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Identification of explanatory factors of the presence and quantification of endocrine disruptors in commercially available bottled waters

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Abstract

To identify the factors that influence the presence and quantification of endocrine disruptors (EDs) in bottled water marketed in Bogotá, the packaging (plastic or glass), gas (sparkling or still water) and origin (international or Colombian) of the water were considered. EDs were divided into plasticizers, drugs and hormones and were quantitatively determined via gas chromatography coupled to mass spectrometry (GC–MS). Principal component and multiple correspondence analyses, the Wilcoxon and Kruskal–Wallis tests, average mutual information and tree-based models were used to identify the factors that affected the ED concentrations. Phthalates, drugs, hormones and synthetic compounds were detected, including 4-*tert*-octylphenol, acetaminophen, caffeine, fluoxetine, gemfibrozil, triclosan, bisphenol A, primidone, carbamazepine and progesterone. Factors such as glass packaging and sparkling water increased the detection and presence of EDs. Fourteen of the 16 identified compounds were detected if the water was bottled in glass; the exceptions were caffeine and acetaminophen. Furthermore, bottled water of international origin had higher concentrations of most EDs than Colombian bottled water. The statistical approaches used are an innovative predictive method for analysing ED concentrations and classifying factors closely correlated with the presence of these compounds.

KEYWORDS
average mutual information, bottled water, endocrine disruptors, linear statistical analysis, toxicity degree, tree-based models

1 | INTRODUCTION

The contamination of water by chemical substances represents one of the most serious problems for human health and the environment. Currently new emerging pollutants have been generated, by the use of chemical substances in manufacturing food containers and drugs, which have caused a strong exposure of humans and animals to emerging pollutants. Thus, it is important to analyse these chemical species in basic products through selective, sensitive and economic techniques (Ali et al., 2005; Basheer, 2018a).

The contamination of water by these newly emerging pollutants is a matter of global concern due to the adverse consequences of traces of these compounds, such as sterility, deterioration of oestrogenic activity, alteration of behavioural habits and growth problems. Thus, a great deal of effort has been focused on discovering the sources of contamination and degree of toxicity of these products (Ali et al., 2017; Basheer, 2018b).

Endocrine disruptors (EDs) are synthetic chemical substances that affect the hormonal balance. Hormones emit chemical signals that can be modified by different interfering chemical compounds. When this modification occurs, biological consequences occur in the hormonal system (HS) (FundAlborada, 2015; Moral, 2015). Since 1991, scientists have been concerned about defining the phenomenon of endocrine alterations: EDs can be defined as 'a large number of chemical products generated by humans with the potential to alter the endocrine system of animals, including humans' (Autrup et al., 2020). Since then, research in this multidisciplinary field has been increasing the ED knowledge base, which continually expands in many aspects of how they affect hormonal pathways (Mustieles et al., 2015). Two decades later, the German Endocrinology Society renewed the demand to prioritize the projections of exposure to these substances in its statement on the Science of Endocrine Disruptors (Marvin et al., 2020). However, understanding the complexity of human exposure to human-made chemicals, including EDs, is compromised by the immense number of compounds in use and the technical limitations of their detection (Petersen, 2019). The cumulative effects of long-term exposure to low doses of EDs start from altering the endocrine system to the appearance of diseases such as overweight, infertility and cancer (Pînzaru et al., 2020). Thus, the daily consumption of bottled water can generate this exposure to low doses of EDs and become a risk for human health (Annamalai & Vasudevan, 2020). The science of exposure focuses on a few chemicals as indicators of the total exposure to EDs, such as bisphenol A (BPA) and phthalates, for which excellent biomonitoring data are available (analytical procedure for identifying and quantifying residues of EDs) (Albouy-Llaty et al., 2016).

The production of compounds such as BPA and phthalates is among the highest worldwide: The annual global output of BPA is estimated at more than 5 million tons (Rhomberg & Goodman, 2012). BPA is a primary component of polycarbonate (PC) plastic, which is an epoxy resin monomer (Li et al., 2010; Muhamad et al., 2016; Rubin, 2011) and is used with phthalates in food and beverage containers, including bottles for drinking water (Fadillah et al., 2020). There have been human losses due to exposure to BPA (Li et al., 2010), which is currently rising worldwide. An analysis by the National Health Unit and Nutrition Survey (NHANES) of the United States revealed that more than 90% of the general population were exposed to BPA (Wang et al., 2020). These data support the hypothesis that polyethylene terephthalate (PET) packaging materials are a source of ED generation, although at high temperatures (>80°C), EDs rapidly migrate from PC packaging into water and exponentially increase exposure (Feng, 2020; Goodson et al., 2004).

This article relates factors that explain ED exposure in bottled water, such as the origin, gas and type of bottle, to discover the degrees of incidence and possible exposure patterns through different multivariate statistical techniques, concepts such as information entropy and mutual information, and tree-based models with data mining.

2 | MATERIALS AND METHODS

From a total of 165 registered bottled water companies in Bogotá, Colombia (INVIMA, 2017), we considered 59 brands due to accessibility problems in the water trade and the discontinuity of the INVIMA registration of some companies. We purchased three bottles of each brand; however, there were four discontinued brands, of which only duplicate samples were obtained, so there were 173 samples in total. A balanced incomplete block (BIB) design was applied to determine whether 173 water samples were sufficient to perform this research using the 'Agricolae' library in the R Statistical software (De Mendiburu, 2016).

We identified and quantified EDs in water samples in the Water Quality Laboratory of the Department of Civil Engineering of the Pontificia Universidad Javeriana (PUJ) in Bogotá. We applied the multiresidue method of gas chromatography coupled to mass spectrometry (GC–MS), which enabled us to quantitatively detect the compounds of interest. Analyses were performed using a Shimadzu 2010 GC–MS system in the electronic impact (EI; 70 eV) ionization mode. The experimental conditions were as follows: capillary column: MS-5 (5% phenyl, 95% dimethylpolysiloxane, 30 m × 0.25 mm i.d., 0.25-μm phase thickness); carrier gas: He (1.0 ml/min): injection volume, 1 μl; injection mode: split; and split ratio, 1:12. The temperatures of the quadrupole mass spectrometer and the source were 150°C and 230°C, respectively. The temperature programme was 80°C (for 3 min) and subsequently increased at 10°C/min to 295°C for 10 min (Gómez et al., 2007; Shimadzu Corporation, 2017). Prior to the chromatographic analysis, 500-ml water samples (saturation volume of C18 cartridges) were filtered, and the pH was measured. If the pH was below 8, it was adjusted with ammonium hydroxide (NH_4OH) to a range of 8–8.5. This range guaranteed the retention of the chemical species of interest, and the chemical species present did not change due to chemical processes that occur at acidic or basic pH values (Gómez et al., 2007; Yanina G. Muñoz Reyes, 2015). We filtered the water through 0.45-μm cellulose filters to retain substances and minerals that affected passage through the C18 silica cartridges for extraction (Gómez et al., 2007).

We analysed five ED groups: organochlorine pesticides, organophosphorus pesticides, pharmaceuticals, hormones, steroids and phthalates. For this analysis, it was necessary to add a solvent to completely saturate the C18 cartridge prior to adding the 500-ml sample; ethyl acetate ($C_4H_8O_2$) was applied as the eluent to elute the EDs in the cartridge to a test tube. Then, the sample in the test tube was evaporated to obtain the sample precipitate. The precipitate of the sample was resuspended in 1 ml of triphenyl phosphate ($C_{18}H_{15}O_4P$) and subjected to chromatographic analysis at 40–350°C. A 30-m Biological Mass Spectrometry (BMS) capillary column (5% polysiloxane 'low polarity') was used, and the compounds with the highest polarity were eluted first.

We analysed the compounds in the bottled water based on the brand RESKEL CORPORATION's calibration standards, and the EDs were divided into four groups (Table 1).

We determined the degree of toxicity of each compound by comparing the levels with a toxicity index provided by the Health Advisory Program (HA), which is sponsored by the Environmental Protection Agency's (EPA's) Office of Water (OW). This index provides the concentrations of contaminants in drinking water where cancerous effects are not expected to occur with lifetime exposure (2015). The HA parameterized these levels for an adult weighing 70 kg who consumed 2 L of water per day for life. We calculated the maximum contaminant level (MCL) for life for each compound in bottled water from the drinking water equivalent level (DWEL), which was obtained from the reference dose (RfD). The RfD is defined as an estimate (with uncertainty spanning an order of magnitude) of daily oral exposure to the human population (including sensitive subgroups) that likely has no appreciable risk of deleterious effects during life (EPA, 2015). This methodology incorporates the relative source contribution (RSC) containing specific data on pollutants or 20% of the total exposure values of all sources (US EPA, 2015).

We applied the principal component analysis (PCA) and multiple correspondence analysis (MCA) (Terrádez, 2017) using the *ade4 library* of R software (Chessel & Dufour, 2017; Dray et al., 2018; Dray & Dufour, 2007). We applied the non-parametric Wilcoxon test to determine whether there was a significant difference in percentages of difference with the MCA, because it was not possible to assume the normality or homoscedasticity (using the Bartlett test and the Shapiro test, respectively) of the target analytes in the water matrix (Whitley & Ball, 2002). We applied the Kruskal–Wallis test to determine the factors that significantly influenced the variability of the concentration of each compound.

TABLE 1 Patterns in the chromatographic analysis

Method	Catalogue no.
EPA Method 8061A Phthalate Esters Mixture	33227
EPA Method Steroids and Mixed Pharmaceuticals Mix	31117
EPA Method Pharmaceuticals Mix #1	31116
EPA Method Pharmaceuticals Mix #2	31118

Abbreviation: EPA, Environmental Protection Agency.
Source: Self-made.

In addition, we used the entropy concept of information through average mutual information (AMI) to find non-linear relationships among the chosen factors (packaging, gas and origin), presence ('detection' when the concentration is greater than zero and 'nondetection' when this concentration is zero) and concentration of the components, where classical statistical analysis cannot infer results (Hernández et al., 2016).

Finally, we used tree-based learning algorithms to map non-linear relationships of the chosen factors (packaging, gas and origin), contaminant presence (as a classification problem) and concentrations (as a regression problem) (Analytics Vidhya, 2016; Kabacoff, 2017).

3 | RESULTS

We obtained eight possible response combinations, classified in families or 'treatments' with different bottled water characteristics, which yielded a lambda parameter of three. This result indicated that some factors were coupled in three groups and exhibited a 0.86 efficiency factor, which was defined as the relationship between the efficiency of the BIB design versus that of the randomized complete block design (RCBD) (De Mendiburu, 2016). Therefore, the number of defined samples (173 samples) was three times higher than that suggested by the BIB design.

Table 2 shows the degrees of toxicity for the analysed compounds. We calculated the percentage of the concentrations of the compounds for the respective MCL to determine which compounds

TABLE 2 MCL, RfD and DWEL values for target compounds (MCL: maximum contaminant level; DWEL: drinking water equivalent level; RfD: reference dose)

Component	MCL (μg/L)	DWEL (μg/L)	RfD (μg/(kg·day))
Dimethylphthalate	7000	35 000	1000
Diethylphthalate	5600	28 000	800
Diisobutylphthalate	700	3500	100
Di-*n*-butylphthalate	700	3500	100
Bis(2-ethyl-hexyl) phthalate (DEHP)	0	700	20
Di-*n*-octylphthalate	280	1400	40
4-*tert*-octylphenol	1190	5950	170
Acetaminophen	30 434	1 521 739	43 478
Caffeine	21 000	105 000	3000
Fluoxetine HCl	58 100	290 500	8300
Gemfibrozil	91 301	456 505	13 043
Triclosan	$42*10^6$	$210*10^6$	$6*10^6$
Bisphenol A (BPA)	35	175	5
Primidone	114 128	570 640	16 304
Carbamazepine	105 000	525 000	15 000
Progesterone	15 218	76 090	2174

Source: Adapted from Gonzales et al. (2014), Katsikantami et al. (2016) and US EPA (2015).

presented adverse effects on an individual's health and at which percentage.

Only two of the 16 compounds presented levels higher than the MCL in some water samples (bis(2-ethyl-hexyl) phthalate [DEHP] in 46% of samples and BPA in 9% of samples). The presence of these two compounds clearly indicated that these compounds migrated into the water, likely due to their chemical properties (Li et al., 2010), particularly their water solubility. For example, the solubility of DEHP in water is 0.27 mg/L, whereas that of BPA is 300 mg/L at 25°C (Nam et al., 2010; National Center for Biotechnology Information, 2017). BPA is much more soluble than DEHP, which is reflected in the order of magnitude difference in the observed concentrations for each

TABLE 3 Percentage of detection and minimum and maximum concentrations of compounds analysed by mass chromatography

Component	Detected (%)	Not detected (%)	Minimum (μg/L)	Maximum (μg/L)
Dimethylphthalate	66.1	33.9	0.0002	0.0116
Diethylphthalate	97.1	2.90	0.0002	0.0006
Diisobutylphthalate	57.5	42.5	0.0002	0.0340
Di-*n*-butylphthalate	85.1	14.9	0.0002	0.0010
Bis(2-ethyl-hexyl) phthalate	54.6	45.4	0.0003	0.0320
Di-*n*-octylphthalate	96.6	3.40	0.0003	0.0010
4-*tert*-Octylphenol	5.70	94.3	0.0003	0.1790
Acetaminophen	32.2	67.8	0.0210	1.9160
Caffeine	0.60	99.4	0.0004	0.2450
Fluoxetine HCl	16.7	83.3	0.0010	0.1640
Gemfibrozil	26.4	73.6	0.0030	2.4680
Triclosan	14.9	85.1	0.0020	0.4450
Bisphenol A	30.5	69.5	0.2060	221.14
Primidone	4.00	96.0	0.0020	0.5100
Carbamazepine	73.0	27.0	0.0200	479.76
Progesterone	4.00	96.0	0.0010	1.7890

Note: Number of samples = 173.
Source: Self-made.

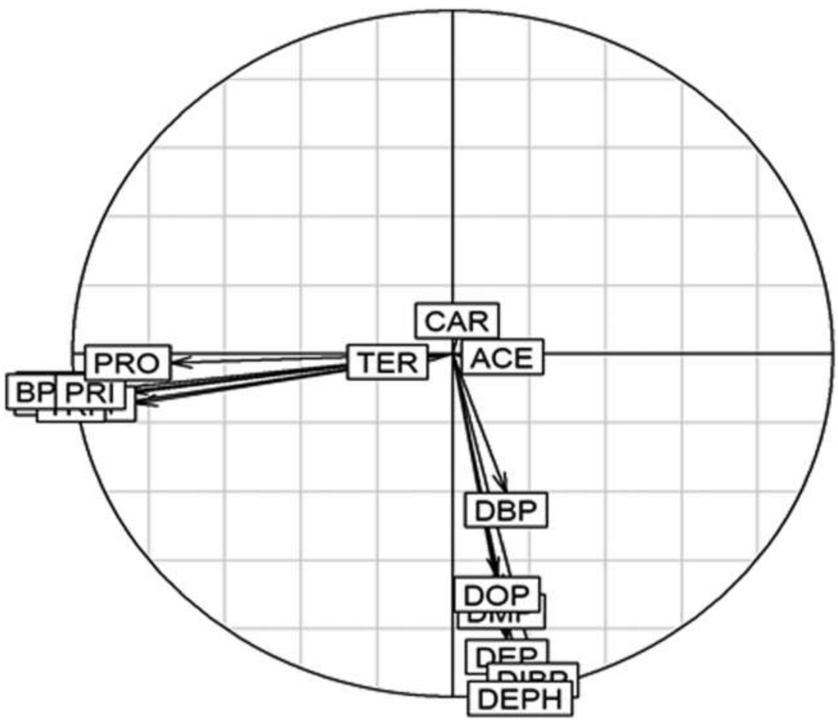

FIGURE 1 Principal component analysis of endocrine disruptors in the water matrix. ACE, acetaminophen; BPA, bisphenol A; CAF, caffeine; CAR, carbamazepine; DBP, di-*n*-butylphthalate; DEHP, bis(2-ethyl-hexyl) phthalate; DEP, diethylphthalate; DiBP, diisobutylphthalate; DMP, dimethylphthalate; DOP, di-*n*-octylphthalate; FLU, fluoxetine HCl; GEM, gemfibrozil; PRI, primidone; PRO, progesterone; TER, 4-*tert*-octylphenol; TRI, triclosan

compound: The maximum observed DEHP and BPA concentrations were 0.032 and 224 mg/L, respectively. Table 3 shows the percentage of detection for each compound and the minimum and maximum concentrations obtained.

Regarding the data analysis, the first two principal components (PCs) (58% of the total variance) from PCA (Figure 1) indicate that many drugs and hormones have greater variability (PC 1—horizontal axis in Figure 1) than phthalates, except for di-*n*-butylphthalate (DBP) (PC 2—vertical axis in Figure 1). The compounds with the highest proportion of original variability were BPA, fluoxetine HCl (FLU), gemfibrozil (GEM), triclosan (TRI), primidone (PRI), caffeine (CAF) and progesterone (PRO). Thus, the observed pharmaceutical compounds and hormones exhibited some similarity.

TABLE 4 Joint entropy, mutual information and factor redundancy values with respect to dimethylphthalate (DMP)

Variables	JE	MI	*R*	*R_max*	%*R*
Plastic bottle	0.99	0.002^{b}	0.12	0.19	65.82
Glass bottle	0.57^{a}		0.57	0.31	181.58^{c}
Colombian water	0.99	0.001	0.21	0.27	78.22
International water	0.78		0.45	0.35	127.57
Still water	1.01	0.001	0.23	0.30	77.9
Sparkling water	0.84		0.41	0.36	115.1

Note: *Variables* are defined as the combinations of the levels of the factors with respect to a given compound; *JE* is the joint entropy: representation of the uncertainty and information of all possible combinations of the analysed variables; *MI* is the mutual information in pairs of variables; *R* is the coefficient of redundancy of the factors with respect to the compounds (predictive capacity); *R_max* is the maximum redundancy; %*R* is the rounding between redundancy and maximum redundancy.
[a]indicates the lower number of JE (glass bottle shares more information with DMP).
[b]indicates the highest value of MI (packaging depends more on DMP than origin and gas).
[c]indicates the highest value of %*R* (predictive capacity of glass bottle with respect to DMP 'highest dependency').
Source: Self-made.

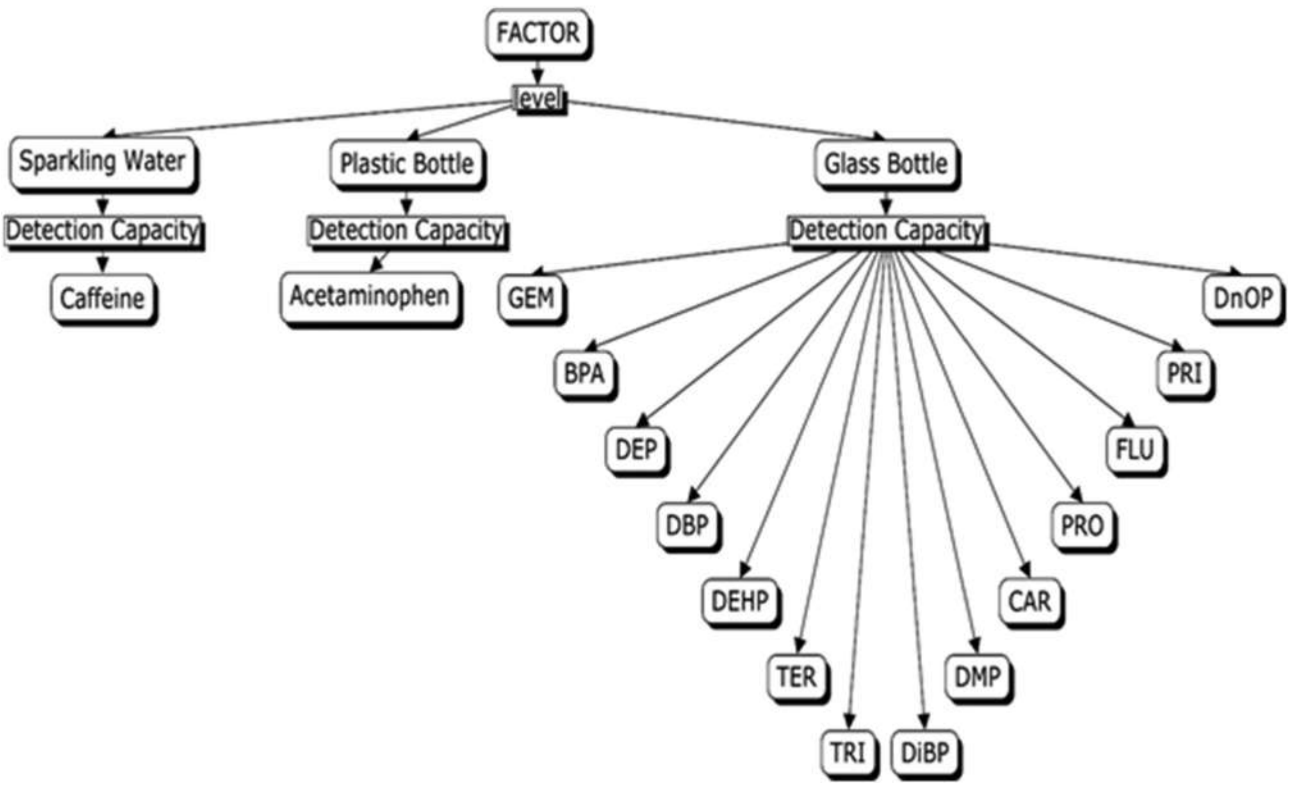

FIGURE 2 Relevant factors for endocrine disruptor detection according to average mutual information. BPA, bisphenol A; CAR, carbamazepine; DBP, di-*n*-butylphthalate; DEHP, bis(2-ethyl-hexyl) phthalate; DEP, diethylphthalate; DiBP, diisobutylphthalate; DMP, dimethylphthalate; DnOP, di-*n*-octylphthalate; FLU, fluoxetine HCl; GEM, gemfibrozil; PRI, primidone; PRO, progesterone; TER, 4-*tert*-octylphenol; TRI, triclosan

The Kruskal–Wallis test in carbonated water samples indicates that the dimethylphthalate (DMP) concentrations in carbonated waters with glass and plastic containers were significantly different (p-value = 0.012) from the other evaluated combinations. Furthermore, the caffeine concentrations in still waters with glass and plastic containers were significantly different (p-value = 0.0168).

Additionally, a multivariate Kruskal–Wallis test indicated significant differences between plasticizer concentrations according to the origin (p-value = 0.005) and gas (p-value = 0.086). The concentrations of drugs and hormones in still waters showed significant differences according to their origin (p-value = 0.035). Similarly, the plasticizer concentrations in international samples with gas were significantly different from those without gas (p-value = 0.0428).

Table 4 indicates the values of entropy, mutual information and redundancy for DMP. We repeated the AMI calculation for each compound and observed that the concentrations of 14 of the 16 EDs showed greater dependence on glass containers than on plastic containers. On the other hand, the predictive ability to find acetaminophen was high when the water was packaged in plastic, with medium dependence and low uncertainty. Furthermore, only caffeine was predicted to be detected in carbonated waters, with high dependence and medium uncertainty (Figure 2).

Figure 3 shows the DMP decision tree composed of nine rectangles called nodes. At each node top, a number (1–9) indicates the order of importance (1 = the most important 'root node'; 9 = least important). Within each node, three lines are indicated: (I) The top line indicates the response variable 'low or not detected'; (II) the node middle line indicates the fraction detected on the right and not detected on the left; and (III) the node bottom line indicates the percentage of the 173 analysed samples in each node. In addition, under each rectangle, the factor (packaging, gas and origin) and classification (plastic or glass, sparkling or still water, and international or Colombian origin) are shown; YES on the left side indicates compliance with those classifications, and NO on the right side indicates noncompliance with those certain classifications. Thus, the shortest path of the decision tree (red line) infers that when a water sample is not packed in plastic or is in a glass container (Node 1) and has gas (Node 3), possibly low concentrations of DMP are present (Node 6); hence, the origin is not an influencing factor to detect DMP (hidden rule).

Decision models were developed for each compound. For example, diisobutylphthalate (DiBP) was detected in low concentrations when the bottled water was of international origin and did not contain gas, and DEHP was detected at high concentrations when the water was packaged in glass and did not contain gas. The classification as low and high concentrations was made according to the MCL: If a concentration exceeded this safety factor, it was considered high (adverse to human health); otherwise, it was considered low (no risk).

From the regression tree for DMP error in the main node of 924×10^{-6} (Figure 4), two rules can be observed where the mean

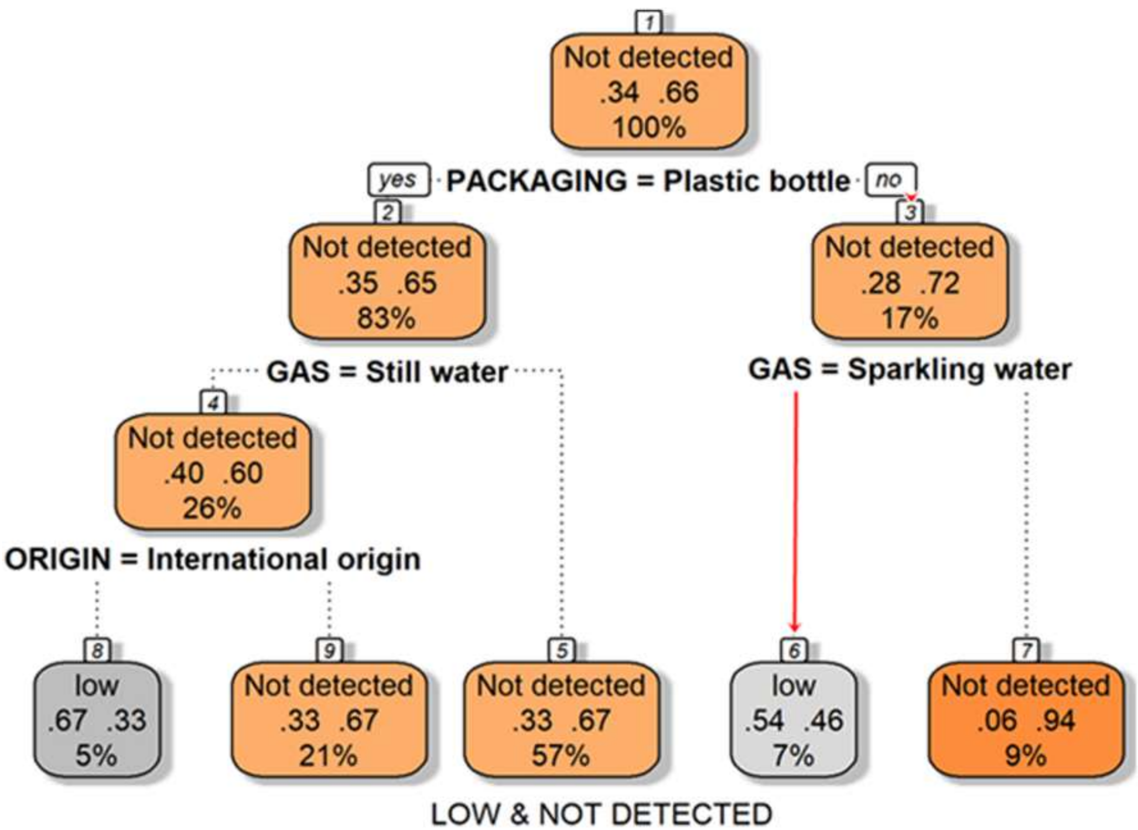

FIGURE 3 Decision tree of dimethylphthalate

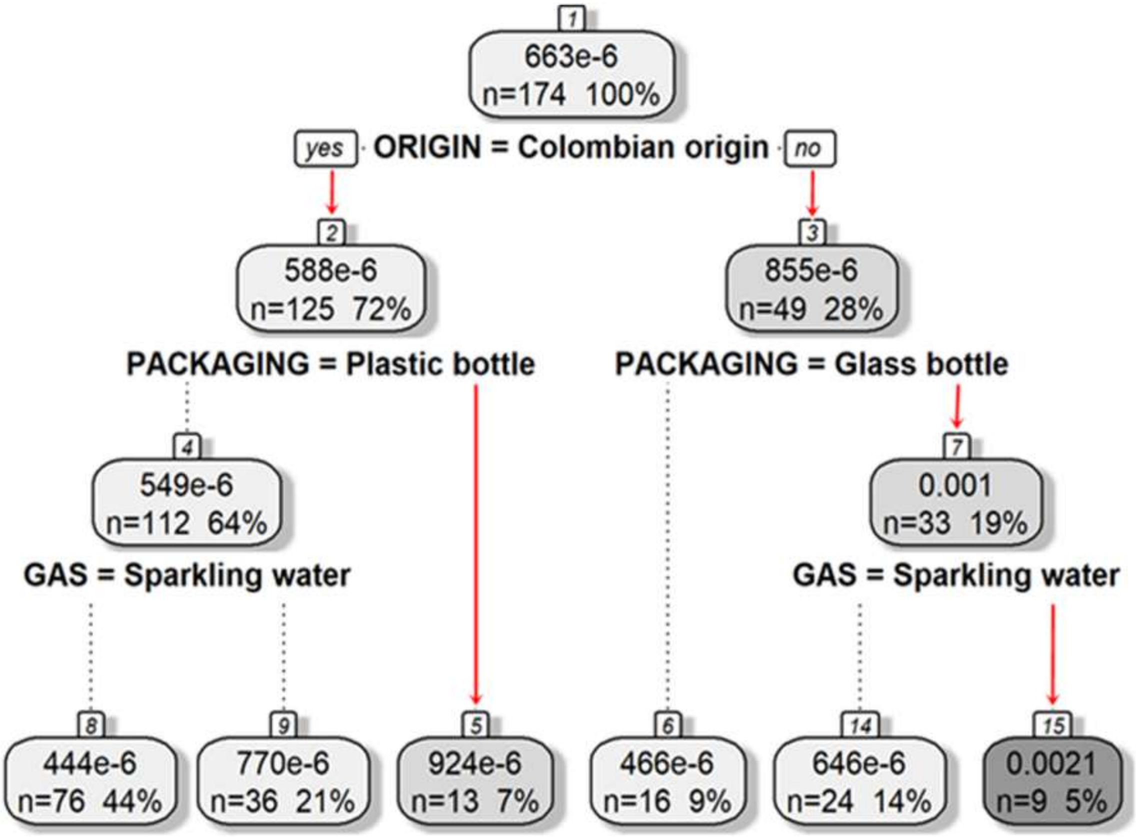

FIGURE 4 Regression tree of dimethylphthalate

concentration of the data matrix is exceeded: (i) When the water was of Colombian origin and packaged in glass (5th rectangle), relatively similar concentrations to the mean of the main node of the tree were quantified ($924 \times 10^{-6} > 663 \times 10^{-6}$); (ii) when the water was of international origin, packaged in plastic and contained no gas (15th rectangle), the predicted concentrations were much larger than those in the main node ($0.0021 >> 663 \times 10^{-6}$), which highlights that although this concentration was much higher than those generally within the average concentration of water samples, it did not represent a risk to human health due to the MCL. This procedure was repeated for each compound: Figure 5 summarizes the most important results in the ED quantification.

In summary, high concentrations of di-*n*-octylphthalate (DnOP) and DEHP are found when the bottled water is of international origin and is carbonated. Meanwhile, high CAR concentrations can be found when the water is of Colombian origin. For the remaining ED, similar concentrations to the mean of the data matrix can be detected regardless of the combination of the three factors.

From the random forest models, Table 5 indicates the importance of the factors for DMP. Figure 6 summarizes the obtained results with all constructed random forest models. The compound concentration depends on the type of container, which highlights that the out-of-bag (OOB) error estimated from each random forest is indicated in each cell.

Finally, regarding the XGBoots algorithm, Figure 7 describes the compounds that are most influenced by the packaging, origin or gas factors. The gas factor is more important for the quantification of four compounds than the origin and container type.

We compared the concentrations obtained at the monitoring points of the Chingaza, Tibitoc and Zumapaz reservoirs that supply drinking water in Bogotá. Figure 8 indicates the maximum ED concentrations in both bottled water and drinking water distributed in the city, which indicates excessively high DEHP concentrations in drinking water and high risks to human health, including low development of the reproductive system and DNA damage (Cooper et al., 2011).

4 | DISCUSSION

First, the percentage of EDs in this study was compared with those in the studies conducted in Spain and Mexico (Figure 9). The comparison shows that the samples of Colombian origin had higher ED detection frequencies. This result suggests that the regulation of these additives at the time of manufacture and processing of the packaging type played a crucial role due to the synthetic substances to give shape and flexibility to the containers. In this sense, 683 resolutions from 2012 and 12 186 from 1991 dictate that

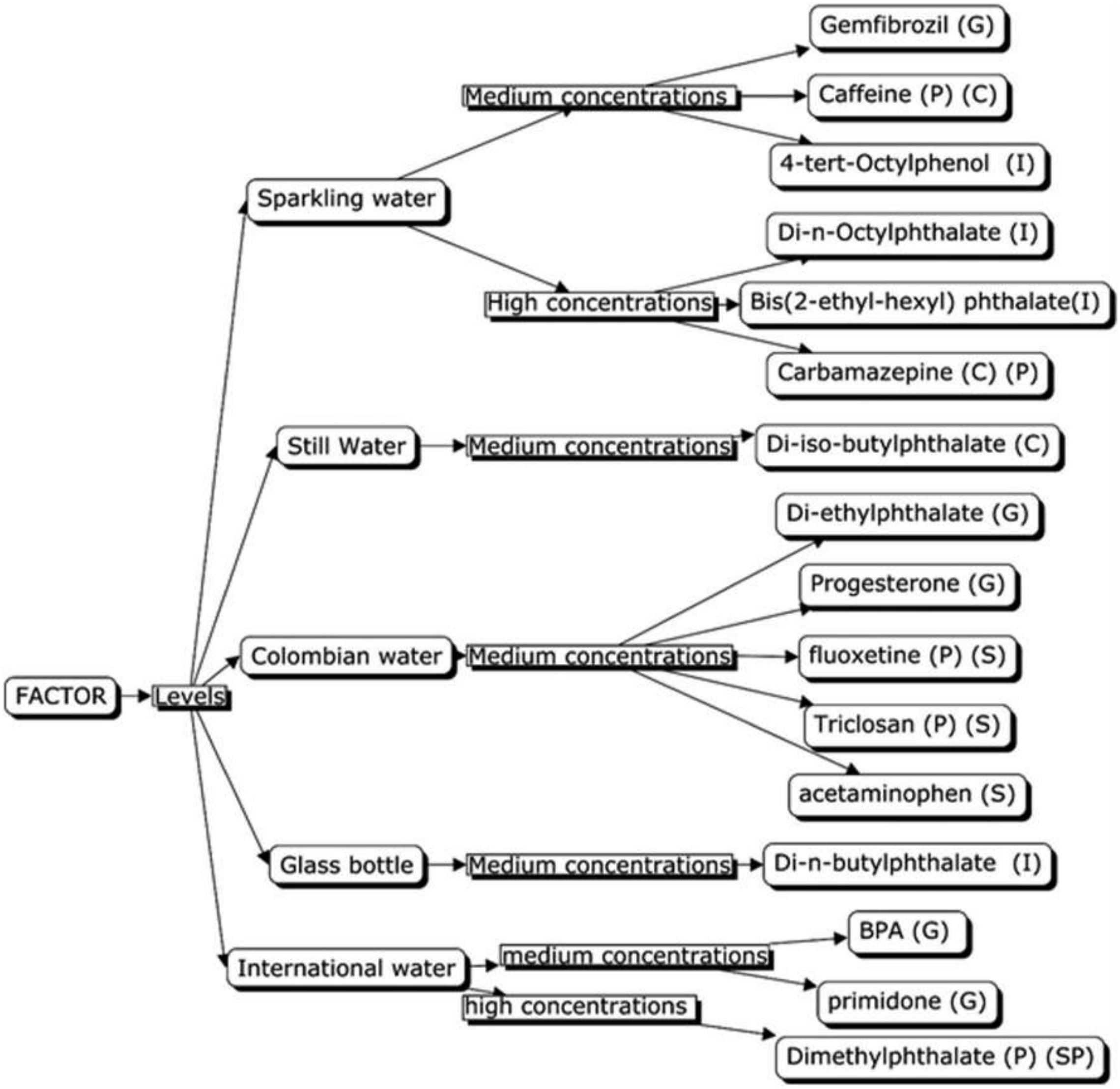

FIGURE 5 Relevant factors to quantify endocrine disruptors according to regression trees. BPA, bisphenol A; C, Colombian water; G, glass bottle; I, international water; P, plastic bottle; S, still water; SP, sparkling water

TABLE 5 Importance of detection of factors for DMP with random forest

Factor	I detected	I not detected	Mean decrease accuracy	Mean decrease Gini	Estimated OOB error
Packaging	25.616[a]	17.961	29.119	2.203[c]	
Origin	22.485	8.016	21.042[b]	2.882	17.24%
Gas	16.549	31.953	36.103	3.658	

Note: *I detected* is the importance of a factor to be detected (the largest number is the most important); *I not detected* is the importance of a factor not to be detected (the largest number is the most important); *mean decrease accuracy* is the number or proportion of observations that are incorrectly classified; *mean decrease Gini* measures the average gain of purity by divisions of the given compound (a higher value indicates a purer node); *out-of-bag (OBB) estimate* is the percentage of the sample model error defined as the average accuracy of the model in predicting the response variable (a higher percentage corresponds to a less accurate random forest).

[a]Greater number (packaging is the most important factor).

[b]Smaller number (origin has fewer incorrect proportions).

[c]Smaller number (packaging has more correctly classified observations in the main node).

Source: Self-made.

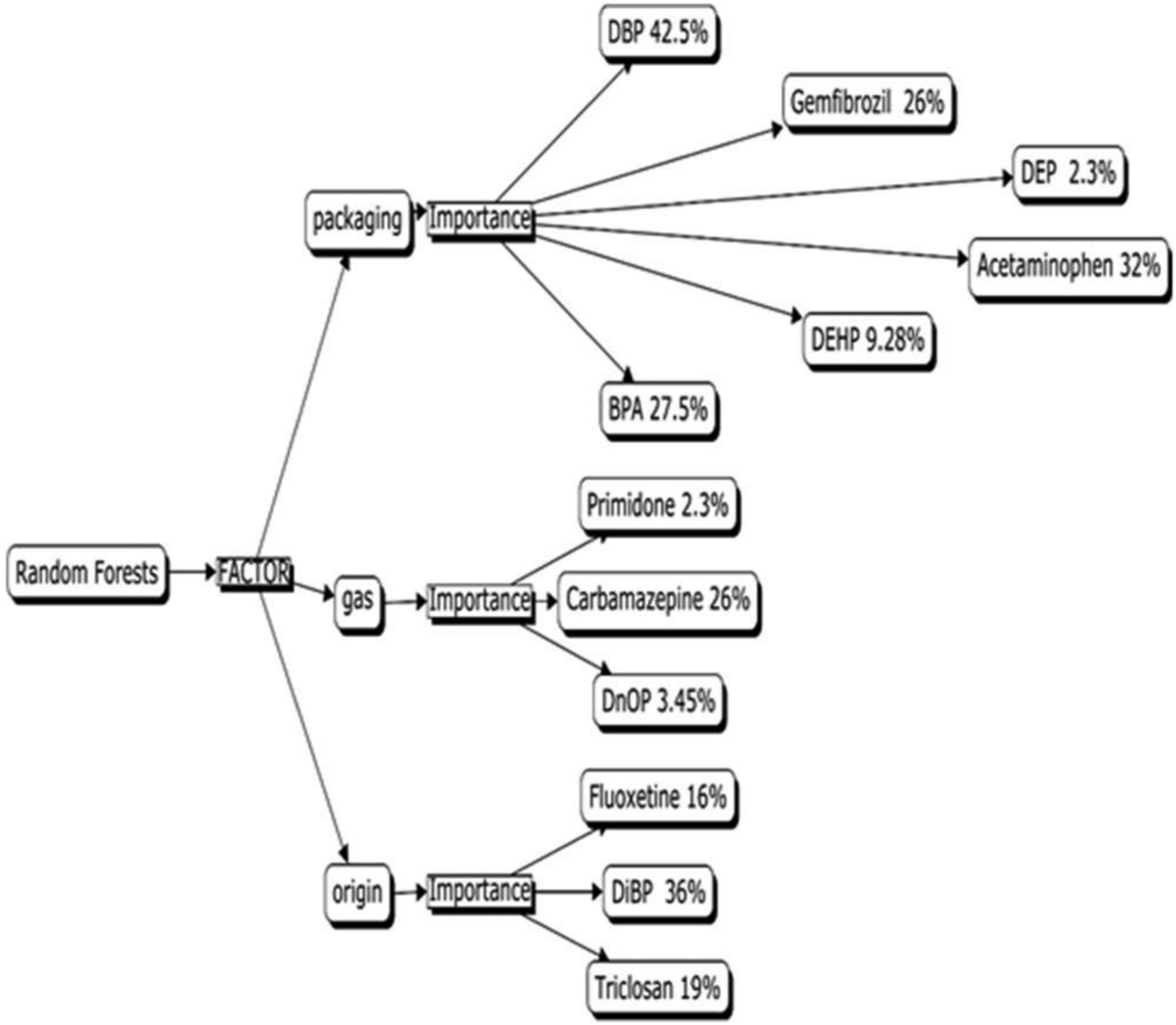

FIGURE 6 Relevant factors for the detection of endocrine disruptors according to random forest. BPA, bisphenol A; DBP, di-*n*-butylphthalate; DEHP, bis(2-ethyl-hexyl) phthalate; DEP, diethylphthalate; DiBP, diisobutylphthalate; DnOP, di-*n*-octylphthalate

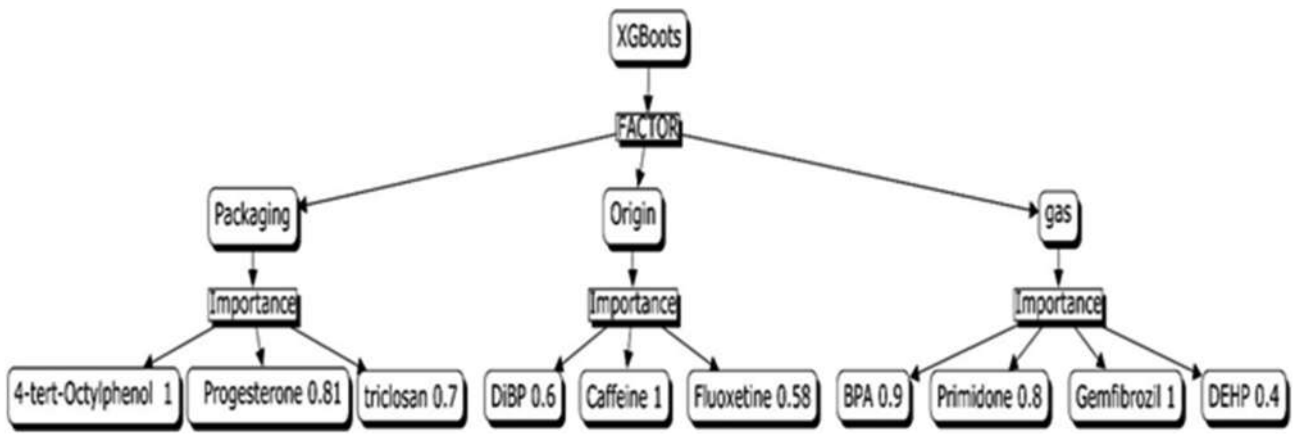

FIGURE 7 Important factors for the endocrine disruptor detection according to the XGBoots algorithm. BPA, bisphenol A; DEHP, bis(2-ethyl-hexyl) phthalate; DiBP, diisobutylphthalate

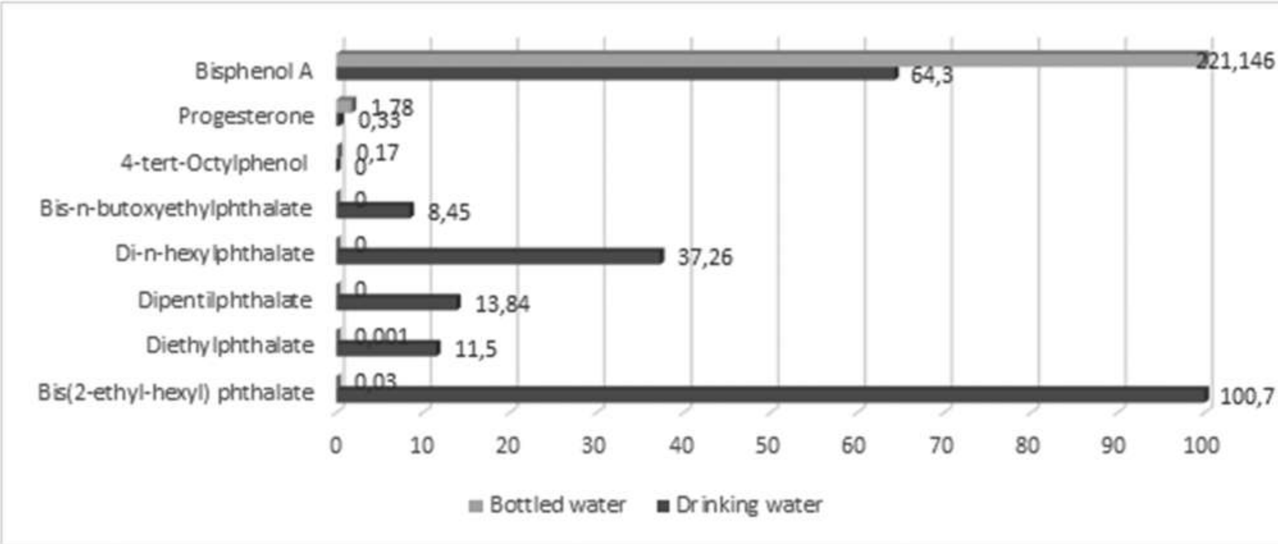

FIGURE 8 Concentrations of endocrine disruptors in drinking water distributed in Bogotá and bottled water marketed in Bogotá

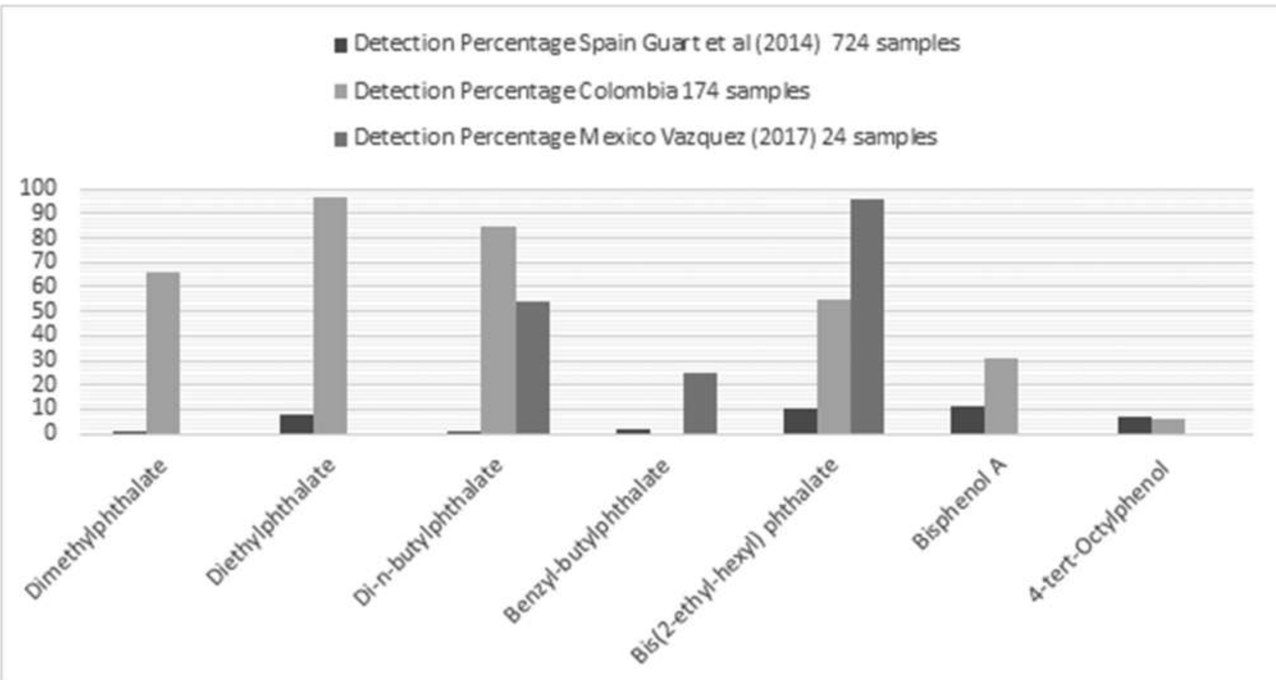

FIGURE 9 Detection percentages of endocrine disruptors in Colombia, Spain and Mexico

these substances can be controlled following specific procedures at the time of water packaging (INVIMA, 2012; Ministerio de Salud, 1991).

This refers to the fact that there is no complete certainty of the origin of EDs in bottled water (Tijani et al., 2015). A comparison of research conducted in Spain and Mexico suggests that the detection frequencies of phthalates such as dibutylphthalate, benzyl-butylphthalate and bis-2-ethyl-hexylphthalate in water of Mexican origin are higher than those in water from Spain (Guart et al., 2014; Vazquez et al., 2017). Thus, the origin of the water is an important factor in the detection of these compounds. In addition, Guart et al. (2014) indicated that carbonated water packed in glass with metal or plastic lids exhibited elevated migration of these compounds to water.

Therefore, a worrisome issue is the relatively high concentration of detected BPA because bottled water sold in Spain had much smaller values than those found in this study: The maximum BPA concentration was 221 μg/L, whereas in the Guart study, it was

24.2 μg/L. This result highlights that Colombian samples in plastic containers have lower BPA concentrations than those found in Spain, which suggest that the additives in water bottles in Colombia with concerning BPA levels could be better regulated than in other countries. These concerning BPA concentrations were due to the migration of BPA onto water as a function of an increase in temperature, where a rapid migration of BPA occurs above 80°C, but BPA can also be released into water at ambient temperatures (Goodson et al., 2004).

In this sense, the current tolerable daily intake (TDI = 50 mg/kg) established by the European Food Safety Agency (EFSA) and US EPA was conducted. The BPA concentrations represent a minimal risk according to the TDI (Cooper et al., 2011; Li et al., 2010; Nam et al., 2010; Wagner & Oehlmann, 2011).

Second, regarding the quantification of these results, international carbonated water had higher BPA concentrations than Colombian still water; these concentrations were relatively high with respect to the mean concentrations of the 173 analysed water samples. However, these concentrations did not imply a risk according to the MCL for human health.

Regarding the influencing factors, the compared studies were divided into detecting some phthalates and compounds such as 4-*tert*-octylphenol and relating their detection to the type and form of packaging, presence of carbonation and storage time. These methods represent a great danger due to their oestrogen properties and persistence in the environment (ALOthman et al., 2019). For example, Guart et al. (2014) observed that neither the shape of the container nor the storage time affected the quality of the water, and only carbonated water could slightly increase the migration processes, which was consistent with the concentrations in the carbonated water analysed in this research (generally, these concentrations are related to the type of monomer or plastic in the manufacture of the container). Moreover, only water packed in glass with metal or plastic lids showed a significant increase in ED concentrations. Hence, a combination of carbonated water packed in glass with any lid may contain higher concentrations of EDs than other combinations of explanatory factors, such as PET bottles with a high-density polyethylene lid (used throughout the world), which have low levels of plasticizers.

5 | CONCLUSIONS

- The main factors that increase the predictive ability of major ED detection are glass containers and carbonated waters with medium dependence and low uncertainty. Thus, water from any source bottled in plastic and without gas can contain fewer EDs and present less risk for individuals.
- Bottled water distributed in Colombia has higher ED concentrations than bottled water distributed in Spain and Mexico; however, the detection frequency is lower than that of international water samples. Furthermore, the analysed samples represent a minimal risk to human health according to the MCL evaluated.
- Still water of Colombian origin and bottled in plastic bottles was a statistically safer combination of factors than other existing combinations, as it suggested a lower presence and concentration of EDs than other combinations to represent the lowest possible risk when people drink water with this kind of explanatory factor combination.
- The concentrations of low-molecular-weight phthalates statistically differed from those of high-molecular-weight phthalates; whereas high-molecular-weight phthalates in water are associated with gas and glass packaging factors, the others are associated only with glass and water origin. Therefore, the compound structure contributes to its association with an influencing factor in the bottle manufacturing process and therefore its presence.

6 | RECOMMENDATIONS

1. The association of acetaminophen with plastic containers should be studied with a focus on toxicology, medicine and wastewater issues, where the water cycle can determine the paths by which acetaminophen enters bottled water.
2. Similarly, the associations of caffeine with carbonation and bottled water should be studied, in addition to whether its association differs from that of caffeine concentrations in soft drinks, tea, juices and so forth.

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DATA AVAILABILITY STATEMENT

I declare that all the data used in the research will be available and without access restrictions.

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