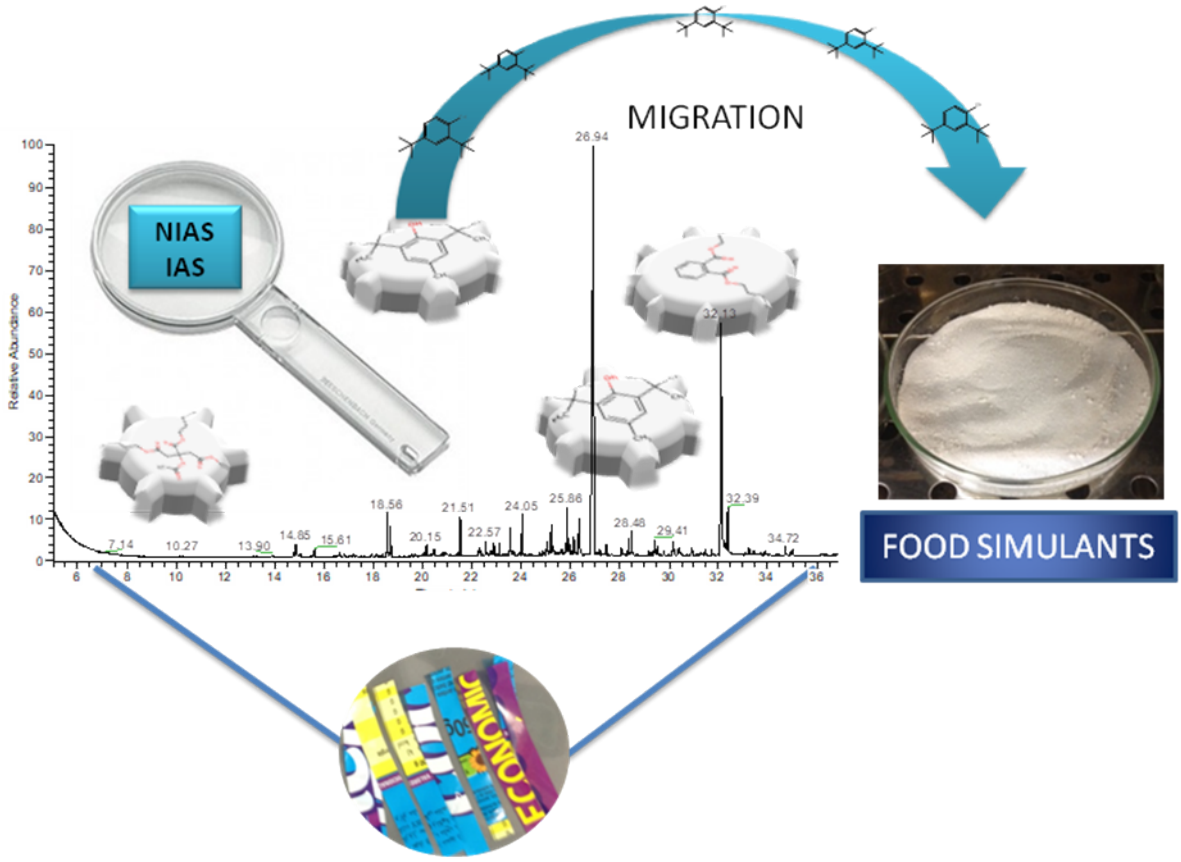
1 Graphical abstract



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NON-TARGET ANALYSIS OF INTENTIONALLY AND NON INTENTIONALLY ADDED SUBSTANCES FROM PLASTIC PACKAGING MATERIALS AND THEIR MIGRATION INTO FOOD SIMULANTS

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ABSTRACT

A wide variety of compounds are used in the manufacture of plastic materials; however, some of them have the potential to migrate in food products.

The main objective of this work was the identification of potential migrants in plastic packaging materials and their migration into food simulants. For this purpose, a total of twelve plastic packaging materials were analyzed using purge and trap (P&T) coupled to GC–MS for volatile compounds and GC-MS for semivolatile compounds after extraction with organic solvents.

A qualitative migration tests were carried out using tenax and isooctane and the migrants were analyzed by GC-MS. About 100 different organic compounds were detected in plastic materials. Of these, 27 compounds migrated into tenax and/or isooctane. In general, migration occurs to a larger extent in tenax than in isooctane. Moreover, most of detected compounds in plastic samples are not included in the Commission Regulation (EU) No. 10/2011 on plastic materials and articles intended to come into contact with food.

Keywords: volatile compounds; semivolatile compounds; migration; food simulants

1. Introduction

Plastic materials are widely used in food packaging applications for their excellent properties. Polymers most widely used in this application include polyethylene (PE), polyethylene terephthalate (PET), polypropylene (PP), polyamide (PA), polystyrene (PS), ethylene vinyl alcohol (EVOH), polyvinylidene chloride (PVDC), polyvinyl chloride (PVC), ethylene vinyl acetate (EVA) and polycarbonate (PC). The mentioned polymers are also used ~~too~~ to produce multilayer materials (Hoppe, de Voogt, & Franz, 2016). Multilayer materials are commonly used in food packaging industry. These materials are produced by combination of various types of plastic and or non-plastic materials (e.g., aluminum foil and paper, among others) with adhesives. Most commonly used adhesives in the manufacturing of multilayer food packaging are polyurethane and acrylic or acrylate based adhesives. The final properties of these materials are a combination of individual material properties, which allows improving the performance of packaging materials (Clemente, Aznar, Nerín, & Bosetti, 2016).

Packaging provides physical protection and extends the shelf life of foods, however when packaging comes in contact with food~~,~~ components from the packaging materials can migrate into the food. ~~there is the possibility that constituents from the same are transferred to the packaged food. In fact, packaging materials contain chemical compounds that potentially can migrate into the foodstuffs; t~~These substances could include authorized substances e.g. residual monomers, starting substances as well additives used to improve the properties of materials. Furthermore, may migrate the so called "non intentionally added substances" or (NIAS). ~~from packaging material into the packaged food.~~ In Europe the substances authorized are included in Regulation N° 10/2011 which contains the list of monomers, starting substances and additives allowed to be used in the manufacture of plastics as well as the list of simulants and the assay conditions to be used for testing migration. ~~of constituents of plastic materials and articles intended to come into contact with foodstuffs.~~ The same Regulation defines NIAS as "any impurities in the substance used or reaction intermediates formed during the production process or decomposition or reaction products". These

substances are not included in the union list, however the safety of NIAS has to be assessed (Commission Regulation (EU) No 10/2011).

~~The presence of NIAS in packaged food could be the result of the impurities present in the raw materials used for their production but one of the most frequent pathway to NIAS formation is degradation processes (Dąrowska, Borcz, & Nawrocki, 2003; Kim et al., 2015). For example, during PET manufacturing, several degradation and decomposition reactions can occur. High temperatures and the presence of oxygen in the PET can promote reactions generating numerous NIAS in the polymer (Kassouf, Maalouly, Chebib, Rutledge, & Ducruet, 2013). In recent years the concern about the risk of NIAS is increasing. Over 50% of compounds migrating from food contact materials are NIAS (Bach et al., 2013; Grob, Biedermann, Scherbaum, Roth, & Rieger, 2006).~~ From the toxicological point of view, particular attention have received low molecular substances, ~~including also NIAS,~~ given that it is generally accepted that substances with molecular weight over 1000 Da are not absorbed by the gastro-intestinal tract (European Food Safety Authority, 2008). ~~Several analytical techniques have been used for the determination of potential migrants in packaging materials used target and non target methodologies.~~ The application of mass spectrometry (MS) in combination with gas chromatography (GC) or liquid chromatography (LC) has been well recognized for both quantification and semi-quantitative screening of food packaging materials. GC is suitable for semi-volatile substances, whereas compounds that are thermally instable, non- or highly volatile should be analyzed by LC (Bradley & Coulier, 2007; Lahimer, Ayed, Horriche, & Belgaied, 2013; Nerin, Alfaro, Aznar, &– Domeño, 2013; Simal-Gándara, Damant, & Castle, 2002).

GC-MS coupled to headspace by solid-phase microextraction (HS-SPME) or combined with a purge & trap (P&T) system have shown to be efficient techniques for screening of volatile compounds in food contact materials (Nerin, Canellas, Aznar, & Silcock, 2009; Skjevrak et al. 2005). More sophisticated technologies such as comprehensive two-dimensional gas

chromatography has also been successfully applied in the analysis of food packaging materials (Biedermann, Castillo, Riquet, & Grob, 2014; Biedermann, & Grob, 2013).

Other techniques such as pyrolysis–GC coupled to mass spectrometry has also been used for compositional analysis of polymers (Rial-Otero, Galesio, Capelo, & Simal-Gándara, 2009).

~~Gas chromatography-mass spectrometry (GC-MS) has been applied successfully for the screening and the identification of potential migrants from films and adhesives as well as for quantitative analysis of migration into food simulants. Rothenbacher & Schwack (2009) developed a GC-MS method for the screening in resins, foils, and multilayer foils intended for the production of food packaging. Toxicological evaluation of the 46 identified compounds was also realized. GC-MS coupled to headspace by solid-phase microextraction (HS-SPME) is another technique selected for its high sensitivity for the screening of volatile compounds coming from adhesives used in packaging materials (Nerin, Canellas, Aznar, & Silcock, 2009).~~

~~Other technique that can trap and analyze simultaneously the vapor emitted from the plastic is the purge & trap (P&T) system coupled with a GC-MS. This system allows the identification and quantification of compounds that arriving at the MS detector. Skjevrak et al. (2005) used Purge-and-trap (P&T) combined with GC-MS (P&T-GC/MS) and solid phase extraction (SPE)-GC/MS for the analysis of volatile and semi-volatile compounds originated from four type of plastic articles. Most migrants were NIAS or compounds originated from non-plastic components, such as printing inks, adhesives, not-listed additives, solvents and coatings.~~

Advances in analytical instrumentation have allowed to address the challenging task to identify unknowns. High resolution mass spectrometry techniques such as Time of Flight (TOF) and Orbitrap have been effectively applied for this purpose (Isella, Canellas, Bosetti, & Nerin, 2013; Cherta et al., 2015; Vaclavikova et al., 2016).

~~the use of new technologies to identify target and non-target compounds such as Time of Flight (TOF) mass spectrometry, which provides the sensitivity and selectivity required for the analysis of compounds with an accurate mass analysis. Ultra-high performance liquid chromatography-~~

~~quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF/MS) has been proved to be a powerful technique to identify NIAS from polyurethane adhesives (Isella, Canellas, Bosetti, & Nerin, 2013). In the same way the identification of unknown substances capable to migrate from plastic materials to food simulants was performed using the combination of two analytical techniques (GC-(EI)TOF/MS) and GC-(APCI)QTOF/MS, which allowed the confirmation of the identity of 8 migrants (Cherta et al., 2015).~~ Recent developments have let that polymers and solid food simulants can be analyzed by direct thermal desorption techniques, in which the extraction steps can be avoided. These techniques include direct analysis in-real-time (DART) MS (Ackerman, Noonan, & Begley, 2009; Lago & Ackerman, 2016), desorption electrospray ionization (DESI) MS (Venter, Nefliu, & Cooks, 2008) and atmospheric solids analysis probe (ASAP) MS (Barrere, Maire, Afonso, & Giusti, 2012).

In this work an approach based on purge and trap and MS (P&T-GC/MS) and an extraction with organic solvents followed by a GC-MS analysis for the determination of volatile and semi-volatile Intentionally added substances (IAS) and non-intentionally added substances (NIAS) in plastic packaging materials is proposed. This methodology could be a valuable screening tool and be used as a first step in identifying potential migrants for compliance with food contact materials legislation. Additionally, migration tests were performed using Tenax and isooctane as food simulants.~~In this work a GC-MS and purge and trap (P&T-GC/MS) method was developed for the determination of volatile compounds in twelve different plastic food-packaging samples. In addition, the semi-volatile compounds were analyzed by GC-MS after an extraction with organic solvents. Migration tests were performed with the aim of identifying the semi-volatile compounds capable to migrate from plastic materials into food simulants Tenax and isooctane.~~

2. Materials and methods

2.1. Chemicals and analytical standards

Analytical standards of butylated hydroxytoluene (BHT) 99% (CAS: 128-37-0), tributyl acetyl citrate (ATBC) 99% (CAS: 77-90-7), bis(2-ethylhexyl) adipate (CAS: 103-23-1), bis (2-ethylhexyl) phthalate (DEHP) 99% (CAS: 117-81-7) were purchased by Fluka (Steinheim, Germany).

Caprolactam (CAS: 105-60-2), diethyl phthalate (DEP) 99.5 %, (CAS: 84-66-2), erucamide (CAS: 112-84-5), tolulene 2,6-diisocyanate 97% (CAS: 91-08-7), benzophenone 99%, internal standard methyl myristate (CAS: 124-10-7), saturated alkane standard mixture C_7-C_{30} (1000 µg/mL each component in hexane) and polyoxide 2,6-diphenyl-p-phenylene TA (Tenax), 80-100 mesh were purchased from Sigma Aldrich (Schnelldorf, Germany). Toluene 2,4 diisocyanate (584-84-9) from Merk (Darmstadt, Germany).

All chemicals were of analytical grade. Acetonitrile (ACN), ethanol, methanol, acetone and isooctane were from Merck (Darmstadt, Germany). Purified water (Type I) was obtained from an Autwomatic Plus purification system (Wasserlab, Navarra, Spain).

2.2. Samples

Twelve samples of plastic films (with and without printing ink)~~-~~ intended to come into contact with food ~~not yet in contact with food~~ (six samples purchased in Quito-Ecuador and six samples purchased in Spain) were independently studied during the investigation of organic compounds. Details of packaging samples are listed in Table 1.

2.3. Sample Treatment (Screening)

The organic compounds originated from the plastic material, were extracted from slices of plastic material (approx. 1 g, 1.58 dm^2) by purging an inert gas (Helium at 40 mL/min) through the sample (heated at 60ºC) during 20 minutes. Purged sample components are trapped in a tube containing a suitable sorbent material (Vocarb 3000 Trap). When purging is completed, the trap is heated

(250ºC) and back flushed with Helium (400 mL/min during 2 min) to desorb the trapped sample components into the GC column. Components eluting from the GC column are identified by MS.

A liquid extraction was also performed with plastic samples. Acetonitrile was selected as extraction solvent due to its extraction power. ~~For this purpose an~~ An area of 0.8 dm^2 ~~(~~0.7 g) was cut from each packaging material and analysed separately. Each specimen was then cut in ~~layers,~~ pieces put in a glass container and extracted with 25 mL of acetonitrile for 24 h at 70 °C, after been hermetically closed. An aliquot of the extract (10 mL) was then removed and evaporated under nitrogen stream (RapidVap Vertex Evaporator, Labconco) up to less than 1 ml. Subsequently, to a 1-mL volumetric flask was added 50 µl of the internal standard methyl miristate (100 mg/L) and the volume was made up with the final extract (evaporated).

Cramer rules were used to estimate the toxicity of identified compounds. An open source application called Toxtree v2.6.13 (Ideaconsult Ltd.) was used for this purpose (Toxtree v2.6.13, 2015). The decision tree allows classifying chemical compounds into three structural classes mainly on the basis of chemical structure and reactivity. Cass I (low toxicity): For substances with simple chemical structures and efficient modes of metabolism; Class II (intermediate toxicity) for substances that may suggest significant toxicity or have reactive functional groups and substances of a chemical structure that permit no strong initial impression of safety and may even suggest a significant toxicity are classified in Class III (high toxicity) (Lapenna & Worth, 2011; Patlewicz, Jeliazkova, Safford, Worth, & Aleksiev, 2008).

2.4. Qualitative Migration Test

Migration test were carried out using two simulants. Isooctane and Tenax® . All migration experiments were done in duplicate.

For migration test performed with Tenax, 0.13 dm^2 of each laminate (the side in contact with food) were placed in a petri dish and covered with 0.52 g of Tenax (4 g Tenax per dm^2 laminate) (UNE-EN-14338, 2004) which had been previously cleaned with acetone in a Soxhlet extraction for 6 h and dried into the oven for other 6 h at 160°C.

192 Petri dishes were wrapped by aluminium foil carefully and stored at 60°C during 10 days. Two
193 independent replicates of each packaging material were analyzed. After this period Tenax was
194 extracted two consecutive times using acetone (10 mL every time) through manual shaking for 1
195 min and ultrasonic bath for 15 min. The samples were then centrifuged (5 min, 2°C at 2000 rpm).
196 The recovered acetone was concentrated under nitrogen stream (RapidVap Vertex Evaporator,
197 Labconco) to approx. 1 mL and transferred to a 1mL volumetric flask with 50 µl of the internal
198 standard methyl miristate (100 mg/L) and analyzed by GC-MS with the same method used for the
199 screening and identification of semivolatile compounds. Blank samples of tenax (without plastic
200 material) were placed in the oven in the same conditions of test specimens.
201 For migration tests carried out with isooctane, 0.08 dm^2 of each plastic films were place in contact
202 with 8 mL of pre-warmed isooctane (100 mL simulant per dm^2 laminate) (UNE-EN 1186-1, 2002)
203 using a glass cell that exposes only one side of the material to the simulant. Two replicates of each
204 packaging material were prepared. The samples were stored at 20°C for 2 days. After this period the
205 simulant was removed and concentrated under nitrogen stream (RapidVap Vertex Evaporator,
206 Labconco) up to less than 1 mL. Then, to a 1-mL volumetric flask was added 50 µl of the internal
207 standard methyl miristate (100 mg/L) and the volume was made up with the final extract ~~to approx.~~
208 ~~1 mL and transferred to a 1 mL volumetric flask with 50 µl of the internal standard methyl miristate~~
209 ~~(100 mg/L)~~ and analyzed by GC-MS with the same method used for the screening and identification
210 of semivolatile compounds. Blank samples (without plastic samples) undergo the same migration
211 procedure same treatment as regular samples
212 *2.5. Instrumentation*
213 *2.5.1. Purge and Tramp- GC-MS analysis*
214 A Stratum Purge and Trap (P&T) instrument (Teledyne, Tekmar) with automatic sample heater
215 coupled in line with a Finnigan Trace GC ultra chromatograph with a Trace DSQ mass detector
216 (Thermo Scientific) and a TriPlus AS autosampler were used for the analysis of volatile
217 compounds. The purge and trap conditions are presented in Table 2.

The column used for separation in GC/MS analysis was a ZB-624 (30 m x 0.25 mm x 1.40 µm) from Phenomenex® (Torrance, CA, USA), with the following oven program: 35 °C during 4 min, then 210°C at 5 °C/min with a holding time of 5 min. Helium was used as carrier gas with a flow rate of 1 mL/min. The temperature of injector inlet and transfer line of the detector was 200 and 250 °C respectively. The mass spectra were also obtained using a mass-selective detector under electron impact ionization and data acquisition was done in full scan mode (range: 20-400 *m/z*).

Before the analysis of each sample, blank runs were obtained to check the likely contamination. Xcalibur 3.0.63 software (Thermo Fisher Scientific Inc) was used to process peak areas. The identification was carried out by using the NIST/EPA/NIH 11 Mass spectral library (version 2.0) and Wiley RegistryTM 8th edition.

2.5.2. GC-MS analysis (liquid extraction)

A Thermo Scientific Trace 1300 Series Gas Chromatograph (Thermo Fisher Scientific, San José, CA, USA) with a Trace ISQ LT mass detector and an AI 1310 automatic injector was used to perform GC analysis of semivolatile compounds. The separation was performed on a ZB-5MS (30 m x 0.25 mm x 0.25 µm) column from Phenomenex ® (Torrance, CA, USA). An unpacked liner was used. Helium was used as carrier gas with a flow rate of 1 mL/min and the temperature of injector inlet and transfer line of the detector was set 300 °C. Injection was performed in a splitless mode, the splitless period was 1 min and the injection volume was 1µL. The oven temperature was programmed as follows: 50°C for 3.00 min, then 300°C at 8°C/min, with a holding time of 3 min. The mass spectra were obtained using a mass-selective detector under electron impact ionization at a voltage of 70 eV and data acquisition was done in full scan mode over a range of 40-500 *m/z*.

Xcalibur 3.0.63 software (Thermo Fisher Scientific Inc) was used to process peak areas. The identification was carried out by using the NIST/EPA/NIH 11 Mass spectral library (version 2.0) and Wiley Registry^{TM} 8th edition.

2.6. FT-IR

Infrared spectra were acquired using an ATR-FTIR spectrometer (FT-IR 4700, Jasco, Japan) with an optical element of diamon in the range from 4.000 to 650 cm^{-1}. ATR-FTIR spectrometer was controlled by the software Spectra Manager™ Suite.

2.7. Film thickness measurement

The thickness of the plastic samples was determined using a manual digital micrometer (Mitutoyo-Japan). Measurements were repeated in 3 different regions of each sample and then an average value was calculated.

3. Results and discussion

3.1. Screening of organic compounds

First of all, the plastic materials used in this study were characterized by FTIR-ATR. External and internal side of packaging materials were characterized by FTIR-ATR. The results shown that the ~~external~~ internal side of most materials were polyethylene, while on the outer side were found different type of materials. For example, in sample 1EC the internal side corresponds to poliethylene (PE) while the external side to polyethylene terephthalate PET. Details of the other plastic films are shown in Table 1.

~~On the other hand, t~~The GC-MS screening analysis of organic compounds of the plastic films studied provided chromatograms with numerous peaks; an example is given in Figure 1. Identification of compounds was performed comparing the mass spectra of the peak obtained in the samples with that of the NIST/EPA/NIH 11 Mass spectral library (version 2.0) and Wiley RegistryTM 8th edition.

In the case of P&T technique parameters such as temperature and time of purge, sorption and desorption steps were optimized. The ~~maximum number of detected compounds~~ highest number of peaks detected as well as their relative abundance in tested samples was used as criteria in the optimization of the method.

Volatile compounds with the best matches found during the library search are listed in Table 3. Compounds with matching factors SI (direct matching factor for the unknown and the library spectrum) and RSI (reverse search matching factor ignoring any peaks in the unknown that are not in the library spectrum) in a value from 800 to 1000 were selected (900 or greater is an excellent match; 800–900, a good match; and 700–800, a fair match).

More than 30 volatile compounds were detected including alkanes, cycloalkanes, alkenes, aldehydes, alcohols, aromatic compounds, cyclic amides, phenolic compounds and phthalate esters. Most of the compounds found are most likely to have come from broken polymeric chains (alkanes) or monomers (alkenes). Alkanes are common components of polymers; they serve as raw materials to produce plastics, fibres and rubbers. Alkenes are also used as starting compounds for several additives and polymers.

More than 77% of the volatile compounds detected were alkanes being the predominant detected compounds, especially in PE/PET films, followed by aldehydes (hexanal, octanal, nonanal), alkenes such as dodec-1-ene, 2-octene, alcohols (1-tetradecanol) and aromatic compounds (benzene, 1,3-bis(1,1-dimethylethyl)-). Phenolic compounds, such as the antioxidant butylated hydroxytoluene (BHT) were detected in four samples (8ES, 10ES, 11ES and 12ES). Caprolactam was detected in sample 2EC, while the plasticizer diethyl phthalate (DEP) was detected in sample 7ES. Only three of the identified compounds listed in Table 3 have specific migration limits detailed in European legislation: 1- dodecene, BHT and caprolactam. In this study, for semivolatile compounds a liquid extraction ~~using~~ with temperature was investigated to leach out the chemical compounds from plastics as a simple procedure for screening purposes. Thus, about 50 semivolatile compounds were identified including citrates, phthalates, adipates, phosphates, alkanes, aldehydes, carboxylic acids, alcohols, phenolic compounds, diisocyanates**,** fatty acids, cyclic amides, among others. Although the identification of some compounds was not possible with the tools used in this work.

As well as volatile compounds, semivolatile compounds with the best matches found during the library search are listed in Table 4. The analysis of available reference standards was performed in

293 order to confirm the identity of some compounds found in the samples. Thus, identity of 21
294 compounds was confirmed based on retention time and their respective spectral data. The remaining
295 detected peaks could not be finally confirmed due to the lack of their corresponding commercial
296 standards and they were considered as tentatively identified.
297 Among the hydrocarbons found in plastic samples alkanes such as dodecane, tridecane, hexadecane,
298 heptadecane, octadecane, eicosane and docosane can be highlighted. Aldehydes such as octanal and
299 some fatty alcohols; heptadecanol, 1-octadecanol and 1-hexadecanol were also detected. 1-
300 Octadecanol was identified in sample 1EC (PE/PET). This compound is used as ink solvent and
301 lubricant, as well as in coatings and as plasticizer in packaging materials applications (Ash & Ash,
302 2004). 1 Hexadecanol, a compound used as adhesive in food packaging materials was identified in
303 samples 3EC, 7ES and 11ES (PP/PP, PE/EVA, PE/PET).
304 Acids such as lauric, palmitic and octadecanoic acid were also found. In this case fatty acids are
305 originating from several oils such as coconut oil (lauric acid) or palm oil (palmitic acid). Lauric acid
306 was found in sample 11ES. The use of this compound includes alkyl resins, wetting agents and
307 detergents, and it is also used as lubricant for easy opening polyolefin bottle cap liners (Bush,
308 Gilbert, & Goenaga, 1993). Palmitic acid was found in nine samples (4EC, 5EC, 6ES, 7ES, 8ES,
309 9EC, 10ES, 11ES, 12ES); it is a common fatty acid that occurs in natural fats and in oils and
310 nondrying oil for surface coatings. This compound is authorized as monomer or additive for food
311 contact materials (Bengtstrom, 2014). Octadecanoic acid is used as lubricant for plastics at low
312 concentrations as well as slip agent and for adhesives in food packaging materials. This compound
313 was detected only in sample 9EC (PE/PA) (Ash, 2004; Ash & Ash, 2004; Kumudini, 2012).
314 Plasticizers such as phthalates, citrates, adipates and phosphates were identified in the plastic
315 materials. Among the phthalates, bis (2-ethylhexyl) phthalate (DEHP) was confirmed in 4 samples,
316 diisobutyl phthalate (DIBP) in 5 samples, while DEP in 6 samples. Of these compounds only DEHP
317 is included as an additive or auxiliary in polymer production in the positive list in Regulation
318 10/2011.

Phthalates are compounds used in a wide range of applications due to their desirable properties. High molecular weight phthalates such as DEHP are used mainly as plasticizers in the production of PVC, although they are also used in other materials such as polyurethane (PU) and polyvinyl acetate (PVA) (Meeker, Sathyanarayana & Swan, 2009). DEP is used as plasticizers for PVC, PVA and nitrocellulose as well as in cosmetic formulations. DIBP is a plasticizer for nitrocellulose and it is often combined with other phthalates for PVC applications (Heudorf, Mersch-Sundermann, & Angerer, 2007; Rodgers, Rudel, & Just, 2014). Besides plasticizers, phathalates have been used as solvents to hold color and also can be present in printing inks (VanHolderbeke et al. 2014, Cao, 2010).

Tributyl acetylcitrate (ATBC) is one of the most frequent identified compound in tested samples of packaging materials, which was found in samples 3EC, 6ES, 7ES, 8ES, 9EC, 10ES, 11ES and 12ES. ATBC is a citrate compound widely used in food packaging applications as plasticizer for vinyl resins, cellulosic resins and rubbers, as well as plasticizer for inks, adhesives and coatings (Ash & Ash, 2004).

The adipate compound bis (2-ethylhexyl) adipate (DEHA) was detected in samples 10ES (PE/EVA), 11ES (PE/PET), and 12ES (PE/PET). This compound just like the ATBC is one of the most widely used plasticizers, used mainly in flexible PVC films as well as in coatings, adhesives and printing inks (Godwin, 2011). When these films are used in contact especially with fatty foodstuffs significant migration of DEHA to the foodstuff can occur. It has been reported that DEHA is associated with reproductive toxicity as well as with liver carcinogenity in ~~animals~~ animals (Dalgaard et al., 2003). ~~However~~However, the International Agency for Research on Cancer (IARC) has concluded that there is limited evidence for the carcinogenic of DEHA in experimental animals and considered that is not classifiable as to its carcinogenicity in humans (Group 3) (International Agency for Research on Cancer, 2000). Very limit information about

DEHA exposure is described in the literature. Fromme et al. (2007) reported values of daily intake via food of 0.7 µg/kg body weight for DEHA.

Regarding phosphates, triphenyl phosphate (TPP) was detected in samples 3EC and 9EC. This compound is used ~~as plasticizer for cellulose acetate articles and~~ in lacquers, as well as a flame retardant and solvent (Sheftel, 2000). This compound classified in class III according Cramer rules.

Tributyl aconitate (TBA), a compound commonly used to protect PVC against effects of light and heat, was detected in samples 6ES, 7ES, 8ES and 12ES (Dupáková, Dobiáš, Votavová, Klaudisová, & Voldrich, 2010). Isopropyl myristate was detected in sample 3EC, and is used as plasticizer for cellulosic, as well as pigment dispersant and binder (Ash & Ash, 2004).

Antioxidants such as BHT were detected in samples of PP/PET, PE/EVA and PE/PET (8ES, 10ES, 11ES and 12ES). This compound is used in the production of plastics, mainly polyolefins and is approved as antioxidant for food contact applications (Sheftel, 2000).

Slip agents were detected in all types of materials analyzed PE/PET, PP/PET, PE/PA, PE/PP and PE/EVA. According to the bibliography these compounds are added to reduce the surface coefficient of friction of polymers and are used to enhance either processing or end applications. Erucamide was found in all tested samples, oleamide in six samples, hexadecanamide in three samples and octadecanamide in two samples. Octadecamide is used as a slip agent, anti-fogging or lubricant for food packaging films (mainly polyolefins) (Ash, 2004). Erucamide is one of the most commercially important slip additives, used in polyolefin closures as well as in food contact materials due to their properties including heat stability as well as better blocking performance (Lahimer et al., 2013; Wypych, 2005). Hexadecanamide is used as slip agent for processed plastics, printing inks, coatings and films (Dupáková et al., 2010). Oleamide is used as slip agent for printing inks, coatings and films however erucamide is more widely used because it is thermally more stable than oleamide (Dupáková et al., 2010, Kumudini, 2012; Wypych, 2005).

Caprolactam was detected in PE/PA materials (samples 5EC and 9EC) and in PE/PET materials (samples 2EC and 4EC). In these last samples probably polyamide (PA) was present in one of the

inner layers of the packaging materials. PA in most cases is combined with polyolefins as a component of multilayer structure. Caprolactam is a monomer used for the manufacture of polycaprolactam (nylon 6), widely used in food packaging materials as well as in the manufacture of printing inks (Pogorzelska & Mielniczuk, 2001; Sheftel, 2000). According to IARC caprolactam is probably not carcinogenic to humans (Group 4) and in experimental animals there is evidence suggesting a lack of carcinogenicity of this compound (International Agency for Research on Cancer,1999). Other compounds of high toxicity, identified in our samples were diisocyanates, which are chemical compounds mainly used in polyurethane applications, such as coatings, adhesives, elastomers, sealants among others (Dupáková et al., 2010). 2,4-toluene diisocyanate was identified in 3 samples (7ES,8ES, 12ES) while 2,6-Toluene diisocyanate in sample 7ES. Their use in food packaging materials is regulated in the European Union, however their levels in final products must not exceed 1.0 mg/kg (Commission Regulation (EU) No 10/2011). The photoinitiator benzophenone was detected in samples 7ES and 12ES, the origin of this compound in tested samples is possibly the printing inks used in the external face of packaging films. This compound widely used as initiator for printing inks cured by UV radiation is possibly carcinogenic to humans. (International Agency for Research on Cancer, 2013).

The compounds benzenesulfonamide, n-ethyl-2-methyl- and benzenesulfonamide, n-ethyl-4-methyl were also detected in two samples (3EC and 9EC). These compounds have been used as component of ink formulations and are classified in class III of toxicity according to Cramer rules. In the European Union, these substances are not included on the list of authorized substances in the manufacture of plastic materials and articles. ~~However~~However, the U.S. Food and Drug Administration (FDA) listed these substances in the Inventory of Effective Food Contact Substances (FCS) Notifications. (U.S Food & Drug Administration, 2017).

Glycols such as triethylene glycol and tripropylene glycol were also identified. Triethylene glicol, a compound widely used as solvent in coating and ink industry, as well as a solvent for nitrocellulose and various resins was detected in sample 12ES (PE/PET) (Lago & Ackerman, 2016). Tripropylene

Glycol was detected in sample 8ES and is used as initiator for urethane polyols, in the manufacture of polyester plastics as well as solvent and homogenizing agent for inks. Synthetic fatty alcohols such as methyl palmitate was detected in sample 7ES (PE/EVA). This compound is used as intermediate for detergents, emulsifiers, stabilizers, resins, lubricant, plasticizers and defoamer in food-contact coatings (Ash & Ash, 2004).

Other identified compounds can be "non-intentionally added substances" (NIAS), such is the case of 2,4-di-tert-butylphenol and 2,6-di-tert-butyl-1,4-benzoquinone. 2,4-di-tert-butylphenol is a degradation product of Irgafos 168 while 2,6-di-tert-butyl-1,4-benzoquinone is a degradation product of antioxidants such as Irganox 1010, Irgafos 168 and Irganox PS 802 (Félix, Isella, Bosetti & Nerín, 2012; Lago &Ackerman, 2016). These compounds were detected in five and three samples respectively and are reported as NIAS in other migration studies (Alin & Hakkarainen, 2011; Félix et al., 2012; Lago & Ackerman, 2016).

The compound tert-butyl-1-oxaspiro (4,5) deca-6-9-diene-2,8-dione, a byproduct of the antioxidant Irganox 1010 was identified in almost all samples of PE/PET, PP/PP, PE/PA, LDPE/PP and PE/PVDC (1EC, 3EC, 4EC, 5EC, 6ES, 7EC, 8EC, 9EC, 10ES, 11ES, 12ES). This compound exhibited high toxicity according to Cramer rules and other authors have also estimated some toxicity (Lago & Ackerman, 2016; Rothenbacher & Schwack, 2009).

Squalene was identified in samples of PE/PET, PE/PA, PE/PP and PE/ EVA (2EC, 4EC, 5EC, 6ES, 7ES and 12ES). This compound is an ethylenic-unsaturated hydrocarbon that had oxygen-scavenging capacity to extend the shelf life of oxygen sensitive products. This compound ~~may be~~may be added to packaging materials such as polyethylene and polypropylene during conventional mixing processes to thermoplastics (Lopez-Rubio et al., 2004).

Lubricants such as glycerol trycaprilate were found in sample of PE/PET (2EC). Lubricants are used to minimize adhesion and viscosity of plastic materials.

Some compounds were identified only in samples from Ecuador, such as caprolactam, benzenesulfonamide, n-ethyl-2-methyl-, benzenesulfonamide, n-ethyl-4-methyl, isopropyl myristate and octadecanal. Others such as BHT and DEHA only in samples from Spain. Scientific information of some compounds listed in Table 4 was not available. Nevertheless, these results provide evidence of the wide range of compounds that can be found in plastics materials intended for food contact, which may be potential migrants to foodstuffs. Most of the identified compounds are not included in the positive list of Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food, and only 3 of the compounds detailed in Table 3 and 16 of the compounds detailed in Table 4 are regulated by these normative.

It is interesting to note that some of the compounds identified are included in the inventory list of the European Printing Ink Association (EuPIAincluir ~~ref~~), in different categories like this octane, undecane and tetradecane are within the solvents; hexane, dodecane, octadecane, hexadecane diethyl phthalate, 2,4-di-tert-butylphenol, isopropyl myristate, diisobutyl phthalate, methyl palmitate and 1-docosanol are included in substances used as additives or ingredients of additive preparations; 1-tetradecanol is included in polymeric resin-monomers/precursors/raw materials; 1-Octadecanol and triphenyl phosphate belong to pigment additives; and benzenesulfonamide, N-ethyl-2-methyl and benzenesulfonamide, N-ethyl-4-methyl are included in both groups substances used as additives or ingredients of additive preparations and polymeric resin - monomers/precursors/raw materials.

3.2 Estimation of migration into food simulants

Considering the large number of compounds detected in the screening of plastic packaging samples, a qualitative migration test was performed to identify the potential of all of these previously identified substances to migrate into food simulants.

Qualitative migration tests were carried out with 12 plastic packaging materials using tenax and isooctane as food simulants in contact with the plastic materials. Migration was performed from one

side of each laminate (side of contact with the food) and two independent replicates of each packaging material were analyzed. The acetone extracts of tenax and isooctane were analyzed by GC-MS with the same conditions used in the identification of semivolatile compounds. Results are listed in Table 5 and Table 6. In total 27 compounds were detected in the migration experiments, of which, 25 compounds migrated from samples from Ecuador while 17 migrated from samples from Spain. Some of them were common in both simulants and others were only observed in one of them.

~~In this work we have proposed an approximation with the purpose of having an idea about~~ To evaluate the differences in the amount of compound present in plastic materials after extraction with acetonitrile and in migration into tenax and isooctane, ~~.~~ The responses were calibrated against ~~estimated concentrations of these compounds were obtained considering~~ the response factor of the internal standard methyl myristate, as reported in Equation 1 (Guazzotti, Giussani, Piergiovanni, & Limbo, 2015; Jenke & Odufu, 2012).

$$C_a = C_i \, x(^{A_a}/_{A_i}) \qquad (1)$$

Where Ca is the analyte concentration (mg/L), C_i the internal standard concentration (mg/L), Aa the analyte area and A_i the internal standard area.

Migration test were performed in two food simulants, tenax and isooctane for dry and fatty food products, respectively. Migration of caprolactam occurred from the samples 2EC, 4EC and 5EC only into tenax, while in isooctane was not detected. It is important to note that caprolactam that was present in an external layer (polyamide) of a packaging material 5EC and 9EC, could migrate through the layers of packaging and reach the food simulant.

2,6-di-tert-butyl-1,4-benzoquinone migrates in tenax from samples PP/PP, PE/EVA and PE/PET (3EC, 7ES, 10ES) in concentrations from 0.00045 to 0.0018 mg/dm^2. 2,4-di-tert-butylphenol migrate from five packaging samples of PP/PP (3EC), PE/PET (4EC, 12ES) and PE/PVDC

(10ES,11ES) into both simulants tenax and isooctane, with higher concentrations in tenax than isooctane in most of the samples. In the case of samples 3EC, 10ES and 12ES, migration of 2,4-di-tert-butylphenol was lower in isooctane than in tenax. In the sample 11ES migration value was similar in both simulants, while in the sample 4EC migration was higher in isooctane than in tenax. Our values were lower than those reported by Félix et al. (2012), except the samples 10ES –and 11ES whose values were similar to those described by these authors.

BHT migrates only into tenax from the sample of PE/PET (12ES) in a concentration of 0.000761 mg/dm^2, while migration was not observed in the samples of PP/PET, PE/EVA and PE/PET. For this compound, the migration value obtained was lower than those reported ~~by Félix~~by Félix et al. (2012).

In terms of phthalates, DEP migrated in both simulants in six samples (3EC, 5EC, 6ES, 7ES, 8ES and 9EC). Its migration was higher into isooctane in samples 3EC, 6ES, 7ES and 8ES, while in sample 5EC the migration was higher in tenax. Migration was almost in the same proportion in both simulants in sample 9EC. Migration values in isooctane were from 0.0012 to 0.084 mg/dm^2, while in tenax were from 0.0010 to 0.017 mg/dm^2. Diisobutyl phthalate migrated from five samples 4EC, 5EC, 7EC, 11ES and 12ES into tenax and isooctane. Its migration was similar in both simulants in samples 7ES and 11 ES, while in the rest of the samples migration values were higher in isooctane than in tenax. Bis (2-ethylhexyl) phthalate migrated from the samples 2EC, 3EC, 9EC and 11ES in tenax and isooctane, with highest migration values in sample 3EC in both simulants.

Benzenesulfonamide, N-ethyl-2-methyl- and benzenesulfonamide,n-ethyl-4-methyl migrated into samples 3EC (PP/PP) and 9EC (PE/PA). Migration of benzenesulfonamide,n-ethyl-4-methyl was higher in tenax than isooctane in both packaging materials. Benzenesulfonamide, n-ethyl-2-methyl migrated more in tenax than isooctane in the sample 3EC, while in the case of sample 9EC migration ranged in a similar level into both simulants.

Isopropyl myristate migrated only in the sample 3EC in both simulants, with higher migration values in tenax than isooctane. 1-Hexadecanol migrated only into tenax from samples 3EC and 7ES,

500 with values from 0.0028 to 0.0084 mg/dm^2. Octadecanal migrated into both simulants from sample
501 3EC. Its migration into isooctane was higher than in tenax. Acetyl tributyl citrate was identified in
502 different types of packaging materials including PP/PP, PE/PET, PE/PA, PE/PP and PE/EVA films
503 in levels up to 2.0 mg/dm^2. This compound migrated from samples 3EC, 6ES, 7ES, 8ES, 9EC,
504 10ES, 11ES and 12ES into tenax and isooctane. In samples 3EC and 12ES migration was higher in
505 isooctane while in sample 6ES migration values were similar in both simulants. In the rest of
506 samples migration was greater in tenax than isooctane. ATBC was one of the predominant migrant
507 in both simulants, with migration values from 0.00026 to 0.96 mg/dm^2 in isooctane and from 0.0013
508 to 0.58 mg/dm^2 in tenax. The highest concentration level was observed in isooctane.
509 Other plasticizers found in migration studies were triphenyl phosphate (TPP) and tributyl aconitate.
510 TPP migrated from packaging samples 3EC and 9EC into both simulants, with higher migration
511 values in tenax. Migration of tributyl aconitate into both simulants occurred from samples 6ES,
512 7ES, 8ES, 9EC and 12ES, with higher migration values in tenax than isooctane in all samples,
513 except in the case of sample 8ES where the migration in isooctane was greater than in tenax.
514 Another compound also relevant in both simulants was 7,9 di-tert-butyl-1-oxaspiro (4,5) deca-6-9-
515 diene-2,8-dione, that migrate in eleven of twelve tested samples. Migration was higher in tenax than
516 isooctane, except in the case of samples 7ES and 11 ES when migration values are similar in both
517 simulants. Migration values in isooctane were from 0.00075 to 0.013 mg/dm^2, whereas in tenax
518 from 0.0011 mg/dm^2 to 0.046 mg/dm^2. Oleamide migrated in sample 3EC in both simulants. The
519 highest concentration level was observed in tenax.
520 DEHA was found in three of twelve tested plastic materials in concentrations from 0.024 to 1.0
521 mg/dm^2 and migrated in both simulants in the three samples of PE/PVDC and PE/PET (10ES, 11ES
522 and 12ES). Its migration was higher into tenax than into isooctane, migration values from 0.023 to
523 0.081 mg/dm^2 were reached in tenax. The slip agent erucamide was detected in all plastic materials
524 with concentrations from 0.082 to 1.3 mg/dm^2. In the same way this compound migrated in all
525 tested samples in tenax and isooctane, with concentrations from 0.0011 to 0.14 mg/dm^2 and from

0.0096 to 0.19 mg/dm^2 in isooctane and tenax, respectively. Migration values were higher in tenax than in isooctane in all cases. Hexadecanamide migrated only in samples 3EC and 9EC, with higher migration values in tenax than in isooctane. Octadecanamide migrated from PE/PA film (9EC) in tenax and isooctane. Its migration into tenax was greater than in isooctane.

Squalene migrated into tenax and isooctane from samples 2EC, 4EC, 5EC, 6ES, 7ES and 12E (PE/PET, PE/PA, PE/PP and PE/EVA), reaching high concentrations in tenax in almost all samples tested. Migration of alkanes such as tetradecane, hexadecane, heptadecane, octadecane and dodecane was also occurred in some samples, with higher migration values into tenax than in isooctane. In general migration results showed higher migration values in tenax than in isooctane. Only nine of out of all migrant compounds appeared in the positive list of Regulation 10/2011.

4. Conclusions

In this work the determination of volatile and semivolatile compounds in 12 packaging materials were performed using P&T coupled to GC-MS for volatile compounds and GC-MS for semivolatile compounds. These techniques have demonstrated to be useful for screening and identification of compounds from plastic materials as well as their migration into food simulants. About 100 volatile and semivolatile compounds including "non intentionally added substances" were detected in plastic materials. Of these, 27 compounds migrated into tenax and/or isooctane. In general, migration occurs to a larger extent in tenax than in isooctane.

On the other hand, it is interesting to point out that most of detected compounds and even more, the migrants detected in the food simulants tested are not included in the positive list of monomers and additives that are allowed to be used in plastic food contact materials; and neither in the ~~–~~inventory list of the European Printing Ink Association.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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Fig.1. Chromatogram of semivolatile compounds sample 9EC (PE/Polyamide). 1) caprolactam, 2) diethyl phthalate, 3) benzenesulfonamide, n-ethyl-2-methyl-, 4) benzenesulfonamide, n-ethyl-4-methyl, 5) 7,9 di-tert-butyl-1-oxaspiro (4,5)deca-6-9-diene-2,8-dione, 6) palmitic acid 7) hexadecanamide, 8) tributyl acetylcitrate, 9) triphenyl phosphate, 10) erucamide.

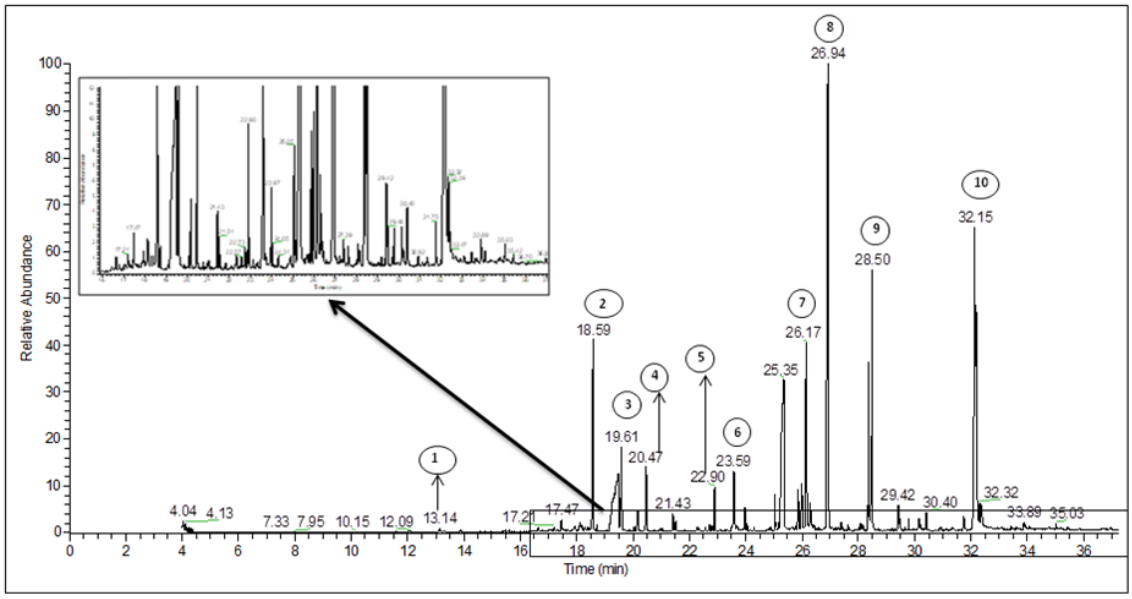

Table 1
Details of the twelve plastic films.

Sample Code	Type of material		Thickness µm	Origin	Observations
	Internal side	External side			
1EC	PE	PET	153	Ecuador	With printing ink
2EC	PE	PET	141	Ecuador	With printing ink
3EC	PP	PP	46	Ecuador	Without printing ink
4EC	PE	PET	146	Ecuador	Without printing ink
5EC	PE	PA	72	Ecuador	Without printing ink
6ES	PE	PP	70	Spain	Without printing ink
7ES	PE	EVA	70	Spain	With printing ink
8ES	PP	PET	35	Spain	With printing ink
9EC	PE	PA	50	Ecuador	With printing ink
10ES	PE	EVA	61	Spain	With printing ink
11ES	PE	PET	54	Spain	With printing ink
12ES	PE	PET	77	Spain	With printing ink

PE: polyethylene
PET: Polyethylene terephthalate
PA: Polyamide
PP: Polypropylene
EVA: Ethylene vinyl acetate

Table 2
Purge and Trap Instrument Conditions

Purge Parameters:	
Valve Oven Temp	140 °C
Transfer Line Temp	140 °C
Sample mount Temp	90 °C
Purge ready Temp	35 °C
Standby Flow	0 mL/min
Pre-Purge Time	0.50 min
Pre-Purge Flow	40 mL/min
Sample Preheat time	1.00 min
Sample Temp	60 °C
Purge Time	20.00 min
Purge Flow	40 mL/min
Condenser Ready Temp	40 °C
Condenser Purge Temp	20 °C
Dry Purge Time	0.50 min
Desorb Parameters:	
Desorb Preheat Temp	245 °C
Desorb Time	2.00 min
Desorb Temp	250 °C
Desorb Flow	400 mL/min
Bake Parameters	
Bake Time	10.00 min
Bake Temp	280 °C
Bake Flow	200 mL/min
Condenser Bake Temp	200 °C

Table 3

Compounds extracted by dynamic Headspace and subsequently identified by GC-MS in the plastic materials with their respective level of toxicity (TC) according Cramer rules

Compound	IUPAC NAME	CAS	RT (min)	TC	Samples											
					1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
Hexane	Hexane	110-54-3	6,07	I							X		X			
Hexane, 2,5-dimethyl-	2,5-dimethylhexane	592-13-2	10.56	I				X								
Hexane, 2,4-dimethyl-	2,4-dimethylhexane	589-43-5	10.67	I				X	X							
Pentane, 2,3,4-trimethyl-	2,3,4-trimethylpentane	565-75-3	11.42	I	X	X	X	X	X				X			
Pentane, 2,3,3-trimethyl-	2,3,3-trimethylpentane	560-21-4	11.65	I	X	X	X	X	X	X	X		X			
Heptane, 3-methyl-	3-methylheptane	589-81-1	12.20	I				X		X	X					
Cyclopentane, 1-ethyl-2-methyl-, cis-	1-ethyl-2-methylcyclopentane	930-89-2	13.05	I				X	X	X						
Octane	Octane	111-65-9	13.21	I	X	X		X	X	X	X		X	X	X	X
3-Heptene, 3-methyl-	3-Methyl-3-heptene	7300-03-0	13.30	I	X											
2-Heptene, 3-methyl-	(E)-3-methylhept-2-ene	3404-75-9	13.39	I	X			X	X							
2-Octene	oct-2-ene	111-67-1	13.95	I				X	X							
Heptane, 2,4-dimethyl-	2,4-dimethylheptane	2213-23-2	14.08	I			X	X								
Heptane, 2,5-dimethyl-	2,5-dimethylheptane	2216-30-0	14.58	I	X	X										
Octane, 3-methyl-	3-methyloctane	2216-33-3	14.58	I				X								
Hexanal	Hexanal	66-25-1	14.92									X				
Heptane, 2,3-dimethyl-	2,3-dimethylheptane	3074-71-3	15.42	I	X			X	X							
Heptane, 3,4-dimethyl-	3,4-dimethylheptane	922-28-1	15.54	I				X								
Heptane, 2,4,6-trimethyl-	2,4,6-trimethylheptane	2613-61-8	16.03	I				X								
Heptane, 2,2,4-trimethyl-	2,2,4-trimethylheptane	14720-74-2	16.17	I	X	X	X	X	X				X			
Octane, 2,2-dimethyl-	2,2-dimethyloctane	15869-87-1	16.46	I	X	X		X	X							

Octane, 3,3-dimethyl-	3,3-dimethyloctane	4110-44-5	16.98	I	X	X		X	X				X			
Nonane, 4-methyl-	4-methylnonane	17301-94-9	17.62	I	X	X		X	X							

Compound	**IUPAC NAME**	**CAS**	**RT (min)**	**TC**	**Samples**											
					1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
Octane, 2,3-dimethyl-	2,3-dimethyloctane	7146-60-3	17.70	I				X								
Octane, 4-ethyl-	4-ethyloctane	15869-86-0	19.01	I	X	X		X								
Nonane, 3-methyl-	3-methylnonane~~3-methylundecane~~	5911-04-6~~1002-43-3~~	19.52	I		X										
Decane	Decane	124-18-5	20.50	I	X	X		X	X	X	X	X	X	X	X	X
Octanal <n->	Octanal	124-13-0	22.24	I								X				
Undecane	Undecane	1120-21-4	23.82	I		X		X		X	X	X	X	X	X	X
1-Tetradecanol	tetradecan-1-ol	112-72-1	24.58	I	X	X				X	X					
Nonanal	Nonanal	124-19-6	25.53	I								X				
1- Dodecene	dodec-1-ene	112-41-4	26.80	I						X			X			
Dodecane	Dodecane	112-40-3	26.89	I	X	X	X	X	X	X	X	X	X	X	X	X
Benzene, 1,3-Bis(1,1-Dimethylethyl)-	1,3-ditert-butylbenzene	1014-60-4	29.32	I										X	X	X
Tridecane	Tridecane	629-50-5	29.80	I		X	X			X	X	X	X		X	
Tetradecane	Tetradecane	629-59-4	32.50	I		X			X	X	X		X	X	X	
Caprolactam	Azepan-2-one	105-60-2	32.87	III		**X**										
Octadecane	Octadecane	593-45-3	35.06	I				X	x	x	x		x	X		
Butylated hydroxytoluene	2,6-ditert-butyl-4-methylphenol	128-37-0	36.79	II								**X**		**X**	**X**	**X**
Diethyl phthalate	diethyl benzene-1,2-dicarboxylate	84-66-2	40.10	I							**X**					

TC: Cramer Toxicity

Table 4

Confirmed and tentative identified compounds extracted by liquid extraction and identified by GC-MS in the plastic materials with their respective level of toxicity (TC) according Cramer rules.

Compound	IUPAC Name	CAS	RT (min)	Function	TC	SML	Samples											
							1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
***Dodecane**	Dodecane	112-40-3	12.09	Alkane	I	NL	X	X	X	X	X	X	X	X	X	X	X	X
Triethylene glicol	2-[2-(2-hydroxyethoxy)ethoxy]ethanol	112-27-6	12.5	Solvent	I	**												X
***Caprolactam**	azepan-2-one	105-60-2	13.14	Monomer in polyamides	III	15		X		X	X				X			
***Tridecane**	Tridecane	629-50-5	13.91	alkane	I	NL		X										
Tripropylene Glycol	1-[2-(2-hydroxypropoxy)propoxy]propan-2-ol	1638-16-0	14.30	Solvent (solubilize resins commonly used in printing-ink) internet	III	NL								X				
***2,6-Toluene diisocyanate**	1,3-diisocyanato-2-methylbenzene	91-08-7	14.75	Used in the production of flexible polyurethane foams	III	ND							X					
***2,4-Toluene diisocyanate**	2,4-diisocyanato-1-methylbenzene	584-84-9	14.85	Used in the production of flexible polyurethane foams	III	ND							X	X				X
***Tetradecane**	Tetradecane	629-59-4	15.61	Alkane	I	NL		X		X	X	X	X					
2,6-di-tert-butyl-1,4-benzoquinone	2,6-ditert-butylcyclohexa-2,5-diene-1,4 dione	719-22-2	16.65	Degradation product	II	NL			X				X			X		
***Butylated Hydroxytoluene**	2,6-ditert-butyl-4-methylphenol	128-37-0	17.29	Antioxidant	II	3								X		X	X	X
2,4-di-tert-butylphenol	2,4-ditert-butylphenol)-	96-76-4	17.32	Degradation product from antioxidants	I	NL			X	X						X	X	X
***Diethyl Phthalate**	diethyl benzene-1,2-dicarboxylate	84-66-2	18.59	Solvent to hold color ~~Plasticizer in the production of cellulose esters (cellulose acetate films) intended for~~	I	NL			X		X	X	X	X	X			

~~contact with food~~

Compound	IUPAC Name	CAS	RT (min)	Function	TC	SML	Samples											
							1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
***Hexadecane**	Hexadecane	544-76-3	18.71	Alkane	I	NL	X	X		X	X	X	X			X		X
***Benzophenone**	diphenylmethanone	119-61-9	19.25	Photoinitiator UV-inks	III	~~NL~~0,6							X					X
Benzenesulfonamide, N-ethyl-2-methyl-	N-ethyl-2-methylbenzenesulfonamide	1077-56-1	19.61	Component of ink formulations	III	NL			X						X			
***Heptadecane**	Heptadecane	629-78-7	20.15	Alkane	I	NL		X					X			X		
Benzenesulfonamide, N-ethyl-4-methyl	N-ethyl-4-methylbenzenesulfonamide	80-39-7	20.47	Component of ink formulations	III	NL			X						X			
***Octadecane**	Octadecane	493-45-3	21.52	Alkane	I	NL				X	X	X	X		X	X		
Isopropyl myristate	propan-2-yl tetradecanoate	110-27-0	21.82	Plasticizer, lubricant	I	NL			X									
***Diisobutyl phthalate**	bis(2-methylpropyl) benzene-1,2-dicarboxylate	84-69-5	22.31	~~Plasticizer for PVC and other polymers~~Present in printing inks	I	NL				X	X		X				X	X
1-Octadecanol	octadecan-1-ol	112-92-5	22.35	Ink solvent, plasticizer	I	NL	X											
1-Hexadecanol	hexadecan-1-ol	36653-82-4	22.57	Adhesive in food packaging materials and coatings.	I	**			X				X				X	
7,9 Di-Tert-Butyl-1-Oxaspiro (4,5)Deca-6-9-Diene-2,8-Dione	7,9-ditert-butyl-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione	82304-66-3	22.90	Degradation product from antioxidant	III	NL	X		X	X	X	X	X	X	X	X	X	X
Methyl palmitate	Methyl hexadecanoate	112-39-0	23.11	Intermediate for resins and defoamer in food-contact coatings.	I	NL							X					

Palmitic acid	Hexadecanoic acid	57-10-3	23.59	Slip agent degradant	I	**				X	X	X	X	X	X	X	X	X
***Eicosane**	Eicosane	112-95-8	24.04	Alkane	I	NL				X	X		X					

Compound	**IUPAC Name**	**CAS**	**RT (min)**	**Function**	**TC**	**SML**	**Samples**											
							1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
Octadecanal	Octadecanal	638-66-4	24.31	-	I	NL			X									
Heptadecanol	Heptadecan-1-ol	1454-85-9	25.05	Used as Plasticizer and in the manufacture of wetting agents and detergents.	I	NL					X				X	X		
Tributyl aconitate	Tributyl (1E)-1-propene-1,2,3-tricarboxylate	7568-58-3	25.85	Plasticizer	I	NL					X	X	X	X				X
Octadecanoic Acid	Octadecanoic Acid	57-11-4	25.99	PVC lubricant, Adhesive in food packaging.	I	**									X			
Hexadecanamide	Hexadecanamide	629-54-9	26.17	Slip agent	III	NL			X			X			X			
***Docosane**	Docosane	629-97-0	26.35	Alkane	I	NL		X		X	X		X			X	X	
***Tributyl acetylcitrate**	tributyl 2-acetyloxypropane-1,2,3-tricarboxylate	77-90-7	26.94	Plasticizer for flexible packaging films	I	60			**X**			X	X	X	X	**X**	**X**	X
Oleamide	(Z)-octadec-9-enamide	301-02-0	28.09	Slip agent	III	**	X		X	X		X	X					X
Octadecanamide	Octadecanamide	124-26-5	28.34	Slip agent, antiblock agent and release agent.	III	**						X			X			
***Bis(2-ethylhexyl) adipate**	bis(2-ethylhexyl) hexanedioate	103-23-1	28.40	Plasticizer in the production of plastic materials.	I	18 60										X	X	
1-Docosanol	Docosan-1-ol	661-19-8	28.42	Used in synthetic fibres and lubricants, thermal papers and	I	NL				X								

				Toners																			
***Tetracosane**	Tetracosane	646-31-1	28.48	Alkane	I					X			X										
Triphenyl phosphate	Triphenyl phosphate	115-86-6	28.50	Pigment additive ~~Plasticizer for cellulose acetate articles~~ and plasticizer for coatings, lacquers and varnishes	III	NL			X							X							

Compound	IUPAC Name	CAS	RT (min)	Function	TC	SML	Samples											
							1EC	2EC	3EC	4EC	5EC	6ES	7ES	8ES	9EC	10ES	11ES	12ES
***Bis(2-ethylhexyl) phthalate**	bis(2-ethylhexyl) benzene-1,2-dicarboxylate	117-81-7	29.85	~~Principal plasticizer in the production of PVC and its copolymers.~~ Substance used as additives or ingredients of additive preparations	I	1,5 60		**X**	X						**X**		X	
cis-11-Eicosenamide	(Z)-icos-11-enamide	10436-08-5	30.17	Used in adhesives and components of coatings	III	**										X	X	X
***Erucamide**	(Z)-docos-13-enamide	112-84-5	32.15	Slip agent	III	**	X	X	X	X	X	X	X	X	X	X	X	X
***Squalene**	2,6,10,15,19,23-hexamethyltetracosa-2,6,10,14,18,22-hexaene	111-02-4	32.39	Used as oxygen-scavenging	I	NL		X		X	X	X	X					X
Glycerol tricaprylate	2,3-di(octanoyloxy)propyl octanoate	538-23-8	33.45	Lubricant	I	NL		X										

*Confirmed compounds
TC: Cramer Toxicity
SML: Specific migration limit
IUPAC:PUB CHEM
NL: Non listed in Regulation 10/2011
** Specific migration limit of 60 mg/kg (Substances for which no specific migration limit or other restrictions are provided in Annex I Regulation 10/2011)

Table 5

Comparison of the amounts of the compounds in packaging materials from Ecuador and migration into tenax and isooctane

Compound	RT (min)	Samples (mg/dm²)																	
		1EC			2EC			3EC			4EC			5EC			9EC		
		PP	I	T	PP	I	T	PP	I	T	PP	I	T	PP	I	T	PP	I	T
Caprolactam	13.12				0.073	nd	0.025				0.68	nd	**0.010**	0.37	nd	0.024			
Tetradecane	15.61				0.015	0.00024	0.0033				0.013	0.0014	0.0030	0.0056	0.00049	0.00095			
2.6-di-tert-butyl-1.4-benzoquinone	16.65							0.013	nd	0.00074									
2.4-di-tert-butylphenol	17.32							0.010	0.00057	0.00092	0.024	0.0016	0.00074						
Diethyl Phthalate	18.56							0.023	0.0039	0.0025				0.0049	0.0012	0.0021	0.42	0.0014	0.0017
Hexadecane	18.71										0.0055	0.0015	0.0033	0.012	0.00055	0.0015			
Benzenesulfonamide. N-ethyl-2-methyl-	19.55							0.049	0.0057	0.017							0.15	0.018	0.017
Heptadecane	20.15				0.0043	0.00015	0.0023												
Benzenesulfonamide. N-ethyl-4-methyl	20.42							0.023	0.0021	0.0085							0.18	0.0054	0.0074
Octadecane	21.52				0.032	0.00049	0.0078				0.031	0.0015	0.0070	0.014	0.00062	0.0029			
Isopropyl myristate	21.82							0.068	0.0041	0.017									
Diisobutyl phthalate	22.31										0.0017	0.0014	0.00039	0.0030	0.0017	0.00038			
1-Hexadecanol	22.57							0.030	nd	0.0084									
7.9 Di-Tert-Butyl-1-Oxaspiro (4.5)Deca-6-9-Diene-2.8-Dione	22.91	0.023	0.0016	0.0041				0.19	0.013	0.046	0.018	0.0024	0.0039	0.012	0.00075	0.0014	0.069	0.0029	0.0050
Octadecanal	24.31							0.017	0.011	0.0043									
Tributyl aconitate	25.85																0.046	0.0096	0.025
Hexadecanamide	26.17							0.031	0.00093	0.0029							0.29	0.015	0.045
Docosane	26.35				0.019	0.0016	0.010				0.024	0.00085	0.013	0.0072	0.0010	0.0047			
Tributyl acetyl citrate	26.94							0.088	0.046	0.010							2.0	0.17	0.27
Oleamide	28.09							0.30	0.016	0.051									
Octadecanamide	28.34																0.22	0.0096	0.094
Triphenyl phosphate	28.50							0.12	0.039	0.044							0.37	0.062	0.15
Bis(2-ethylhexyl) phthalate	29.85				0.010	0.0011	0.0012	1.8	0.37	0.34							0.029	0.014	0.015
Erucamide	32.13	0.16	0.011	0.049	0.28	0.0011	0.024	0.52	0.085	0.13	1.3	0.14	0.19	0.55	0.026	0.063	0.81	0.088	0.18

Squalene	32.39	0.38	0.13	0.0072		0.065	0.023	0.010	0.051	0.0076	0.0035	

PP: Plastic packaging; I: Isooctane; T: Tenax; nd: not detectable

Table 6
Comparison of the amounts of the of compounds in packaging materials from Spain and migration into tenax and isooctane

Compound	RT (min)	Samples (mg/dm^2)																	
		6ES			7ES			8ES			10ES			11ES			12ES		
		PP	I	T	PP	I	T	PP	I	T	PP	I	T	PP	I	T	PP	I	T
Tetradecane	15.61	0.0043	0.00026	0.00045	0.0075	0.00034	0.00066												
2.6-di-tert-butyl-1.4-benzoquinone	16.65				0.013	nd	0.00045				0.034	nd	0.0018						
Butylated hydroxytoluene	17.29																0.0031	nd	0.00076
2.4-di-tert-butylphenol	17.32										0.030	0.0095	0.011	0.041	0.0075	0.0077	0.0088	0.00069	0.0010
Diethyl Phthalate	18.56	0.13	0.0040	0.0026	0.085	0.084	0.0010	0.048	0.027	0.017									
Hexadecane	18.71	0.0099	0.00063	0.0013	0.034	0.00093	0.0035										0.0073	0.00041	0.0025
Heptadecane	20.15				0.0046	0.00050	0.0029												
Octadecane	21.52	0.016	0.0012	0.0046	0.039	0.0018	0.012				0.023	0.00037	0.0036				0.0032	0.00055	0.0069
Diisobutyl phthalate	22.31				0.012	0.0016	0.0019							0.0045	0.0019	0.0019	0.0073	0.0047	0.0019
1-Hexadecanol	22.57				0.0075	nd	0.0028												
7.9 Di-Tert-Butyl-1-Oxaspiro (4.5)Deca-6-9-Diene-2.8-Dione	22.91	0.12	0.0058	0.0092	0.0084	0.0027	0.0023	0.013	0.0030	0.0090	0.034	0.016	0.0034	0.029	0.0013	0.0019	0.017	0.0014	0.0011
Tributyl aconitate	25.85	0.050	0.012	0.023	0.059	0.013	0.036	0.022	0.014	0.0029							0.066	0.011	0.054
Tributyl acetyl citrate	26.94	1.7	0.24	0.28	2.0	0.24	0.36	1.1	0.48	0.58	0.0016	0.00026	0.0014	0.0073	0.00033	0.0013	1.0	0.96	0.087
Bis(2-ethylhexyl) adipate	28.4										0.21	0.0014	0.081	1.0	0.0039	0.040	0.024	0.00083	0.023
Bis(2-ethylhexyl) phthalate	29.85													0.086	0.0010	0.0095			
Erucamide	32.13	0.60	0.034	0.047	0.42	0.011	0.037	0.082	0.0025	0.0096	0.19	0.018	0.032	1.0	0.022	0.045	0.64	0.021	0.064
Squalene	32.39	0.067	0.028	0.0067	0.027	0.014	0.0062										0.45	0.0031	0.091

1 PP: Plastic packaging; I: Isooctane; T: Tenax; nd: not detectable