥ 98%, CAS number: 41481-66-7), D-90 (CAS number: 191680-83-8), Pergafast-201 (purity ≥ 98%, CAS number: 232938-43-1), 2,4-BPS (CAS number: 5397-34-2), BPS-MAE (CAS number: 97042-18-7), BPS-MPE (CAS number: 63134-33-8) and four internal standards of BPA-$^{13}C_{12}$ (purity ≥98%), BPF-$^{13}C_{12}$ (purity ≥98%), BPS-$^{13}C_{12}$ (purity ≥98%) and BPAF-d4 (purity ≥98%) were obtained from Toronto Research Chemicals (Toronto, Canada). The D-90 copolymer standard is sold as a mixture of the n=1 to 6 monomer units, but the D-90 monomer (n=1) represents >99% of the total signal, and only traces (~1% of the signal) can be recorded for n=2. Other D-90 copolymers (n=3,4,5 and 6) were not detected in the commercial D-90 standard.

2.2. Sample collection and sample preparation

Part I - Occurrence Study: A total of 140 samples of food packaging materials, including labels, plastic films, pads and styrofoam trays, were collected from six local supermarkets in Montreal, QC, Canada and the United States from 2021 to 2022 (**Fig 1**). All packaging samples were wrapped in aluminum foil right after collection to avoid contamination and stored in a -20 °C freezer until analysis. Information on each sample (sample type, food type, location of purchase, supplier, year of collection and plastic film type (identified by ATR-FTIR) is provided in **Table S1**. Direct extractions were carried out to investigate the occurrence of bisphenols and alternatives (**Fig S2-I**); portions of labels (thermal price tags and other stickers) with underlying film, plain

films, pads and styrofoam trays were extracted with 95% ethanol (HPLC grade) in 250-mL amber glass jars and kept at 20 °C (± 1.2°C) for 10 days. Results were expressed as µg of the target analyte per cm^2 of the packaging material (**Table 1**).

Part IIA - Fish Migration Study: A batch of 24 packaged fish fillets were collected from local markets in Montreal (QC, Canada), Victoria (BC, Canada), Raleigh (NC, USA) and Hudson (MA, USA) in 2021-2022 (**Fig S1B, Table S2)**. All packaged fish samples were wrapped in aluminum foil and stored in a freezer (-20°C) or cooler (with ice packs) and shipped within 2 days. Fish were thawed and a portion of each fish fillet (around 30 g) was collected in glass vials to serve as the control (subsequently labelled as '*initial fish'*) sample. The remaining fish samples were wrapped in their original plastic film with its thermal price tag label and stored in the fridge (4°C) for 5 days as the experimental group (**Fig S2-IIA**). After 5 days, the fillets were cut into two parts: portions that were in direct contact with the thermal label were collected in glass containers as the '*label-contact'* fish while portions in contact with only the plastic film were collected as the '*film-contact'* fish. All fish samples were freeze-dried for 3-4 days and ground into powder for further sample extraction; the wet and dry weights of each fish sample were recorded. Extraction was carried out using the method developed by Tian et al.[18] with minor modifications. Briefly, around 0.5 g (± 0.05 g) of each freeze-dried fish sample was extracted with 6 mL of methanol in a 15 mL polypropylene centrifuge tube; samples were spiked with 60 µL of an internal standard mixture (BPA-$^{13}C_{12}$, BPF-$^{13}C_{12}$, BPS-$^{13}C_{12}$ and BPAF-d4; 4 mg L^{-1}). Tubes were vortexed for 1 min using a Vortex Mixer (Fisher Scientific, Hampton, NH), sonicated for 30 min using a Branson 3510 ultrasonic bath (40 kHz), and finally centrifuged at 4500 rpm for 10 min at room temperature. The supernatant was collected and filtered through a 0.22-µm filter (Norm-Ject, Tuttlingen, Germany) into HPLC amber glass vials and stored at -20 °C until analysis. Results were expressed as ng of

the target analyte per g wet weight (ww) of the fish samples (**Fig 3, Table S7**).

Part IIB - Label Migration Study: The migration test was based on the "Commission Regulation (EU) No 10/2011 of 14 January 2011[13] on plastic materials and articles intended to come into contact with food" (**Fig S2-IIB**). Migration studies were conducted on *'fish-wrapped'* film samples to study the migration of bisphenols and alternatives from plain film vs. film with overlying thermal labels. Briefly, *'non-label' and 'label'* film samples were extracted with 50 mL of solvent (95% ethanol, HPLC grade) using a migration cell (MigraCellR (MC-60), FABES Forschungs-GmbH, Munich, Germany) kept at 20°C (± 1.2°C) for 10 days. The contact area of the migration cell was 0.5 dm^2, and each label takes up > 60% of the area. The extracts were collected and stored in amber glass vials at -20°C until analysis. Results were expressed as ng of the target analyte per cm^2 (**Fig S13, Table S7)**.

Fig 1. Examples of packaged fresh food samples with thermal labels (A: sausage; B: vegetables; C: cheese; D: chicken breast; E: tilapia fish; F: salmon fish; G: tuna fish; H: cod fish).

2.3. ATR-FTIR analysis

The polymer type of different plastic film samples was identified using the Cary 630 ATR-FTIR spectrometer (Agilent Technologies, Santa Clara, USA) with three Agilent polymer libraries (Agilent Elastomer Oring and Seal Handheld ATR library, Agilent Polymer Handheld ATR library,

and ATR Demo library) containing 1009 compounds. The available spectral range is set between 650 – 4000 cm^{-1}. 64 scans were acquired for each sample at a resolution of 8 cm^{-1}. FTIR measurements were conducted on each plastic sample in triplicates to obtain the average match quality score (**Figs S3-6**). The "match quality" was used to qualify the strength of the identification (ranging from 0 to 1) of the sample compared to the reference spectra from Agilent Technologies polymer libraries (Agilent Elastomer Oring and Seal Handheld ATR library, Agilent Polymer Handheld ATR library, and ATR Demo library). The identification results were also summarized in **Table S1**.

2.*4. LC-QTOF-MS analysis*

Extracts were analyzed using an Agilent 1290 Infinity II HPLC system (Agilent Technologies, Santa Clara, USA) coupled with a 6545 Quadrupole TOF mass analyzer (Agilent Technologies, Santa Clara, USA). Liquid chromatographic separation was conducted on a Poroshell 120 EC-C18 column (Agilent Technologies, 2.7 µm × 3.0 mm × 100 mm) equipped with a Poroshell 120 EC-C18 guard column (Agilent Technologies, 2.7 µm × 3.0 mm × 5 mm). The mobile phases consist A: water (with 5 mM ammonium acetate) and B: methanol (with 5 mM ammonium acetate). The injection volume was set to 4 µL and the column temperature was maintained at 30°C. The inlet gas flow rate and temperature were 10 L min^{-1} and 175°C, respectively. Samples were analyzed in both positive (ESI+) and negative (ESI-) electrospray ionization modes. HRMS data were acquired in the 50-750 *m/z* range.

LC-MS data were analyzed using Agilent MassHunter Quantitative Analysis (B07.01) software to confirm the presence of analytes in food and packaging samples and procedural blanks. The following *m/z* were extracted from the total ion chromatogram (± 10 ppm) for quantification:

227.1072 (BPA), 249.0222 (BPS), 291.0690 (D-8), 329.0848 (TGSA), 569.0940 (D-90), and 459.0684 (PF-201). The following qualifier ions (*m/z*) were used to confirm the identity of the compound detected in pure calibration solvents and sample matrices: 211.0754 and 133.0648 (BPA), 108.0206 and 155.9876 (BPS), 248.0138 and 184.0519 (D-8), 132.0570 and 148.0519 (TGSA), and 411.0897 and 249.0216 (D-90), 170.0270 and 262.0532 (PF-201) (**Figs S7-S12**). All packaging extracts were quantified using matrix-matched calibration curves at concentration of 1-200 μg mL^{-1}. Mass measurement errors were all below 3 ppm for standards both in pure solvent and different sample matrices. The relative intensity of qualifier ions (% of base peak) of the analytes in pure solvent and in different sample matrices were statistically compared (**Tables S3 and S4**). Following the recommendation in the Document No. SANCO/12495/2011[19] for pesticides, the maximum tolerance should be ±30% if the relative intensity (% of base peak) is in the range of 10% to 20%; and should be ±50% if the relative intensity (% of base peak) is <10%.

2.5. Method validation and quality assurance

Method limit of detection (MDLs) and method limit of quantification (MQLs) were assessed as 3σ and 10σ of the signal using 10 procedural blanks, respectively [20]. Matrix-matched calibration was conducted by spiking standard solution of analytical standards at concentrations in the 1-200 ng mL^{-1} range to plastic sample matrices. The linearity of calibration was determined as the correlation coefficient (r^2) of the calibration curve and the working range was from LOQ to 200 ng mL^{-1}. The results of the instrumental validation of the LC-MS analysis were shown in **Supplemental Tables S3-S5**. Good instrumental linearity ($r^2 > 0.96$) was achieved in the range of 1-200 ng/g for all standards. Matrix effects (ME%) was calculated by the equation (1):

$$ME\% = \frac{bm}{bs} * 100$$

where b_m is the slope of the matrix-matched calibration curve, and b_s is the slope of solvent calibration curve.

There was some signal enhancement recorded for analytes in the packaging sample matrices. Matrix effects were balanced by adding internal standards when performing fish sample analysis. The general matrix effects of analytes in pure solvent (methanol) and sample extracts were acceptable (<20%) according to SANCO/12495/2011 guideline[19].

Quality control (QC) samples were tested at regular interval (n=20). The intra-day (n=5) and inter-day (n=3) repeatability of the method were evaluated by analyzing five QCs over the working range (**Table S6**). The intra-day (n=5) and inter-day (n=3) repeatability of the experiment were evaluated by analyzing five replicates of fish samples that contains certain incurred levels of analytes over the working range of the method. Recovery test was conducted by spiking sample extracts with analytes (n=3) at concentrations of 20, 100, and 200 μg L^{-1}, respectively. The mean recovery of all analytes are within the range of 70-120 %, with an associated repeatability RSD ≤ 20% [21].

2.6. Statistical analysis

The paired sample Wilcoxon test [22] was used to examine significant differences between the 'label' and 'non-label' groups of data. Statistical analysis was performed using IBM SPSS Statistics (version 27, IBM Corporation, New York, USA).

3. RESULTS AND DISCUSSION

3.1 Occurrence of BPS and other color developers in food contact materials

Our first objective was to assess the occurrence of bisphenols and their alternatives in

materials (n=140) used in North America in the packaging of a variety of fresh foods, as depicted in **Fig 1**. Interestingly, BPA was not detected in any of the packaging materials tested **(Table 1**). In contrast, BPS was found in most thermal price labels (29/40), a few non-price labels (6/29) and some plain films (11/39) while D-8, D-90, TGSA and PF-201 were above the level of detection in 10-30% of the thermal price labels. BPS had a relatively high average content in the labels (66 μg/cm^2) with a maximum value of 193 μg/cm^2; D-8, TGSA and PF-201 were also detected at high levels in some samples. In addition, relatively high concentrations of BPS (up to 17.3 μg/cm^2) were also found in 'other label stickers' (not price-related), whose color disappeared during the solvent extraction, an observation also made for all of the thermal labels, suggesting that they may have been thermally printed. In contrast, several stickers did not lose color during extraction and almost no BPS was detected. Traces of BPS and alternative color developers were also detected on some occasions in pads and trays (less than 15%).

The present data are comparable to those reported for paper products from the Chinese market by Yang et al. [9], with BPS detected in up to 93% of the thermal (weight/price tag) labels, while D-8, D-90 and TGSA were detected in 6.7 - 27%. The present results suggest that the tray and absorbent pad materials, although in direct contact with food, are not a main source of BPS in food. However, thermal price tag labels and some types of stickers (possibly thermally printed) containing large amounts of different color developers were found on the cling films from a wide range of food products, including fish, meat, dairy, fruits, vegetables and bakery products.

Table 1. Occurrence of BPS and other color developers in food packaging materials.

	BPS	**D-8**	**D-90**	**TGSA**	**PF-201**	**$\sum_{all}$**
Group 1. Thermal price tags (n=40)						
Conc. (μg/cm^2)	66.0 ± 50.8	124 ± 34.0	6.04 ± 8.12	61.1 ± 84.7	37.9 ± 41.8	
Range	ND – 193	ND - 175	ND – 22.6	ND – 214	ND – 133	ND - 214
Occurrence (%)	29/40	4/40	8/40	7/40	11/40	40/40
Group 2. Stickers (n=29)						
Conc. (μg/cm^2)	2.96 ± 7.02	ND	0.002	0.004	ND	
Range	ND – 17.3	ND	ND – 0.002	ND – 0.004	ND	ND - 17.3
Occurrence (%)	6/29	ND	1/29	1/29	ND	7/29
Group 3. Plain film (n=39)						
Conc. (μg/cm^2)	0.31 ± 0.30	0.052	0.039 ± 0.044	0.049	0.22	
Range	ND – 0.96	ND – 0.052	ND – 0.089	ND – 0.049	ND – 0.22	ND – 0.96
Occurrence (%)	11/39	1/39	4/39	1/39	1/39	15/39
Group 4. Pad (n=14)						
Conc. (μg/cm^2)	0.14 ± 0.12	0.008	0.012 ± 0.012	0.22	ND	
Range	ND – 0.23	ND – 0.008	ND – 0.02	ND – 0.22	ND	ND – 0.22
Occurrence (%)	2/14	1/14	2/14	1/14	ND	5/14
Group 5. Tray (n=18)						
Conc. (μg/cm^2)	0.15	ND	0.11	ND	ND	
Range	ND – 0.15	ND	ND – 0.11	ND	ND	ND – 0.15
Occurrence (%)	1/18	ND	1/18	ND	ND	2/18

Note: Concentrations are the means ± SD for samples where the analyte was detected. BPA (MDL = 1.87 ng/cm^2), 2,4-BPS (MDL = 0.01 ng/cm^2), BPS-MAE (MDL = 0.11 ng/cm^2) and BPS-MPE (MDL = 0.2 ng/cm^2) were not detected (ND) in packaging materials.

3.2 Occurrence of individual bisphenols in thermal price tag labels

The Venn diagrams in **Fig 2** compare the occurrence of BPS, D-8, D-90, TGSA and PF-201 in the thermal price tag labels (n=40) from six different shops (different franchises) in Montreal. The overall profiles of the five color developers in food thermal labels varied significantly among the shops, although BPS was detected in samples from all six stores. D-90 was detected in labels from four shops (A, D, E and F), PF-201 (A and E) and TGSA (C and E) in labels from two shops and D-8 only one shop (F). These findings may explain some of the variability among products and sources observed in the Canadian Total Diet Study [17].

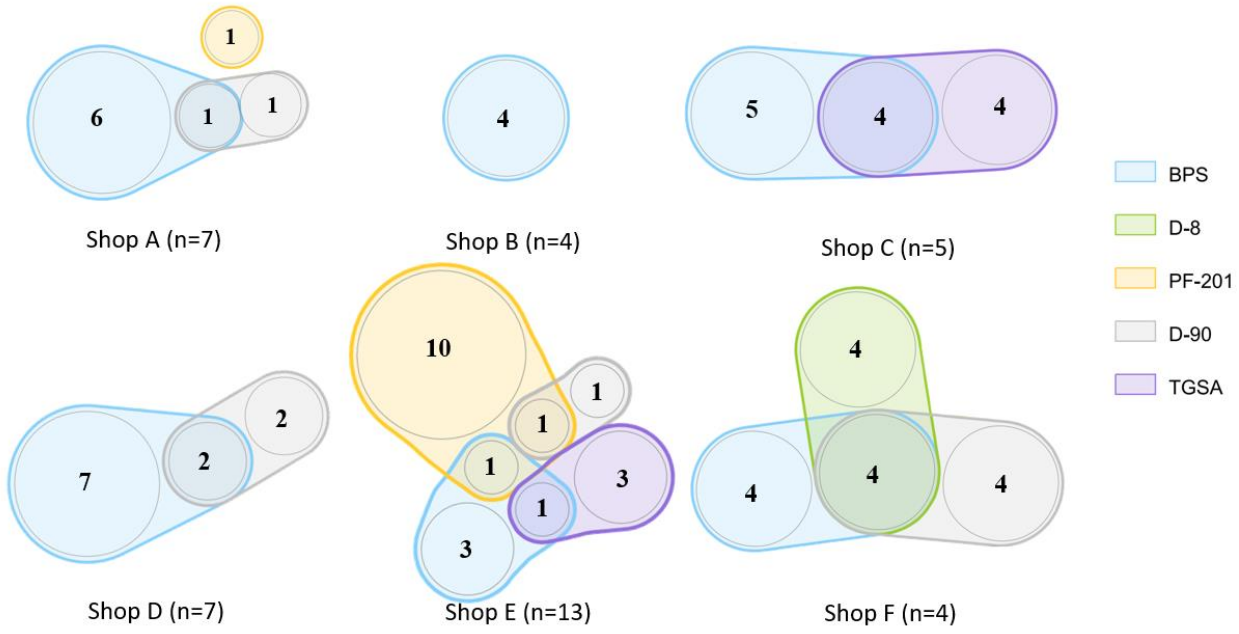

Figure 2. Venn-diagram of occurrence of bisphenols and alternative color developers in thermal price tag labels (n=40) from six shops in Montreal.

3.3 Migration of BPS and other color developers in fish

To test the hypothesis of thermal labels being a source of exposure to BPS and other color developers, our second objective was to conduct a specific controlled laboratory study on samples of store packaged fish (n=24) from Canada and the USA (**Table S2**; **Fig. S2-IIA**) and compare the migration of these color developers into fish samples wrapped with cling films, with or without thermal labels. After removal of a portion of each fish ('*initial*' fish, not in contact with the label) as a reference, each fish fillet was wrapped directly in its cling wrap film, with a portion in contact with the film and the thermal price tag label ('*label-contact'*), and another portion in contact only with the film (*'film-contact'*). These wrapped fish samples were stored at 4°C for 5 days to mimic storage conditions used in stores and by consumers. All fish samples were then extracted and analyzed (**Table S7**). BPS and other color developers were either not detected or present at trace levels (<1.3 ng/g, ww) in the 'initial' fish portions. In contrast, a number of these chemicals were detected frequently in the 'label-contact' fish portions and, to a lesser extent, in 'film-contact' fish. Significantly higher levels of BPS (p<0.001), D-8 (p<0.05) and D-90 (p<0.05) were found in the *'label-contact'* compared to *'film-contact'* fish (**Table S8**). Relatively high amounts of BPS were recorded in *label-contact* sole (Fish 1: 1140 ng/g ww) and salmon (Fish 2: 1090 ng/g ww) from the USA, and in basa (Fish 12: 437 ng/g ww) from Canada (**Fig 3, Table S7**). D-8 was detected mainly in fish from shop I in the USA, with concentrations up to 230 ng/g ww in *label-contact* Tilapia (Fish 7). D-90 was detected in several fish (e.g. up to 3.41 ng/g ww in a salmon sample [Fish 2] from the USA). PF-201 was recorded in fish samples from one shop in Canada, with concentrations up to 1.87 and 1.32 ng/g ww in *label-contact* and *film-contact* salmon, respectively (Fish 22). To the best of our knowledge, this is the first report on the migration of D-8, D-90 and PF-201 into food.

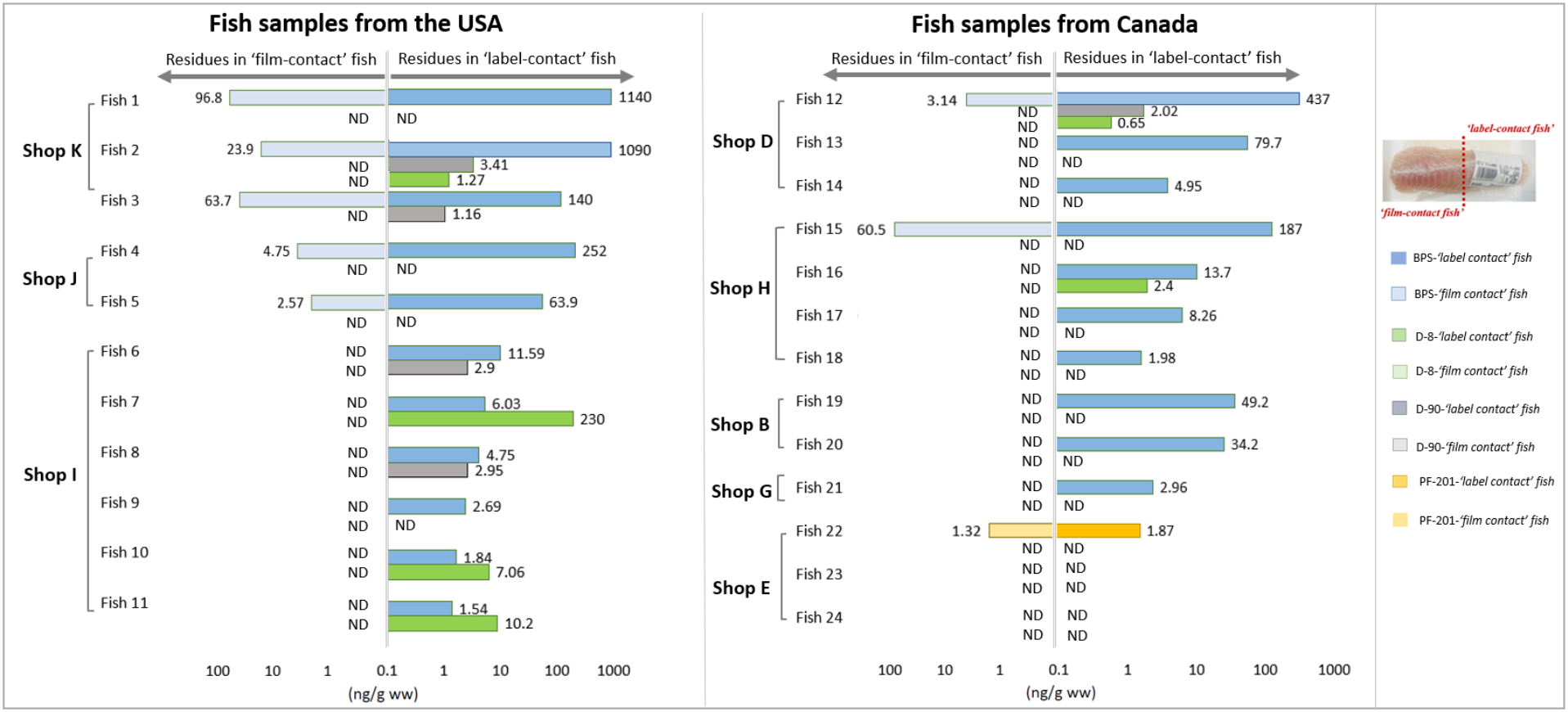

Figure 3. Contents of BPS, D-8, D-90 and PF-201 (ng/g ww) in *'film-contact'* and *'label-contact'* fish samples from the USA and Canada. BPA and TGSA were not detected. Analyte concentrations below MDL were marked as non-detectable (ND).

3.4 Residual bisphenols in packaging films by migration cell

After five days, the film material was rinsed with milli-Q water and tested using specific migration cells and the EU food-related protocols (95% ethanol, 20˚C, 10 days) to estimate the residual migration from both plain film and from film with a thermal label (**Fig S2-IIB**). **Fig 4** shows the residual concentrations (ng/cm^2) of BPS, D-8, D-90 and PF-201 migrating from the two types of fish packaging films. These experiments confirmed that the color developers migrate across the cling film; significantly higher BPS (p<0.001), D-8 (p<0.05), and D-90 (p<0.1) were observed systematically from the films with thermal labels compared to plain films (Table S8). Relatively high residual BPS migration (up to 33.8 µg/cm^2) was observed for the films with thermal labels for shop K collected in the USA, these data are consistent with those in **Fig 3**. D-8 was also confirmed to be migrating from food labels of the tilapia (fish 7) from shop I, with residual concentrations of up to 61.8 µg/cm^2.

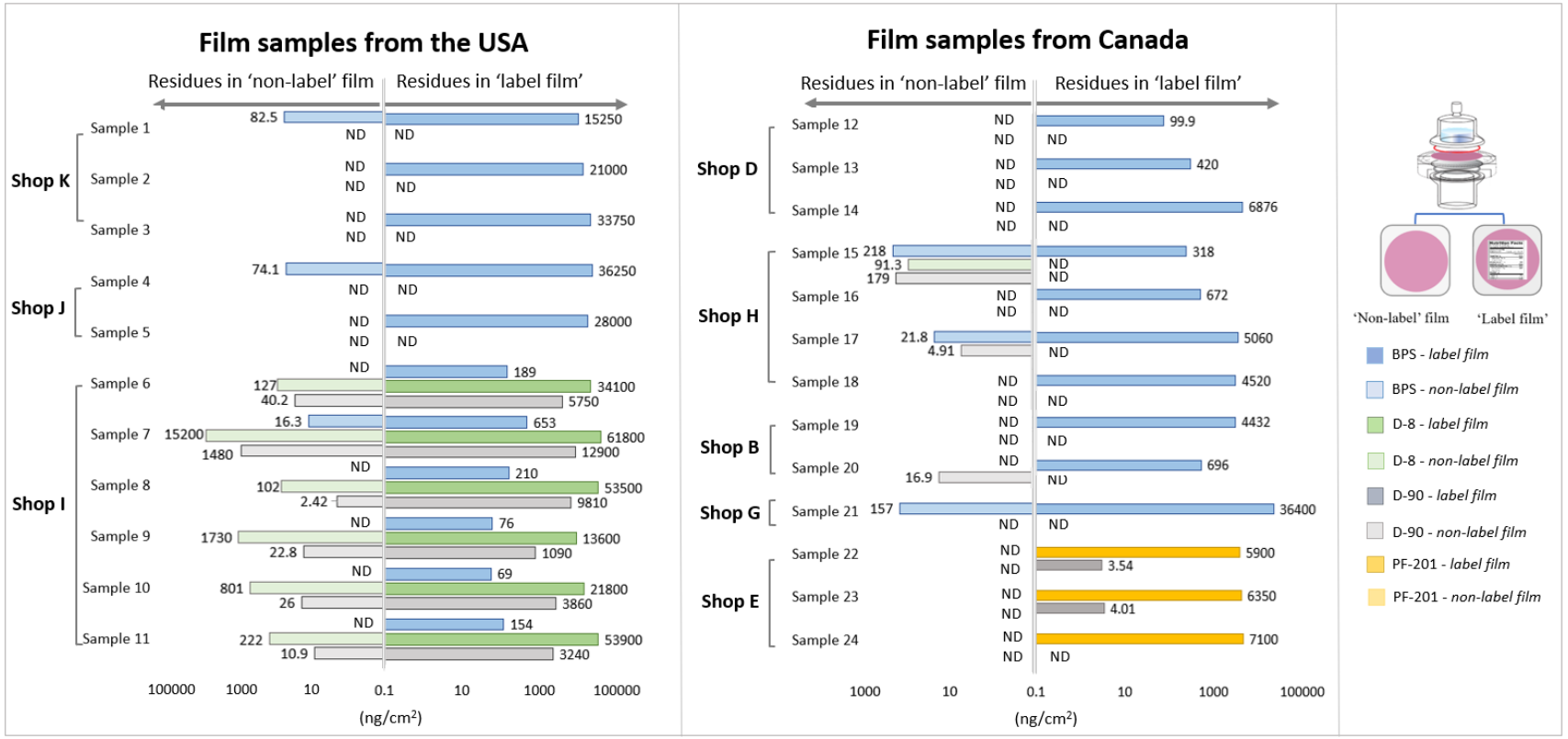

Figure 4. Content of BPS, D-8, D-90 and PF-201 (ng/cm^2) migrating from '*non-label*' and *'label'* films into food simulant. BPA and TGSA were not detected in any film samples. Analyte concentrations below MDL were marked as non-detectable (ND).

3.5 Migration pathway of thermal label color developers in films

A hypothetical migration pathway for thermal label color developers in packaged fish is presented in **Fig 5**. In this model, BPS, D-8, D-90 and PF-201 diffuse from the thermal layer of the paper across the adhesive layer and the cling film to reach the fish matrix. Various parameters, including the size of the fish fillets, their composition (fat and water contents), thickness/composition of the cling films, storage conditions, structure of the thermal paper and intrinsic physicochemical properties of the color developers are anticipated to influence their migration into fish. In the present study, two simple parameters (the thickness of the film or water content of the fish) did not correlate with the levels of BPS in fish (**Table S9**), suggesting the need for more specific and standardized experiments to identify the factors that affect the migration mechanism.

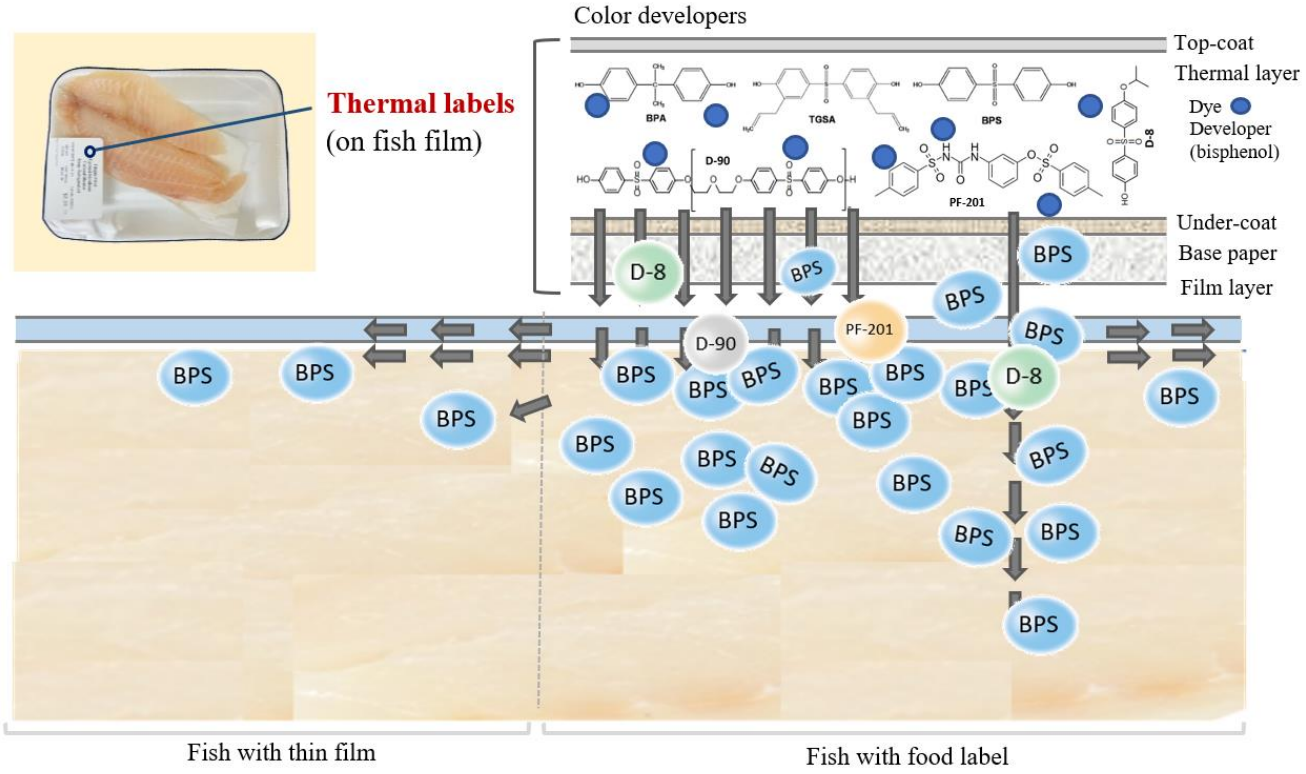

Fig 5. Hypothetical migration pathway of thermal label color developers into fish

4. RESEARCH IMPLICATIONS

After 5 days, the BPS levels (mean: 147 ± 316; range: ND-1140 ng/g ww) recorded in fish wrapped with cling film with a thermal label frequently exceeded the specific migration limit (SML) of 50 ng/g ww proposed by the European Union [13]. To the best of our knowledge, there are as yet no SMLs for D-8, D-90 or PF-201, although US EPA[6] classified D-8 and PF-201 with a 'Moderate Hazard' for repeated doses for humans. In 2015, fish consumption in Canada (both sexes, all ages) averaged 0.22 g/day/kg bw, with a 95th percentile (P95) of 1.59 g/day/kg bw [23]. Based on this information, consumption of contaminated fish (based on a maximum concentration of 1140 ng/g in fish) would represent a BPS exposure of 0.25 (mean) or 1.81 µg/d/kg bw (high consumers; P95), respectively. These levels from fish consumption alone are orders of magnitude higher than the dermal exposure dose reported in the literature. Yang et al.[9] estimated the average dermal exposure to the sum of BPA and alternatives is 0.025 µg/d/kg bw for a 70 kg person, with BPS representing about 10-20% [9]. Similarly, Russo et al.[24] reported an average BPS intake of 0.0244 µg/day through dermal handling of thermal papers for the general population in Italy (15.6 µg/day for the worst case occupational exposure).

High BPS concentrations have been reported for other food commodities: e.g. up to 257.61 ng/g in roast beef [17] and up to 291.4 ng/g in chicken meat [18]. Thermal labels have been observed in supermarkets on marinated food (i.e. oil/marinade in direct contact with wrapped films), but occurrence data on BPS and other color developers for these products are currently unavailable. Considering the elevated number of packaged food commodities sold with thermal labels, the actual dietary intake of BPS and other color developers is likely to be high. In addition, BPS, TGSA, D-90 and D-8 were detected in recent breast milk

samples in China, indicating accumulation of such compounds in human tissues [25]. These reports suggest a more thorough risk assessment of BPS and alternative color developers and their ability to migrate into food from thermal labels is needed, to help develop regulatory guidelines in the food sector.

In conclusion, no BPA was found in the packaging samples or in the thermal labels. However, significant amounts of BPS and alternative color developers (up to 214 μg/cm^2) were present in the labels. Interestingly, their relative occurrence varied from store to store, suggesting that the use of specific color developers in the manufacture of thermal labels is quite variable. Our findings reinforce the need to include non-targeted analysis in food surveillance to help identify unknown or unexpected contaminants, like new color developers. Investigation of the mechanisms by which the color developers are migrating is also needed in order to identify strategies to reduce exposure.

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