Review article

Analytical strategies for organic food packaging contaminants

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ABSTRACT

In this review, we present current approaches in the analysis of food-packaging contaminants. Gas and liquid chromatography coupled to mass spectrometry detection have been widely used in the analysis of some relevant families of these compounds such as primary aromatic amines, bisphenol A, bisphenol A diglycidyl ether and related compounds, UV-ink photoinitiators, perfluorinated compounds, phthalates and non-intentionally added substances.

Main applications for sample treatment and different types of food-contact material migration studies have been also discussed. Pressurized Liquid Extraction, Solid-Phase Microextraction, Focused Ultrasound Solid-Liquid Extraction and Quechers have been mainly used in the extraction of food contact material (FCM) contaminants, due to the trend of minimising solvent consumption, automatization of sample preparation and integration of extraction and clean-up steps.

Recent advances in analytical methodologies have allowed unequivocal identification and confirmation of these contaminants using Liquid Chromatography coupled to High Resolution Mass Spectrometry (LC–HRMS) through mass accuracy and isotopic pattern applying. LC–HRMS has been used in the target analysis of primary aromatic amines in different plastic materials, but few studies have been carried out applying this technique in post-target and non-target analysis of FCM contaminants.

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1. Introduction

Food contact materials are all materials and articles intended to come into contact with food, such as packaging and containers, kitchen equipment, cutlery and dishes. Modern food packaging materials are designed to fulfil multiple purposes including the protection of food products from external sources of contamination and damage, and the information of consumers about ingredients and nutritional data [1]. Furthermore, food packaging provides preservation, ease of transportation and storage of food products [2,3]. Thus, the production and use of packaging materials has increased during the last decades, comprising an indispensable part of food manufacturing. The packaging manufacturing industry is making an effort to combine low cost manufacturing with appearance improvement for consumer appeal, maintenance of food safety and a minimal environmental impact. Concerning food safety, one of the major considerations of manufacturers must be the migration of harmful chemical compounds from packaging materials to food, as they could adversely affect consumer health [4]. In this context, strict national and international regulations, applicable to all materials which come in direct contact with food, have been established. In a European Framework, Regulation 1935/2004/EC [5] regulates materials and articles intended to come into contact with food, providing the basis for securing a high level of protection of human health. In addition, Regulation 2023/2006 [6] describes the good manufacturing practices (GMP) that industry should follow to protect the interest of consumers.

The majority of studies published in the literature are mostly focused on the analysis of FCM contaminants in materials rather than in food matrices and food simulants. Fig. 1 shows that non-intentionally added substances (NIAS), primary aromatic amines (PAAS) and inks (photoinitiators) have only been analyzed in food contact materials [7–11]. Although contaminants such as perfluorinated compounds (PFCs) and bisphenol A (BPA) have been mainly determined in materials [12–14], these contaminants have also been determined in food, in some studies [15,16]. Instead, phthalates have been more frequently studied in food [17–28,29,30] (see Fig. 1). NIAS, BPA, phthalates, PAAS and inks have been analyzed in food simulants [7,8,10,11]. Table 1 shows food contact contaminants that could be transferred to the food.

Seventeen different materials such as ceramics, cork, rubber, glass, plastics, metals, paper and board, silicones, wood and so on, are described in the Regulation 1935/2004/EC [5] to be in contact with food materials. In the present study, we have focused our work mainly on plastic materials, due to plastic is one of the main material used and, consequently, analyzed in FCM studies. Plastic materials are composed by monomers and other starting substances transformed through chemical reactions in a polymer,

which represents the principal component. The most widely produced synthetic plastic polymers are poly vinyl chloride (PVC), polyvinyl acetate (PVA), polyethylene (PE) and polypropylenes (PP), in which polymerization is made by monomers of vinyl chloride, vinyl acetate or simple alkenes (ethane and propene), respectively. Between the most widely used plastic materials are kitchen equipment such as nylon utensils, plastic laminates (plastic films) and other enamelware made of polycarbonates [7,8]. Polycarbonates (PC) are one of the high-performance heterochain polymeric materials that comprise the family of engineering thermoplastics with a wide variety of applications due to excellent mechanical properties, high impact strength, heat resistance and high modulus of elasticity, as well as excellent toughness, clarity and transparency. These properties make it an ideal choice for tableware, microwave ovenware, reusable bottles, food storage containers and water pipes [30,35]. European Regulation 10/2011 is based on a positive list of authorized substances which may be intentionally used in the manufacture of plastic layers in plastic materials and articles and related restrictions, such as specific migration limits (SML). SML means the maximum permitted amount of a given substance released from a material or article in to food or food simulants [36].

Other commonly used materials are paper and paperboard. They are used in corrugated boxes, wrapping paper, milk cartons, folding cartons, bags and sacks, paper plates and beverage cups, fast-food containers, microwave popcorn bags, ice cream cups, dessert containers, baking paper, etc. More specifically, paperboard, due to its thickness, is commonly used for shipping-packages, such as boxes and cartons, but also as packaging material for fast food, such as pizza. Plain paper does not possess good heat-sealing and barrier properties, so it is almost always treated, coated, or impregnated with additives in order to improve its functional and protective properties, before its use as packaging material [37]. In addition, recycled paper is mainly used in direct contact with dry foodstuff like flour, grain, sugar, salt, rice and pasta. A large number of chemicals are used in the paper recycling process, such as bleach, paper strengthening agents and inks. Cardboard packaging materials are mainly contaminated with mineral oil via the fibre recyclate stream [34]. There is an increasing public demand for avoiding the use of waste paper, as packaging material that comes into contact with food products. This demand can be attributed to the shortage of available data concerning migration models of the referred contaminants, but also due to the lack of specific laws for paper and paperboard food packaging. The European regulation (Reg. CE 1935/2004) [5] only affirms that recycled paper can be used for solid, dry foods. To date European laws have not yet provided formal guidelines for reclaimed-fibre testing to assess fibre risk, despite suggesting an approach similar to that for plastics.
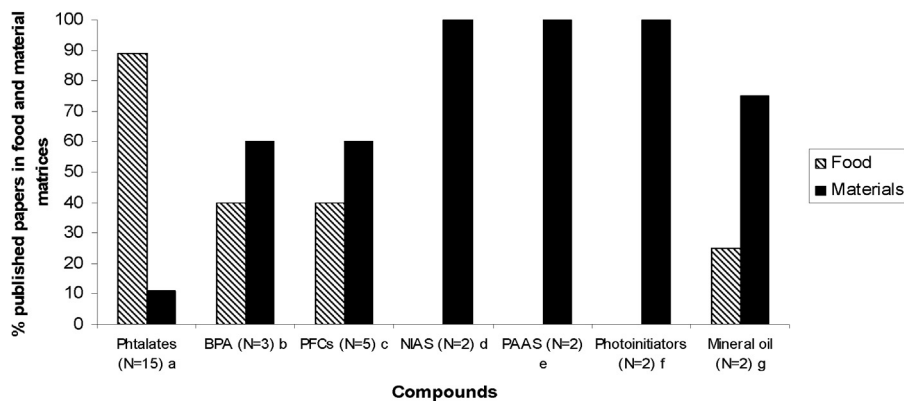

Fig. 1. Publications in food and materials for some food packaging contaminants. (N = number of papers published for each compound; Letters = references). a: [12,17,18,21,22,23,24,25,26,27,28,29,33,101,102]; b: [15,30,31]; c: [12,13,16,32,96]; d: [9]; e: [7,8]; f: [10,12], g [98,99].

Table 1
Food contact material contaminants, food products and food contact materials.

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
Primary aromatic amines (PAAS)					
Aniline	62-53-3	ANL		Plastic (nylon kitchen utensils)	[8]
2,4 Dimaminetluene	95-80-7	2,4 TDA		Plastic (nylon kitchen utensils)	[8]
Benzidine	92-87-5	BNZ		Plastic (plastic laminate)	[7]
o-Ansidine	90-04-0	o-ANS		Plastic (plastic laminate)	[7]
4,4′ Diaminodiphenylether	101-80-4	4,4′ DPE		Plastic (nylon kitchen utensils)	[8]
o-Toludine	95-53-4	o-TOL		Plastic (plastic laminate)	[7]
4,4′ Methylenedianiline	101-77-9	4,4′ MDA		Plastic (nylon kitchen utensils)	[8]
o-Diansidine	119-90-4	o-DANS		Plastic (plastic laminate)	[7]
o-Tolidine	119-93-7	o-TOLI		Plastic (nylon kitchen utensils)	[8]
p-Chloroaniline	106-47-8	p-ANL		Plastic (plastic laminate)	[7]
p-Cresidine	120-71-8	p-CRS		Plastic (plastic laminate)	[7]
4,4′ Methylene-bis-(2-methylaniline)	838-88-0	4,4′ MBM		Plastic (nylon kitchen utensils)	[8]
4,4′ Thiodianiline	139-65-1	4,4′ TDA		Plastic (plastic laminate)	[7]
2-Naphtylamine	91-59-8	2-NAPH		Plastic (plastic laminate)	[7]
4-Chloro-o-toludine	95-69-2	4-Cl-TOL		Plastic (plastic laminate)	[7]
5 Nitro-o-toludine	99-55-8	5-N-O-TOL		Plastic (plastic laminate)	[7]
2,4,5 Trimethylaniline	137-17-7	2,4,5 MTA		Plastic (plastic laminate)	[7]
4-Aminobipheny	92-67-1	4-ABF		Plastic (plastic laminate)	[7]
4,4′ Methylene-bis-(2-chloroaniline)	101-14-4	4,4′ M(2Cl)		Plastic (plastic laminate)	[7]
3,3′ Dichlorobenzidine	91-94-1	3,3′ DCB		Plastic (plastic laminate)	[7]
p-Aminobenzene	60-09-3	p-ABZ		Plastic (plastic laminate)	[7]
m-Phenyldiamine	108-45-2	m-PDA		Plastic (nylon kitchen utensils)	[8]
1,5 Diamine naphtalene	2243-62-1	1,5 DAN		Plastic (nylon kitchen utensils)	[8]
o-Aminoazotoluene	97-57-3	o-AaT		Plastic (plastic laminate)	[7]
BPA, BADGEs and related compounds					
Bisphenol A 2,2-bis(4-hydroxyphenyl)propane	80-05-7	BPA	Canned food		[15]
Bisphenol F bis(4-hydroxyphenyl)METHANE	620-62-8	BPF		Recycled paper	[31]
Bisphenol A diglycidyl ether	1675-54-3	BADGE		Recycled paper	[31]
Bisphenol f diglycidyl ether	2095-03-6	BFDGE		Recycled paper	[31]
Perfluorinated compounds (PFCs)					
Perfluorooctanesulfonic acid tetraethylammonium salt	1763-23-1	PFOS	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluorobutanoic acid	375-22-4	PFBA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluoropentanoic acid	2706-90-3	PFPeA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluorohexanoic	307-24-4	PFHxA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluroheptanoic acid	375-85-9	PFHpA	Popcorn	Plastic (popcorn bags)	[32]
Perfluorooctanoic acid	335-67-1	PFOA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluorononanoic acid	375-95-1	PFNA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluorodecanoic acid	335-76-2	PFDA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluoroundecanoic acid	2058-94-8	PFUnA	Popcorn	Plastic (popcorn bags)	[32]
				Paper	[12]
Perfluorododecanoic acid	307-55-1	PFDoA		Paper	[12]
Perfluoroctylsulfonamide	754-91-6	FOSA		Paper	[12]
Perfluorobutanesulfonic acid	29420-49-3	PFBS		Paper	[12]
Perfluorooctanephosphonic acid	-	PFOPA		Paper	[12]
Perfluorohexanesulphonic acid	355-46-4	PFHxS		Paper	[12]
Perfluorohexanephosphonic acid	–	PFHxPA		Paper	[12]
Perfluorododecanoic acid	307-55-1	PFDoA	Popcorn	Plastic (popcorn bags)	[32]
Perfluorodecanephosphonic acid	–	PFDPA		Paper	[12]
Phthalates					
Dimethyl phtalate	131-11-3	DMP	Olive oils		[17]
		DMP	Food products	Plastics, paperboard	[18]
		DMP	Fatty foods		[19]
		DMP	Hydroalcoholic food beverages		[21]
		DMP	Fatty foods		[22]
		DMP	Wine		[20]
		DMP	Soybean milk		[23]
		DMP	Vegetables		[24]

Table 1 (*Continued*)

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
Bis (2-methoxyethyl)phtalate	117-82-8	DMEP	Fatty foods		[19]
		DMEP	Fatty foods		[25]
Bis(2-ethoxyethyl)phtalate	605-54-9	DEEP	vegetables		[24]
Diethyl phtalate	84-66-2	DEP		Paper	[12]
		DEP	Cow milk/power milk		[17]
		DEP	Hydroalcoholic food beverages		[21]
		DEP	Fatty foods		[19]
		DEP	Olive oils		[17]
		DEP	Meat roasted		[26]
		DEP		Plastics, paperboard	[18]
		DEP	Vegetables		[24]
Diallyl phtalate	131-17-9	DAP	Fatty foods		[22]
		DAP	Soybean milk		[23]
Diisopropyl phtalate	605-45-8	DIPrP	wine		[20]
		DIPrP	Bottle milk		[27]
Diphenyl phtalate	84-62-8	DPhP	Soybean milk		[23]
		DPhP	Fatty food		[25]
		DPhP		Paper	[12]
		DPhP	Milk and milk products		[33]
Dibutyl phtalate	84-74-2	DBP	Hydroalcoholic food beverages		[21]
		DBP	Milk and milk products		[33]
		DBP	Olive oils		[17]
		DBP	Meat roasted		[26]
		DBP		Paper	[12]
		DBP	Vegetables		[24]
		DBP	Fatty foods		[22]
		DBP	Fatty food		[25]
		DBP	Bottled milk		[27]
		DBP	Chicken soup		[28]
		DBP	Fatty foods		[19]
		DBP	Wine		[20]
		DBP	Soybean milk		[23]
Diisobutylphtalate	84-69-5	DIBP	Vegetables		[24]
		DIBP	Olive oils		[17]
		DIBP		Paper	[12]
		DIBP		Plastics, paperboard	[18]
		DIBP	Fatty foods		[22]
		DIBP	Wine		[20]
		DIBP	Hydroalcoholic food beverages		[21]
		DIBP	Meat roasted		[26]
		DIBP	Fatty foods		[19]
Bis(2-butoxyethyl)phtalate	117-83-9	DBEP	Fatty foods		[19]
		DBEP		Plastic (plastic bags)	[28]
Dibenzyl phtalate	523-31-9	DBeP	Milk/milk products		[33]
Benzylbutylphtalate	85-68-7	BBP	Bottle milk		[27]
		BBP		Plastics, cardboard	[18]
		BBP	Wine		[20]
		BBP	Olive oils		[17]
		BBP	Hydroalcoholic food beverages		[21]
		BBP	Vegetables		[24]
		BBP	Fatty foods		[22]
		BBP	Meat roasted		[26]
Di-n-butylphtalate	84-74-2	DnBP	Vegetables		[24]
Dipentyl phtalate	131-18-0	DPP	Hydroalcoholic food beverages		[21]
Dipentylphtalate			Fatty foods		[22]
Dicyclohexyl phtalate	84-61-7	DCHP	Fatty food		[25]
		DCHP	Fruits and vegetables,milk, cereals meat, fish, fat and oils, snacks, condiments, beverages, and baby food		[18]
		DCHP	Meat samples(roasted chicken)		[26]
		DCHP		Paper	[12]
Dihexyl phtalate	84-75-3	DHXP	Wine		[20]
Diheptylphtalate	3648-21-3	DHP	fatty foods		[22]
		DHP	Meat roasted		[26]
Diisononyl-phtalate	28553-12-0	DINP		Paper	[12]
		DINP	Olive oils		[17]
		DINP	Bottle milk		[27]
		DINP	Fatty foods		[22]

Table 1 (*Continued*)

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
Dioctyl phtalate, bis(2-ethylhexyl) phtalate	117-81-7	DNOP, DEHP	Meat roasted		[26]
		DNOP, DEHP		Paper	[12]
		DNOP, DEHP	Soybean milk		[23]
		DNOP, DEHP	Fatty foods		[19]
		DNOP, DEHP	Bottle milk		[27]
		DNOP, DEHP		Plastics, cardboard	[18]
		DNOP, DEHP		Plastics, cardboard	[18]
		DNOP, DEHP	Meat samples(roasted chicken)		[26]
		DNOP, DEHP		Paper	[12]
		DNOP, DEHP	Fatty foods		[22]
		DNOP, DEHP	Olive oils		[17]
		DNOP, DEHP	Wine		[20]
		DNOP, DEHP	Vegetables		[24]
		DNOP, DEHP	Fatty foods		[19]
		DNOP, DEHP	Hydroalcoholic food beverages		[21]
Di-n-heptyl phthalate	3648-21-3	DiHP	olive oils		[17]
Di-n-octyl phthalate	117-84-0	DOP	Olive oils		[17]
		DOP	Meat roasted		[26]
		DOP	Vegetables		[24]
		DOP	Olive oils		[22]
Di-isodecyl phthalat	26761-40-0	DiDP	Olive oils		[17]
		DiDP		Paper	[12]
		DiDP		Plastics, cardboard	[18]
		DiDP	Meat samples(roasted chicken)		[26]
Ethylene terephthalate dimers and trimers Polymer	-	PET		Plastics(PET)	[9]

Non-intentionally added substances (NIAS)

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
(Z)-9-Octadecenamide	301-02-0	9-ODA		Plastics (PE)	[9]
3-[3,5-Di-tert-butyl-4-hydroxybenzyl]propionic acid	20170-32-5			Plastics (PE)	[9]
Carbonyl and vinyl species	–			Plastics (PE)	[9]
2,4-Dit-butyl-6-nitro-phenol	–	2,4di-6-P		Plastics (PE)	[9]
2,4-Dit-butyl-6-nitro-phenol and 2-cyclohexene-1-dione				Plastics (PE)	[9]
3,5-Dimethyl o-methyloxime	–	3,5 M-o-M		Plastics (PE)	[9]
Nonylphenol	25154-52-3	NP		Plastics (PET)	[9]
Octylphenol	1806-26-4	OP		Plastics (PET)	[9]
N2-dodecanoyl-l-arginine	–	LAS		Plastics (Active packaging)	[9]
1,4,7-Trioxacyclotridecane-8,13-dione	6607-34-7			Adhesives	[9]
Abietic acids	514-10-3	ABC		Adhesives	[9]
1-Hexanol-2-ethyl	104-76-7	HE		Adhesives	[9]
2-Ethylhexylacetate	103-09-3	2-Eac		Adhesives	[9]
Cyclic lactone	–	LAC		Adhesives	[9]
Nonylphenol etoxilated	–			Adhesives, Plastics (PET)	[9]

Additives

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
Tinuvin 234	70321-86-17	TNV 234		Plastics (polycarbonate)	[30]
Tinuvin 326	3896-11-5	TNV 326		Plastics (polycarbonate)	[30]
Tinuvin 327	3864-99-1	TNV 327		Plastics (polycarbonate)	[30]
Tinuvin 328	25973-55-1	TNV 328		Plastics (polycarbonate)	[30]
Cyasorb UV9	131-57-7	Cys UV9		Plastics (polycarbonate)	[30]
Cyasorb UV12	131-54-4	Cys UV12		Plastics (polycarbonate)	[30]
Cyasorb UV24	131-53-3	Cys UV24		Plastics (polycarbonate)	[30]
Cyasorb UV 5411	3147-75-9	Cys UV5411		Plastics (polycarbonate)	[30]
Irgafos 168	31570-04-4	I-168		Plastics (polycarbonate)	[30]
Advastab 800	115628-90-5	Adv-800		Plastics (polycarbonate)	[30]
UVINUL 400	92092-63-2	UV-400		Plastics (polycarbonate)	[30]
Cyanox 2246	119-47-1	Cyx-2246		Plastics (polycarbonate)	[30]
Chimassorb 81	1843-05-6	Ch-81		Plastics (polycarbonate)	[30]
Uvitex OB	7128-64-05	Uv-OB		Plastics (polycarbonate)	[30]
Irganox 1076	2082-79-3	I-1076		Plastics (polycarbonate)	[30]
Irganox 1010	6683-19-8	I-1010		Plastics (polycarbonate)	[30]
Irganox 1330	1709-70-2	I-1330		Plastics (polycarbonate)	[30]
Irganox 1081	90-66-4	I-1081		Plastics (polycarbonate)	[30]

Organic contaminants

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
1,2-Dimethylnaphthalene	573-98-8	12DMNa		Paper	[12]
1,4-Dimethylnaphthalene	571-58-4	14DMNa		Paper	[12]
1,6-Dimethylnaphthalene	575-43-9	16DMNa		Paper	[12]
1-Methylfluorene	1730-37-6	1mfLN		Paper	[12]

Table 1 (*Continued*)

Compound	CAS number	Abbreviation	Food product	Food contact material	Reference
1-Methylnaphthalene	90-12-0	1MNa		Paper	[12]
2,6 dimethylnaphthalene	581-42-0	26DMnA		Paper	[12]
2,7-Diisopropylnaphthalene	40458-98-8	27DiPNa		Paper	[12]
2-Methylanthracene	613-12-7	2MAnt		Paper	[12]
2-Methylnaphthalene	91-57-6	2MNa		Paper	[12]
9-Methylanthracene	779-02-2	9MAnt		Paper	[12]
Acenaphthene	83-32-9	Ace		Paper	[12]
Acenaphthylene	208-96-8	Acy		Paper	[12]
Anthracene	120-12-7	Ant		Paper	[12]
Benzo(a)anthracene	56-55-3	BaA		Paper	[12]
Dibenzo(ah)anthracene	53-70-3	BaP		Paper	[12]
Benzo(b)fluoranthene	205-99-2	bBf		Paper	[12]
Benzo(ghi)perylene	191-24-2	BghiP		Paper	[12]
Benzo(a)pyrene	50-32-8	BkF		Paper	[12]
Fluorene	86-73-7	Fln		Paper	[12]
Fluoranthene	206-44-0	Flt		Paper	[12]
Chrysene	218-01-9	Chr		Paper	[12]
Indeno(1,2,3-cd)pyrene	193-39-5	IcdP		Paper	[12]
Naphtalene	91-20-3	Na		Paper	[12]
Phenanthrene	85-01-8	Phe		Paper	[12]
Pyrene	129-00-0	Pyr		Paper	[12]
Printing inks (photoinitiators)					
2-Isopropylthioxanthone	5495-84-1	2ITX		Paper	[12]
4-Isopropylthioxanthone	83846-86-0	4ITX		Paper	[12]
4-Methylbenzophenone	134-84-9	4MBFN		Paper	[12]
Benzophenone	119-61-9	BFN		Paper	[12]
Ethyl-4-dimethylamino benzoate	10287-53-3	EDB		Paper	[12]
2-Ethylhexyl-4-dimethylamino benzoate	21245-02-3	EHDB		Paper	[12]
Mineral oil					
Mixture of saturared hydrocarbons (C16-C24)		MOSH		Recyclated Paper	[34]
Mixture of unsaturared hydrocarbons (<C24)		MOAH		Recyclated Paper	[34]

Until now, some studies have reviewed the analytical methods for phthalates [38] NIAS [9] and PFCs [39] compounds in food and FCMs. LC-MS analysis of phthalates, bisphenol A and related compounds in food-packaging materials was reviewed until 2013 by Gallart-Ayala and co-workers [4]. The present review focuses on the most recently published information for the analysis of different chemical families of food-packaging contaminants, through the identification and discussion of the most relevant methods published between 2010 and 2016. Likewise, we include for the first time the analytical methods for the determination of food-packaging contaminants using gas chromatography. Gallart-Ayala et al. reviewed [4] the analytical methods for FCMs using liquid chromatography until 2013. The present review shows the most recent advances in analytical methods using liquid chromatography (2013–2016) and as a novelty includes the most novel techniques, particularly high resolution mass spectrometry (HRMS).

In many fields such as food safety or environmental control the development of LC-HRMS platform, using both Orbitrap and TOF analyzers, has grown rapidly in the last years. However, in the FCM area it not seems so clear, or at least not so fast. We also discuss this challenge in the present work.

2. Compounds

There are hundreds of compounds that can migrate from food contact materials. In this review, we have focused on some relevant families of organic compounds (primary aromatic amines, bisphenol A, bisphenol A diglycidyl ether and related compounds, UV-ink photoinitiators, perfluorinated compounds, phthalates and non-intentionally added substances and mineral oil) where there has been increasing interest in their analysis by liquid chromatography (LC) and gas chromatography (GC) in recent years.

Several of these compounds are of particular concern because, although they are generally present in very small amounts, they are nonetheless often dangerous to human health [4].

2.1. Primary aromatic amines (PAAs)

Primary aromatic amines appear in food products through food contact materials mainly from plastics such as kitchen utensils [8] or plastic laminates [7]. These amines are formed by hydrolysis of aromatic isocyanates in polyurethane adhesives, and by degradation of azodyes used as colorants in nylon kitchen utensils and other plastic materials [40]. Brede et al. [40] identified the polyamide cooking utensils as a common source of PAAs.

Taking into account that many aromatic amines are classified as toxic compounds and/or as suspected human carcinogens [8], their migration into foodstuff from food contact material is subjected to restrictions. The European Regulation 10/2011 establishes that plastic material and articles shall not release primary aromatic amines in detectable quantity in food or food simulants. The SML are set to 0.01 mg of substances per kg of food or food simulant and it applies to the sum of primary aromatic amines (ANL, 2-4 TDA, 2-6 TDA, 4-4′MDA, 1-5DAN, m-PDA, 3-3′DCB and 4-4′DPE) released [8,35].

From these early studies onwards, numerous alerts have been issued by the European rapid alert system for food and feed (RASFF) for excessive concentrations of PAAs migrating from FCMs [41].

2.2. Bisphenols and related compounds

Bisphenol A (BPA) is used as a monomer for polycarbonate production, and it is considered to be an endocrine disrupter [4]. Recent studies highlight the potential of BPA to disrupt thyroid hormone action, to causes proliferation of human prostate cancer cells and to block testosterone synthesis [42] at very low part-per-trillion doses. Use of BPA in food contact materials is permitted in the European Union (EU) under Regulation 10/2011/EU [36]. This Regulation permits use of BPA in plastic materials and articles intended to come into contact with foodstuffs, with a SML of 0.6 mg/kg [36]. However, the European Commission adopted Directive 2011/8/EU [43] in January 2011, prohibiting its use for the manufacture of polycarbonate infant feeding bottles [4,44]. BPA has also been found in recycled paper and paperboard used for food packaging (pizza cardboard, paper bags) and in kitchen towels made from recycled paper, probably due to its use in printing inks [42]. For this reason, it is very important to establish the criteria to ensure that paper containing recycled pulp is safe enough to be used as food contact material. Further data would be needed to quantify the impact of these sources in terms of BPA exposure in the population [31]. The European Food Safety Agency conducted a risk assessment of BPA, setting a Tolerable Daily Intake of 4 μg/kg bw [4]

Other related compounds are bisphenol F (BPF), bisphenol A diglycidyl ether (BADGE) and bisphenol F diglycidyl ether (BFDGE). The toxicity of BPF, which has also been proven, is mainly related to its oestrogenic and antiandrogenic effects [45]. In turn, BADGE and BFDGE, have cytotoxic effects, which make them tumorigenic and mutagenic [46]. The most popular coating varnishes and lacquers used in drink and food cans are those based on vinyl organosols (novolacs), which include epoxy resins obtained from BADGE or from BFDGE in their composition. With respect to BADGEs, the EU has set SMLs of 9 mg/kg for the sum of BADGE and its hydrolyzed derivatives and 1 mg/kg for the sum of BADGE·HCl, BADGE·2HCl and BADGE·HCl·H2O [47].

2.3. Perfluorinated compounds (PFCs)

Poly- and per-fluoroalkyl substances (PFASs) are chemicals that have been found to be persistent and to bio-accumulate causing adverse human health effects [48–52]. They comprise a diverse group of compounds that have been widely used in consumer product applications such as cookware and food contact papers [53]. In fact, the chemical properties such as thermal stabilities, in addition to the hydrophobic and lipophobic nature of these compounds, have made them highly valued in consumer products [53]. Among the PFASs are the per-fluoroalkyl sulfonates (PFSAs) and the per-fluoroalkyl carboxylates (PFCAs) of which the per-fluorooctane sulfonate (PFOS) and the per-fluorooctanoic acid (PFOA) are the most important [54,55]. Recently, PFOS has been listed as a persistent organic pollutant (POP) under the Stockholm Convention on POPs in Annex B, banning their production and use [56].

Exposure to PFOS and PFOA might have occured directly due to their manufacture and use in commercial products [57]. Indirect exposure might also have occured through the release of PFOS and PFOA precursors that degrade to PFOS and PFOA, and were released into the environment during production and through treated commercial products [58–60]. Examples of such precursors include: fluorotelomer alcohols (FTOHs), perfluorooctane sulfonamides (FOSAs), and perfluorooctane sulfonamidoethanols (FOSEs). Polyfluoroalkyl phosphate esters (PAPs), mainly used in food-packing materials, are precursors of FTOHs and subsequently also of PFOA [15,61]. Recently PAPs have become a focus of attention due to their wide use in packaging materials made of paper and paperboard, including wrapping paper, milk and juice cartons, fast-food containers and microwave popcorn bags. Mono and diPAPs

have been reported in food packaging materials [27,62]. EFSA has completed a risk assessment on PFOS and PFOA in the food chain and established TDIs of 150 ng/kg body weight/day and 1500 ng/kg body weight/day, respectively. [4]

2.4. Phthalates

Phthalates (PAEs) or esters of phthalic acid (1,2-benzenedicarboxylic acid) have been commonly used as plasticizers to increase flexibility, transparency, durability, and longevity of plastic materials since the 1930s [63]. Millions of tons of PAEs are produced all over the world annually, of which di-2-ethylhexyl phthalate (DEHP) is one of the most popular plasticizers and accounts for ~50% of global production, followed by dibutyl phthalate (DBP), di-iso-decyl phthalate (DIDP) and di-iso-nonyl phthalate (DINP) [4,64]. In general, the content of PAEs in plastic materials, such as polyvinyl chloride (PVC), polyethylene terephthalate (PET), polyvinylacetates (PVA) and polyethylene (PE), varies from10% to 60% by weight [39].

Phthalates and their metabolites have been reported to cause detrimental effects to human health. For instance, researchers showed that di-n-butyl phthalate (DnBP), benzylbutyl phthalate (BBP), DEHP and DiNP can adversely affect the male reproductive system. Duty et al. [65] found an association between DNA damage in sperm and exposure to diethyl phthalate (DEP). Furthermore, Latini et al. [66] revealed that DEHP can disrupt the human endocrine system and can induce premature delivery in humans.

PAEs may easily migrate from food-packaging materials into food under certain conditions, particularly when they are in contact with fatty and oily food. However, PAEs are not labelled as ingredients on food-packaging materials [67,68]. Human exposure to PAEs occurs mainly via food ingestion [69–71]. For example, in 2011, six PAEs were detected in milk samples with plastics packaging, indicating that PAEs could migrate from plastic packaging into milk [27]. In addition to liquid milk, [72] found that milk powder was also contaminated with DEHP at the highest level of 25 μg/kg. However, PAEs in foods did not capture special attention until 2011 – when a food scandal was reported in Taiwan, revealing that DEHP was being used illegally as a clouding agent in beverages to increase profits, resulting of major public health concern [64,73,74].

In view of the potential hazards to human and animal health, some PAEs (e.g., DMP, BBP, DBP, DEP, DNOP and DEHP) have been listed as priority pollutants and their use in foods and plastic products have been restricted in the European Union (EU), USA and China [29,75,76]. Using food simulants, the European Union has established SMLs for several PAEs in food-contact materials [77–82]. For example, the SMLs (mg/kg food simulant) for BBP, DEHP and DBP are 30, 1.5 and 0.3, respectively [36]. Regarding those without SMLs, a limit of 60 mg/kg in food products is applied [83]

2.5. Non-intentionally added substances (NIAS)

Packaged food may contain non-intentionally added substances (NIAS) as a result of the interactions between different ingredients in the packaging materials, from degradation processes and mainly from the impurities present in the raw materials used for their production [84]. Most NIAS and unknown compounds are regularly detected when using high-sensitivity advanced analytical techniques, although their chemical structure is often difficult to establish. It is likely that in the majority of cases, due to the very low levels found, these substances will not be of any health concern. However, at present no guidance exists on what should be done when an unknown peak is detected.

The Regulation on Food Contact Materials (Regulation 10/2011/EU) [36] recognizes that during the manufacture and use of plastic materials and articles, NIASs can be formed. Being

relevant for risk assessment, the main NIAS of the final packaging material should be considered and included under the restrictions of the positive substance list. Any potential health risk in the final material or article arising from NIASs should be assessed by the manufacturer in accordance with internationally recognized scientific principles of risk assessment. However, NIAS identification is very difficult because of the lack of information about the real composition of the various ingredients and materials used for polymers and final packaging manufacturing. For this reason, it is almost impossible to know in detail what is included in the final packaging material.

In order to avoid the presence of NIASs in packaged food, especially when risk assessment is involved, it is very important to know their origin. Traceability of food packaging materials is obligatory and this includes a description of NIAS [9]. Degradation processes, additive degradation and impurities are important sources of NIAS. Degradation processes can take place in the polymer itself and also in the additives used for improving its physicochemical characteristics. Some additives such as antioxidants or light stabilizers added to the polymer for improving their properties can also be degraded. As a result, new potential migrants will be present in the packaging material. Some of the most common degradation products that have been studied due to toxicity are alkylphenol, nonylphenol (NP) and octylphenol (OP), which are known to be endocrine disrupters [85]. NP and OP can be generated by the oxidation of tris(nonylphenyl)phosphate (TNPP), used as an antioxidant in polymeric materials such as poly-(vinyl chloride) (PVC), polyolefins and acrylics. They can also be generated by the degradation of polyethoxylated nonylphenols (APEOs), which are common surfactants in cleaning agents used in PET (polyethylene terephthalate) bottle manufacturing and in other materials such as adhesives or polymeric dispersions [9].

Another frequent reason for finding NIAS in migration from food packaging is the presence of impurities coming from the raw materials or additives used during polymer manufacturing. Impurities from adhesive additives used in food packaging have also been found in migration. The compounds 1-hexanol-2-ethyl, 2-ethylhexylacetate and 2,4,7,9-tetramethyl-5-decyl-4,7-diol (TDMM) were found in migration from multilayer materials based on acrylic adhesives. The first two compounds were impurities from commercial 2-ethylhexylacrylate, a monomer used in the production of acrylic adhesives, and the last one was an impurity or residual surfactant monomer from ethoxylated TDMM, used as a surfactant in adhesive production [86].

2.6. Printing inks (photoinitiators)

Inks are commonly used in food packaging materials and therefore, migration of ink components to food must be studied. Printing inks (2ITX, 4ITX, 4MBFN, BFN and so on), provide information about the packaged food. When multilayer materials are used in food packaging, migration can take place, not only from the internal side of the packaging (food contact surface) but also from internal layers due to diffusion and partition processes [10,87]. In the case of inks applied on the external side of the packaging, there can be ink transference from the external side to the internal side (side in contact with food) during material production and storage in rolls, increasing the possibility of ink-component migration to food. The transference of ink components from the external printed surface of food packaging to the food contact surface is called set-off [10].

Inks, defined as a coloured fluid or paste used for writing, drawing or printing, are mainly composed by a pigment or dye, suspended or dissolved, in a solvent. The use of printing inks for food packaging is regulated by the European Printing Ink Association (EuPIA) [88]. Different groups of raw materials can be used in the manufacture of food packaging inks such as additives, colorants,

(pigments, dyes), pigment additives, polymeric resins, solvents or photo-initiators [89].

Although intermediate aluminium layers are commonly used to prevent the migration of ink components into food products, the unintentional transfer of printing ink components from the outer printed surface onto the food-contact surface can occur when the printed material is rolled on spools or stacked during storage. Although ink photoinitiators are widely used, there are no specific EU controls for migration of inks and their associated coatings. A specific migration limit SML for benzophenone of 0.6 mg/kg has been established in a specific legislation for food-contact plastics [36]. Regarding those without SMLs, a limit of 60 mg/kg in food products is applied.

2.7. Additives

Additives such as antioxidants, stabilizers and plasticizers have a major influence in the processing and shelf-life of plastics and are responsible for many properties of these materials. These additives are present in small amounts in plastics (generally ranging from 0.1% and 1%), dispersed in the polymer matrix, with the aim of avoiding such effects as thermo-oxidative deterioration, which initiates scission and cross-linking of the macromolecular chains consequently leading to polymer deterioration [35]. The polymer has got an inert structure with a high molecular weight that represents a low potential risk for human health since the organism cannot absorb molecules with a molecular weight greater than 1000 Da [30]. On the contrary, as plastic additives and organic colorants have a generally low molecular weight, they may migrate from plastics into foods, representing a potential risk for human health [30].

2.8. Mineral oil

Mineral oil components found in packaging cardboard are complex mixtures of saturated hydrocarbons (MOSH) and unsaturated hydrocarbons (MOAH). MOSH are linear and branched hydrocarbons whereas MOAH are alkylsubstituted poly aromatic compounds [34].

The migration of contaminants from cardboard packaging materials into foodstuffs is a complex process. The contaminants need to be vaporized into the gas phase. From the gas phase the contaminants permeated through the functional barrier into the food. The gas phase migration process requires an evaporation of the mineral oil components with subsequent re-condensation onto packaging materials or food.

Regarding consumers safety the migration of contaminants from recycled fibres into food should be reduced down to levels below of any toxicological concern. The German Federal Ministry of Food and Agriculture (BMEL) presented a draft document for the regulation of mineral oil from recycled fibres in cardboard food packaging materials. According to this draft document, the maximum concentration of mineral oil components in cardboard packed food should be 2 mg/kg and 0.5 mg/kg for MOSH and MOAH, respectively. For MOSH the mineral oil components between n-C20 and n-C35, whereas for MOAH the compounds between C16 and C35 should be considered [34].

3. Analytical methods

3.1. Sample preparation

The analysis of FCM contaminants can be performed in food, in food simulants or in food contact materials. The analysis of contaminants in FCMs requires to perform a first stage of specific migration of substances to food simulants. There are European legislation that

regulates these migration studies. For instance, migration studies on food contact materials (plastic materials and articles not yet in contact with food) are regulated by Regulation (EU) N° 10/2011 [36]. Migration studies using food simulants are necessary in order to characterise new packaging materials and the amount of non-desirable contaminants that can migrate into food. Various food simulants, such as ethanol, acetic acid, vegetable oil and Tenax®, are listed in Regulation (EU) N° 10/2011 [36].

Recent works have described the use of these simulants in the migration of FCM contaminants. For instance, Sanchis et al. (2015) [8] studied the migration of some PAAs (primary aromatic amines) from nylon kitchen utensils following the migration test established in the European Standard EN 13130-1:2004 [14,90]. In this study, each sample was placed in a beaker which was, in turn, filled with a volume of simulant (acetic acid, 3%) enough to cover the piece of utensil used for migration. Regarding printing inks, Aznar et al. [10] carried out migration experiments with two different simulants, ethanol 95% as fat simulant and Tenax® as dry-food simulant. Two different sets of food packaging materials were studied in this work. In both studies, a polyethylene layer (PE) was in contact with food, and a printing ink was applied on the outer side in order to study the set-off effect. For ethanol experiments, pouches were filled with ethanol 95% [36]. For Tenax® migration experiments, pouches were filled with 0.64 g of Tenax®

Tables 2 and 3 show a selection of the relevant conventional and novelty analytical procedures for the three studied matrixes (food, food simulants and food contact materials) using gas and liquid chromatography, respectively, proposed in recent literature.

Some conventional techniques like Soxhlet, solid–liquid (S–L) extraction, Solid Phase Extraction (SPE), Ultrasonic extraction and liquid–liquid (L–L) extraction have been generally used for the extraction of FCM contaminants from food and food packaging (Figs. 2 and 3). Soxhlet and SPE have been used for extracting phthalates from paper materials and beverages followed by gas chromatography analysis [21,84]. For more polar compounds, determined by liquid chromatography, S–L extraction has been applied to extract BPA and BADGEs from canned food [15]. Another conventional extraction method is ultrasonic extraction. This extraction has been employed in sample preparation of phthalates from food (milk and wine) and plastic material [20,27], and in sample preparation of PFCs from paper materials [12].

Gel permeation chromatography (GPC) and gas purge microsyringe extraction (GP-MSE) clean-up steps were used for extracting phthalates from widely consumed food such as fruits, vegetables, milk, beverages, baby food and so on, after L–L and S–L extraction, respectively [18,26]. In addition, SPE has been used as clean-up method when extracting PFCs from different paper materials (baking paper, paper bags and more) after ultrasonic extraction and final determination by liquid chromatography [12].

The disadvantages of the conventional techniques are that sample preparation is usually manual and a large amount of organic solvent is required for compound extraction. In addition, a clean-up step is usually necessary when conventional extraction techniques are applied. To minimise the use of organic solvents and avoid clean-up steps, several pre-treatment methods have been described as an alternative for extraction, clean-up and concentration. Fig. 4 presents the extraction methodologies used for phthalates, PFCs, BPA, BADGEs and NIAS contaminants in food and FCMs (paper and plastics). Solid-phase microextraction (SPME) [103], focused ultrasond solid–liquid extraction (FUSLE) [104], Pressurized liquid Extraction (PLE) [105] and Quechers [106] have been currently applied to extract FCM contaminants in food and materials. SPME is a widely used technique for the analysis of volatile and semi-volatile compounds in gas chromatography [26]. SPME is commonly applied in the headspace mode (HS-SPME), in which the fibre used for extraction does not come into direct

contact with the sample but with the headspace above the sample, instead. SPME can also be applied in direct-immersion mode (DI-SPME), in which the extraction fibre is placed in direct contact with the sample, with the advantage of increased extraction efficiency. DI-SPME may have an even greater efficiency when a cooling system is applied to the fibre. The extraction process consists of the analyte sorption into a fibre, an exothermic process, and cooling the fibre to accelerate the transfer of the analyte into the fibre. Recently, a solid-phase microextraction fibre cooled by liquid nitrogen (CF-SPME) was selected as a sampling technique to analyze eight plasticizers (phthalates) in spices and roasted chicken meat stored in plastic bags by gas chromatography–mass spectrometry [26]. In addition, SPME has been the selected technique to extract NIAS from plastics and cans [9]. This approach has the major advantage of no sample manipulation, therefore minimising cross contamination from glassware, solvents and samples. However, its main drawbacks are that the fibres tend to break and are relatively expensive.

FUSLE is a simple, safe and inexpensive methodology with a 100-fold higher extraction power than the traditional ultrasonic bath used as extraction technique when liquid chromatography is applied [104]. This technique has been recently used for the extraction of bisphenol-type endocrine disrupters in food-contact recycled-paper materials [31] and for perfluorinated alkyl acids in corn, popcorn and microwave popcorn packaging [32]. FUSLE factors affecting the extraction efficiency (solvent volume, extraction time and ultrasonic irradiation power) were optimized in these studies. Bisphenol-type endocrine disrupters (BPA, BPF, BADGE and BFDGE) were extracted with 20 mL methanol at the ultrasonic amplitude of 100% for 5 s. and 2 extraction cycles [31]. Selected perfluorinated alkyl acids (PFAAs) [nine perfluorocarboxylic acids (PFCAs) and perfluorooctane sulfonate (PFOS)] were efficiently extracted in a single 10-s cycle from microwave popcorn bags and from the inside popcorn before and after cooking under FUSLE conditions [32]. Better recoveries were obtained when extracting BPA, BPF, BADGE and BFDGE from recycled paper (72–97%) [31], than when extracting PFCs in corn and popcorn (65–105%) [32], when using the FUSLE extraction method.

PLE has also been used for sample treatment of BPA-related compounds and UV-ink photoinitiators in liquid chromatography [4]. This technique has recently been used for the extraction of perfluorinated compounds (PFCs) used in food packaging materials (baking paper and beverage cups) as coatings/additives for oil and moisture resistance. After a PLE extraction, a solid-phase extraction (SPE clean-up) with 1.5 g florisil, 1 g basic alumina and 1 g of sodium sulphate was applied prior to the injection into the LC–MS/MS. The PLE extraction method with a SPE clean-up obtained recoveries between 60 and 90% [13].

The Quick, easy, cheap, effective, rugged and safe (QuEChERS) method was proposed by Anastassiades et al. in 2003 [106]. The QuEChERS approach was first used to extract pesticides from foods. Nowadays, in addition to pesticides, the QuEChERS method is being increasingly applied to the extraction of other compounds. In 2014, the QuEChERS method was successfully applied to extract 23 phthalate esters (PAEs) from grape jelly, seasoning powder, egg noodles and grapefruit sauce [97]. In 2016, QuEChERS was applied after ultrasonic extraction using a mixture of acetonitrile and water for the determination of 68 potential contaminants: specifically phthalates, polycyclic aromatic hydrocarbons, photoinitiators, bisphenols and polyfluorinated compounds in paper FCMs [12]. Quechers has been used in FCMs methodologies as a extraction and clean-up technique obtaining good recoveries (75–115%) as an extraction technique in food samples for phthalates [33,97] and as a clean-up technique for PFCs in paper materials (70–120%) [12] by liquid chromatography. However, when extract-

Table 2

Analysis of food packaging contaminants in food, food simulants and packaging materials by gas chromatography and mass spectrometry detection.

Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	Technique	GC conditions	Ionisation source	Recovery	LOD	LOQ	Refs.
Phthalates: DEA,DiBA, DBA, DMP,DEP, DiBP, DBP, BBP,DiHP, DEHP, DOP, DiNP,DiDP, DEHS	–	Olive oil	–	Liquid–liquid extraction with Acetonitrile	–	HRGC–MS	Supelco SPB-5MS (5%polydiphenylsiloxane,95% polydimethylsiloxane) (0.25 μm × 30 mm × 0.25 mm)	EI mode	93–101%	0.003–1.200 mg/kg	0.001–4 mg/kg	[17]
Phthalates, organic contaminants and photoinitiators: Na, 2MNa,1MNa, 26DMNa,16DMNa,14DMNa,12DMNa,Acy,DMP,Ace, DEP, Fln,27DiPNa, BFN,1MFln,EDB, 4MBFN, DiBP, Phe,Ant, DBP, 2MAnt,9MAnt, Ant,DNPP, Flt, Pyr, EHDB, DEHP,DiNP, 4ITX, 2ITX,DiDP, BaA,DNOP,Chr,BbF,BkF,BaP, IcdP, BghiP.	–	–	Paper	Liquid–liquid extraction with Quechers	–	GC–MS/MS	Rxi–PAH column (0.10 μm × 30 mm × 0.25 mm)	EI mode	52–135%		0.001–0.22 mg/kg	[12]
Phthalates: DMP, DEP, DiBP, DnBP, BBP, DEHP, DCHP, DNOP	–	Fruits, vegetables, milk, cereals, meat, fish, fat, oils, snacks, condiments, sauces, beverages, miscella-neous and baby food	–	Liquid–liquid extraction	gel per-meation chro-matog-raphy (GPC)	GC–MS	DB–XLB column (0.25 μm × 60 mm × 0.25 mm)	EI/CI MSD mode	89–101%		0.01–145 μg/kg	[18]
Phthalates: DMP, DEP, DiBP, DnBP, BBP, DEHP, DCHP, DNOP	60 min with 40 mL n-hexane in an ultrasonic bath	–	Plastics, paperboard		–	GC–MS	DB–XLB column (0.25 μm × 60 mm × 0.25 mm)	EI/CI MSD mode	82–99%		0.1–1.5 μg/kg	[18]
Phthalates: DEP,BBP, DEHP, DBP DOP, DiBP, DCHP	–	Meat samples (roasted chicken)	–	Solid-phase microex-traction	fibre cooled by liquid nitro-gen (CF-SPME)	GC–MS	HP-5MS Agilent column (0.25 μm × 30 mm × 0.25 mm)	EI mode		0.01–0.18 μg/kg	0.07–0.26 μg/kg	[26]

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Table 2 (*Continued*)

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Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	Technique	GC conditions	Ionisation source	Recovery	LOD	LOQ	Refs.
Phthalates ans esters: DEP, DEHP,DBP, DNOP, DMP,BBP	–	78 samples of widely consumed food	–	Solid-phase extraction	gas purge microsyringe extraction (GP-MSE)	GC–MS	DB5 fused-silica capillary column (0.25 μm × 30 mm × 0.25 mm)	EI mode	90–100%	0.14–0.38 ng/g for solid 0.0021–0.0096 ng/mL for liquid		[26]
Phthalates: DMP,DEP,DBP,BBP,DNOP	–	Bottled milk	–	Ultrasound-assisted dispersive liquid–liquid microextraction	–	GC–MS	KB-1 (0.25 μm × 30 mm × 0.25 mm)	–	93–106%	0.64–0.79 ng/g		[27]
Phthalates: DMP,DEP,DIBP,DBP,DAP, DHP,BBP,BBEP,DEHP,DOP	–	Olive oil	–	Headspace solid-phase microextraction	–	GC–MS	ZB-5MS (0.25 μm × 30 mm × 0.25 mm)	–			0.02–0.05 mg/kg	[22]
Phthalates: DMP,DBP,DEP,DEHP	–	Fatty food	–	Liquid–liquid extraction	–	GC–MS	DB-5 MS (0.25 μm × 30 mm × 0.25 mm)	–		0.4 μg/g	1.2 μg/g	[25]
Phthalates: DMP,DBP,DEP,BBP,DIBP, DEHP	–	Wine	–	Ultrasound-vortex-assisted dispersive liquid–liquid microextraction	–	GC–MS	SE-54 (0.25 μm × 30 mm × 0.25 mm)	–	85–100%	0.0022 μg/L	0.075 μg/L	[20]
Phthalates: DMP,DEP,DBP,DAP,DNOP	–	Soybean milk	–	Molecular imprinted solid-phase extraction (MISPE)	–	GC–MS	DB-5MS (0.25 μm × 30 mm × 0.25 mm)	–	76–108%	0.013–0.022 μg/mL		[23]
Phthalates: DMP, DEP, DBP, BBP, DIBP, DEHP	–	Hydroalcoholic food beverages	–	Solid phase extraction (SPE) with Amberlite XAD-2 adsorbent.	–	GC–MS	SE-54 (0.24 μm × 30 mm × 0.25 mm)	–	94–103%	1.21–2.51 pg/μL	2.42–5.03 pg/μL	[21]
Phthalates: DBP,DEHP	–	Chicken soup	–	Magnetic micro-solid phase extraction	–	GC–MS	DB-5(0.25 μm × 30 mm × 0.25 mm)	–	70–118%	26.3–36.4 μg/mL		[28]
Phthalates: DMP,DEP,DBP,BBP,DEHP,DOP	–	Vegetables	–	Stir bar sorptive extraction	–	GC–MS	DB-17 MS (0.25 μm × 30 mm × 0.25 mm)	–	83–118%	15.8–106 pg/g		[24]
Phthalates: MP,DEP,DBP,DIBP,DMEP,DNOP	–	Fatty foods	–	Dispersive solid phase extraction	–	GC–MS	DB-5 MS (0.25 μm × 30 mm × 0.25 mm)	–	71–115%	0.4–0.8 μg/mL		[19]
Phthalates: DMP, DEP, DBP,DIBP,DMEP,BBP, DHXP, DCHP, DNOP	–	Various food	–	Liquid–liquid extraction	gel permeation chromatography (GPC)	GC–MS	DB-5 MS (0.25 μm × 30 mm × 0.25 mm)	–			1.5 mg/kg (fatty food) 0.05 mg/kg other food	[29]
Ethyl carbamate	–	Alcoholic beverages and soy	–	Solid-phase extraction	–	GC–MS	DB Innowax capillary (1.25 μm × 30 mm × 0.25 mm)	–	96–107%		5 μg/kg	[91]

Compounds	Conditions	Simulant	Material	Extraction		Technique	Column	Detection	Recovery	LOD	LOQ	Ref.
Additives: I-168, I-1076, TNV 326, Ch-81	24 h at 60 °C, total inmersion with hexane	–	Polypropylene films	–	–	HPLC-GC	12 m × 0.25 mm column coated with a 0.13 μm film of PS-255, a cross linked dimethyl polysiloxane	Flame ionisation detection (FID)		0.1–1 mg/kg		[11]
BPA, DEHP	–	–	Paperboard	BPA-extraction in ethanol, DEHP in acetone–hexane 4:1, Soxhlet extraction	–	GC–MS	SLB-5ms type (5%polysilarylene-95% polydimethylsiloxane) (0.25 μm × 30 mm × 0.25 mm)	–	101–108%	0.015–0.017 mg/L	0.05–0.064 mg/L	[84]
BPA, DEHP	migration with simulant Tenax	Salt, sugar	–	–	–	GC–MS	SLB-5ms type (5%polysilarylene-95% polydimethylsiloxane) (0.25 μm × 30 mm × 0.25 mm)	–	70–120%	0.015–0.017 mg/L	0.05–0.064 mg/L	[84]
BPA, DEHP	migration with simulant Tenax	–	Recycled paper and paperboard	–	–	GC–MS	Supelco SLB-5ms type (5% polysilarylene–95% polydimethylsiloxane; (0.25 μm × 30 mm × 0.25 mm)	–	70–120%		0.06–25 mg/L for BPA, 0.5–60 mg/Lfor DEHP	[92]
Ethyl acetate, Methyl methacrylate, Toluene, Hexanal, Paraldehyde, P-xylene, Butyl acrylate, Styrene, P-cymene, 2-octanone, 1-hexanol, 2-ethylhexylacetate, Nonanal, Cyclohexanol, Acetic acid, 2-ethyl-1-hexanol, Camphor, Propanoic acid, Benzaldehyde, 1-octanol, butyric acid, Methylbenzoate, naphtalene, allylbenzoate.	Migration with Tenax in the oven 40 °C for 10 days	–	Multilayer materials for packaging dry food	–	–	GC–MS	BP-20 (0.25 μm × 30 mm × 0.25 mm)	–		0.01–25.7 μg/g		[93]

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Table 2 (*Continued*)

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Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	Technique	GC conditions	Ionisation source	Recovery	LOD	LOQ	Refs.
Volatile compounds: hexanal, octanal, 2-heptenal, 1-hydroxy-2-propanone, nonanal, 2-octenal, furfural, decanal, 2-nonenal, 2-furanmethanol, 2-decenal, 2,4 decanienal isomers, hexanoic acid	Migration with Tenax in the oven 40 °C for 10 days	Powdered milK	–	–	–	GC–MS	DB WAX (0.20 µm × 50 mm × 0.40 µm)	–				[94]
Melamine		Powdered milK		Liquid–liquid extracction	–	GC–MS	HB-5MS (0.25 µm × 30 mm × 0.25 mm)	EI mode	95–101%		0.025 mg/kg	[95]
Perfluorinated compounds: FTOHs, FOSAs, and FOSEs	Two migrations, first acetic 3%, second methanol	–	–	–	SPE (solid phase extraction)	GC–MS	DB-WAX column (0.25 µm × 30 mm × 0.25 mm)	Positive chemical ionisation (PCI)		3.9–30 pg		[96]
133 Volatile compounds (esters, acids, saturated alcohols, unsaturated aliphatic alcohols, ketones, aldehydes, furans, ethers, lactones, sulphur containing compounds)	–	Camel milk	–	Solid phase microextraction, solvent assisted flavour evaporation, and simultaneus destillation extraction.	–	GC–MS	DB-WAX column (0.25 µm × 30 mm × 0.25 mm)	–				[97]
Mineral oil: MOSH, MOAH	–		paperboard	Liquid–liquid extraction with etanol–hexane 1:1 during three days	–	HPLC–GC–FID	HPLC column (25 cm × 2 mm, silica gel) and a 10 m × 0.25 mm separation column coated with a 0.13 m film of PS-255 in the GC	–		0.1 mgç/kg	–	[98]
Mineral oil: MOSH, MOAH		food	paperboard	Food: extraction with hexane, 8 hours. Paperboard: extarction with etanol–hexane 1:1 2 hours	–	HPLC–GC–FID	HPLC column (25 cm × 2 mm, silica gel); GC: Separation columns were coated with a dimethyl polysiloxane stationary phase (KLZH: 10 m × 0.25 mm, 0.13 m PS-255; BfR: DB1-HT, 15 m × 0.32 mm, 0.10 m)	–	72.9% MOSH, 27.1% MOAH	0.5 mg/kg		[99]
NIAS	Migration with Tenax		Acrylic adhesives	HS-SPME extraction and liquid extraction	–	APGC–MS/Q-TOF)	HP-5MS (30 m × 0.25 m × 250 mm)	Atmospherie-pressure gas chromatography (APGC)		2.2–4.3 µg/kg		[100]

Table 3

Analysis of food packaging contaminants in food, food simulants and packaging materials by liquid chromatography and mass spectrometry detection.

Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	LC conditions	Technique	Ionisation source	Recovery	LOD	LOQ	Refs.
Amines: ANL,2,4 TDA, 2,6 TDA, m-PDA, 1,5 DAN, 3,3′ DMB, 4,4′DPE,4,4′ MDA	Migration with acetic acid 3%, 2 hours at 100 °C	–	Nylon kitchen utensils	–	–	C18 Phenyl hexil column (2.1 μm x 100 × 2.1 mm), Methanol 2/water 98	LC–HRMS	ESI(+)	70–120%		2.5 μg/kg	[8]
Amines: ANL, 2,4 TDA, BNZ, o-ANS,4,4′ DPE, o-TOL, 4,4′ MDA,o- DANS, o-TOLI, p-ANL, p-CRS, 4,4′ MBM,4,4′ TDA, 2-NAPH, 4-Cl-TOL, 5-N-O-TOL, 2,4,5 MTA, 4-ABF,4,4′ M(2Cl),3,3′ DCB,p-ABZ,o-AaT	Migration:0.6 dm of plastic laminate was cut and then inmersed in 100 mL de acetic 3% the solution incubated 70 °C for 2 h.	–	Plastic laminate	–	–	C18 (2.6 μm × 100 × 2.1 mm) water 4.7 mM perfluropropanoic acid(PPFPA)/4.7 mM PFPA en methanol	HPLC–HRMS	ESI(+)		0.06–5.27 μg/kg	0.09–5.45 μg/kg	[7]
BPA, BADGEs and related compounds: BPA, BPF,BADGE,BFDGE	–	–	Recycled paper	Focused ultrasonic solid–liquid extraction (FUSLE)	–	C18 (1.7 μm × 50 × 2.1 mm) ACN:water/0.5 mM sodium acetate 8.5 mM acid acetic	UPLC–Q-TOF-MS	ESI(+)	72–97%	16–47 ng/mL		[31]
BPA, BPB, BPF, BPE, BFDGE, BADGE, BADGE-H$_2$O, BADGE-2H$_2$O, BADGE-H–O–HCl, BADGE-HCl, BADGE-2HCl, BFDGE-2HCl	–	Canned food	–	Solid–liquid microex-traction	–	C18 (5 μm × 250 × 4.5 mm)ACN/water in isocratic conditions	Liquid chromatography fluorescence detection		80–110%		0.9–3.5 μg/kg	[15]
BPA,BADGE	–	–	Polycarbonate	Chloroform/ Methanol	–	C18 Acclaim PepMapRSLC (2 μm × 150 × 0.3 mm)1 mM ammonium formate in 10:90 methanol:water (v/v)/1 mM ammonium formate inmethanol	UHPLC	ESI(+)(−)	95–98%			[30]

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Table 3 (*Continued*)

Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	LC conditions	Technique	Ionisation source	Recovery	LOD	LOQ	Refs.
Perfluorinated compounds: Perfluorooc-tanesulfonic acid tetraethy-lammonium salt PFOS, perfluo-robutanoic acid PFBA, perfluo-ropentanoic acid PFPeA, perfluo-rohexanoic PFHxA acid, per-fluroheptanoic acid PFHpA, per-fluorooctanoic acid PFOA, per-fluorononanoic acid PFNA, per-fluorodecanoic acid PFDA, perfluo/unde-canoic acid PFUnA, perfluo-rododecanoic acid PFDoA	–	–	Microwave popcorn bags	Focused ultasound solid–liquid extraction (FUSLE)	–	C18 (1.7 μm × 50 × 2.1 mm) 0.8% formic–acetonitrile/0.8% formic	UHPLC–QTOFMs/Ms analysis	ESI(−)	80–106%	0.2–0.5 ng/g	0.4–1.6 ng/g	[32]
Perfluorinated com-pounds:PFOS, PFBA,PFPeA, c PFHxA, PFHpA,PFOA, PFNA, PFDA, PFUnA, PFDoA	–	Corn and popcorn	–	Focused ultasound solid–liquid extraction (FUSLE)	–	C18 (1.7 μm × 50 × 2.1 mm) 0.8% formic–acetonitrile/0.8% formic)	UHPLC–QTOFMs/Ms analysis	ESI(−)	65–105%	0.2–0.7 ng/g	0.2–0.6 ng/g	[32]
Perfluorinated com-pounds:PFBA, PFOA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDOA, PFBS, PFHxS, PFOS, PFTrDA, PFTeDA, PFHxDA, PFODA, PFDS	–		Aluminium foil wrap-pers,baking paper materials or beverage cups	Pressurized liquid extraction (PLE) with methanol and	Clean-up with Florisil-Basic Alu-mina column	Hypersil GOLD C8 (3 μm,150 mm, 2.1 mm) 5 mM ammonium acetate–MeOH	LC–MS/MS analysis		60–90%	from 0.20 to 0.94 ng/g		[13]
PFCs, PFCA,PFAAS,PFAPA,PAP,FOSA,PFCs, and bisphenols	–		Paper,Cardboard, Paper filters for coffee	Ultrasonic extraction by mixture of acetonitrile and water	Clean-up with quech-ers	EC-C18 column (2.7 μm, 150 mm, 3 mm)	HPLC–MS/MS		70–120%		0.0027–0.13 mg/kg	[12]

PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnA, PFBuS, PFHxS, PFHpS, PFOS	–	Chicken eggs	Solid–liquid extraction with methanol solvent.	–	C18 column (5 μm, 50 mm, 2.1 mm)/ammonium formate in water/methanol.	LC–MS/MS analysis		90–120% 0.15 ng/g	0.5 ng/g	[16]
Phthalates:DMP, DMEP, DEEP, DEP, DAP, DIPrP, DPrP, DPhP, DIBP, BBP, DIPP, DPP, DCHP, DMPP, DHXP, DHP, DEHP, DNOP, DINP, DNP, DIPP.	–	Food samples including milk-based products, distilled liquor, wine, beverage, grain, meat, oil, biscuit (cookie), and canned food.	Liquid samples extracted by acetonitrile. Solid samples by QuEChERS of glass-based SPE methods	–	Poroshell 120 EC-C18 column (100 × 4.6 mm, 2.7 μm)	LC–MS/MS analysis		75.5–115.2% 0.8–15 μg/kg	10–100 μg/kg	[101]
Phthalates:DMP,DEP,DiBP, DnBP, BBP, DEHP, DOP, DiNP, DiDP	–	wine	Liquid–liquid extraction	–	Synergi Hydro-RP HPLCcolumn with a (2 mm, 4 μm, 80A) 10 mM ammoniumacetate/methanol	HPLC–MS/MS		95–105%	1.6–26.6 μg/L	[102]
Phthalates:DMeP, DMP, DMEP, DEEP,DEP, DAP, DlPrP, DPrP, DPhP, DBP, DIBP, DBEP,DBeP,BBP, DBuP, DIPP, DPP,DCHP, BMPP, DHXP, DHP,DEeP, DINP, DNP,DIDP, (DNOP) and bis(2-DEHP.	–	Milk and milk products	Liquid–liquid extraction with quechers	–		UHPLC/ESI Q-Orbitrap)	ESI(+)(−)	90,7–104.6% 0.32–2.6 μg/kg		[33]
Ink and photoinitiatos: 3,90.217.1080, 4,62.285,1315, 5,35.251,1260, 5,44.453.1770, 5,50.473.1448, 5,71.337,1627, 6,50.273.2067, 6,50.259.1911, 6,82.389.1118, 6,97.403.2334, 7,05.287.2230, 7,19.297.2412, 7,22.341.2655, 7,23.385,2928, 7,36.315.2549, 7,39.315.2549, 7,62.343.2855, 7,80.371.3174	Migration With simulants ethanol 95% and Tenax	Multilayer material	–	–	C18 (1.7 μm × 100 × 2.1 mm) water 0.1% formic/methanol 0.1% formic)	UPLC–QTOF-Ms analysis	ESCI			[10]

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Table 3 (*Continued*)

Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	LC conditions	Technique	Ionisation source	Recovery	LOD	LOQ	Refs.
Non-intentionally added substances (NIAs): Formaldehyde Polymer (PET), Acetaldehyde Polymer (PET), Ethylene terephthalate dimers and trimers Polymer (PET), 2,4-di-tertbutyl-phenol (2,4-DBTP) Polymer (pp), 2,6-di-tertbutyl-p-benzoquinone (2,6-DTBQ) polymer (PP), 3,5-ditertbutyl-4-hydroxyphenylpropionic acid polymer (PP), 2,6-ditertbutyl-4-methoxyphenol polymer (PP), 3,5-ditertbutyl-4-hydroxybenzoic acid polymer (PP), triph-enylphosphate polymer (PP), tri-o-tolylphosphate polymer (PP), diphenylphos-phate polymer (PP), dimethyl-benzaldehyde polymer (PP), 4-hydroxy-1H-indole-3-carboxilic acid polymer (PP), 7,9-di-tert-butyl-1-oxaspiro(4,5)deca-6,9-diene-2,8-dione polymer (PP), methyl-3-(3,5-ditertbutyl-4-hydroxyphenyl)propionate Polymer (PP),												

| 3-[3,5-di-tert-butyl-4-hydroxybenzyl]propionic acid polymer (PP), carbonyl and vinyl species polymer (PE), (Z)-9-octadecenamide polymer (PE), 2,4-dit-butyl-6-nitro-phenol polymer (PE), 2,4-dit-butyl-6-nitro-phenol and 2-cyclohexene-1-dione, 3,5-dimethyl, o-methyloxime polymer (PE), nonylphenol (NP) Polymer (PET), Octylphenol (OP) polymer (PET), primary aromatic amines (PAAS),N2-dodecanoyl-l-arginine (LAS), C10H16O2 active packaging, 1,4,7-trioxacyclotridecane-8,13-dione adhesives, BADGE derivates, ESBO clorohydrins PVC, Abietic acid derivates adhesives, 1-hexanol-2-ethyl adhesives, 2-ethylhexylacetate adhesives, cyclic lactone Adhesives, nonylphenol etoxilated | - | Polymers: PET,PP,PE,Printed materials, active packaging, adhesives, cans, PVC | Headspace, Solid Phase Microextraction, Liquid-Liquid extraction, Liquid-liquid Microextraction | - | volatiles GC–MS(QTOF), non volatiles LC–MS(QTOF) | ESI | [9] |

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Table 3 (*Continued*)

Compound	Food simulant	Food product	Food contact material	Extraction	Clean-up	LC conditions	Technique	Ionisation source	Recovery	LOD	LOQ	Refs.
Additives: BHT,BHA, TNV 234, TNV 326, TNV 327, TNV328, Cys UV 9, Cys UV12, Cys UV 24, Cys UV 5411, I-168, Adv-800, UV-400, Cyx-2246, Ch-81,Uv-OB, I-1076, I-1010, I-1330, I-1081	–		polycarbonate	Chloroform/Methanol		C18 (2,0 μm × 150 × 0.3 mm) ACN:water/0.5 mM sodium acetate 8.5 mM acid acetic	UHPLC–HRMS	ESI(+)(−)	95–98%			[30]
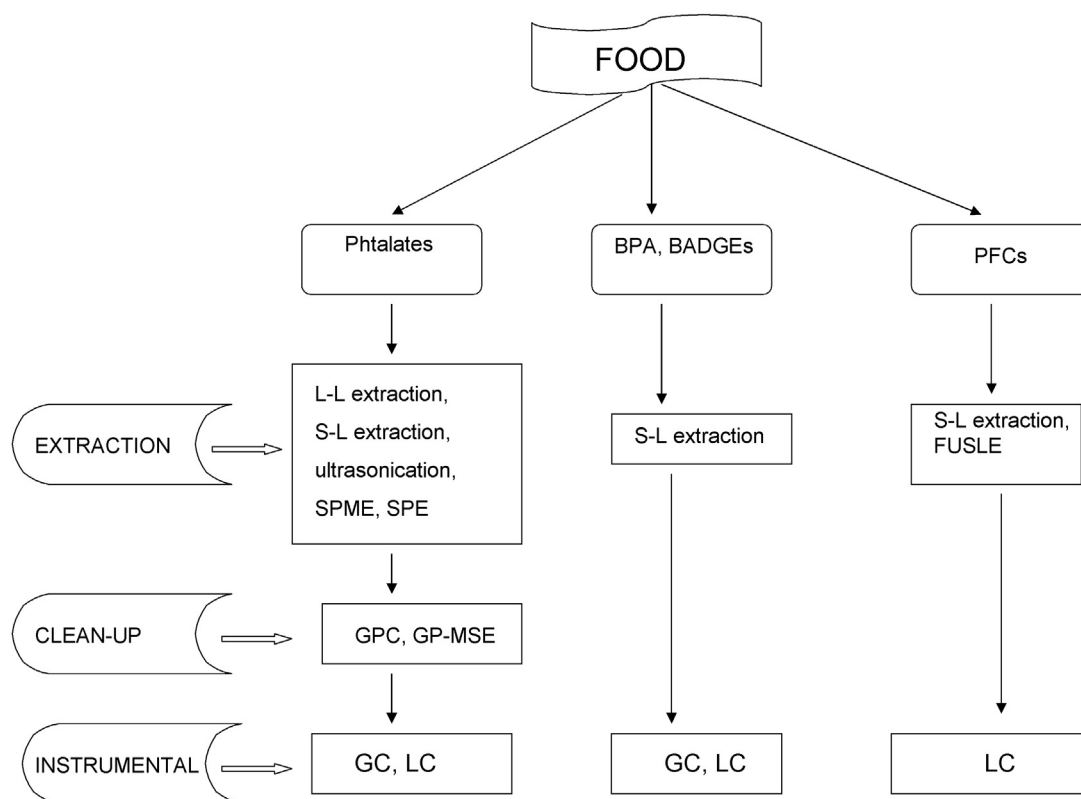
Fig. 2. Analytical strategies (extraction, clean-up and instrumental techniques) for food samples.

ing phthalates from paper materials using gas chromatography, poor recoveries were described (52–135%) [12].

In summary, in the field of FCMs. migration studies using food simulants are regulated for some FCMs. However, it will be interesting that these studies will be regulated in a wider scope of FCMs. Regarding to extraction methodologies for FCM contaminants in food and FCMs (paper and plastics) there are not a clear trend because some conventional techniques are still applied in this field. As a novelty, QuEChERS has been used in FCM methodologies as a extraction and clean-up technique. In general, few clean-up steps are applied after the extraction of FCM contaminants. Trends towards sample preparation automation and minimisation of organic solvent use are observed (PLE, SPME, FUSLE). Overall, good recoveries are generally obtained for all families of compounds using the selected methodologies.

3.2. Instrumental techniques

The selection of the instrumental technique depends on the physicochemical properties of the target substances and their concentration. For the analysis of FCM organic contaminants, both GC and LC are commonly used coupled to mass spectrometry detectors (MS and MS/MS). GC is the technique best suited for the apolar and volatile compounds (e.g., phthalates). However, the second technique, LC, is selected for more polar compounds with lower volatility or lower thermal stability, including PFCs, PAAS, NIAS and photoinitiators.

Tables 2 and 3 summarise the analytical techniques by GC and LC, respectively, and their main characteristics used in recently published studies for the analysis of the food-packaging contaminants addressed in this review, in food simulants, food and different food contact materials.
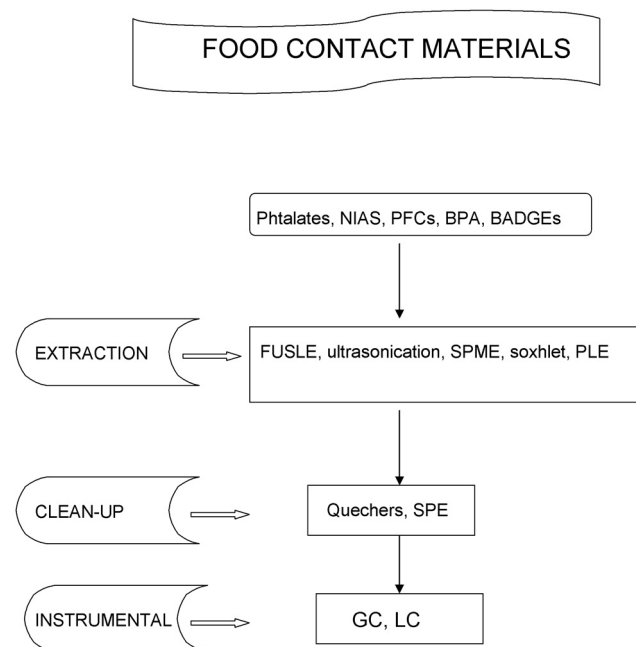
Fig. 3. Analytical strategies (extraction, clean-up and instrumental techniques) for food contact materials.

3.2.1. Gas chromatography (GC)

Phthalates and BPA are the families of organic FCM compounds mainly analyzed by GC (Fig. 5, Table 2). Recently published methods have a narrow scope, of usually between 1 and 25 of these compounds. This is in clear contrast with the present tendency observed in other fields such as water that presents a prevalence
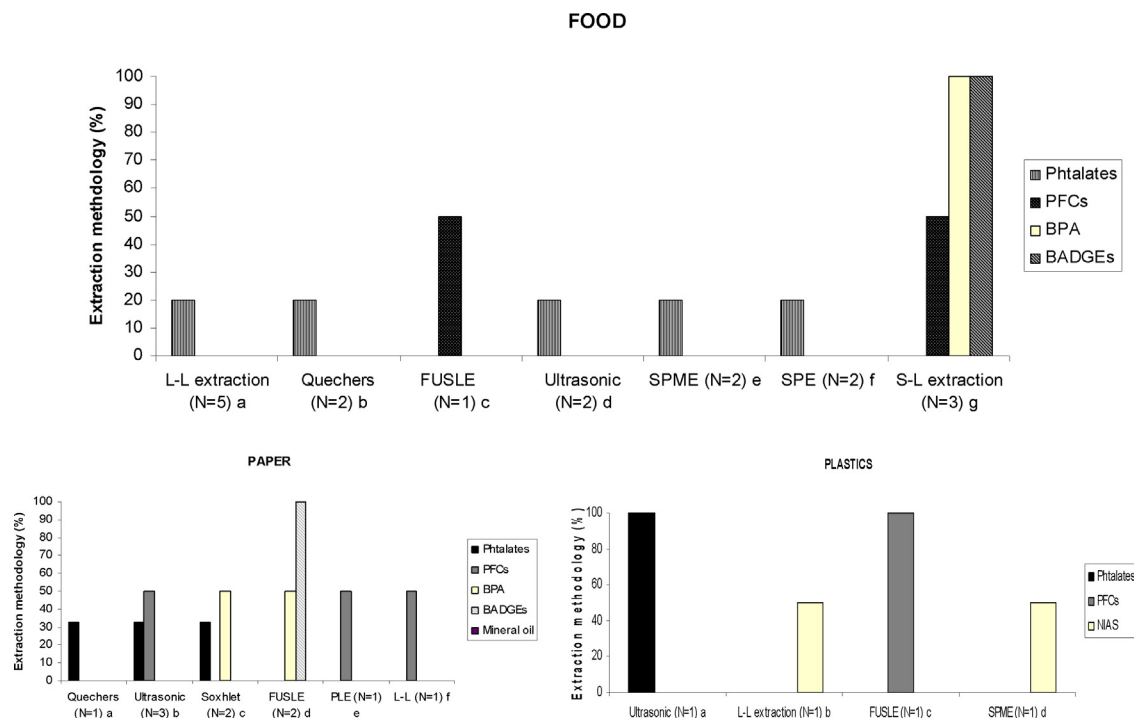
FOOD

PAPER

PLASTICS

Fig. 4. Publications on methodologies to extract contaminants from food and materials (paper and plastic). (N = number of papers published for each extraction technique; Letters = references). *Food*: a: [17,18,25,27,29]; b: [12,33]; c: [32]; d: [20,27]; e: [22,26]; f: [21,101]; g: [15,16,32]. *Paper*: a: [12]; b: [12,18,97]; c: [84,97]; d: [31,32]; e: [13], f: [98]. *Plastic*: a: [18]; b: [9]; c: [32]; d: [9].
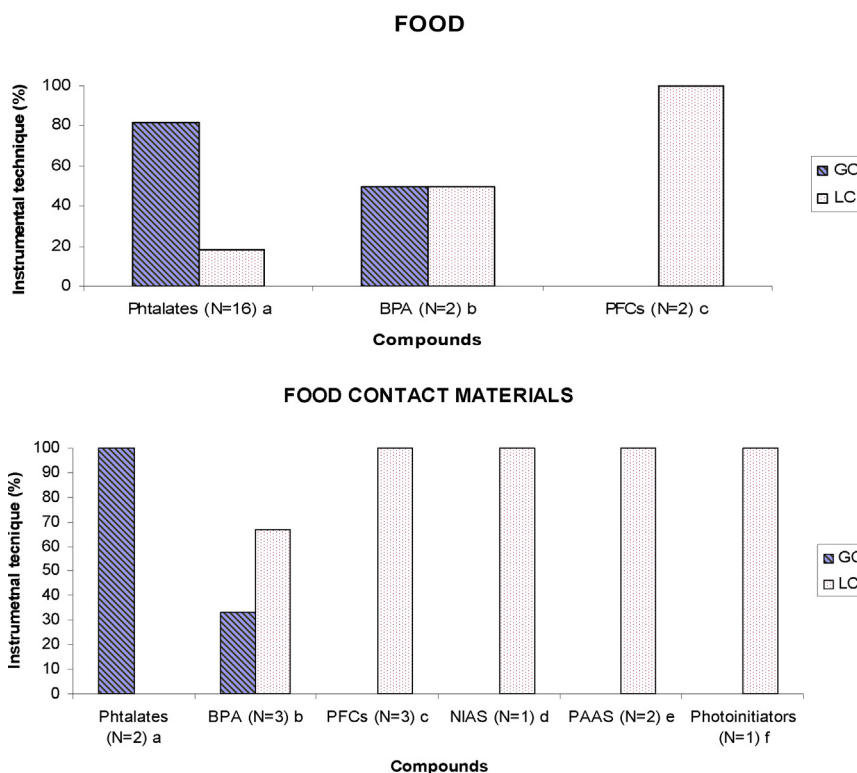
FOOD

FOOD CONTACT MATERIALS

Fig. 5. Publications on Instrumental techniques used in food and food contact materials for some families of compounds. (N = number of papers published for each compound; Letters = references). *Food*: a: [17,18,19,20,21,22,23,24,25,26,27,28,29,33,101,102]; b: [15,84]; c: [16,32]. *Food contact materials*: a: [12,18]; b: [31,84,92]; c: [12,13,32]; d: [9]; e: [7,8]; f: [10].

of multiresidue/multiclass methods for more than 150 substances on average [107].

Phthalates have been detected in oil [17,22], milk [27], meat [18], beverages [19], wine [20], vegetables [19] and fat [25]) and

in FCMs (paper [12] and plastics [18]) using GC–MS In general, the polarity of analytes is the most important parameter for the selection of an analytical column. Due to the relatively low polarity of PAEs, a non-polar column (5% phenyl-95%dimethylpolysiloxane)

and a mid-polar column (50% phenyl-50% dimethylpolysiloxane) are frequently used [108] Table 2 shows typical GC methods reported for the analysis of PAEs in foods and FCMs. Electron Impact (EI) is the ionisation technique most commonly applied. Since the contents of PAEs in food samples are generally at ultratrace levels, highly-sensitive detectors are indispensable for positive identification and quantification. Consequently, GC–MS, has been the main approach to determine PAEs due to its high sensitivity and reliability [17–28,29]. In addition, the enhanced selectivity (using SIM mode) is another advantage of the MS detector, which reduces the requirement for chromatographic separation and increases the sensitivity of PAE detection to some extent. In paper packing materials, a mass spectrometry in tandem mode was developed for the analysis of PAEs (GC–MS/MS) [12]. Good sensitivity and recoveries were obtained for PAEs in food samples ranging from 70% in chicken soup [28] to 118% in chicken soup and vegetables [24]. In materials, migration of PAEs from cardboard, tetrabrick and plastics presented good recoveries ranging from 82 to 99% and low detection limits using GC–EI-MS [18]. However, in paper materials the recoveries obtained were poorer (52–135%) but limits of detection were also low employing the GC–MS/MS technique [12].

The high efficiency and low cost of plastics materials containing phthalates stimulate their wide use in various practical applications, leading to their ubiquity in laboratories. In general, excessively high background signals account for poor LODs. Accordingly, sample contamination by these compounds cannot be ignored in the analysis. According to the literature, seven major measures were advised to avoid the contamination with phthalates: (1) all plastics consumables should be avoided; (2) organic solvents used should be purified with aluminium oxide; (3) all glassware should be cleaned up with blank tested organic solvents (e.g., acetone, hexane) and dried prior to use; (4) all reagents, including laboratory water, should be tested to establish the blank value; (5) all clean laboratory consumables should be kept in a desiccator containing aluminium oxide to avoid recontamination; (6) the chromatographic system, especially the inlet and the caps of sampler vials, should be checked initially and regularly by injecting the blank for indication of the contamination levels; and (7) use of personal-hygiene products containing PAEs should be avoided [38].

BPA has been analyzed in salt and sugar and in paperboard by gas chromatography [84]. In all these matrices a 5% polysilarylene-95% polydimethylsiloxane column and EI ionisation source were employed. Simple mass spectrometry quadrupole (MS) was using providing low detection limits, and a LOQ between 0.05 and 0.064 mg/L in food and packing material was obtained [84].

Apart from mass spectrometry detection (applied to phthalates and BPA analysis) other detectors were employed to analyze NIAS in polypropylene films. GC-FID provided good LOD (0.1–1 mg/kg) in these plastic matrices. Mineral oil in paperboard was also detected using on line HPLC-GC-FID with LOD of 0.1 mg/kg [98].

In addition, atmospheric pressure gas chromatography coupled to a quadrupole-time of flight mass spectrometry (APGC-MS/Q-TOF) has demonstrated to be a powerful tool for indentification of NIAS in acrylic adhesives used in food packaging materials. The results were compared to those obtained in a target analysis by conventional GC–MS-Q (quadrupole), and three new compounds were identified and their structure were elucidated working with the spectra obtained by APGC-MS/Q-TOF in a non-target analysis [100].

In summary, GC analytical methodologies mainly developed in FCMs field are coupled to low resolution mass spectrometers (LRMS) working in SIM [22,26,27]. More recently, GC in tandem (MS/MS) mode [12] have been also employed. No trend was observed in the studied period (2010–2016) towards the use of HRMS detection, where only one study analyzed NIAS in acrylic adhesives used in food packaging materials with Q-TOF detector [100].

3.3. Liquid chromatography (LC)

Gallart-Ayala et al. reviewed [4] the analytical methods for FCMs using liquid chromatography until 2013. They concluded that MS/MS (QqQ) continues to be the method of choice in the analysis of food packaging contaminants. The present review shows the most recent advances in analytical methods using liquid chromatography (see Table 3). Although MS/MS continues to be the method of choice, the use of HRMS is one of the best ways to prevent false positives or even false negatives, and we present some relevant examples concerning the analysis of FCM organic contaminants.

LC–MS has been the selected technique in the analysis of PFCs, PAAS and photoinitiators in plastic packaging [7,10,12,13,32], plastic utensils [8] (see Fig. 5). In addition, LC has been used for the analysis of PFCs in food such as corn and popcorn [32] and chicken eggs [16], as well as of BPA and BADGEs in canned food [15] and of phthalates in milk-based products [33], beverages [101,102], grain, meat, oil, biscuit and canned food [101], wine [102] (see Table 3). Similarly to GC, recently published methods in LC, have a narrow scope, of usually between 1 and 25 of compounds.

Generally, column sizes are in the range of 100–250 mm, with a particle size from 2 to 5 μm (see Table 3) [7,10,31]. This is a typical LC set-up for the determination of a low number of compounds (e.g. <50). As previously mentioned by Gallart-Ayala et al. [4], ultra-high performance liquid chromatography (UHPLC) is the most convenient approach to achieve reliable, fast LC separations in the analysis of food-packaging contaminants, because of lower particle size (<2.1 μm), and better resolution is provided. According to Gallart-Ayala et al. [4], RP separations continue to be the chromatographic mode of choice for the analysis of many of these compounds.

Acetonitrile and methanol continues to be the organic components of the mobile phases currently used in LC. Besides, solvent modifiers, mainly formic acid and PFPA as a proton donors, are added for enhancing ionisation efficiencies or improving peak separation or peak shape of target compounds.

Regarding ionisation of food packaging contaminants in LC, electrospray ionisation (ESI) is the most commonly used technique. The positive-ionisation mode is usually employed to analyze PAAS, BADGEs and BFDGEs, UV-ink photoinitiators, and phthalate diesters, while the negative ionisation mode gives the best sensitivity for the detection of phthalate-monoester metabolites, BPA, other bisphenols (e.g., BPE, BPB, BPF and BPS) and PFCs (Table 3). In general, negative ESI and positive ESI are dominated by the deprotonated molecule, [M-H]-, or the protonated molecule, [M+H]+, respectively, and no further fragmentation is usually observed. However, in-source fragmentation can occasionally be observed, e.g., with some UV-ink photoinitiators (2-Hydroxy-2-methylpropiophenone (HMPP), 1-Hydroxycyclohexyl phenyl ketone (HCPK), 2,2-dimethoxy-2-phenylacetophenone (DMPA), 4,4-Bis(diethylamino)-benzophenone (DEAB)) [109] In some cases, the formation of adduct ions with components of the mobile phase was also observed. BADGEs and BFDGEs showed a high tendency to form adducts such as [M+Na]+, [M+K]+, [M+NH4]+ and [M+ACN]+ ions. However, some of these cluster ions {e.g., [M+Na]+} are very stable and no further fragmentation in MS/MS was obtained, but efficient fragmentation occurred for ammonium adducts with a stable signal under MS/MS [110,111]. In these cases, to enable the formation of ammonium adducts and ensure signal reproducibility, formic acid/ammonium formate buffer is generally used as an additive in the mobile phase in positive ESI for the analysis of these compounds.

Although MS/MS continues to be the method of choice, the use of HRMS method using TOF or Orbitrap mass analysers has been recently introduced for the analysis of inks [109], PFCs [32] additives [30] and phatalates [33] in FCMs. This technique has allowed the identification of NIAS such as unknown molecules possibly deriving from polycarbonate degradation [30] or phthalates possibly deriving from nylon kitchen utensils in a non-target analysis [8]. In target analysis, PFCs were analyzed by UHPLC–QTOF-MS/MS in corn, popcorn and popcorn bags [32]. Better recoveries were obtained in microwave popcorn bags (80–106%) than in food matrices (corn and popcorn) (65–105%), although a better LOQ was validated in food (0.2–0.6 ng/g) [32]. Mattarozzi et al. [7] developed a target methodology for the analysis of 22 PAAS from plastic laminates by LC–HRMS, with the LOQ ranging between 0.099–5.45 μg/kg [7]. LC–HRMS has also been used for determination of PAAS from nylon kitchen utensils [8], achieving an LOQ of 2.5 μg/kg.

4. Conclusions and future trends

In this work, we have reviewed the recent analytical strategies for the most relevant food-packaging-contaminant families (PAAS, BPA, BADGEs and related compounds, UV-ink photoinitiators, PFCs, phthalates and NIAS), in FCMs, food and food simulants. For some contaminants (NIAS, PAAS and photoinitiators) studies have only focused on FCMs. More studies on food samples will be necessary in the near future.

Armonization will be necessary for sample preparation and analytical methods for the analysis of FCMs in food, food simulants and food contact materials. PLE, SPME, FUSLE and Quechers are sample preparation methods recently used in these type of analysis due to the integration of the extraction and clean-up procedures, automation of sample preparation and minimisation of organic solvent use. FCMs contaminants in food simulants are regulated, but more legislation will be necessary in food and FCMs. However, there is a lack of regulation about the most suitable extraction and clean-up technique to be applied in these matrixes. SML are regulated for many substances and groups of them, but more specific or individual migration level will be interesting to be established in the near future.

The GC–MS technique is mainly used for the analysis of phthalates, BPA and NIAS in food and food packaging materials. On the other hand, for the more polar substances including PFCs, PAAS and photoinitiators, LC-MS/MS has been the selected technique. Standarization of the analytical methods for FCMs in food simulants, food and food contact materials will be also useful in future.

A clear trend towards the application of HRMS in LC for target, post-target and non-target analysis has been observed in the last three years (since 2013). However, this tendency was not observed in the case of GC. Recently, the LC–HRMS method using TOF or Orbitrap mass analysers has been introduced for the analysis of some FCMs contaminants such as PFCs, PAAs, additives and phatalates in FCMs. Nowadays, the analytical challenges in this field should be the development of FCMs contaminants methodologies in food, food simulants and food contact materials applying the HRMS technique.

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