Scientific Research Publishing

Journal of Environmental Protection, 2023, 14, 711-724
https://www.scirp.org/journal/jep
ISSN Online: 2152-2219
ISSN Print: 2152-2197

Bisphenol A (BPA) Contamination in Whole Milk Marketed in Different Packages

Patrícia dos Santos Souza[1*], Thomas Manfred Krauss[2], André Victor Sartori[2], Shirley de Mello Pereira Abrantes[2]

[1]Graduate Program in Sanitary Surveillance (PPGVS), National Institute for Quality Control in Health (INCQS), Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil
[2]Chemistry Department, National Institute for Quality Control in Health (INCQS), Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil
Email: *souzas.patricias@gmail.com

How to cite this paper: dos Santos Souza, P., Krauss, T.M., Sartori, A.V. and de Mello Pereira Abrantes, S. (2023) Bisphenol A (BPA) Contamination in Whole Milk Marketed in Different Packages. *Journal of Environmental Protection*, **14**, 711-724.
https://doi.org/10.4236/jep.2023.149040

Received: August 7, 2023
Accepted: September 9, 2023
Published: September 12, 2023

Abstract

Bisphenol A (BPA), an important endocrine disruptor, is used in the manufacturing of various materials, including food packaging. Ingestion of contaminated foodstuffs is, in fact, the most relevant form of exposure to this substance. However, scarce data on the presence of this contaminant in milk, or whether different types of food packaging influence food contamination are available in Brazil. This study, therefore, aimed to evaluate the BPA contamination of whole milk (fluid and powder) samples packaged in different types of packaging (Tetra Pak®; PET: Poly (ethylene terephthalate; Metallic can (epoxy resin); Polyethylene (PE) and poly (vinylidene chloride) (PVDC); Laminated Film - Metallized Polyester-Polyethylene and glass) and marketed metropolitan region of Rio de Janeiro, Brazil. An analytical method for the BPA determination in milk was optimized for both fluid (pasteurized and ultra-high temperature) and powdered milk samples. A modified QuEChERS method was applied, and BPA determinations were conducted by ultra-performance liquid chromatography coupled with sequential mass spectrometry (HPLC-MS/MS). The validated method was then applied to 51 milk samples, where BPA was detected in five samples (9.8%) and quantified in two (3.8%).

Keywords

Bisphenol A. Packaging, Migration, Milk, Endocrine Disruptors

1. Introduction

According to the United States Environmental Protection Agency (U.S.EPA),

some chemical substances, known as endocrine disruptors, can alter the regulatory mechanisms of natural hormones in the human body [1]. Several effects are associated to exposure to these substances in animals, such as abnormal sexual development in reptiles and mammals, feminized responses in fish and birds, pseudohermaphroditism in marine gastropods, reproductive failures in mammals, fecundity decreases in fish and embryonic deformations in birds [2] [3] [4]. Recently, the increased prevalences of disorders in humans, such as obesity, neurobehavioral deficit, diabetes, hypothyroidism, endometriosis, autism, breast, prostate, testicular, thyroid and endometrial cancers, as well as precocious puberty, have also been associated with exposure to endocrine disruptors [5] [6] [7].

Endocrine disruptors include a class of diphenylalkane substances, with 2,2-bis(4-hydroxyphenyl)propane (CAS n˚80-05-7), commonly known as bisphenol A (BPA), as the most representative analogue of the bisphenol group. This compound constitutes the basic unit of high-performance polymers and coating, mainly plastics, polycarbonates, and epoxy resin [8].

Due to its known reproductive toxicity and potential for endocrine disruption, the use of BPA in baby bottles and toys is prohibited in the United States, Canada, and the European Union [9]. In Brazil, its use in baby bottles and similar items intended for infant feeding has also been banned since 2011 [10]. However, despite the ongoing debate concerning more effective measures to protect particularly vulnerable populations from BPA exposure and studies on the subject, BPA production and consumption continue to increase, with a global production projection for 2028 of about 30 billion dollars [11].

Several studies have reported the transfer of this compound to foods from packages produced with BPA monomers as a constituent [12] [13]. Several countries have established specific migration limits (SML) aiming at consumer safety. The European Union, for example, has established a SML of 0.1 mg·L^{-1} BPA for chemicals used in toys intended for use by children under the age of 36 months old or in other toys intended to be placed in the mouth [14] and 0.05 mg of BPA per kilogram of food (mg/kg) for plastic materials and articles to ensure that exposure to BPA remains below the daily dose [15]. Brazil maintains the European Union SML recommendation for the preparation of plastic packaging and equipment in contact with food [10]. However, despite all efforts, BPA has been detected in several foodstuffs, including milk and its derivatives, even when the chemical nature of its packaging does not allow for its release, such as milk packaged in polyethylene bags [16] [17] [18].

The quality of milk production is directly associated to the environment and depends significantly on human activities. Soil exposure to contaminated inputs, such as sewage or industrial waste, as well as atmospheric deposition from industrial activities close to producing farms, results in a wide range of environmental contaminants entering the milk production chain [19]. Many of them, including BPA, are fat soluble, and can be stored in adipose tissue, secreted with

milk fat, and accumulated in dairy products along the dairy chain. Furthermore, BPA can also be introduced into the milk chain during milking, due to exposure to plastic parts derived from plastic resins present in milking machines and has been detected in several dairy products due to the use of PVC pipes used during the milking process or transferred from bulk milk to storage tanks [20]. At the end of milk production process, contaminants already present in the milk are usually not affected by further dairy processing and, in some cases, residues may become concentrated in the final product, increasing contaminant levels. Finally, BPA can also migrate to milk or dairy products when employed as an additive in packaging material [21] [22]. Due to the above, the aim of this study was to determine BPA levels in 51 whole milk samples (fluid and powder) sold in different packages marketed in southeastern Brazil.

2. Methodology

2.1. Materials and Reagents

A bisphenol A standard (purity 99%) was purchased from Sigma-Aldrich (Pennsylvania, USA). Acetonitrile (HPLC grade), sodium chloride (99% purity), anhydrous magnesium sulfate (98% purity) and 25% ammonium hydroxide (for analysis) were purchased from Merck (Darmstadt, Germany). Methanol (HPLC grade) was purchased from Tedia (Darmstadt, Germany). Hexane (purity 96%) was obtained from J.T. Baker (Pennsylvania, USA). Ultrapure water was obtained from a Milli-Q Gradient water system (Millipore, Bedford, MA, USA).

2.2. Standard Solution Preparation

A BPA stock solution (1000 μg·mL^{-1}) was prepared by dissolving 10 ± 0.1 mg of the BPA standard in methanol (MeOH) and making the volume up to 10 mL in a volumetric flask. This solution was stored in a glass vial with a screw cap at −18˚C in the dark. Working solutions were prepared weekly by serially diluting the stock solution with MeOH to 5 ng·mL^{-1}. These solutions were stored at 5˚C and used for calibration curve preparation and sample fortification.

2.3. Milk Samples

Bisphenol A detection and quantification were carried out in 51 whole fluid milk (ultra-high temperature (UHT) and pasteurized) and whole milk powdered samples from different manufacturing batches obtained from retailers in the city of Rio de Janeiro between April/2019 and July/2019. A total 19 powdered milk and 27 fluid milk UHT samples and five pasteurized milk samples were purchased from 27 different brands.

The samples were further classified into six categories according to packaging type, namely glass, poly (ethylene terephthalate) (PET) polyethylene (PE) and poly (vinylidene chloride) (PVDC) and Tetra Pak® cartons containing whole fluid milk, metal cans and metallized polyester-polyethylene (laminated film) for whole powdered milk (**Figure 1**).

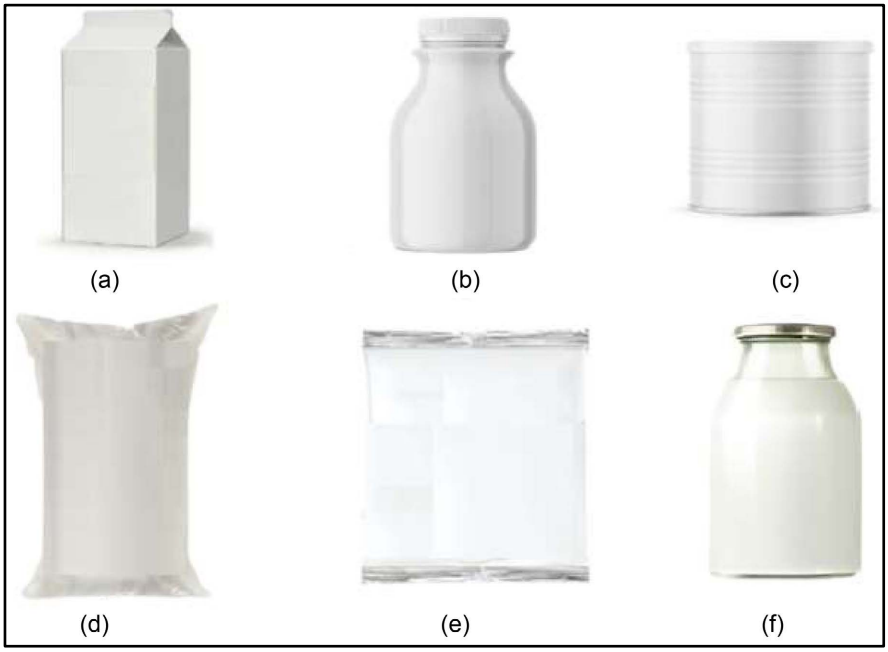

Figure 1. Different fluid and powdered milk packaging materials investigated herein. (a) Carton; (b) PET-Poly (ethylene terephthalate); (c) Metal can; (d) Polyethylene (PE) and poly (vinylidene chloride) (PVDC); (e) Laminated film (metalized Polyester-Polyethylene); (f) Glass.

Table 1 depicts the total number of analyzed milk samples per packaging type.

2.4. Samples Preparation Procedure Employing the QuEChERS Treament

The BPA analysis methodology applied herein was based on [23] and [24] with some QuEChERS treatment modifications as described by [25]. Briefly, powdered milk samples (0.3 g) were weighed in 15 mL Falcon tubes (polypropylene) and mixed with 3 mL of type 1 ultrapure water. The Falcon tubes were then vortexed for 30 seconds (Marconi, MA 162), subsequently mixed with 3 mL of acetonitrile and 2 mL of filtered hexane and vortexed again for 2 minutes. Then, 1.2 g of magnesium sulfate ($MgSO_4$) and 0.3 g of sodium chloride (NaCl) were added to each sample followed by vortexing for 2 minutes. The samples were then centrifuged (Eppendorf, 5804R) at 3000 rpm for 7 minutes at 20˚C. A 1 mL aliquot of the acetonitrile extract of each sample was then transferred to a glass flask and evaporated to complete dryness under a gentle N_2 flow at room temperature (Reacti-Therm III, 18935/Reacti-Vap III, 18785). The dry extracts were then resuspended in 1 mL of MeOH/H_2O (80:20, v/v) with 0.1% ammonium hydroxide and maintained in an ultrasound bath for 5 minutes. The final solutions were then filtered through disposable filtration membranes (Millex-FG, 0.22 µm, hydrophobic PTFE) using a glass syringe, and the filtered extracts were directly placed into vials for the subsequent instrumental analysis. Fluid milk samples (3.0 g) were weighed in polypropylene (PP) centrifuge tubes and treated the same way as the powdered samples.

Table 1. Total number of analyzed whole fluid and whole powdered milk samples per packaging type.

	Packaging					
	Can	Carton (TetraPak®)	Polyethylene metallized polyester	Poly (ethylene terephthalate)	Polyethylene and polyvinylidene chloride	Glass
Whole fluid milk - UHT	0	24	0	3	0	0
Whole fluid milk - Pasteurized	0	0	0	0	4	1
Whole powdered milk	8	0	11	0	0	0

2.5. HPLC-MS/MS Analysis

Liquid chromatography was performed employing an Ultra Performance Liquid Chromatograph (ULC) model UPLCTM I-Class ACQUITYTM apparatus (Waters, USA). An AcquityTM UPLC column BEH C18 (100 mm × 2.1 mm i.d., particle size 1.7 μm) was used as the stationary phase. Column temperature was maintained at 35˚C. Methanol and water (70:30, v/v) were used as the mobile phase at an isocratic elution flow rate of 0.3 $mL \cdot min^{-1}$. The system was washed with acetonitrile:methanol:isopropanol:water (1:1:1:1, v/v/v/v) at the end of each run for five minutes and stabilized under the initial analysis conditions for 5.0 minutes. An injection volume of 5 μL was applied to each sample. Detections were performed using a tandem quadrupole mass spectrometer (Waters, Xevo® TQ-S), equipped with an electrospray ionization (ESI) source. The source parameters were optimized as follows: ion spray voltage, 2 kV for ESI (-), capillary temperature 400˚C, source temperature 150˚C. Nitrogen was used as the cone and desolvation gas at 150 $L \cdot h^{-1}$ and 750 $L \cdot h^{-1}$ flow rates, respectively. Argon was used as the collision gas at a 0.15 $mL \cdot min^{-1}$ flow rate. Collision energies of 15 and 20 V were used for the quantification (Q - m/z 227 > 212) and qualification (q - m/z 227 > 133) transitions, respectively.

2.6. Analytical Method Validation

The applied analytical method was previously validated and proven adequate for fluid and powdered milk BPA determinations [25]. The validated parameters of merit were selectivity, matrix effect, linearity, accuracy/trend, precision (repeatability and intermediate precision), limit of detection (LD) and limit of quantification (LQ) and the absence of matrix effects [25] [26].

2.7. Internal Quality Control

Several quality controls were applied to ensure method accuracy, as cross contamination is a serious problem in BPA analyses and should be avoided as much as possible. Blank tests were carried out in all experiments with the reagent blank (without the samples) to verify potential reagent/solvent interferences and BPA

contamination. The reagent blanks were also analyzed after every batch of 10 sample injections, confirming no interferences. A reconstituted powdered milk (1:10) sample fortified with 0.5 ng·mL^{-1} BPA, was also analyzed, confirming no contamination.

The same reconstituted milk powder (1:10) sample fortified with 0.5 ng·mL^{-1} BPA was analyzed after every batch of 10 sample injections, to verify method recovery values.

To avoid any BPA contamination in the employed system, all exogenous BPA contamination sources were measured, and glassware was used whenever possible and cleaned with MeOH using an ultrasonic bath. The $MgSO_4$ and NaCl used in the QuEChERS treatment were both heated to 400˚C overnight in a muffle furnace and stored in glass vials with screw cap after cooling. Hexane was filtered using a vacuum filtration system coupled to a membrane (ENVITM_18 DSK 47MM - Sigma-Aldrich).

3. Results

3.1. Modified QuEChERS Method Optimization

A miniaturized sample preparation method was optimized and validated for whole milk BPA determinations. The proposed extraction procedure is based on the modified QuEChERS method according to [23] [24]. Hexane and acetonitrile were used for the extraction, followed by drying with magnesium sulfate and applying sodium chloride for the extraction step (salting out effect). A solid-phase extraction clean-up step was not performed, as no need for additional cleaning steps was verified.

The optimization of a modified QuEChERS method reduced milk sample pre-treatment steps, minimizing error sources. A mean recovery of 93.8% and an RSD of 8.3% for six powdered milk samples fortified with BPA at 1.0 ng·mL^{-1} (1:10 reconstituted milk) were obtained. Resuspension in MeOH:H_2O (80:20, v/v) with the addition of 0.1% ammonium hydroxide in the resuspension solvent led to a superior response, as depicted in **Figure 2**. The optimization of the modified QuEChERS method was, in fact, relatively quick and simple.

3.2. Method Validation

Method selectivity was evaluated by the absence of interference signals eluted at the same BPA retention time using reconstituted whole milk powder samples (1:10) fortified with 0.5 ng·mL^{-1} BPA and an unfortified reconstituted whole milk powder sample (1:10). Method selectivity was clear due to the absence of interfering substances at the same BPA retention time, eluting at 1.350 ± 0.005 minutes (**Figure 3**). Confirmation was performed by comparing the signal intensity ratios of the two transition ions (Q - m/z 227 > 212 and q - m/z 227 > 133) of each sample analyte with those of the standard solution.

The BPA calibration curves were constructed from 0.5 ng·mL^{-1} to 2.0 ng·mL^{-1} and good linearity was achieved, with correlation coefficients (r) over 0.99. To

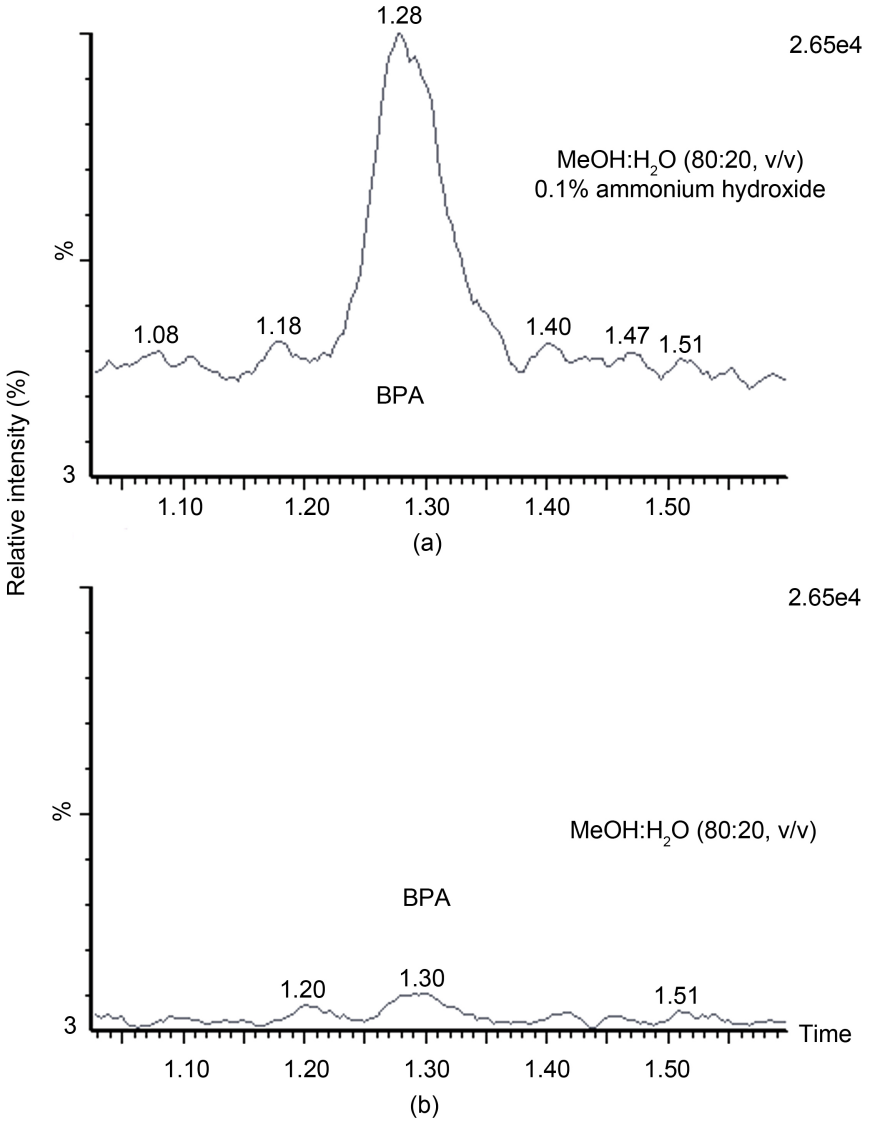

Figure 2. Chromatograms demonstrating the effect of adding 0.1% ammonium hydroxide in the final solvent used for milk sample resuspension at 1.0 ng·mL^{-1} BPA. (a) Chromatogram representing 1.0 ng·mL^{-1} BPA in the matrix with the addition of 0.1% ammonium hydroxide in the final solvent used in sample resuspension; (b) Chromatogram representing 1.0 ng·mL^{-1} BPA in the matrix without the addition of 0.1% ammonium hydroxide in the final solvent used in sample resuspension.

assess any potential matrix effects, matrix and solvent curves were prepared at the same concentration range from 0.5 ng·mL^{-1} to 2.0 ng·mL^{-1} and compared. Matrix/solvent slope ratios and intersections were calculated for BPA. The slopes and intersections of the analytical curves prepared in both the solvent and the matrix were equivalent at a 95% confidence level, confirming the absence of any matrix effect.

The limits of detection (LD, S/N = 3) and limits of quantification (LQ, S/N = 10) for milk sample BPA concentrations were calculated as 0.12 ng·mL^{-1} and 0.36 ng·mL^{-1}, respectively.

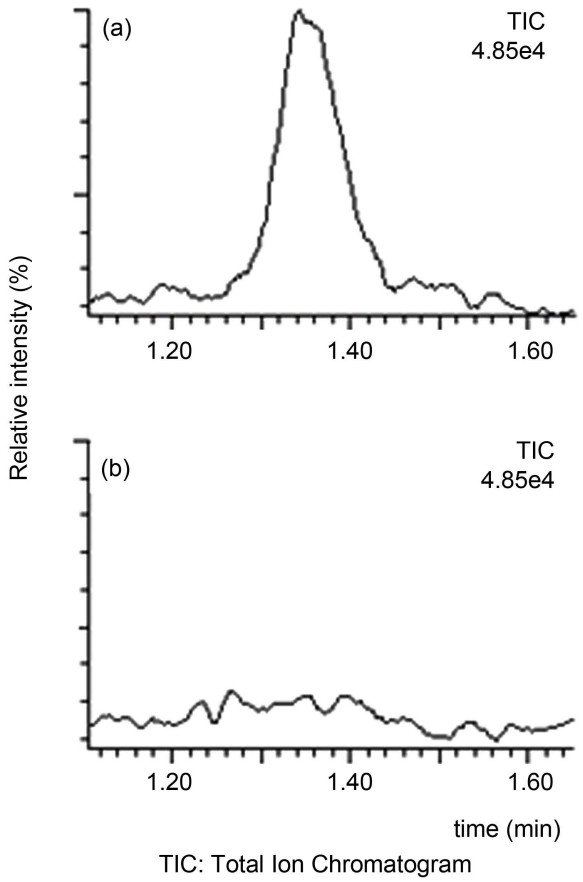

Figure 3. Chromatograms demonstrating the absence of interferences at the same BPA retention time (tR 1.35 minutes). (a) Reconstituted whole milk powder sample (1:10) fortified with BPA (0.5 ng·mL^{-1}) and (b) Non-fortified reconstituted whole milk powder sample (1:10).

Concerning method accuracy, the BPA recovery results $\left(\overline{R}\%\right)$ of 70.8% and 93.6% at 0.5 ng·mL^{-1} (n = 3) and 1.0 ng·mL^{-1} (n = 4), respectively, indicate reliable accuracy and acceptable when compared to [27] [28] standards, which establish ranges between 40% to 120% and 50% to 120%, respectively, for ≤1 ng·g^{-1} of the analyte.

Repeatability was evaluated through the analysis of a reconstituted powdered milk sample (1:10) fortified with 0.5 ng·mL^{-1} BPA (n = 3). Repeatability was calculated using the repeatability relative standard deviation (RSDr), while reproducibility was calculated using the reproducibility relative standard deviation (RSDR), established as 11% and 22%, respectively. The RSDr was compared to the [27], which sets values below 30% for ≤1 ng·g^{-1} of the analyte. The applied method, therefore, exhibited good accuracy and precision for the evaluated BPA levels.

3.3. Validated Method Application to the Analysis of BPA in Ilk Samples

The validated BPA determination method was then applied to 51 whole milk

(fluid and powdered) samples from 27 commercial brands packaged in six different types of packaging. The results are depicted in Table 2.

Only two samples (3.9%) contained BPA levels above the LQ (0.36 ng·mL^{-1}), of 0.53 ng·mL^{-1} in one reconstituted powdered whole milk (1:10) sample and 0.50 ng·mL^{-1} in one pasteurized whole fluid milk sample, respectively. The remaining samples (44 samples) contained BPA levels below the method LD (0.12 ng·mL^{-1}), while five samples (9.8%) contained BPA levels above the LD, but below the LQ.

Bisphenol A was detected in two of the 19 investigated milk powder samples packaged in metallic polyester-polyethylene packaging (laminated film) and in one sample packaged in a metal can. One powdered milk sample packaged in laminated film contained 0.53 ng·mL^{-1} BPA, above the LQ.

Among the 32 whole fluid milk samples, BPA was detected in two samples submitted to UHT thermal treatment packed in Poly (ethylene terephthalate) PET and Tetra Pak® packaging (below the LQ), while one milk sample submitted to pasteurization heat treatment packaged in polyethylene (PE) and poly (vinylidene chloride) (PVDC) packages contained 0.50 ng·mL^{-1} of BPA, above the LQ. Figure 4 displays the chromatogram of the whole powdered milk sample naturally contaminated with BPA.

Milk contamination by BPA has been assessed in several countries, with very variable levels. For example [29] [30] [31] reported no BPA detection in milk samples, although they did not specify what types of packaging were investigated. [32] on the other hand, when evaluating different foods, including milk, detected an average value of 1.47 ng·g^{-1} BPA in this product, while [33] and [34] reported 0.49 ng·g^{-1} and 0.22 ng·g^{-1} BPA in milk, respectively, although also not indicating the type of packaging.

Contact food time with certain types of packaging may or may not contribute to greater migration of packaging compounds to food. Thus, identifying the type of packaging and type of food, in addition to the time and temperature applied during packaging, is paramount to adequately evaluate any migration of substances present in food packages.

[35] who analyzed whole fluid milk packed in polyethylene and high-density polyethylene packages, reported BPA values of 2.6 ng·mL^{-1} and 1.6 ng·mL^{-1}, respectively, with no BPA detected in Tetra Pak®-packed samples.

Table 2. Determination of BPA in whole milk (fluid and powder) samples.

Sample	Number of samples	Number of samples positive for BPA
Fluid milk		
UHT[1]	27	2
Pasteurized	5	1
Powdered milk	19	4

[1]Ultra High Temperature.

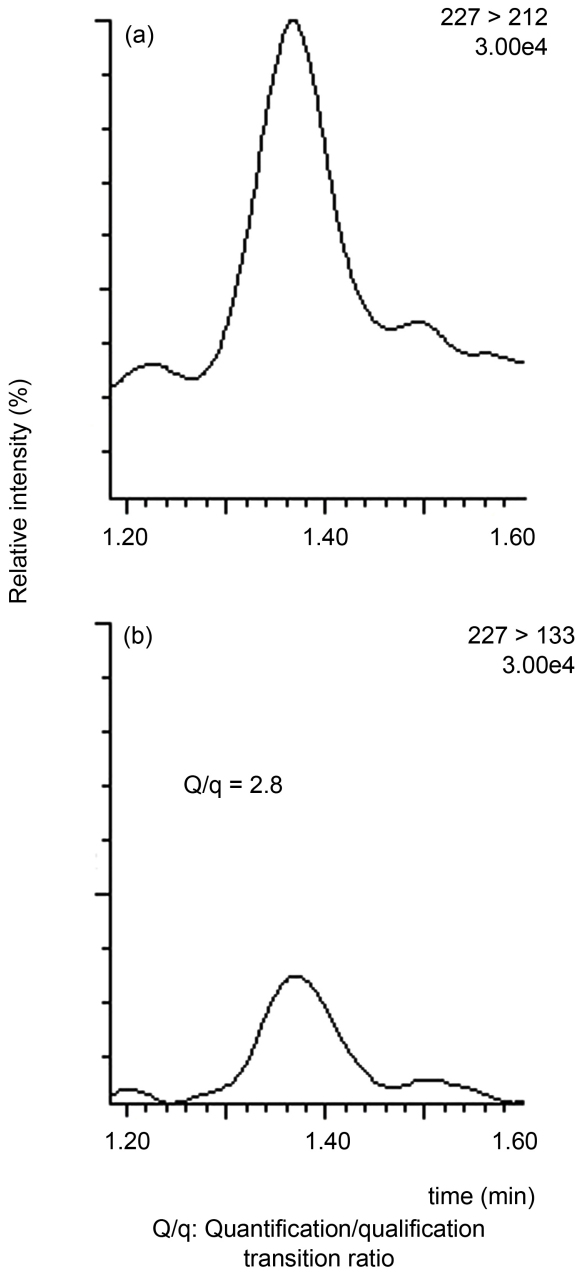

Figure 4. Chromatogram of the reconstituted whole milk powder sample (1:10), packaged in laminated film naturally contaminated by BPA (0.53 ng·mL^{-1}). This was confirmed by comparing the signal intensity ratios of the two ion transitions (a) Q - m/z 227 > 212 and (b) q - m/z 227 > 133.

Concerning the fluid milk samples analyzed herein, BPA was detected below the LQ in two whole milk samples packaged in Poly (ethylene terephthalate) (PET) and Tetra Pak® packages, while one milk sample packaged in polyethylene PE and poly (vinylidene chloride) PVDC contained 0.50 ng·mL^{-1} BPA, above the LQ.

Bisphenol A contamination has been frequently reported in dairy products, powdered milk and infant formulas packed in metal cans, due to epoxy resin

migration [36] [37] [38]. In the present study, BPA was detected below the LQ in one sample packaged in a metal can and quantified (0.53 $ng \cdot mL^{-1}$ BPA) in one sample packaged in a metallic polyester-polyethylene package (laminated film).

It is important to note that milk BPA contamination can take place not only due to the packaging migration, as this contaminant can enter the milk chain via multiple paths, such as animal feed, the farm environment and various points during milk production (tubes used during milk processing, milk transfer to storage locations and filling equipment, among others), in addition to during the technological processing employed in the final production stage.

4. Conclusions

The proposed analytical method was applied to BPA screening in commercial milk (fluid and powder) samples presented in different packages. This compound was detected in five out of the six types of analyzed packages and quantified in metallized polyester-polyethylene (laminated film) and polyethylene (PE) and polyvinylidene chloride (PVDC) packages.

As packaging materials vary and BPA is a ubiquitous substance, it is plausible to assume that the investigated packages may have been cross-contaminated. In addition, milk sample contamination can take place during the entire milk production chain, from animal feeding, to milking and milk processing.

Acknowledgements

This study was financially supported by the Coordination for the Improvement of Higher Education Personnel (CAPES), and the Graduate Program in Sanitary Surveillance (PPGVS), National Institute for Quality Control in Health (INCQS), Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Environmental Protection Agency EPA (1997) Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis.

[2] Bila, D.M. and Dezotti, M. (2007) Desreguladores endócrinos no meio ambiente: Efeitos e consequências. *Química Nova*, **30**, 651-666. https://doi.org/10.1590/S0100-40422007000300027

[3] Ghiselli, G. and Jardim, W.F. (2007) Interferentes endócrinos no ambiente. *Química Nova*, **30**, 695-706. https://doi.org/10.1590/S0100-40422007000300032

[4] Peña-Corona, S.I., Vargas-Estrada, D., Juárez-Rodríguez, I., Retana-Márquez, S. and Mendoza-Rodríguez, C.A. (2023) Bisphenols as Promoters of the Dysregulation of Cellular Junction Proteins of the Blood-Testis Barrier in Experimental Animals: A Systematic Review of the Literature. *Journal of Biochemical and Molecular Toxicology*, e23416. https://doi.org/10.1002/jbt.23416

[5] Pontelli, R.C.N., Nunes, A.A. and Oliveira, S.V.B. (2016) Impacto na saúde humana de disruptores endócrinos presentes em corpos hídricos: Existe associação com a obesidade? *Ciência e Saúde Coletiva*, **21**, 753-766. https://doi.org/10.1590/1413-81232015213.25212015

[6] Wang, T., Li, M., Chen, B., Xu, M., Xu, Y., Huang, Y., Lu, J., Chen, Y., Wang, W., Li, X., Liu, Y., Bi, Y., Lai, S. and Ning, G. (2012) Urinary Bisphenol A (BPA) Concentration Association with Obesity and Insulin Resistance. *The Journal of Clinical Endocrinology & Metabolism*, **97**, E223-E227. https://doi.org/10.1210/jc.2011-1989

[7] Ige, A., Adebayo, O., Adele, B., Odetola, A., Emediong, I. and Adewoye, E. (2022) Genistein Mitigates the Gastro-Toxic Effects of Bisphenol A in Male Wistar Rats. *Journal of Biosciences and Medicines*, **10**, 60-78. https://doi.org/10.4236/jbm.2022.109006

[8] National Library of Medicine (2017) Compound Summary Bisphenol A. https://pubchem.ncbi.nlm.nih.gov/compound/6623

[9] Almeida, S., Raposo, A., Almeida-González, M. and Carrascosa, C. (2018) Bisphenol A: Food Exposure and Impact on Human Health. *Comprehensive Reviews in Food Science and Food Safety*, **17**, 1503-1517. https://doi.org/10.1111/1541-4337.12388

[10] Brasil (2012) RDC nº 56, de 16 de novembro de 2012. Ministério da Saúde (anvisa.gov.br).

[11] Emergen Research (2022) Bisphenol A Market, by Application (Epoxy Resins, Polycarbonate Resins, Unsaturated Polyester Resins, Flame Retardants, Polysulfone Resins, Polyacrylate), by Industry Vertical (Automotive, Electronics, Medical, Paints & Coatings, Packaging), by Distribution Channel (Direct, Indirect), and by Region Forecast to 2028. Bisphenol A Industry Forecast|BPA Market Report 2021-2028. https://emergenresearch.com

[12] García Ibarra, V., Quirós, R.R.A., Losada, P.P. and Sendón, R. (2019) Non-Target Analysis of Intentionally and Non-Intentionally Added Substances from Plastic Packaging Materials and Their Migration into Food Simulants. *Food Packaging and Shelf Life*, **21**, Article ID: 100325. https://doi.org/10.1016/j.fpsl.2019.100325

[13] Tumu, K., Vorst, K. and Curtwiler, G. (2023) Endocrine Modulating Chemicals in Food Packaging: A Review of Phthalates and Bisphenols. *Comprehensive Reviews in Food Science and Food Safety*, **22**, 1337-1359. https://doi.org/10.1111/1541-4337.13113

[14] European Commission (2014) Commission Directive 2014/81/EU: Amending Appendix C of Annex II to Directive 2009/48/EC of the European Parliament and of the Council on the Safety of Toys, as Regards Bisphenol A.

[15] European Commission (2018) Commission Regulation (EU) 2018/213: On the Use of Bisphenol A in Varnishes and Coatings Intended to Come into Contact with Food and Amending Regulation (EU) No 10/2011 as Regards the Use of That Substance in Plastic Food Contact Materials.

[16] Guart, A., Bono-Blay, F., Borrell, A. and Lacorte, S. (2011) Migration of Plasticizers Phthalates, Bisphenol A and Alkylphenols from Plastic Containers and Evaluation of Risk. *Food Additives & Contaminants*, **28**, 676-685. https://doi.org/10.1080/19440049.2011.555845

[17] Casajuana, N. and Lacorte, S. (2003) Presence and Release of Phthalic Esters and Other Endocrine Disrupting Compounds in Drinking Water. *Chromatographia*, **57**, 649-655. https://doi.org/10.1007/BF02491744

[18] Casajuana, N. and Lacorte, S. (2004) New Methodology for the Determination of Phthalate Esters, Bisphenol A, Bisphenol A Diglycidyl Ether, and Nonylphenol in

Commercial Whole Milk Samples. *Journal of Agricultural and Food Chemistry*, **52**, 3702-3707. https://doi.org/10.1021/jf040027s

[19] Bano, S., Hayat, M., Samreen, T., Asif, M., Habiba, U. and Uzair, B. (2020) Detection of Pathogenic Bacteria *Staphylococcus aureus* and *Salmonella sp.* From Raw Milk Samples of Different Cities of Pakistan. *Natural Science*, **12**, 295-306. https://doi.org/10.4236/ns.2020.125026

[20] van Asselt, E.D., van der Fels-Klerx, H.J., Marvin, H.J.P., van Bokhorst-van de Veen, H. and Groot, M.N. (2017) Overview of Food Safety Hazards in the European Dairy Supply Chain. *Comprehensive Reviews in Food Science and Food Safety*, **16**, 59-75. https://doi.org/10.1111/1541-4337.12245

[21] Geens, T., Aerts, D., Berthot, C., Bourguignon, J.P., Goeyens, L., Lecomte, P., Maghuin-Rogister, G., Pironnet, A.M., Pussemier, L., Scippo, M.L., Van Loco, J. and Covaci, A. (2012) A Review of Dietary and Non-Dietary Exposure to Bisphenol A. *Food and Chemical Toxicology*, **50**, 3725-3740. https://doi.org/10.1016/j.fct.2012.07.059

[22] Danaher, M. and Jordan, K. (2013) Identification of Existing and Emerging Chemical Residue Contamination Concerns in Milk. *Irish of Journal Agricultural and Food Research*, **52**, 173-183. http://hdl.handle.net/11019/533

[23] Przybylski, C. and Segard, C. (2009) Method for Routine Screening of Pesticides and Metabolites in Meat Based Baby-Food Using Extraction and Gas Chromatography-Mass Spectrometry. *Journal of Separation Science*, **32**, 1858-1867. https://doi.org/10.1002/jssc.200900016

[24] Sartori, A.V., Mattos, J.S., de Moraes, M.H.P. and Nóbrega, A.M. (2015) Determination of Aflatoxins M1, M2, B1, B2, G1, and G2 and Ochratoxin A in UHT and Powdered Milk by Modified QuEChERS Method and Ultra-High-Performance Liquid Chromatography Tandem Mass Spectrometry. *Food Analytical Methods*, **8**, 2321-2330. https://doi.org/10.1007/s12161-015-0128-4

[25] Souza. P.S., Krauss, T.M., Sartori, A.V. and Abrantes, S.M.P. (2023) Simplified QuEChERS Technique Followed by UHPLC-MS/MS Analysis for the Determination Bisphenol A in Whole and Powdered Milk. *International Food Research Journal*, **30**, 524-535. https://doi.org/10.47836/ifrj.30.2.21

[26] Souza, S.V.C. and Junqueira, R.G. (2005) A Procedure to Assess Linearity by Ordinary Least Squares Method. *Analytica Chimica Acta*, **552**, 25-35. https://doi.org/10.1016/j.aca.2005.07.043

[27] Association of Official Analytical Chemists (2016) International, Official Methods of Analysis of AOAC International. Appendix F: Guidelines for Standard Method Performance Requirements.

[28] European Commission Decision. Commission Decision nº 2002/657/CE. https://op.europa.eu/en/publication-detail/-/publication/ed928116-a955-4a84-b10a-cf7a82bad858

[29] Kang, J.H. and Kondo, F. (2003) Determination of Bisphenol A in Milk and Dairy Products by High-Performance Liquid Chromatography with Fluorescence Detection. *Journal of Food Protection*, **66**, 1439-1443. https://doi.org/10.4315/0362-028X-66.8.1439

[30] Sajiki, J., Miyamoto, F., Fukata, H., Mori, C., Yonekubo, J. and Hayakawa, K. (2007) Bisphenol A (BPA) and This Source in Foods in Japanese Markets. *Food Additives & Contaminants*, **24**, 103-112. https://doi.org/10.1080/02652030600936383

[31] Niu, Y., Zhang, J., Duan, H., Wu, Y. and Shao, B. (2015) Bisphenol A and Nonylphenol in Foodstuffs: Chinese Dietary Exposure from the 2007 Total Diet Study and Infant Health Risk from Formulas. *Food Chemistry*, **167**, 320-325.

https://doi.org/10.1016/j.foodchem.2014.06.115

[32] Liao, C. and Kannan, K. (2014) A Survey of Bisphenol A and Other Bisphenol Analogues in Foodstuffs from Nine Cities in China. *Food Additives & Contaminants. Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment*, **31**, 319-329. https://doi.org/10.1080/19440049.2013.868611

[33] Shao, B., Han, H., Tu, X. and Huang, L. (2007) Analysis of Alkylphenol and Bisphenol A in Eggs and Milk by Matrix Solid Phase Dispersion Extraction and Liquid Chromatography with Tandem Mass Spectrometry. *Journal of Chromatography B*, **850**, 412-416. https://doi.org/10.1016/j.jchromb.2006.12.033

[34] Bemrah, N., Jean, J., Rivière, G., Sanaa, M., Leconte, S., Bachelot, M., Deceuninck, Y., Bizec, B.L., Dauchy, X. and Roudot, A.C., Camel, V., Grob, K., Feidt, C., Picard-Hagen, N., Badot, P.M., Foures, F. and Leblanc, J.C. (2014) Assessment of Dietary Exposure to Bisphenol A in the French Population with A Special Focus on Risk Characterisation for Pregnant French Women. *Food and Chemical Toxicology*, **72**, 90-97. https://doi.org/10.1016/j.fct.2014.07.005

[35] Liu, X., Ji, Y., Zhang, H. and Liu, M. (2008) Elimination of Matrix Effects in the Determination of Bisphenol A in Milk by Solid-Phase Microextraction-High-Performance Liquid Chromatography. *Food Additives & Contaminants*, **25**, 772-778. https://doi.org/10.1080/02652030701713921

[36] Ackerman, L.K., Noonan, G.O., Heiserman, W.M., Roach, J.A. and Begley, W.L. (2010) Determination of Bisphenol A in U.S. Infant Formulas: Updated Methods and Concentrations. *Journal of Agricultural and Food Chemistry*, **58**, 2307-2313. https://doi.org/10.1021/jf903959u

[37] Maragou, N.C., Lampi, E.N., Thomaidis, N.S. and Koupparis, M.A. (2006) Determination of Bisphenol A in Milk by Solid Phase Extraction and Liquid Chromatography-Mass Spectrometry. *Journal of Chromatography A*, **1129**, 165-173. https://doi.org/10.1016/j.chroma.2006.06.103

[38] Bomfim, M.V.J., Silvestre, F.B., Zamith, H.P. and Abrantes, S.M.P. (2015) Determinação de bisfenol A em fórmulas infantis. *Revista Visa em Debate*, **3**, 85-90. https://doi.org/10.3395/2317-269x.00415