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A multi-residue method for determining twenty-four endocrine disrupting chemicals in vegetables and fruits using ultrasound-assisted solid–liquid extraction and continuous solid-phase extraction

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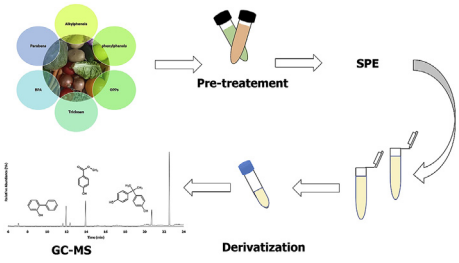
HIGHLIGHTS

- Monitoring of 24 endocrine disrupting chemicals (EDCs) in fruit and vegetables samples is proposed.
- This approach is an effective tool to analyse different classes of EDCs in fruits and vegetables.
- Sample treatment is optimized using a multivariate optimization strategy.
- Most of the 19 samples analyzed contain some of the EDCs studied.
- The levels of EDCs found in the samples vary between 5.8 and 580 ng kg^{-1}.

GRAPHICAL ABSTRACT



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ABSTRACT

In this work, we developed an analytical approach using an ultrasound-assisted extraction (UAE) followed by continuous solid-phase extraction (SPE) and gas chromatography–mass spectrometry (GC–MS) detection in order to determine simultaneously 24 endocrine disrupting chemicals such as alkylphenols, organophosphorus pesticides, parabens, phenylphenols, triclosan and bisphenol A in vegetable and fruit samples. Different variables influencing UAE and SPE performance were optimized in order to maximize removal of the sample matrix and preconcentration of the analytes. The optimized extraction and GC–MS quantitation conditions provided acceptable sensitivity, selectivity, accuracy and precision. Limits of detection spanned the range 0.6–25 ng kg^{-1}, recoveries were near-quantitative and relative standard deviations ranged from 4.5 to 7.6%. The proposed method was used to analyse 11 vegetable samples and 7 fruit samples purchased at various Spanish and Moroccan supermarkets. Most samples contained more than three of the analytes, at levels between 5.8 and 580 ng kg^{-1}.

1. Introduction

Endocrine disrupters are extraneous natural or man-made chemicals that can alter the functioning of the endocrine system and have deleterious impact on human health as a result

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(Diamanti-Kandarakis et al., 2009). Endocrine disrupting chemicals (EDCs) comprise a broad range of contaminants including natural compounds such as phyto-estrogens present in a wide variety of plants [e.g., soybean genistein, mycotoxins such as zearalenone] and synthetic substances such as polychlorinated and polybrominated biphenyls, dioxins, bisphenol A, alkylphenols, parabens, pesticides, fungicides, phthalates and various pharmaceuticals interfering with the endocrine system (Grzeskowiak et al., 2016). The effects of EDCs and their mechanisms of action have been extensively studied (Lauretta et al., 2019). EDC exposure is often behind corticoid and/or thyroid dysfunction, and also behind adverse effects on the reproductive and neurological systems (Gore et al., 2015; Jagne et al., 2016). EDC-induced reproductive alterations namely cancer in breast and ovarian, early menopause, ovarian cysts, endometriosis in female, tumors in prostate or testicles, sexual organ failure and reduced male fertility (Kabir et al., 2015). EDCs are rather ubiquitous as a result of some processing methods using certain products to preserve the nutritional and sensory quality of foods that ultimately become harmful to human health (Ravichandran et al., 2019). For example, Lu et al. (2013) found bisphenol A (BPA), nonylphenol and 17-β-estradiol at concentrations from 0.2 to 18.5 μg kg^{-1} in fruits and vegetables from the USA. Also, Song et al. (2017)found parabens in 50 fresh-cut vegetable samples from different farmer markets in Beijing (China), and Dos Santos et al. (2019) identified organophosphorus pesticides in lettuce, carrot, tomato, collard greens, strawberry and green pepper from Brazil. There are varied sources of EDCs in fruits and vegetables could be owing to naturally occurring contaminants in the environment or introduced artificially through human activity. As well as the various stages of processing, packaging, transport and storage of fruits and vegetables are also important factors in the contamination of fruits and vegetables (Rather et al., 2017).

Determining EDCs in foods often requires extensive sample preparation, which is the bottleneck of the process. The preparation stage typically includes sample pretreatment, extraction, clean-up, concentration and —occasionally— some derivatization reaction (Grzeskowiak et al., 2016) or a special treatment of the matrix depending on its composition. Liquid–liquid extraction (Blasco et al., 2002), matrix solid-phase dispersion (Albero et al., 2017), QuEChERS (Andraščíková et al., 2013; Huskova et al., 2009; Rai et al., 2016) and acid hydrolysis (Lu et al., 2012, 2013) have been used to extract various types of EDCs from fruits and vegetables. Some authors have used ultrasound to facilitate the process (Bidari et al., 2011; Albero et al., 2017, 2014; Mijangos et al., 2015; Ravelo-Pérez et al., 2009; Tadeo et al., 2010). Thus, Dos Santos et al. (2019) used ultrasound-assisted matrix solid-phase dispersion to successfully extract various pesticide classes from fruits and vegetables with good precision.

EDC extracts from vegetable and fruit samples frequently require clean-up to avoid interferences from compounds co-extracted alongside the target analytes. Solid-phase extraction (SPE) with a suitable sorbent is often used for this purpose. For example, Oasis-HLB was used to isolate bisphenol A from the aqueous portion of canned fruits and vegetables (Yoshida et al., 2001). Also, Strata NH_2 was used to clean up extracts from fruit and vegetable samples for the determination of bisphenol A and various parabens (Liao et al., 2013a,b; Liao and Kannan, 2013), and magnetic molecularly imprinted polymer was used to extract parabens from fruit juices (You et al., 2016). EDC extracts from vegetable and fruit samples have also been purified by using dispersive liquid–liquid microextraction (Andraščíková et al., 2013; Rai et al., 2016; Ravelo-Pérez et al., 2009), solid-phase microextraction (Blasco et al., 2003), magnetic solid-phase microextraction (Viñas et al., 2016) and dispersive solid-phase extraction (Aparicio et al., 2018; Mijangos et al., 2015; Satphaty et al., 2011).

Most analytical methods for determining EDCs in foods such as fruits and vegetables are based on the combination of gas chromatography with a sensitive, specific detection technique such as mass spectrometry (GC–MS) (Andraščíková et al., 2013; Dos Santos et al., 2019; Lu et al., 2012; Rai et al., 2016; Yang and Ding, 2005), tandem mass spectrometry (GC– MS/MS) (Albero et al., 2017; Lu et al., 2013) or quadrupole-time of flight mass spectrometry (Cheng et al., 2017). Liquid chromatography in combination with fluorescence (Saad et al., 2004), ultraviolet (You et al., 2016), mass spectrometry (Blasco et al., 2002) or tandem mass spectrometry detection (Mijangos et al., 2015; Aparicio et al., 2018; Montiel-León et al., 2019; Song et al., 2017) has also been used for this purpose.

In this work, we developed a sensitive, expeditious multi-residue methodology for the quantitation of 24 EDCs including alkylphenols, BPA, phenylphenols, parabens, organophosphorus pesticides and triclosan in various types of vegetables and fruit matrices. Removal of the complex sample matrix was maximized by using an efficient, environmentally friendly closed-circuit pretreatment that requires minimal volumes of organic solvents. The method extracts the analytes by ultrasound-assisted extraction (UAE) of the sample and subsequent continuous SPE and microwave-assisted derivatization for their subsequent determination by GC–MS. The target analytes were bisphenol A, two alkylphenols (nonylphenol and 4-*tert*-octylphenol), two phenylphenols (*o*-phenylphenol and *p*-phenylphenol), seven parabens (methylparaben, propylparaben, ethylparaben, butylparaben, isopropylparaben, isobutylparaben and benzylparaben), eleven organophosphorus pesticides (bromophos-methyl, chloropyrifos, dichlorovos, dimethoate, diazinon, fenthion, fenthion sulphoxide, parathion-methyl, parathion-ethyl, malathion and methidathion) and one personal care product (triclosan). After validation, the strategy was employed to quantify the EDC contents of eleven vegetable and seven fruit matrices from Spain and Morocco.

2. Experimental

2.1. Standards and reagents

Standards of the 24 EDCs (viz., BPA, 4-*tert*-octylphenol, nonylphenol, *o*-phenylphenol, *p*-phenylphenol, methylparaben, ethylparaben, propylparaben, butylparaben, isopropylparaben, isobutylparaben, benzylparaben, triclosan, bromophos-methyl, chloropyrifos, dichlorovos, dimethoate, diazinon, fenthion, fenthion sulphoxide, parathion-methyl, parathion-ethyl, malathion and methidathion) and triphenylphosphate (internal standard, IS) were purchased from Sigma–Aldrich (St. Louis, MO, USA) with purity >98.0%. A standard mixture of target compounds (1 g L^{-1}) in methanol, and working standard solutions with a 100 mg L^{-1} concentration each, were prepared and stored in amber glass bottles at −20 °C prior to use.

HPLC-grade acetone, acetonitrile, methanol, dichloromethane, 2-propanol, ethyl acetate, ethanol and hexane were obtained from Merck Corporation (Darmstadt, Germany). The polymeric adsorbents LiChrolut EN (particle size: 40–120 μm) and Oasis-HLB (particle size: 50–65 μm) were supplied by Waters (Milford, USA) and Merck, respectively. The other sorbents [RP-C18 (particle size: 40–63 μm), Florisil (particle size: 16–30 μm), Silica Gel (particle size: 15–35 μm), Amberlite XAD-4 (particle size: 20–60 μm) and Amberlite XAD-2 (particle size: 20–60 μm)] were obtained from Sigma–Aldrich. The silylating reagents, trimethylchlorosilane (TMCS) and *N,O-bis*(trimethylsilyl)trifluoroacetamide (BSTFA) were obtained from Fluka (St. Louis, MO, USA). Hydrophilic Millex-LG PTFE filtering units (pore size: 0.20 μm; diameter: 25 mm; filtration area: 3.9 cm^2) were purchased from Millipore (Bedford, MA,

USA). Finally, ultra-pure water was obtained from a Milli-Q system from Millipore.

2.2. Instruments and apparatus

GC–MS analyses were done on a Focus GC instrument coupled to a DSQ II quadrupole mass spectrometer and checked via a computer operating the software XCalibur (Thermo Electron SA, Barcelona, Spain). The GC column installed was a 30 m × 250 μm i. d. DB-5MS capillary column of 0.25 μm film thickness from J & W (Folson, CA, USA). Helium (purity 99.9999%) at a flow rate of 1 mL min^{-1} was used as the carrier gas. The oven temperature was programmed as follows: 70 °C, held for 1 min, ramped to 150 °C at 14 °C min^{-1} ramp to 150 °C, ramped to 215 °C at 6 °C min^{-1}, and ramped to 285 °C at 10 °C min^{-1}. The injector, ion source and transfer line temperature were 285, 200 and 280 °C respectively. The time for solvent delay was fixed at 8 min. The selected ion monitoring mode (SIM) (ionization energy, 70 eV) was employed to quantify the target compounds. The mass ranging between 60 and 400 amu was used for full scan detection. Each silyl derivative was monitored for $M^{\bullet+}$, [$M-15$] and various additional ions (Table 1), where $M^{\bullet+}$ is the molecular mass and [$M-15$] that involving to the loss of a $CH_3^{\bullet}$ radical from the Si $(CH_3)_3$ group.

The continuous SPE system (Fig. 1S) consisted of a Gilson Minipuls-3 peristaltic pump (Villiers-le-Bel, France) equipped with poly(vinyl chloride) tubes, two Rheodyne 5041 injection valves (Cotati, CA, USA), and PTFE laboratory-made columns of variable length and 3 mm i. d. packed with each sorbent material. Sudden modifications in column compactness upon soaking of the LiChrolut EN or Oasis HLB adsorbent were avoided by placing a segment ca. 0.5 cm long of an inert material (PTFE beads) between successive 1.0 cm long segments of sorbent. The adsorbent columns were conditioned by passing 1 mL of acetonitrile and then 1 mL of deionized water. In these circumstances, they are still useful with no appreciable change in their properties for at least 1–2 months (~100 extractions).

2.3. Sample collection and storage

Eleven fresh vegetables (potato, onion, garlic, tomato, carrot, zucchini, eggplant, lettuce, pepper, white turnip, cucumber) and seven fresh fruits (banana, apple, pear, kiwi, orange, mandarin orange and lemon) were purchased from different supermarkets in Spain and Morocco. The samples were kept at 4 °C until preparation and analysis, which were done within 3 days after purchase. All samples were analyzed unwashed and with an intact peel. A 250 g portion of each vegetable or fruit sample was chopped into small pieces and after a homogenization step in an A320R1 grinder from Moulinex (Barcelona, Spain) immediately before the extraction.

2.4. Sample preparation

Fig. 1 depicts the principal stages of the sample preparation procedure. In the first, an amount of 2 g of vegetable or fruit sample was introduced into a 15 mL polypropylene conical tube and supplied with six mL of acetonitrile. After that, the homogenized sample was processed by ultrasound-assisted extraction (UAE) at 200 W during 10 min. This was followed by centrifugation at 4 °C at 4500 rpm on a JP Selecta Centrofiger BL-II apparatus during 10 min. The resulting supernatant was filtered into a hydrophilic Millex-LG PTFE filter (diameter = 25 mm, pore size = 0.20 μm, and filtration area = 3.9 cm^2) and cautiously evaporated to near-dryness (~200 μL) under a gentle stream of nitrogen. Each UAE extract was reconstituted with 10 mL of ultra-pure water and adjusted to

Table 1
Analytical figures of the proposed method for the determination of 24 EDC in vegetable and fruit samples.

EDCs	Analytes	r[a]	Linear range (ng kg^{-1})	LOD[b] (ng kg^{-1})	RSD (%)[c]		t_R[d] (min)	*m/z*[e]		
					Intra-day	Inter-day		$[M]^{+\cdot}$	$[M-15]^{+}$.[b]	Additional ion(s)[c]
Organophosphorus pesticides	Dichlorvos	0.995	35–2000	10	6.5	7.5	7.06	220	-[f]	**109**, 145, 185
	Dimethoate	0.993	32–2000	10	5.2	6.3	13.80	229	-[f]	87, 93, **125**,143
	Diazinon	0.997	50–2000	15	5.9	7.2	14.73	304	-[f]	137, **179**, 199
	Parathion methyl	0.996	85–2000	25	5.4	6.7	16.39	**263**	-[f]	109, 200
	Malathion	0.998	40–2000	12	5.2	6.6	17.27	332	-[f]	93, 125, 158, **173**
	Parathion ethyl	0.993	85–2000	25	6.5	7.6	17.41	**291**	-[f]	125, 137, 186, 234
	Chloropyrifos	0.996	21–2000	7.0	5.3	6.2	17.54	349	-[f]	199, 258, 286, **314**
	Fenthion	0.993	35–2000	10	6.0	7.3	17.82	**278**	-[f]	109, 125, 169
	Bromophos methyl	0.992	65–2000	20	5.9	7.1	18.28	366	-[f]	109, 125, 213, **331**
	Methidathion	0.994	65–2000	20	6.0	7.4	19.48	302	-[f]	85, 125, **145**
	Fenthion sulfoxide	0.995	35–2000	10	5.5	6.3	21.19	294	-[f]	125,169, **279**
Parabens	Methylparaben	0.999	15–2000	4.5	5.0	6.5	10.11	224	**209**	135,149,177, 193
	Ethylparaben	0.997	16–2000	4.6	4.5	5.8	11.22	238	**223**	135, 151, 193
	Isopropylparaben	0.999	10–2000	3.0	4.4	6.0	11.63	252	237	151, **193**, 195, 210
	Propylparaben	0.998	15–2000	4.5	4.8	6.1	12.69	252	237	**193**, 195, 210
	Isobutylparaben	0.996	10–2000	3.0	5.5	6.5	13.48	266	251	151, **193**, 195, 210
	Butylparaben	0.999	15–2000	4.9	4.8	5.8	14.22	266	251	193, 195, **210**
	Benzylparaben	0.999	16–2000	5.0	4.6	5.7	20.32	300	285	91, **193**, 255
Phenylphenols	2-Phenylphenol	0.998	2.1–2000	0.7	5.0	6.1	11.96	242	**227**	105, 152, 211
	4-Phenylphenol	0.996	2.0–2000	0.6	5.3	6.5	14.40	**242**	227	113,152, 207, 211
Alkylphenols	4-*tert*-Octylphenol	0.997	2.0–2000	0.6	4.6	5.9	12.33	278	263	151, 191, **207**
	Nonylphenol	0.994	2.1–2000	0.7	5.0	6.5	13.99	292	277	179, **207**, 221, 263
Others	Bisphenol A	0.995	3.0–2000	0.9	4.3	5.5	20.73	372	**357**	207, 285
	Triclosan	0.998	3.5–2000	1.0	4.8	6.0	19.76	362	**347**	200, 310

[a] r, correlation coefficient (r^2).
[b] LOD, limit of detection.
[c] RSD, relative standard deviation. Values obtained for samples fortified with 150 ng kg^{-1} of each EDCs.
[d] t_R, retention time.
[e] The peaks used for quantification are boldfaced; *m/z* for IS (triphenylphosphate): 77, 170, 325, **326** (t_R: 22.53 min).
[f] Analyte non derivatized.

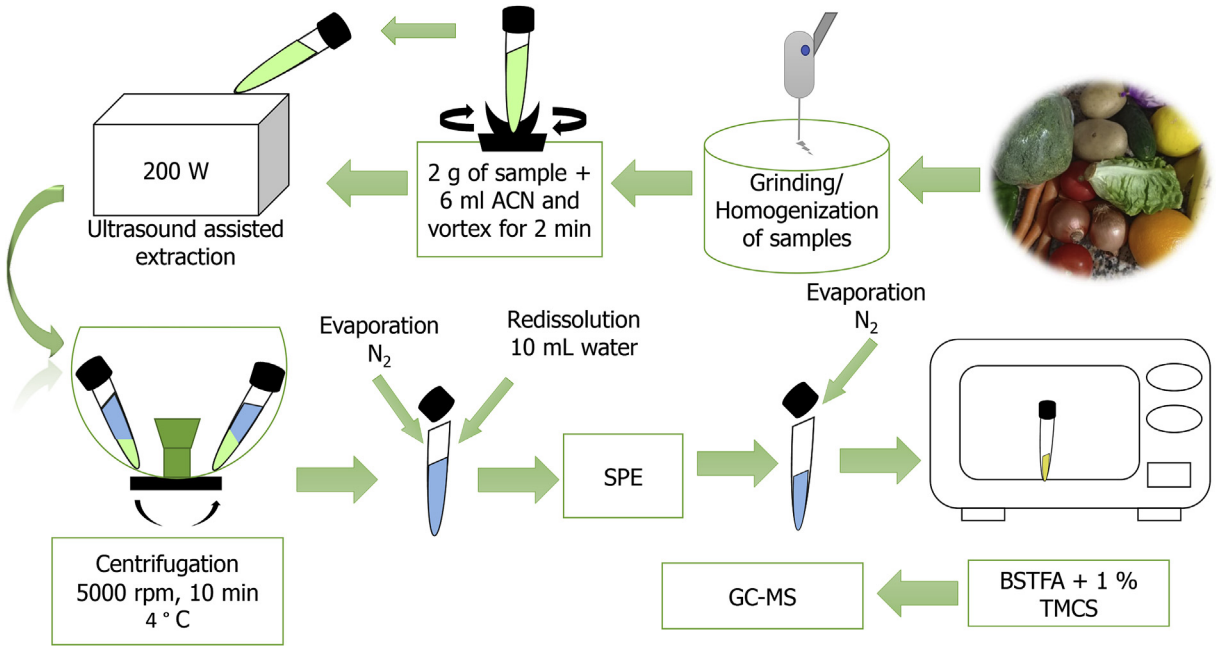

Fig. 1. Sample treatment for the clean-up and preconcentration of EDCs in vegetable and fruit samples. ACN acetonitrile; BSTFA N,O-bis(trimethylsilyl)trifluoroacetamide; GC–MS gas chromatography–mass spectrometry; SPE solid-phase extraction; TMCS trimethylchlorosilane.

pH 4 with dilute HCl or NaOH as required.

Redissolved extracts were subjected to continuous SPE (Fig. 1S) by passing at a flow rate of 4 mL min^{-1} through the SPE column (80 mg of LiChrolut EN, located in the loop of IV_1). In this step EDCs were thus retained on the sorbent surface while the sample matrix was shipped to the residues (Azzouz and Ballesteros, 2012). Any residual water remaining inside the sorbent column and the connectors was eliminated by passing an air stream at 4 mL min^{-1}. After which valve IV_2 was switched to pass 400 μL of the eluent carrier (acetonitrile containing 500 μg L^{-1} triphenylphosphate as IS). Organic extracts were manually collected in air-tight 0.5 mL conical glass inserts and evaporated to ~25 μL under a gentle flow of N_2. Potential errors in measuring final extract volumes were prevented by employing the IS. After that, 70 μL of a BSTFA +1% TMCS mixture was manually added and the vials were hermetically sealed for placement in a household microwave oven where the target compounds were derivatized at 350 W during 3 min (Azzouz et al., 2019).

3. Results and discussion

3.1. Optimization of sample preparation step

In a recent article, we elaborated an approach to identify 24 different compounds in fish and seafood (Azzouz et al., 2019). In this work, we optimized the variables influencing variables of the SPE clean-up procedure including type and amount of sorbent, volume of eluent, pH, nature of the solvent and factors governing the microwave-assisted derivatization (silylation) of EDCs including reaction time, microwave power and the proportion of TMCS in BSTFA.

The conditions of the sample treatment preceding continuous SPE required re-optimization as the samples (fruits and vegetables) were rather different in nature from those of the previous work (fish and seafood). Thus, fruits and vegetables contain water and carbohydrates in quite significant quantities, while the content of proteins and other nutrients is lower. Most of these sample components can produce a strong impact on EDC extraction and determination and require efficient removal prior to insertion of the samples in a clean-up system for their subsequent analysis by GC–MS.

3.2. Variables influencing sample pretreatment

The UAE technique has been increasingly used to prepare environmental and food samples for analysis in recent years. Thus, UAE has been used with a number of contaminants including pesticides, pharmaceuticals and polycyclic aromatic hydrocarbons (PAHs). This is in fact an efficient, environmentally friendly technique by virtue of its using smaller solvent volumes and shorter extraction times than classical extraction procedures (Tadeo et al., 2010). These advantages led us to choose it for sample preparation here.

Based on previous reports, UAE performance is influenced mainly by the polarity and volume of the organic solvent, and the extraction time. We assayed eight different solvents (viz., acetone, ethanol, *n*-hexane, 2-propanol, dichloromethane, acetonitrile, ethyl acetate and methanol) to identify the most suitable choice for extracting EDCs from vegetable and fruit samples. For this purpose, a 500 ng kg^{-1} concentration of each target EDC was added to an amount of 2 g of each vegetable (potato, onion, garlic, tomato, carrot, zucchini, eggplant, lettuce, pepper, white turnip, cucumber) or fruit sample (banana, apple, pear, kiwi, orange, mandarin orange and lemon). And then, the mixture was mixed with 1 mL of each solvent for sonication at 200 W during 15 min. The supernatant was centrifuged and processed as described in Section 2.4. Acetonitrile was found to provide the highest extraction efficiency —up to 1.5 times higher than the other solvents—, so it was selected for further testing. This solvent was previously used for the ultrasound-assisted extraction of pesticides from bananas (Ravelo-Pérez et al., 2009), but Mijangos et al. (2015) chose to use an acetone/*n*-hexane mixture to extract EDCs from carrots and lettuces, achieving similar results in the efficiency of the extraction of the analytes than those obtained with acetonitrile.

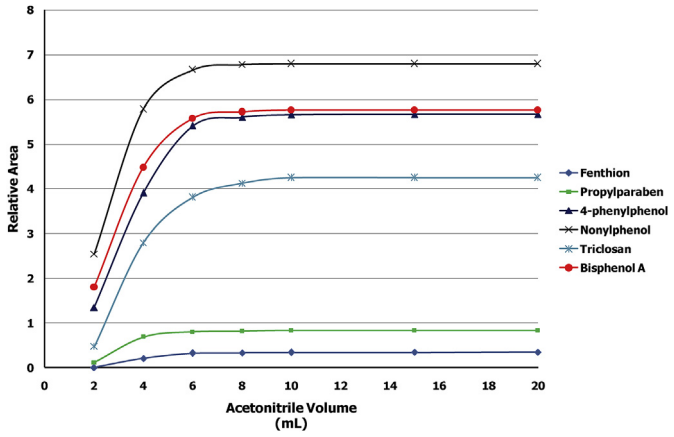

Fig. 2. Influence of the acetonitrile volume on the extraction of six representative compounds from the different EDC families present in vegetable and fruit samples.

Other UAE variables such as solvent volume and extraction time were also considered. Tests with 2–20 mL of extractant revealed that for a solvent volume ≥5 mL the extraction efficiency is maximum. This led us to use 6 mL of acetonitrile for UAE of the analytes from vegetable and fruit samples (Fig. 2). Likewise, tests with sonication times of 0–30 min revealed that 8 min was long enough for efficient extraction of all analytes, so a treatment time of 10 min was selected for further testing (Fig. 3).

We also studied the effects of the variables influencing centrifugation of the UAE extracts for efficient removal of the target compounds from the sample matrix. The effect of the centrifugation rate, temperature and time were studied in the ranges between 1500 and 5000 rpm, 4 and 20 °C and 1 and 30 min, respectively. Analytical signals were observed to increase with increasing centrifugation speed up to 3500 rpm, above which they remained constant. A setting of 4500 rpm was chosen. The optimum centrifugation temperature and time were taken to be 4 °C and 10 min, respectively.

The supernatant from the centrifugation step, which contained the analytes in acetonitrile, was checked for compatibility with the continuous system for preconcentration and cleanup. For this purpose, we optimized the proportion of acetonitrile by using 500 ng kg^{-1} solutions of each EDC in mixtures containing a 0–50% proportion of the solvent in water. An acetonitrile proportion higher than 15% was found to considerably decrease retention of the EDCs in the sorbent column. This led us to evaporate the supernatants to near dryness (ca. 200 μL) under a gentle stream of nitrogen and redissolving them in 10 mL of deionized water (pH 4) prior to introduction into the continuous system.

3.3. Sensitivity and validation of method

The performance and accuracy of this approach was examined on the basis of the regression equation, sensitivity and precision for the 24 target EDCs. For this reason, an amount of 2 g of uncontaminated vegetable (onion) or fruit sample (kiwi) was fortified with concentrations over the range 2.0–2000 ng kg^{-1} of each individual EDC. The fortified onion and kiwi samples were pretreated and clean-up as reported in Section 2.4 (Fig. 1).

Standard curves were constructed by plotting analyte-to-internal standard peak area against analyte concentrations (15 points per curve) (Azzouz and Ballesteros, 2012). The analytical features of the suggested approach are illustrated in Table 1. Thus, the correlation coefficient (r^2) was between 0.992 and 0.999. The limit of detection (LOD, described as the compound concentration level providing a chromatographic peak equal to three times the associated regression standard deviation, $S_{y/x}$, divided by the slope of the calibration graph) ranging between 0.6 and 25 ng kg^{-1}. The precision as the relative standard deviation (RSD) was assessed by analyzing eleven vegetables and fruit samples spiked with different concentrations (150, 250 or 500 ng kg^{-1}) of each analyte on the same (within-day precision) or 7 different days (inter-day precision), ranging from 4.5 to 6.3% and 5.2–7.6%, respectively.

The presented approach was validated for application to vegetable and fruit samples in regard of recovery. For this reason, different kinds of vegetable (potato, onion, garlic, tomato, carrot, zucchini, eggplant, lettuce, pepper, white turnip and cucumber) and fruit samples (banana, apple, pear, kiwi, orange, mandarin and lemon) were fortified with 150, 250 or 500 ng kg^{-1} of a standard mixture of the compounds prior to pre-treatment and were

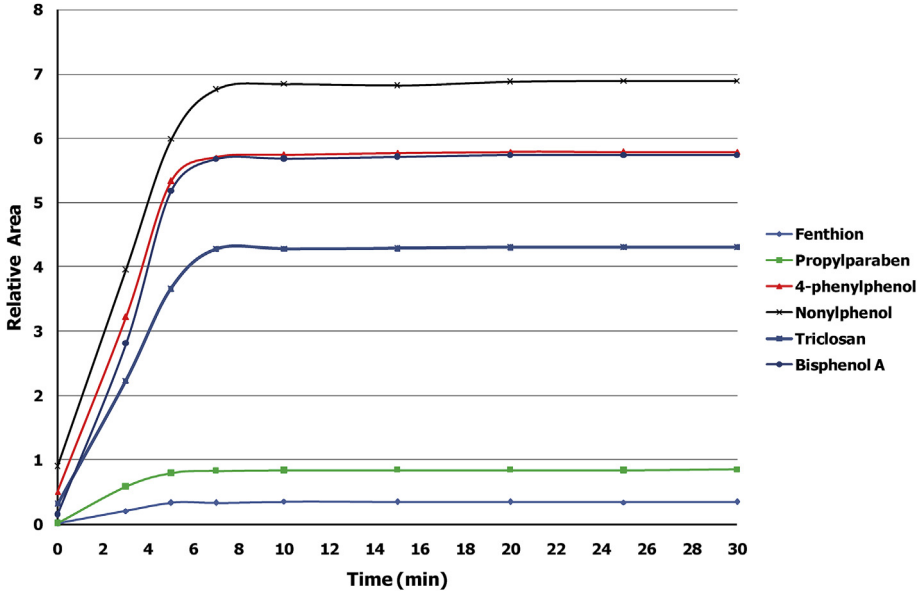

Fig. 3. Influence of the sonication time on the extraction of six representative compounds from the different EDC families present in vegetable and fruit samples.

Table 2
Determination of endocrine disrupting chemicals in vegetable samples from Spain (S) and Morocco (M) (mean values ± standard deviation, ng kg−1, n = 3).

Analyte	Potato (S)	Onion (S)	Garlic (M)	Tomato (M)	Carrot (S)	Zucchini (S)	Eggplant (S)	Lettuce (M)	Pepper (M)	White turnip (S)	Cucumber (S)
Dichlorovos	–	–	290 ± 20	120 ± 10	–	510 ± 30	330 ± 20	490 ± 30	–	280 ± 20	–
Dimethoate	–	–	–	–	–	–	–	–	–	140 ± 10	52 ± 3
Diazinon	–	–	180 ± 10	–	–	–	–	–	–	–	–
Parathion methyl	220 ± 10	–	–	–	290 ± 20	160 ± 10	–	–	–	95 ± 6	410 ± 30
Malathion	–	–	190 ± 10	150 ± 10	–	–	–	55 ± 3	–	–	–
Parathion ethyl	–	–	–	–	500 ± 30	230 ± 10	250 ± 20	460 ± 30	420 ± 30	–	360 ± 20
Chloropyrifos	–	–	–	56 ± 4	–	75 ± 4	–	–	–	–	–
Fenthion	310 ± 20	–	94 ± 6	–	–	370 ± 20	–	200 ± 10	–	490 ± 30	–
Bromophos methyl	–	–	–	–	–	–	–	–	–	–	–
Methidathion	360 ± 20	–	250 ± 10	160 ± 10	470 ± 30	150 ± 10	210 ± 10	410 ± 30	190 ± 10	–	240 ± 10
Fenthion sulfoxide	–	–	85 ± 5	–	–	450 ± 30	340 ± 20	530 ± 30	230 ± 10	–	–
Methylparaben	–	–	–	–	–	–	–	–	30 ± 2	41 ± 2	–
Ethylparaben	–	–	–	–	–	–	–	–	–	–	–
Isopropylparaben	140 ± 10	–	–	–	–	–	–	–	–	–	–
Propylparaben	–	–	–	–	–	–	–	–	–	–	–
Isobutylparaben	–	–	–	–	–	–	–	–	–	–	–
Butylparaben	–	–	–	–	–	–	–	–	–	–	–
Benzylparaben	–	–	–	–	–	–	–	–	–	–	–
2-Phenylphenol	–	–	–	–	–	–	–	–	–	–	–
4-Phenylphenol	–	–	–	–	–	–	–	–	–	–	–
4-*tert*-Octylphenol	73 ± 4	–	–	25 ± 1	60 ± 4	87 ± 5	66 ± 4	55 ± 3	40 ± 2	–	51 ± 3
Nonylphenol	–	–	320 ± 20	62 ± 4	–	–	–	–	72 ± 4	47 ± 3	66 ± 4
Bisphenol A	7.4 ± 0.4	–	16 ± 1	70 ± 4	48 ± 3	68 ± 4	21 ± 1	41 ± 3	5.2 ± 0.3	42 ± 2	36 ± 2
Triclosan	–	–	–	–	–	–	–	–	–	–	–

measured in triplicate. The mean recoveries thus achieved are shown in Tables 1S and 2S. As can be observed, all target compounds were accurately monitored; as well as, recoveries (mean 83–110%) were quite acceptable for all matrices. Therefore, ultrasound-assisted extraction, precipitation/centrifugation or clean-up by SPE efficiently reduced or even completely suppressed matrix interferences.

3.4. Analysis of vegetables and fruits

The proposed method was successfully used to determine twenty-four EDCs in vegetables (potato, onion, garlic, tomato, carrot, zucchini, eggplant, lettuce, pepper, white turnip and cucumber) and fruits (banana, apple, pear, kiwi, orange, mandarin orange and lemon) from Morocco and Spain. The different samples were tested in triplicate as described in Section 2.4. Any samples containing some target compound at a level exceeding the upper end of the linear range (Table 1) was diluted as required with eluent (500 μg L^{-1} triphenylphosphate in acetonitrile) and then derivatizing the targets EDCs with BSTFA + 1% TMCS. The analytical results are reported in Tables 2 and 3.

As can be observed in Table 2, the onion sample contained none of the EDCs. On the other hand, most of the vegetable samples contained bisphenol A and el 4-*tert*-octylphenol, at concentrations over the range 5.2–70 and 25–87 ng kg^{-1}, respectively. Table 4 summarizes previous findings of EDCs in vegetable and fruit samples. As can be seen, nonylphenol has been found in garlic, tomato, pepper, white turnip and cucumber, at concentrations from 47 to

Table 3
Determination of endocrine disrupting chemicals in fruit samples (mean values ± standard deviation, ng kg−1, n = 3) from Spain (S) and Morocco (M).

Analyte	Banana (S)	Apple (S)	Pear (S)	Kiwi (S)	Orange (M)	Mandarin orange (S)	Lemon (M)
Dichlorovos	–	–	–	–	–	–	–
Dimethoate	–	–	–	–	–	–	–
Diazinon	–	150 ± 10	570 ± 30	–	–	230 ± 20	–
Parathion methyl	–	200 ± 10	–	–	–	–	420 ± 30
Malathion	310 ± 20	210 ± 10	–	–	–	–	–
Parathion ethyl	240 ± 20	250 ± 20	350 ± 20	–	–	–	–
Chloropyrifos	–	–	–	–	330 ± 20	150 ± 10	–
Fenthion	580 ± 30	140 ± 10	–	–	–	–	–
Bromophos methyl	–	–	–	–	–	–	–
Methidathion	260 ± 20	–	–	–	–	550 ± 30	–
Fenthion sulfoxide	–	80 ± 5	200 ± 10	–	160 ± 10	360 ± 20	340 ± 20
Methylparaben	47 ± 3	–	–	–	14 ± 1	–	250 ± 20
Ethylparaben	–	37 ± 3	–	–	–	–	–
Isopropylparaben	–	–	16 ± 1	–	–	–	40 ± 2
Propylparaben	–	–	–	–	–	–	–
Isobutylparaben	–	–	–	–	–	–	–
Butylparaben	–	–	–	–	–	–	–
Benzylparaben	–	–	–	–	–	–	–
2-Phenylphenol	–	8.4 ± 0.5	48 ± 3	–	85 ± 5	7.0 ± 0.4	8.9 ± 0.5
4-Phenylphenol	–	–	–	–	–	–	–
4-*tert*-octylphenol	240 ± 20	16 ± 1	61 ± 4	–	–	50 ± 3	70 ± 4
Nonylphenol	190 ± 10	25 ± 2	54 ± 3	–	140 ± 10	150 ± 10	–
Bisphenol A	–	7.2 ± 0.4	12 ± 1	–	5.8 ± 0.3	8.2 ± 0.5	–
Triclosan	–	–	–	–	–	–	–

Table 4
Comparison of the proposed method and alternative methods for determining EDCs in vegetable and fruit samples.

Analytes	Samples	Countries	Pretreatment of samples and clean-up	Analytical techniques	Performance	Concentration in real samples	References
Bisphenol A, nonylphenol and 4-*tert*-octylphenol	Lettuce, tomato, potato and citrus	USA	UAE	GC–MS/MS	LOD: 0.03 –0.3 μg kg^{-1} RSD: 8.7 –24.8% R: 93–102%	0.2–18.9 μg kg^{-1}	Lu et al. (2012)
Nonylphenol, 4-*tert*-octylphenol, bisphenol A and nonylphenol	Lettuce, tomato, pumpkin, potato, carrot, citrus, apple and strawberry	USA	Acid hydrolysis	GC–MS	LOD: 0.01 –0.1 μg kg^{-1} RSD: 1.8–9.0% R: 95.2 –104.2%	0.2–18.5 μg kg^{-1}	Lu et al. (2013)
Bisphenol A, nonylphenol and triclosan	Carrot, onion, tomato and lettuce	Spain	MSPD	GC–MS/MS	LOD: 0.1 –1.0 μg kg^{-1} RSD: 1–19% R: 56–120%	1.7–16.3 μg kg^{-1}	Albero et al. (2017)
Nonylphenols, 4-*tert*-octylphenol, n-octylphenol, bisphenol A and triclosan	Carrot and lettuce	Spain	FUSLE–dSPE	LC–MS/MS	LOD: 0.1 –99.7 μg kg^{-1} RSD: 2–27% R: 70–130%	9.1–10.9 μg kg^{-1}	Mijangos et al. (2015)
Nonylphenol, bisphenol A and triclosan	Lettuce, spinach, chard, carrot, turnip and potato	Spain	UAE–dSPE	LC–MS/MS	LOD: 0.025 –0.5 μg kg^{-1} RSD: 1–10% R: 87–114%	–	Aparicio et al. (2018)
Diazinon, parathion methyl, malathion, fenthion and others pesticides	Tomato	Iran	UAE, DLLME	GC–FPD	LOD: 0.2 –0.4 μg kg^{-1} RSD: 7.9–10%	22.7 –34.3 μg kg^{-1}	Bidari et al. (2011)
2-Phenylphenol	Apples and oranges	Malaysia	–	LC–FD	LOD: 5.0 μg kg^{-1} R: 84.0 –108.8%	3–20 μg kg^{-1}	Saad et al. (2004)
Parathion methyl, fenthion, diazinon, dimethoate, malathion, chlorpyrifos and others pesticides	Apple, pear, tomato, cucumber and cabbage	China	QuEChERs	GC-MS (TOF)	LOD: 0.13 –5 μg kg^{-1} RSD: <19.7% R: 70.0 –115.9%	<LOQ	Cheng et al. (2017)
2-Phenylphenol	Banana, chard, lemons, onions, oranges and pepper	Spain	MSPD	LC–MS	LOQ: 10 μg kg^{-1} RSD: 6.1 –11.9% R: 52.5–91.1%	10–2160 μg kg^{-1}	Blasco et al. (2002)
Nonylphenol, 4-*tert*-octylphenol and others alkylphenols	Fruit juices (orange, pineapple, apple, peach and grapefruit)	Spain	MSPE	LC–MS/MS	LOD: 1.7 –6.8 μg L^{-1} RSD: 8.1 –13.1% R: 91–107%	30–106 μg L^{-1}	Viñas et al. (2016)
Methylparaben, ethylparaben, propylparaben, isopropylparaben, butylparaben and isobutylparaben	Cabbage, carrot, celery, potato and broccoli	China	QuEChERS	LC–MS/MS	LOQ: 50 μg kg^{-1} RSD: 1–10% R: 81–113%	81 μg kg^{-1}	Song et al. (2017)
Dimethoate and other pesticides	Lettuce, apples, grapes, and tomatoes	Canada	QuEChERS	LC-MS/MS	LOD: 0.1 –1.0 μg kg^{-1} RSD: 1–18% R: 70–110%	6.3–215 μg kg^{-1}	Montiel-León et al. (2019)
Benzylparaben, heptylparaben, butylparaben, propylparaben, methylparaben and ethylparaben	Walnuts, chestnuts, jujubes, plums, hawthorns, raisins, mushrooms, peanuts, peppers, sea-weed, bamboo shoots, potatoes, edible tree fungus, Chinese cabbage, salted mustard	China	SPE	LC–MS/MS	LOQ: 0.01 μg kg^{-1} RSD: 6–22% R: 67–107%	0.006 –14.7 μg kg^{-1}	Liao et al. (2013a)
Chlorpyrifos and dimethoate	Lettuce, carrot, tomato, collard greens, strawberry and green pepper	Brazil	UAE–MSPD	GC–MS and LC–MS/MS	LOQ: 5.0 –500 μg kg^{-1} RSD: 1–22% R: 63–140%	20–60 μg kg^{-1}	Dos Santos et al. (2019)
4-*tert*-Octylphenol and 4-nonylphenol	Apple, nectarine, pear, grape, plum, guava, tomato, carrot, cucumber, lettuce, green pepper, broccoli, celery, spinach, mushroom and alfalfa sprout	Taiwan	Nielson–Kryger steam distillation extraction	GC–MS	LOQ: 0.2 μg kg^{-1} RSD: 1–9.6% R: 64–101%	0.7–16 μg kg^{-1}	Yang and Ding (2005)

(*continued on next page*)

Table 4 (*continued*)

Analytes	Samples	Countries	Pretreatment of samples and clean-up	Analytical techniques	Performance	Concentration in real samples	References
Methylparaben, ethylparaben, propylparaben and butylparaben	Fruit juices (orange, grape, apple and peach)	China	SPE (MMIP)	LC–UV	LOD: 21 –28 μg L^{-1} RSD: 2.6–8.9% R: 72.5–89.4%	89 μg L^{-1}	You et al. (2016)
Organophosphorus pesticides, parabens, alkylphenols, phenylphenols, bisphenol A and triclosan	Potato, onion, garlic tomato, carrot, eggplant lettuce, pepper, turnip, cucumber, zucchini, banana, apple, pear, kiwi, orange, mandarin and limon	Spain and Morocco	UAE and SPE	GC–MS	LOD: 0.6 –25 ng kg^{-1} RSD: 4.5–7.6% R: 83–110%	5.8–580 ng kg^{-1}	The proposed method

ASE: Accelerated solvent extraction; BAμE: Bar adsorptive microextraction; DLLME: Dispersive liquid–liquid microextraction; dSPE: Dispersive solid-phase extraction; FUSLE–dSPE: Focused ultrasonic solid–liquid extraction dispersive solid phase extraction; GC–FPD: Gas chromatography–flame photometric detection; GC-MS: Gas chromatography-mass spectrometry; GC-MS/MS: Gas chromatography-tandem mass spectrometry; GC-MS (TOF): Gas chromatography quadrupole-time-of-flight mass spectrometry; LC-FD: Liquid chromatography-fluorescence detector; LC_MS/MS: Liquid chromatography-tandem mass spectrometry; LC–UV: Liquid chromatography-ultraviolet detection; LLE: Liquid-liquid extraction; LOD: Limit of detection; LOQ: Limit of quantification; MMIP: Magnetic molecularly imprinted polymer; m-MISPE: Membrane-based molecularly imprinted solid-phase extraction; MSPD: Matrix solid-phase dispersion; MSPE: Magnetic solid phase extraction; QuEChERs: Quick, easy, cheap, effective, rugged and safe extraction; R: Recovery; RSD: Relative standard deviation; SPE: Solid phase extraction; TD-GC-MS: Thermal desorption and gas chromatography-mass spectrometry; UAE: Ultrasonic assisted extraction.

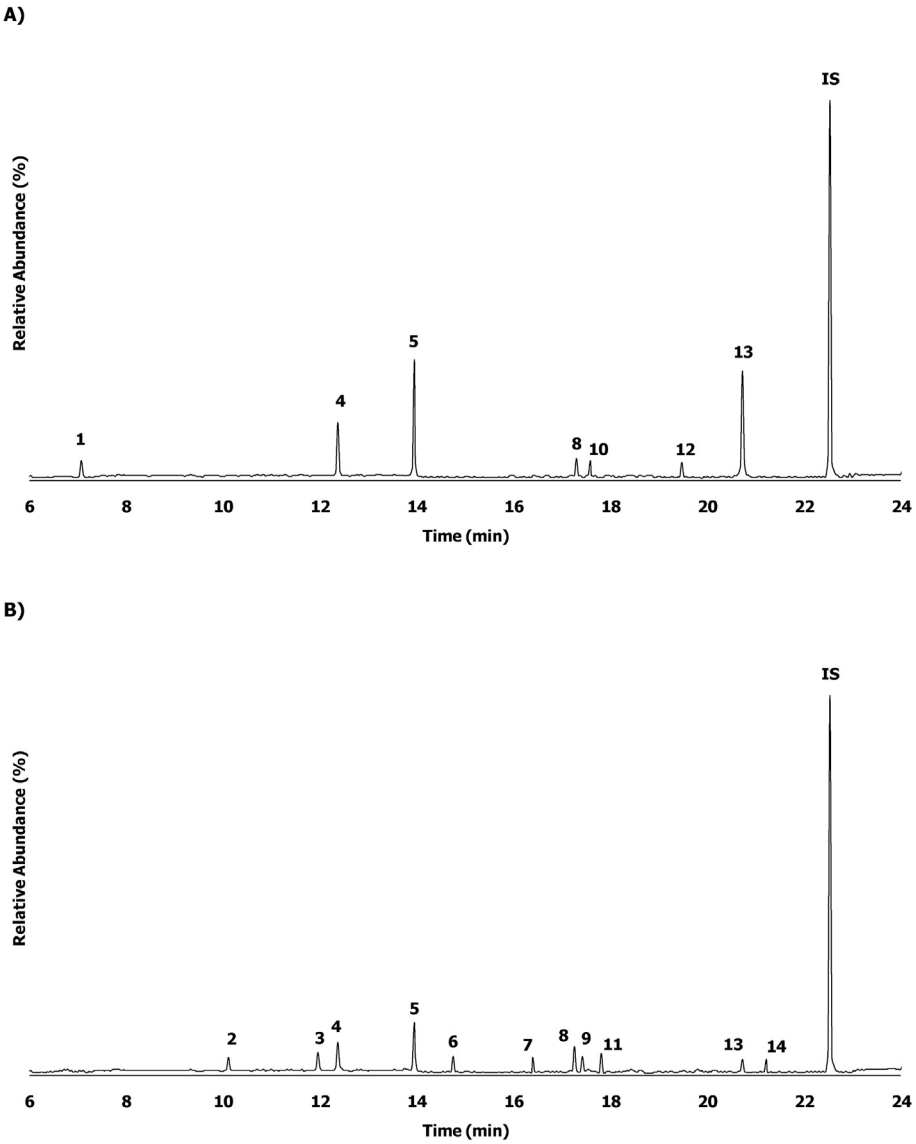

Fig. 4. GC–MS chromatograms in the SIM mode obtained for an amount of 2 g of tomato (A) and apple sample (B). 1: dichlorovos; 2: ethylparaben; 3: 2-phenylphenol; 4: 4-tertoctylphenol; 5: Nonylphenol; 6: diazinon; 7: parathion-methyl; 8: malathion; 9: parathion-ethyl; 10: chloropyrifos, 11: fenthion; 12: methidathion; 13: bisphenol A; 14: fenthion sulfoxide; IS triphenylphosphate.

370 ng kg^{-1}. Lu et al. (2013) found bisphenol A and nonylphenol at concentrations over the range 0.2–9 and 5.3–18.5 μg kg^{-1}, respectively, in vegetable samples from the USA. Bisphenol A was also found, at concentrations level between 9.1 and 10.9 μg kg^{-1}, in carrot and lettuce from Spain, (Mijangos et al., 2015). The European Food Safety Authority set a maximum acceptable daily intake of bisphenol A at 50 μg kg^{-1} body weight/day in CD 2004/19/EC (EFSA, 2014).Yang et al. (2005)found 4-*tert*-octylphenol and nonylphenol at concentrations from 0.4 to 16 μg kg^{-1} in various types of vegetables from Taiwan. Isopropylparaben at 140 ng kg^{-1} in potato, and methylparaben in pepper (30 ng kg^{-1}) and white turnip (41 ng kg^{-1}) were the only parabens detected here. By contrast, Song et al. (2017) found methylparaben (81 μg kg^{-1}) in only one type of vegetable sample from China (celery). Triclosan was detected in none of our vegetables samples, which is similar to the results previously obtained byMijango et al. (2015). Also, neither phenylphenol was detected here.

The proposed method detected organophosphorus pesticides in a large number of samples. Thus, all samples contained at least three pesticides, at concentrations from 52 to 510 ng kg^{-1} —by exception onion contained no EDC. Bidari et al. (2011) detected diazinon, malathion and parathion methyl at levels between 22.7 and 34.3 ng kg^{-1} in tomato matrix from Iran. Also, lettuce samples from Canada were found to contain dimethoate (6.3–215 μg kg^{-1}) and other pesticides not studied here. By way of example, Fig. 4A shows the chromatogram for a tomsato sample.

Most of the fruit samples —kiwi excluded— contained a number of EDCs. Thus, 2-phenylphenol and the two alkylphenols were found at concentrations from 8.4 to 240 ng kg^{-1}. Also, bisphenol A was found at concentrations over the range 5.8–12 ng kg^{-1} in apple, pear, orange and mandarin orange. Our concentrations levels are lower than those reported by other authors. Thus, Blasco et al. (2002) found 2-phenylphenol at concentrations of 10–2160 μg kg^{-1} in banana, lemon and orange from Spain, and Saad et al. (2004)found this EDC at 3–20 μg kg^{-1} in apple and orange from Malaysia. Viñas et al. (2016) detected 4-*tert*-octylphenol and nonylphenol at 31–106 μg L^{-1} in fruit juices. Some of fruit samples (banana, apple, pear, orange and lemon) contain some paraben (methylparaben, ethylparaben and isopropylparaben) at levels from 14 to 250 ng kg^{-1}. By contrast, Young et al. (2016)only found propylparaben in an orange juice sample.

Like the vegetables, all fruits —kiwi excepted— contained some organophosphorus pesticide, with apple containing the greatest number (80–250 ng kg^{-1}; Fig. 4B). In any case, the pesticide concentrations found were lower than the maximum residue limits (MRLs) established by the European Union (2017)and the Codex Alimentarius (2020): 0.01–7 mg kg^{-1}. Such concentrations were also lower than those reported by other authors such as Dos Santos et al. (2019), who found dimethoate and chlorpyrifos at concentrations over the range 20–60 μg kg^{-1} in strawberry samples.

4. Conclusions

The proposed analytical approach, which uses a combination of UAE, continuous SPE and GC–MS, proved an accurate, sensitive, convenient choice for the multi-detection of 24 EDCs (organophosphorus pesticides, alkylphenols, parabens, phenylphenols, triclosan and bisphenol A) in fruits and vegetables. The recovery, repeatability, linearity and relatively low detection limits of the method make it suitable for the quantitative determination of EDCs in real samples. In fact, LODs ranged between 0.5 and 25 ng kg^{-1} according to the specific target, recoveries spanned the range 83–110% and RSDs were all lower than 7.6%. In addition, continuous SPE allowed the extracts from UAE and centrifugation to be cleaned up, and afforded highly efficient preconcentration and subsequent elution of the analytes from the sorbent by using only 400 μL of solvent (acetonitrile). The involved strategy employs a reduced volume of organic solvents (6.5 mL) in a closed system and is thus environmentally friendly. This method was checked by analyzing 18 different types of vegetable and fruit samples. All samples except onion and kiwi were found to contain some EDC. In any case, the EDC levels found (5.8–580 ng kg^{-1}) were inferior than those reported by other researchers (Table 4) and also than MRLs fixed by the European Union (2017)and the Codex Alimentarius (2020).

Authorship contribution statement

Lamia Hejji, Conceptualization, Methodology. Abdelmonaim Azzouz, Methodology, Formal analysis, Validation, Writing - original draft. Laura Palacios Colón, Formal analysis. Badredine Souhail, Validation. Evaristo Ballesteros, Project administration, Validation, Writing - review & editing, Funding acquisition, Supervision.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2020.128158.

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