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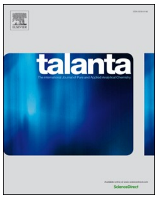

Analytical methods for the determination of emerging contaminants in sewage sludge samples. A review

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ABSTRACT

Emerging contaminants are a heterogeneous group of chemicals that includes daily personal care products and pharmaceuticals (PPCPs), flame retardants, endocrine disrupting chemicals (EDCs) and nanoparticles (NPs). The present work is an overview focused in the research published in the scientific literature for the determination of this type of pollutants in sewage sludge samples in the last 5 years. Instrumental and sample preparation methods for the detection and quantification of the analytes of interest are reviewed, with an emphasis on the sample treatment techniques. Liquid chromatography (LC) and gas chromatography (GC) coupled to mass spectrometry are generally employed as the analytical technique of preference. Sample preparation techniques include conventional methods such as Soxhlet, solid-phase extraction (SPE), pressurized liquid extraction (PLE) or ultrasound-assisted extraction (UAE), but also other recent techniques, including novel microextraction techniques such as microextraction by packed sorbent (MEPS) or solid-phase microextraction (SPME).

1. Introduction

In recent years, continuous industrial development has propitiated the generation of a wide variety of new chemicals applied in daily anthropogenic practices. These substances, which range from organic and inorganic compounds to nanoparticles, are considered to be pollutants and represent a cause of concern for society [101]. A number of families of compounds, such as pharmaceuticals and personal care products (PPCPs), flame retardants, nanoparticles or endocrine disrupting chemicals (EDCs) among many substances, form this heterogeneous group, often referred as "emerging contaminants". These substances are ubiquitous and present potential risks to human health and the environment, although their toxicological effects are not yet fully known in many cases [134]. Research, however, has determined that

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Abbreviations: ACN, acetonitrile; AOX, halogenated organic compounds; APs, alkylphenols; BFRs, brominated flame retardants; BPA, bisphenol A; BSTFA, N,O-bis (trimethylsilyl)trifluoroacetamide; CID, collision-induced dissociation; DAD, diode array detector; DCM, dichloromethane; DDT, dichlorodiphenyltrichloroethane; decaBDE, decabromodiphenylether; DEHP, bis(2-ethylhexyl) phthalate; ECNI, electron capture negative ion mass spectrometry; EDCs, endocrine disrupting chemicals; EI, electron ionization; ESI, electrospray ionization; EtAc, ethyl acetate; FLD, fluorescence detector; GC-HRMS, gas chromatography–high-resolution mass spectrometry; GC-LRMS, gas chromatography–low-resolution mass spectrometry; GC-MS^n, gas chromatography-mass spectrometry; HBCDs, hexabromocyclododecanes; HESI-II, electrospray interface heated electrospray ionization; HS-SPME, headspace solid-phase microextraction; ICP-MS, inductively coupled plasma mass spectrometry; LAS, linear alkylbenzene sulfonates; LC-MS^n, Liquid chromatography-mass spectrometry; LOD, limit of detection; MAE, microwave-assisted extraction; MeOH, methanol; MEPS, microextraction by packed sorbent; MRM, multiple reactions monitoring; MS, single mass spectrometry; MS/MS, tandem mass spectrometry; MSTFA, N-methyl-N-(trimethylsilyl)-trifluoroacetamide; MTBSTFA, N-tert-Butyldimethylsilyl-N-methyltrifluoroacetamide; NCI, Negative chemical ionization; NPs, nanoparticles; NPEs, nonylphenol ethoxylates; NSAIDs, non-steroidal anti-inflammatory drugs; octaBDE, octabromodiphenylether; OPEs, octylphenol ethoxylates; OPFRs, organophosphorus flame retardants; PBs, parabens; PBBs, polybrominated biphenyls; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls; PCPs, personal care products; PHWE, pressurized hot water extraction; PLE, pressurized liquid extraction; POPs, persistent organic pollutants; PPCPs, personal care products and pharmaceuticals; QuEChERS, Quick, Easy, Cheap, Effective, Rugged & Safe; QqLIT, hybrid triple quadrupole/linear ion trap; QqQ, triple quadrupole; ROS, Reactive oxygen species; SPE, solid-phase extraction; SPME, solid-phase microextraction; STPs, sewage treatment plants; TCC, triclocarban; TCS, triclosan; TMCS, trimethylchlorosilane; TMS, methoximated trimethylsilyl; UAE, ultrasound-assisted extraction; WWTPs, Wastewater treatment plants

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prolonged exposure to EDCs, including alkylphenols (APs), phthalates, parabens (PBs) or bisphenol A (BPA) provokes disorders on the normal development and reproductive system of wildlife and humans [14,72,103]. Polybrominated diphenyl ethers (PBDEs) used in foams, resins and adhesives among other materials; or PPCPs cause neurotoxicity and alter the normal function of the endocrine system [21,76,91,105] Nanoparticles (NPs) contained in many industrial and consumer products, especially metal NPs such as silver nanoparticles (AgNPs) or zinc oxide nanoparticles (ZnONPs), cause cytotoxicity and potentially cell damage [16,143].

Modernization and urban expansion has led to an increase in the generation of global waste derived from touristic, residential and industrial activities [101]. Wastewater treatment plants (WWTPs) are not properly equipped to remove emerging contaminants contained within household and industrial wastewater at trace levels ($\mu g\,L^{-1}$ range and below). Moreover, insufficient removal of these substances leads to discharge to the aqueous effluent, which results in pollution of aquatic environments; or sorption onto the sludge [65]. Sewage sludge is the by-product resulting from the treatment processes occurring in WWTPs. It may contain microorganisms separated from the liquid phase, as well as a wide spectrum of organic and inorganic substances [31]. While there are several disposal routes for sewage sludge (incineration, landfill, composting, etc), most of them result in the deposition of the treated or untreated sludge into the environment, with the consequent potential ecotoxicological risks [101,171]. Sludge deposition on agricultural land is associated with hazardous consequences to the environment and human health. Groundwater contamination from leaching or land runoffs could indirectly prompt a risk to human health through the food chain due to drinking water or consumption of contaminated crops [65].

Land application of sewage sludge for agricultural purposes is the most widespread method for sludge disposal, due to its low economic cost and biological advantages to the soil [34]. The total production of sewage sludge from municipal WWTPs in the European Union in 2015 was of 9.4 million tonnes, from which 39.6% was recycled for agricultural purposes, while the remaining 60.4% was landfilled or used for compost and other applications. These numbers have slightly decreased since 2010, in which the total production of sludge achieved 9.7 million tonnes in the EU, from which 45.2% was applied to land. The greatest producers of sludge remain Germany, Spain, the UK and France [131]. Sewage sludge reuse is encouraged by European Directives [38] in order to prevent further aquatic environment pollution and encourage an efficient management of the sludge. For this objective, limits in the concentration of metals and nutrients present in the sludge have been set by EU [37] and Spanish [124] legislation. Some emerging contaminants have been detected and measured in digested sewage sludge for several years [61,151,153]. Currently, no regulations exist for the presence of these contaminants in sewage sludge, although an ongoing working document containing limit values for concentrations of seven groups of organic contaminants (11 polycyclic aromatic hydrocarbons (PAHs); linear alkylbenzene sulfonates (LAS); bis(2-ethylhexyl) phthalate (DEHP); nonylphenol ethoxylates (NPEs); halogenated organic compounds (AOX); and 7 polychlorinated biphenyls (PCBs) as well as dibenzofuranes (PCDD/F) and polychlorinated dibenzodioxines i.e. chlorinated dioxins and furans) is currently under review by the European Commission [49,70].

Furthermore, analyzing emerging contaminants in sewage sludge is a difficult task. Sludge is a complex matrix in which the contaminants are often found at trace levels. Signal intensity of the analytical instrument may be suppressed in the interface of the system when several matrix components co-elute, which would result in underestimation of real concentrations, especially with LC-MS/MS [129]. Moreover, the low concentrations at which the compounds are found in the sludge makes developing an efficient pre-treatment method to extract the target contaminants extremely challenging [86,87,113]. As a result, there is need to develop sensitive and robust methods for determination of a wide variety of emerging contaminants in sewage sludge.

In recent years, several papers regarding emerging contaminants and their presence in sewage sludge have been published [22,43,64,121,151,157,163,171]. Most literature, however, focuses on a selected number of compounds or family of compounds. Zuloaga et al. [171] comprehensively reviewed with meticulous detail the main extraction techniques, clean-up procedures and instrumental techniques for analysis of emerging contaminants until 2012. However, no information about analysis of nanoparticles in sewage sludge is given. The goal of this review is to provide an update on the extraction, clean-up procedures and instrumental techniques of emerging contaminants in solid samples (biosolids and sewage sludge) collected from different WWTPs or surroundings since 2012 onwards. Due to the lack of previous analytical information on nanoparticles in this type of matrix, 10 years' worth of literature were selected for these compounds. In this study, an introduction of the compounds of interested is firstly presented, as well as an overview of the collection process of the samples (sampling, sample transfer, sample preservation) and the main procedures followed in order to pre-treat the sludge samples. The focus of the study is placed on the current sample preparation techniques, clean-up procedures and instrumental techniques employed for multiple classes of emerging contaminants.

2. Compounds of interest

The compounds selected for review are emerging contaminants chosen due to their potential risks and increasing occurrence in sewage sludge.

2.1. Flame retardants

Brominated flame retardants (BFRs) are organobromine chemicals which reduce the flammability of products [84]. Among the several classes of BFRs, the most widespread compounds in industrial production are PBDEs. Those are additive flame retardants that can be found in a large variety of consumer goods, including computers, plastics or textiles [80,161].

PBDEs are hydrophobic substances that have high persistence. Therefore, they are prone to bioaccumulate in all environmental fields, presenting risks to ecosystems and human health [58,105,146]. Three PBDE commercial mixtures have been marketed: pentabromodiphenylether (pentaBDE), octabromodiphenylether (octaBDE) and decabromodiphenylether (decaBDE) [2]. However, due to their hazardous properties, pentaBDE and octaBDE were catalogued as persistent organic pollutants (POPs) at the Stockholm Convention in 2009 and their production and use have since been eliminated in the European Union (EU) and North America [135]. In 2013, USA companies phased out the production of decaBDEs [146]. In addition, decaBDE has been recently included in Annex XVII of the REACH Regulation, where it is specified that decaBDE production, use or commercialization will be restricted after 2 March 2019 [50].

PBDEs enter WWTPs through disposal of human wastewater due to washing of rugs, carpets or gray water; leachate from landfilled PBDE-containing products and discharge water from industrial material containing PBDEs [80,146]. Wastewater treatment processes are often not effectively designed to remove PBDEs from water [80]. These compounds have low water solubility and limited biodegradability, having higher octanol-water partition coefficients (log K_{ow}) and soil organic carbon-water coefficients (log K_{oc}) than other classic emerging contaminants. For instance, PBDEs log K_{ow} and log K_{oc} range from 5 to 7 [48], whereas values for EDCs such as estradiol or BPA are significantly lower (3–4 for these examples) Hence, PBDEs rapidly sorb to organic and particulate matter, being more likely to be found and partition into the sewage sludge in WWTPs [36]. Thus, PBDEs are introduced into the environment through biosolids land application [34,60]. PBDEs could also diffuse to aquatic environments through run-offs from contaminated soils [112]. However, sewage sludge and biosolids are complex matrices in which the levels of organic chemicals such as PBDEs may vary depending on different geographical sources of wastewater discharge [80]. Human exposure to PBDEs occurs normally due to inhalation or trophic transfer, mainly through contaminated fish and seafood via sewage sludge [106]. The possible adverse health effects of these chemicals include thyroid hormone disruption or neurodevelopmental problems. Moreover, sensitive groups of population, such as pregnant women or infants are more susceptible to these effects [76,105] Due to their hazardous properties and potential negative impacts on human health, PBDEs are considered emerging contaminants and have become a growing concern over the past years.

2.2. Pharmaceuticals and personal care products

PPCPs consist of a large and unique group of organic substances which include daily personal care products (PCPs), pharmaceutical drugs, veterinary medicines and more. PCPs include fragances (e.g., polycyclic musks), sunscreens (UV-filters), insect repellents or cosmetic products; whereas among the pharmaceutical drugs considered include antibiotics, hormones, β-blockers, or blood lipid regulators among many others [39].

PPCPs involve a wide variety of chemicals with significantly diverse chemical properties. A large number of these compounds have high polarity and low volatility and can be found in aquatic media, hence one of the main pathways of environmental contamination by PPCPs is through wastewater effluent from WWTPs. Their widespread use has led these substances to become ubiquitous in the environment [125]. Additionally, conventional sewage treatment plants (STPs) are often incapable of removing PPCPs [91,155]. Some PPCPs do not dissociate in water to a significant extent, having K_{ow} values over 3 for naproxen or ibuprofen, for instance and K_{oc} values of over 2 for other compounds such as tiamulin or indomethacin [122,152]. Thus, incomplete elimination of these compounds produces variable removal efficiencies which, ultimately, result in detection of various classes of PPCPs at concentrations of $\mu g\,kg^{-1}$ or $mg\,kg^{-1}$ in sludge [56].

PPCPs introduction into the environment occurs through direct and indirect pathways [111]. Direct wastewater discharge originating from hospitals, industries and households frequently contains high concentrations of PPCPs [39]. These compounds are later ineffectively processed in STPs and can be adsorbed onto the sludge, which will contaminate agricultural land if it is spread, as common practice. PPCPs can also pass into the soil by irrigation with treated or untreated wastewater. Furthermore, PPCPs can reach groundwater by leaching, bank filtration or wet atmospheric deposition [91,125,155].

Moreover, pharmaceutically active phenolic compounds or steroid estrogens (natural or synthetic) can interfere with the endocrine system at low concentration and cause developmental abnormalities or decreased fecundity among other effects [21]. Another hazardous effect provoked by persistent exposure to PPCPs is the potential emergence of antibiotic-resistant bacteria. Furthermore, combined action of various chemicals could produce further unwanted synergic effects [42]. Given the constant presence of PPCPs in daily life and their potential risks to wildlife and human beings, these compounds have been regarded as emerging contaminants.

2.3. Endocrine disrupting chemicals

EDCs are a group of structurally diverse organic substances that can affect the endocrine system of humans and wildlife by altering the normal function of hormones [24,42]. In the International Program on Chemical Safety, the World Health Organization [71] described an endocrine disrupting compound as "*an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations*" [71]. EDCs interfere with receptor binding and metabolism of hormones through nuclear hormone receptors, non-steroid receptors, metabolic and biosynthetic pathways of steroids and orphan receptors [42,123,128].

This group of chemicals is highly heterogeneous and includes natural occurring compounds such as lignans, coumestans, isoflavones or mycotoxins and substances found in human and animal food, as phytoestrogens. Other synthetic EDCs consist of PCBs, polybrominated biphenyls (PBBs), dichlorodiphenyltrichloroethane (DDT), dioxins, alkylphenols, phtalates, BPA or dioxins [24,42,57]. All these compounds have been used as industrial solvents or lubricants, pesticides, plasticizers or plastics in food containers, electronics or water bottles [42,115].

EDCs normally bioaccumulate in aquatic organisms and especially in groundwater, river and lakes [12]; due to their stability and persistence. EDCs are mainly introduced into the environment through run-offs from farmlands and effluents from WWTPs. Consequently, EDCs are frequently found in sediments and sludge at trace levels ($\mu g\,kg^{-1}$). Hence, the detection of these compounds in sludge requires an efficient pre-treatment of the sample and highly sensitive methods [14,26,59].

2.4. Nanoparticles

The term nanoparticle (NP) refers to engineered solid particles with at least one dimension whose length is lower than 100 nm [47,95]. The production and use of nanoparticles has increased tremendously in the recent years due to their unique and versatile properties. NPs can be found in multiple consumer goods, from medical and antimicrobial products and textiles (AgNPs), electronic equipment containing gold nanoparticles (AuNPs), toothpastes, food storage containers, coating materials, liquid fabric softeners containing titanium dioxide nanoparticles (TiONPs) to plastics or packaging (ZiONPs) [16,77].

The widespread presence of nanoparticles in industrial and consumer products has increased concern over their potential toxic or harmful effect to the environment [73]. Engineered nanoparticles are released into the environment indirectly from products during their production and their increasingly common use (cosmetics, sunscreen formulations, drugs, paints, etc) through wastewater discharge [63]. During the treatment process, nanoparticles are often not entirely removed and may be incorporated into the sewage sludge matrix through aggregation or sorption reactions, and over time, become concentrated [54,77,95]. After sludge application to agricultural land, the potential hazardous effects nanoparticles pose could affect biological soil communities, as well as aquatic species through leaching, run-off lands or erosion [104]. However, assessing nanoparticles' occurrence and behavior once they re-enter the environment through sludge disposal to agricultural soil, incineration, or landfilling remains difficult [77,78,143].

Human exposure to nanoparticles occurs mainly during the manufacturing of the nanomaterial, through absorption for drug systems or possibly through inhalation of nanoparticles released into the atmosphere too. NPs differ in physical and chemical properties depending on their origin, size or composition, some of which can result in long-term environmental and health risks [143]. Under certain environmental and biological conditions, metal containing NPs can react with other contaminants and cause cytotoxicity [78]. Reactive oxygen species (ROS) may be particle-induced generated in combination with UV-light, potentially causing cell damage [16,54]. Moreover, nanoparticles can serve as carriers for other toxins which may be released into the environment and alter aquatic ecosystems [78,143].

3. Methods and applications

The number of publications regarding determination of emerging contaminants in sewage sludge has notably increased over the last 10 years. Tables 1–3 review some of the most relevant publications from an analytical point of view over 5 years for emerging contaminants and 10 years for NPs.

Table 1
Determination of emerging substances of concern in solid waste/sewage sludge samples by gas chromatography.

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
CG-MS (EI)							
EDCs	Estrogenic compounds	– UAE (EtAc) – Treatment with H_2SO_4 – SPE (HLB) – Clean-up (neutral Al_2O_3-Silica gel column) – Derivatization (BSTFA-pyridine, (1:1, v/v))	LOQs: 1.2–5.5 ng L^{-1}	80–98.5% (removal efficiencies)	Activated sludge (Tunisia)	2.52–3.55 L kg^{-1} (K_d: distribution coefficients between water and activated sludge)	[17]
	Estrogenic compounds	– UAE (EtAc-MeOH) – SPE (Oasis HLB cartridges) – Clean-up (neutral Al2O3-silica gel column) – Derivatization (BSTFA-pyridine, (1:1, v/v))	LOQs: 0.9–1.4 ng g^{-1} dw	87–101%	Sewage sludge (Tunisia), 2013	8.3–935 µg kg^{-1} dw	[18]
	E1, E2, E3, EE2; 4tOP, 4-CP, NP1EO, NP2EO; BPA	– Freeze-dried, ground and teflon-lined extraction vessels – MAE – Cleanup by GPC (Bio-Beads S-X3 column, cyclohexane-EcAt (1:1, v/v)) – Filtered with Millipore 0.45 µm GF/F, glass fiber filters. – pH adjusted to 4.0–4.5 with hydrochloric acid – SPE (Supelco) – Derivatization with BSTFA (1 % TMCS) plus 40 µL pyridine (estrogens and phenols) – Derivatization with MSTFA-TMIS-DTE, (1000:2:5, v/v/w) (progestogens and androgens)	LOQs: 0.2–9.5 ng g^{-1} dw	74.8–101.6%	Sludge (Dianchi Lake, China), 2012	1.1–4386.0 ng g^{-1} dw (phenols) 0.6–13.4 ng g^{-1} dw (estrogens) 0.8–43.3 ng g^{-1} dw (androgens) 1.3–3.8 ng g^{-1} dw (progestogen) 14.7–557.5 ng g^{-1} dw (BPA)	[68]
	Hormonal steroids, PAH, PCBs	– Dried and grounded – UAE (hexane-acetone, (3:2, v/v)) – Filtered (Whatman filter paper)	No data	92–98%	Biosolids (Argentina)	< LOD (Steroids) < LOD (PAHs, PCBs) DBP, DEHP detected. No quantification data.	[142]
	PBs, phenylphenols, APs, NP, 4tOP, TCS, BPA	– Freeze-dried – MAE (MeOH, 350 W, 3 min), UAE (MeOH) or Soxhlet extraction (anhydrous Na_2SO_4, MeOH) – Continuous SPE (PTFE column, LiChrolut EN sorbent) – Derivatization with BSTFA containing 1% TMCS	0.5–4.5 ng kg^{-1}	93–99% (MAE) 81–95% (UAE) 70–89% (Soxhlet)	Sewage sludge (Spain)	36–164 ng kg^{-1} (MAE-SPE)	[14]
	E1, E2, EE2, NP, OP and their metabolites (including MeTCS)	– Freeze-dried – LSE (phosphate buffer, pH2 and ACN, twice; ACN, once) – Rotary evaporation and diluted with water – SPE (HLB)	MQLs: 0.5–20 µg kg^{-1}	40.2–89.4 %	Sludge and suspended solids (China), 2016	< LOD (E3, E1, EE2, OP) < LOD – 122 µg kg^{-1} (NP) 120–180 µg kg^{-1} (E2) 130–380 µg kg^{-1} (MeTCS)	[11]

(continued on next page)

Table 1 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
APs	OP, NP, NP1EO, NP2EO	– LLE (Cyclohexane, by manual shaking) (sludge leachates)	0.0002–0.05 mg kg^{-1}	88–112%	Dried and fresh sewage sludge, sludge leachates (Spain)	0.01–1.9 mg kg^{-1} (dried sludge) 0.006–19.3 mg kg^{-1} (fresh sludge)	[109]
EDCs, PPCPs	Antiinflamatory pharmaceuticals, BPA, TCS, NP, OP and E1	– UAE (MeOH 1% (v/v) formic acid) – SPE (Envi-carb) – Derivatization with MTBSTFA	0.1–25 ng g^{-1}	83–107%	Sewage sludge (California), 2010	1502–5327 ng g^{-1} dw	[164]
PPCPs	Analgesics, antiinflammatories, lipid regulator, TCS, anti-epileptic, β-Blockers, antibacterials and estrogenic compounds	– MAE (MeOH-H_2O, (3:2, v/v), 500W, 6min) – SPE (Oasis HLB) – Derivatization with BSTFA containing 1%TMCS	0.8–5.1 ng kg^{-1}	91–101%	Sewage sludge (Spain),	6.5–3100 ng kg^{-1}	[13]
PCPs	Macrocyclic musk fragrances	– HS-SPME (PDMS/DVB 65 µm fiber)	MDLs: 5.0–25.0 pg g^{-1} dw	–	Sewage sludge (Spain)	< LOD – 0.89 ng g^{-1} dw	[148]
PCPs (*EI,NCI,PCI*)	M3TPh	– UAE (Acetone-DCM) – SPE (ENV+)	No data	54% (sludge) 78% (sediments)	Sewage sludge (Sweden), 2013 Lake sediments (Sweden, Norway), 2009, 2012	470–530 ng g^{-1} dw (sludge) 0.015–1.7 ng g^{-1} dw (sediments)	[107]
APEs, BFRs	PBDEs, OPEs, NPs, TBBPA, HBCD	– UAE (Hexane-acetone, (4:1, v/v)) – Cleanup with acidic silica column – Derivatization with HFBA + triethylamine	0.12–5.0 ng g^{-1}	39–79%	Sludge sample (South Africa)	2.009–642.07 ng g^{-1} 38.58 ng g^{-1} (alkylphenols) < LOQ – 642 ng g^{-1} (APEs) < LOQ – 161 ng g^{-1} (BFRs)	[33]
BFR	HBB, BDE-99	– PLE (ASE 300, DCM-hexane (50:50, v/v), 100 °C, 3 cycles) – Syringe-filtered (0.45 µm PTFE) – Clean-up with GPC column – Treatment with concentrated H_2SO_4 – LLE (hexane)	No data	63–97%	Biosolids/sewage sludge (North Carolina), 2006–2010	< 2 – < 10 ng g^{-1} dw (HBB) 274–810 ng g^{-1} dw (BDE-99)	[40]
GC-MS/MS (EI)							
PBDEs	BDEs congeners	– Mixed with Florisil and Na_2SO_4 – PLE (ASE 200, hexane-DCM, (50:50, v/v), 40 °C, one cycle) – MEPS (C18, Acetone-H_2O)	0.01–0.04 ng g^{-1}	92–102%	Sewage sludge (Spain)	16.2–45.6 ng g^{-1}dw (ΣBDEs)	[97]
PCPs	BTRs UV-filters	– LSE (acetone-hexane, (1:1, v/v) by orbital shaking) – Clean-up with de-activated silica gel and sodium sulfate column	LOQs: 0.1–0.5 ng mL^{-1}	72.94–103.19%	Sewage sludge (China)	0.34–408.32 ng g^{-1} dw	[169]
FRs	PBDEs, NBFRs, OPFRs	– UAE (EtAc -cyclohexane, (5:2, v/v)) – SPE (Florisil)	4.8–25 µg kg^{-1} (PBDEs) 3.7–375 µg kg^{-1} (NBFRs) 28–575 µg kg^{-1} (OPFRs)	64–131%	Sludge sample (Spain)	3.2–2971 µg kg^{-1}	[35]

(*continued on next page*)

Table 1 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
EDCs	Synthetic and natural strogenic compounds	– MSPD – Derivatization (BSTFA + pyridine)	0.01–0.3 ng g^{-1}	80–110%	Sludge-amended soil (Spain)	0.21–3.3 ng g^{-1}	[4]
	Natural and synthetic hormonal esteroids: estrogenic compounds, *t*-ANDR, ANDT, TEST and PROG	– UAE (H_2O-ACN, (2:3, v/v)) – $MgSO_4$ and NaOAc added – QuEChERS ($MgSO_4$, PSA and C18) – SPE (Evolute ABN) – Derivation (MSTFA-TMIS-DTE, (1000:2:5, v/v/w))	0.5–2.1 ng g^{-1}	76–124%	Pelletized sewage sludge (Spain)	5–3078 ng g^{-1} (androgens) 1–52 ng g^{-1} (estrogens) 48–62 ng g^{-1} (progestogen)	[5]
PCPs	PBs	– MSPD (filter with two paper circles 2 cm diameter and cleanup with Florisil) – Derivatization (BSTFA-TMCS, (99:1, v/v))	0.1–2.0 ng g^{-1} dw	85–125%	Sewage sludge (Spain), 2010	5.1–26.2 ng g^{-1} dw (MPB) 44.1 ng g^{-1} dw (PPB)	[3]
EDCs	N-nitrosamines	– PHWE: ASE200, water at pH 7.5, 125 °C, 1500 psi, twice) – HS-SPME (DVB/CAR/PDMS fiber)	0.03–0.15 µg kg^{-1} dw	-	Sewage sludge (Spain)	0.2–371 µg kg^{-1} dw	[94]
GC-NICI-MS							
BFRs PBDEs	PBDEs congeners and emerging compounds (HBB, PBEB, DBDPE)	– PLE (ASE 200, hexane-DCM, (1:1, v/v), 100 °C, twice) – Treatment with concentrated H_2SO_4 – Purification with SPE (two different cartridges: silica and alumina).	0.19–0.67 ng g^{-1} dw (PBDEs) 0.17–0.56 ng g^{-1} dw (PBEB and HBB) 3.63–12.1 ng g^{-1} dw (DBDPE)	31–81% (PBDEs) 23–29% (PBEB, HBB) 44% (DBDPE) 39–120% (HBCDs, TBBPA)	Sewage sludge (Spain), 2009	20.7–2326 ng g^{-1} dw (PBDEs) 5.71 ng g^{-1} dw (HBB) 2.33 ng g^{-1} dw (PBEB) 257 ng g^{-1} dw (DBDPE)	[58]
GC-NCI-MS							
PBDEs	PBDEs congeners	– Soxhlet extraction with DCM – Clean-up with multi-layer silica gel column	No data	77.3–97.3%	Sewage sludge (Italy)	0.5–9410 ng g^{-1} dw	[32]
PBDEs	PBDEs congeners	– UAE (MeOH 1% ammonium hydroxide, v/v; DCM-hexane (2:1, v/v)) – Treatment with H_2SO_4 – SPE (Florisil)	No data	59–100 %	Biosolids from WWTPs (Australia)	1.8–2500 ng g^{-1} dw (ΣPBDEs)	[52]
PCPs	TCS and chloro bromo derivatives	– MAE and *in situ* acetylation (Acetone-hexane, (20:80, v/v) in presence of acetic anhydride) – Filtered through Celite – NaOH to remove acetic acid – Clean-up with silica gel column	MDLs: 300.0 ng g^{-1} (TCS) 5.0 ng g^{-1} (Halogenated TCSs)	86–101%	Biosolids (grab and digested sludge) (Canada), 2011–2012	3.9–273.6 ng g^{-1}	[83]

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Table 1 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
GC-ECNI-MS							
HFRs	PBDE congeners, DP, BTBPE, TBB, DBDPE	– Homogenization (sodium sulfate) – Soxhlet extraction (acetone-hexane) – Activated copper powder to remove sulfur – Concentrated H_2SO_4 to remove lipids – Clean-up with alumina/silica column	0.2–1.5 ng g^{-1}	82.7–133.5% 73.6–89.2%, 77.9–127.6% 71.6–105.6%	Sewage sludge (China), 2013–2014	19–72.1 ng g^{-1} (ΣPBDEs) 7.2–16.0 ng g^{-1} (DP) 2.4–6.8 ng g^{-1} (BTBPE) 676.6–27,438.6 ng g^{-1} (DBDPE)	[159]
BFR *(ECNI, EI)*	PBDEs congeners and DP	– PLE (ASE 300, DCM-hexane (50:50, v/v), 100 °C, 3 cycles) – Syringe-filtered to (0.45 µm PTFE) – Clean-up with GPC column – Treatment with concentrated H_2SO_4 – LLE (hexane)	No data	79% (F-BDE-69) 73% (^{13}C-BDE-209)	Biosolids/sewage sludge (North Carolina), 2006–2010	1750–6358 ng g^{-1} dw (ΣPBDEs) 2–29 ng g^{-1} dw (DP)	[40]
SPME-GC-MS (EI)							
EDCs	Chlorophenols, estrogenic compounds, androsterone, DHT; NE; TCS, BPA	– UAE (MeOH) – SPE (silica gel with sodium sulfate) – Coupled SPME (polyacrylate fiber, Supelco)	1.0–42.5 ng g $^{-1}$	–	Activated sludge (biosolids) (Greek)	54.9–786.7 ng g $^{-1}$ dw (hormonal steroids) N.D – 634.4 ng g $^{-1}$ dw (chlorophenols) 13.3–412.36 ng g $^{-1}$ dw (TCS) 1.71–4.53 ng g $^{-1}$ dw (BPA)	[147]
GC-ICP-MS							
PBDEs	PBDEs congeners	– Dried, ground and sieve – Sterilized by g-irradiation (to eliminate any bacterial activity) – LSE (0.1 mol L^{-1} HCl in MeOH by mechanical shaking) or MAE (0.1 mol L^{-1} HCl in MeOH, 1200 W) – Addition of Tris-citrate buffer solution (pH 6) and iso-octane, mechanical shaking	0.182–0.302 n-g g^{-1} dw (LSE)	95–104%	Sewage sludge (Slovenia), 1998, 2000, 2014	$<$ 0.209–66.6 ng g^{-1} dw 1.12–38.6 ng g^{-1} dw 1.40–20.1 ng g^{-1} dw	[116]
HRGC/HRMS (EI)							
PBDEs	PBDEs congeners	– Soxhlet extraction with dichloromethane – Clean-up with GPC, silica gel, and Florisil or alumina chromatography.	0.80–290,000 -pg g^{-1}	–	– Primary sludge (PS) – Waste biological sludge (WBS) – Treated biosolids (Canada)	230–82,000 ng g^{-1} (PS) 530–8800 ng g^{-1} (WBS) 420–6000 ng g^{-1} (Treated biosolid)	[79]
HRGC/LRMS (ECNI)							
HFRs	BFRs, CFRs	– Mixed with Na_2SO_4 – PLE (ASE 350, DCM-Hexane, (1:1, v/v), 100 °C, 3 cycles) – Acidic silica to remove lipids – Clean-up: multilayer silica column	0.01–0.5 ng g^{-1}	92.6%	Sewage sludge (China), 2010–2013	0.09–298 ng g^{-1} dw	[167]

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Table 1 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
HRGC-TQMS-MS (EI)							
BFR	BDE-209, DBDPE	– PLE (ASE 100, Hexane-DCM, (1:1, v/v), 100 °C, 10.3 MPa) – Mixed with anhydrous sodium sulphate and activated copper powder to remove sulfur. – Solvent exchanged with hexane – and liquid extracted with concentrated H_2SO_4 – Clean-up with Power Prep System (FMS Inc., USA), acidic silica gel, basic alumina and carbon columns	0.3 pg g^{-1}dw	63%	Sewage sludge (Spain), 2006	5.45–843 ng g^{-1} (BDE-209) 3.25–125 ng g^{-1} (DBDPE)	[41]

Abbreviations: ACN, acetonitrile; ANDT, 4-androstene-3,17-dione; APs, alkylphenols; APEs, alkylphenol ethoxylates; ASE, accelerated solvent extraction; BFRs, brominated flame retardants; BDEs, brominated diphenylethers; BPA, bisphenol A; BSTFA, N,O-Bis(trimethylsilyl)trifluoroacetamide; BTRs, benzotriazoles; BTBPE, 1,2-bis(2,4,6-tribromophenoxy)ethane; 4-CP, 4-cumylphenol; CFRs, chlorinated flame retardants; DBDPE, decabromodiphenylethane; DCM, dichloromethane; DHT, 5α-androstan-17b-ol-3-one; DP, Dechlorane Plus; DTE, 1,4-Dithioerythritol; dw, dry weight; E1, estrone; E2, 17β-estradiol; E3, estriol; ECNI, electron capture negative ion; EDCs, endocrine disrupting chemicals; EE2, 17α-ethinylestradiol; EI, Electron ionization; EtAc, ethyl acetate; FRs, flame retardants; GC-MS, gas chromatography–mass spectrometry; GPC, gel permeation chromatography; HBB, hexabromobenzene; HBCD, hexabromocyclododecane; HFBA, heptafluorobutyric anhydride; HFRs, halogenated flame retardants; HRGC/HRMS, high-resolution gas chromatography/high resolution mass spectrometry; HRGC/LRMS, high-resolution gas chromatography/low resolution mass spectrometry; HS-SPME, headspace solid-phase microextraction; IPC-MS, inductively coupled plasma mass spectrometry; LLE, liquid-liquid extraction; LOD, limit of detection; LOQ, limit of quantification; LSE, liquid-solid extraction; M3TPh, phenyl-tris(trimethylsiloxy)silane; MAE, microwave-assisted extraction; MDL, method detection limit; MeOH, methanol; MEPS, microextraction by packed sorbents; MSPD, matrix solid-phase dispersion; MSTFA, N-Methyl-N-(trimethylsilyl)trifluoroacetamide; MTBSTFA, N-tert-butyldimethylsilyl-N-methyltrifluoroacetamide; NBFRs, novel bromitated flame retardants; NCI, negative chemical ionization; NE, 19- norethindrone; NICI, negative-ion chemical ionization; NP, nonylphenol; NP1EO, nonylphenol monoethoxylate; NP2EO, nonylphenol diethoxylate; OP, octylphenol; OPEs, octylphenol ethoxylates; OPFRs, organophosphorus flame retardants; PAHs, polycyclic aromatic hydrocarbons; PBs, parabens; PBEB, pentabromoehytlbenzene; PBDEs, polybromitaded diphenyl ethers; PCBs, polychlorinated biphenyls; PCPs, personal care products; PHWE, pressurised hot water extraction; PLE, pressurized liquid extraction; PPB, propyl paraben; PROG, progesterone; PTFE, polytetrafluoroethylene; SPE, solid-phase extraction; SPME, solid-phase microextraction; t-ANDR, trans-androsterone; TBBPA, tetrabromobisphenol A; TCS, triclosan; TEST, testosterone; TMCS, trimethylchlorosilane; TMIS, Iodotrimethylsilane; 4tOP, 4-tert-octylphenol; TQMS-MS, mass spectrometry triple quadrupole; UAE, ultrasound-assisted extraction; WWTPs, wastewater treatment plants.

Table 2

Determination of emerging substances of concern in solid waste/sewage sludge samples by liquid chromatography.

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
HPLC-MS/MS (ESI-)							
FRs	HBCDs	– UAE (MeOH 1% ammonium hydroxide, v/v; DCM-hexane (2:1 v/v)) – Treatment with H_2SO_4 – SPE (Florisil) – SPE (fractioned on LC-Si silica)	No data	32–126% (range) 80–86% (mean)	Biosolids from WWTPs (Australia)	< LOD – 129 ng g^{-1} dw (ΣHBCDDs)	[52]
EDCs	Estrogenic compounds, BPA	– PLE (ASE 350, DCM-Hexane, (3:1, v/v), 80 °C, twice) – 4 steps for cleanup: LLE, Florisil, aqueus alkali extraction and hydrophilic-lipophilic balance (HLB) enrichmnet	0.05–0.1 ng g^{-1}	88–97%	Sewage sludge (China)	0.7–7.1 ng g^{-1} (estrogens) 92.9 ng g^{-1} (BPA)	[29]
	BPs analogues	– Freeze-dried – UAE (phosphate buffer-ACN, (3:4, v/v), ACN) – SPE (Oasis HLB)	MQLs: 0.188–7.28 μg kg^{-1}	40.1–128%	Sewage sludge (China), 2016	0.804–1980 μg kg^{-1} dw	[140]
	SPAs, BHT	– Mixed with Na_2SO_4 – PLE (ASE 350, DCM-Hexane, (3:1, v/v), 90 °C, 3 cycles) – SPE (silica column)	MQLs: 0.1–15.0 ng g^{-1}	65–103% 63–106%	-Sewage sludge (China), 2010–2011 -Sewage sludge (China), 2013	0.07–30,300 ng g^{-1} (SPAs) 51.7– 30,300 ng 1.1–2325 ng g^{-1} (SPAs) 1325–2325 ng g^{-1} (BHT)	[92] [93]
	BPs analogues	– Freeze-dried – LSE (MeOH-H_2O, (5:3, v/v) by orbital shaking, twice) – SPE (Oasis MCX)	LOQ: 1.79 ng g^{-1} dw	78–101%	Sewage sludge (United States), 2006–2007	< 1.79–4700 ng g^{-1} 12.8–4730 ng g^{-1} (ΣBPs)	[165]
	BPs analogues	– LSE (MeOH by shaking, 3 times) – SPE (ENVI-Carb) – SPE (Sep-Pak C18)	MQLs: 0.08–12.8 ng g^{-1}	62–108% Means: 81% (10 ng spiked) 88% (100 ng spiked)	Sewage sludge (China), 2010–2011	0.06–259 ng g^{-1} 5.37–599 ng g^{-1} (ΣBPs)	[133]
	HIS	– PLE (ASE 2000, MeOH-H_2O, (1:1, v/v), 40 °C, one cycle) – SPE (Oasis HLB)	5.0–10.0 μg kg^{-1}	> 61%	Sewage sludge (Spain)	< LOQ – 591 μg kg^{-1} dw	[9]

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Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
PPCPs	NSAIDs	– QuEChERS (ACN, NaCl and $MgSO_4$) – On line SPE (Strata-X)	0.33–36 ng L^{-1} MDLs: 0.065–6.7 ng g^{-1}	36–55% 50–76% (ASA, SAL, KET)	Sewage sludge (Italy), 2015	< 0.39–57 ng g^{-1}	[127]
	PBs	– Oven dried – UAE (MeOH-acetone, (1:1, v/v) with 10 mM of acetic acid) – SPE (Oasis MCX)	0.2–0.5 ng L^{-1} MDLs: 0.28–0.97 ng g^{-1}	78–113% 65–72% (Average absolute recoveries)	Sewage sludge (United States), 2009–2010	21.2–213.2 ng g^{-1} dw (ΣPBs)	[30]
	TCS	– Homogenization (sodium sulfate) – PLE (ASE 300, DCM-hexane, (50:50, v/v), 100 °C, 3 cycles) – Purification with concentrated H_2SO_4 – LLE (DCM-hexane, (50:50, v/v)) – SPE (Sep-Pak Plus Silica)	No data	53%	Municipal biosolids/ domestic sludge (North Carolina), 2006–2010	490–13,866 ng g^{-1} dw	[40]
	TCS, TCC and their metabolites	– Freeze-dried – LLE (phosphate buffer, pH (2) and ACN, twice; ACN, once) – Rotary evaporation	MQLs: 0.2–0.5 µg kg^{-1}	56.1–92.2%	Sludge and suspended solids (China), 2016	229–1170 µg kg^{-1} (TCC) 515–1120 µg kg^{-1} (TCS) 0.876–33.6 µg kg^{-1} (metabolites)	[11]
PCPs	PBs and metabolites	– Freeze–dried, ground and sieved – PLE (ASE 350, MeOH, 70 °C, twice) – SPE (Oasis HLB)	MDLs: 0.1–0.8 µg kg^{-1}	87.8–112% 81.5–113% (PLE) 86.8–103% (SPE)	Sewage sludge (China), 2013–2014	0.28–1940 µg kg^{-1} 273–556 µg kg^{-1} (MPB)	[85]
	PBs and their metabolites	– Freeze-dried – LSE (MeOH-H_2O, 5:3 v/v; by orbital shaking, twice) – SPE (Oasis MCX 3 cm^3)	0.01–10.0 ng g^{-1} dw	52–109% (PBs) 87–105% (benzoic acid)	Activated sludge (Albany, United States), 2011	27.0–107 ng g^{-1} dw (ΣPBs) 331.0–4120 ng g^{-1} dw (Σmetabolites)	[154]
	PBs	– Homogenized, freeze-dried – LSE (MeOH-H_2O, (5:3, v/v) by orbital shaking) – SPE (Oasis MCX)	LOQs: 0.05–0.1 ng g^{-1} dw	81–119% (spiked samples)	Sewage sludge (Korea), 2011	4.63 – 545 ng g^{-1} dw (ΣPBs)	[89]
	PBs and their metabolites	– Freeze-drying – LSE (MeOH-H_2O, (5:3 v/v) by orbital shaking, twice) – SPE (Oasis MCX 6 cm^3)	0.01–5 ng L^{-1} dw	76.8–91%	Sewage sludge (India)	104–1090 ng g^{-1} dw (ΣPBs) 1220–35,900 ng g^{-1} dw (Σmetabolites)	[75]
HPLC-MS/MS (ESI+)							
FRs	OPs	– Dried with anhydrous sodium sulfate – Soxhlet extraction (DCM-EtAc, (1:1, v/v)) – SPE (aminopropyl and neutral silica column)	0.01–0.5 ng g^{-1} dw	83.1–124%	Biosolids/ activated and primary sludge (Canada), 2014	4.5–2236 ng g^{-1} dw	[158]

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Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
PPCPs	SAs antibiotics	– PLE (ASE 300, ACN-water, (25:75, v/v), 50 °C, 3 cycles) – SPE (Oasis HLB)	0.03–2.23 ng g^{-1}	60–130%	Sewage sludge (Spain), 2009	0.22–301.92 ng	[53]
	Antibiotics	– pH adjustment to 3.0 – Filtration using 0.22 µm acetate cellulose membrane – On-line SPE (Oasis HLB)	MDLs: 0.800–600 ng L^{-1}		Domestic sewage and bioreactor effluent (Brazil)	0.018–1097 µg L^{-1} (sewage) 0.023–308 µg L^{-1} (effluent)	[90]
	TCs and SAs antibiotics	– PLE (ASE200, Citric acid (pH 3)-MeOH, (1:1, v/v), RT, 2 cycles) – SPE (Oasis HLB)	0.006–0.043 µg L^{-1} (SAs), 0.129 µg MDLs: 0.6–4.2 ng g^{-1} (SAs) 3.2–13 ng g^{-1} (TCs)	86.4–100.3%	Sewage sludge (Spain), 2011	$<$ MDL – 103.8 ng g^{-1}	[117]
	Quinolone antibiotic derivatives	– UAE (MeOH-McIlvaine buffer, (50:50, v/v)) – MAE (MeOH-McIlvaine buffer, (50:50, v/v), 100 W, 17 min) – PLE (MeOH-McIlvaine buffer, (50:50, v/v))	2–5 ng g^{-1}	97.9–104%	Sewage sludge (Spain)	12–834 ng g^{-1}	[45]
ECs	BTRs, BTHs, BzPs, and BPs	– Freeze-dried – LSE (MeOH-H_2O, (5:3, v/v) by orbital shaking, twice) – SPE (Oasis MCX 6 cm^3)	0.5–2 ng mL^{-1} (BTRs) 0.33–2 ng mL^{-1} (BTHs) 0.1–0.8 ng mL^{-1} (BzPs) 0.2–1.8 ng mL^{-1} (BPs)	52–102%	Sewage sludge (India), 2012	$<$ LOQ – 58.4 ng g^{-1} dw (BTRs) $<$ LOQ – 85,700 ng g^{-1} dw (BTHs) $<$ LOQ – 231 ng g^{-1} dw (BzPs) 0.7–185.7 ng g^{-1} (BPs)	[74]
HPLC-MS/MS (ESI+/-)							
EDCs	Antibiotic and anti-inflammatory pharmaceuticals	– UAE (H_2O-MeOH)	MDLs: 2–12 ng g^{-1} dw	76–131%	Sewage sludge (Spain), 2011	2–1125 ng g^{-1} dw	[55]
	Steroid hormones, APEOs, PAEs (phthalates)	– UAE (MeOH; DCM-hexane, (1:1, v/v)) – SPE (C18)	0.01–1 ng L^{-1}	70–120%	Sewage sludge (Hong Kong, China), 2013	0.1–238 ng g^{-1} dw (hormones) 10–19,743 ng g^{-1} dw (APEOs and BPA) 0.3–37,016 ng g^{-1} dw (PAEs)	[159,160]
ECs	Pharmaceuticals and a fungicide	– Aqueous phase: – SPE (Oasis HLB) – Solid phase: - UAE (MeOH-H_2O, (50:50, v/v), 0.5% HCOOH)	LOQs: 0.2–220 µg L^{-1} (Aqueous phase) 1.2–46 µg kg^{-1} (Solid phase)	70–120% $<$ 40% (4-AA)	Liquid and solid phase of sewage sludge (Mediterranean area), 2014–2015	No data	[20]
PPCPs	Pharmaceuticals, TCS, TCC, BPA, PBs and UV-filters	– MSPD	MQLs: 0.117–5.55 µg kg^{-1}	50–120%	Sewage sample (China), 2011–2013	2270 µg kg^{-1} (ofloxacin) 1440 µg kg^{-1} (TCC)	[86,87]
	Pharmaceuticals: analgesics, stimulants, anti-seizures, NSAIDs and antibiotics	– LLE (MeOH-phosphate buffer) – SPE (Oasis H LB)	LOQs: 0.001–0.122 µg g^{-1}	74–122%	Sewage sludge (Korea), 2008	2.622–422.8 mg kg^{-1}	[46]

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Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
	Pharmaceuticals, BPA, TCS, TCC	– MSPD (C18 sorbent, MeOH, MeOH-acetone, ACN-5% oxalic acid)	0.02–2 µg kg^{-1}	42–107%	Sewage sludge (China), 2014	< LOD – 4020 µg kg^{-1} (PPCPs) < LOD – 1830 µg kg^{-1} (BPA) 354–608 µg kg^{-1} (TCS) 1130–2180 µg kg^{-1} (TCC)	[139]
	Pharmaceuticals, TCS, UV-filter	– Freeze-drying – UAE (MeOH-H_2O, (5:3, v/v), MeOH) – SPE (Oasis HLB)	LOQs: 0.5–50.0 ng L^{-1}	75–100%	Activated sludge (India), 2013	2.0–970 ng g^{-1} dw (pharmaceuticals) 10,000–28,000 ng g^{-1} dw (TCS) < LOQ – 36 ng g^{-1} dw (UV-filter)	[138]
	Pharmaceuticals	– Freeze-drying – UAE (MeOH-H_2O (5:3, v/v)) – SPE (C18)	0.5–20.0 ng g^{-1}	90–131% < 56% (ketoprofen)	Digested sludge (South Korea), 2011	< LOQ – 6930 ng g^{-1} dw	[136]
PPCPs	Pharmaceuticals: barbiturates and benzodiazepines	– Freeze-dried and sieved – PLE (ASE 200, MeOH, 100 °C, one cycle) – Filtered 0.22 µm nylon filter	0.2–12.0 µg kg^{-1}	88–112% (PLE) 41–122%	Sewage sludge (Spain)	2.8–18.9 µg kg^{-1} dw	[8]
	NSAIDs, PBs, TCC, BPA, herbicides, an antidepresive and a fungicide	– LSE (ACN 1% acetic acid, by hand-shaking and vortex) – $MgSO_4$ and NaCl to partioning organic phase – d-SPE, QuEChERS (C18, PSA,PSA + C18, chitin or and GCB adding $MgSO_4$)	0.3–15 µg kg^{-1}	50–120%	Sludge samples (Brazil)	No data	[28]
HPLC-MS/MS (APCI)							
EDCs	BPA, Cl-BPAs	– PLE (ASE200, Ethyl acetate, 100 °C, 3 cycles)	4–8 ng g^{-1}	97.7–100.6%	Sewage sludge (Spain)	23.5–680 ng g^{-1} (BPA) Cl-BPAs not detected	[44]
HPLC-DAD-FLD							
PPCPs	Anti-inflammatory drugs, strogens, antibiotics, lipid regulators, β-blockers, antiepileptic and stimulant drugs	– UAE (MeOH-acetone) – pH adjustment to 2.0 – SPE (Oasis HLB)	1.22–360 µg kg^{-1}dw	41.1–115% < 15% (acetaminophen)	Primary, secondary and digested sludge (Spain), 2008–2009	2.18–3237 µg kg^{-1}dw 524–3237 µg kg^{-1}dw (IBF) 19.8–160 µg kg^{-1}dw (EE2) 7.69–836 µg kg^{-1}dw (E2)	[98]
	Anti-inflammatory drugs, strogens, antibiotics, lipid regulators, β-blockers, antiepileptic and stimulant drugs	– UAE (MeOH-acetone) – pH adjustment to 2.0 – SPE (Oasis HLB)	0.45–126 µg kg^{-1}dw (DAD) 0.13–128 µg kg^{-1}dw (Fl)	41.1–115% < 15% (acetaminophen)	Primary, secondary and digested sludge and compost (Spain)	3.29–4105 µg kg^{-1} dw (Sludge) 9.19–974 µg kg^{-1} dw (Compost)	[99]
HPLC-UV							
	Antibiotics	– LSE (MeOH, by orbital shaking, once) – SPE (Phenomenex C18)	LOQ: 50 ng g^{-1}	–	Sludge (Kenya), 2014–2015	50–276 ng g^{-1}	[81]

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Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
UHPLC-MS/MS (ESI-)							
EDCs	Hormonal steroids: glucocorticoids	– Freeze-dried – PLE (ASE 200, hexane; MeOH-acetone, (80:20, v/v), 45 °C, one cycle) – SPE (Bond Elut Plexa cartridges)	0.5–1.0 µg kg^{-1}	8–20% (high polar) 28–43% (medium-polar) 73% (low-polar)	Sewage sludge (Spain)	< LOQ – 6.1 µg kg^{-1} dw	[66]
	PFCAs, PFSAs	– UAE (1% acetic acid in MeOH; MeOH-ACN, (50:50, v/v)) – SPE (Oasis WAX)	MDLs: 3–4 pg g^{-1}	50–104%	Sewage sludge (Nigeria), 2012	10.8–596.5 pg g^{-1}	[132]
	BPs analogues	– UAE (MeOH-acetone, (50:50, v/v)) – SPE (HLB and MAX)	0.02–0.2 ng g^{-1} dw (sediments) 0.03–0.86 ng g^{-1} dw (sludge)	57.1–103.2%	Sediment and activated sludge (China)	0.07–2009.80 ng g^{-1} dw (sediments) 1.37–20.56 ng g^{-1} dw (BPA) No data for sludge	[162]
PCPs	Antimicrobials: TCS, TCC	– PLE (ASE 300 H_2O-isopropyl alcohol, (20:80, v/v), 120 °C, one cycle) – SPE(Oasis HLB) – pH adjustment to 2.0 – SPE (HyperSep™ Retain PEP or Oasis HLB)	MDLs: 8.5–112.9 ng L^{-1} 0.0024–0.006 µg g^{-1}	62.3–91.1% 105.7–117.4% (TCS) 33.1–36.1% (TCC)	Wastewater solids/biosolids (Mid Atlantic UE), 2005–2015 Biosolids (Ireland), 2015	13,008–16,839 ng g^{-1}dw (TCS) 102–3006 ng g^{-1} dw (TCC) 0.08–4.9 µg g^{-1}	[10] [12]
	PBs	– Freeze-dried – UAE (MeOH) or PLE (MeOH)	3–7 ng g^{-1} (UAE) 3–4 ng g^{-1} (PLE)	94.0–105.9%	Compost samples (Spain)	No data	[19]
UHPLC-MS/MS (ESI+)							
FRs	Flame retardants: OPEs	– PLE (ASE 350, ACN, 170 °C, two cycles) – Filtered (GF/C membrane) – SPE (Oasis HLB)	0.02–3.00 µg kg^{-1}	56–119%	Sewage sludge (China), 2016	– Wheat straw-doped: 7.22–29.9 µg kg^{-1} – Corncob: 0–29.9 µg kg^{-1} – Sawdust: 3.33–23.0 µg kg^{-1}	[118]
	OPEs: OOPEs, MOPEs	– Freeze-dried – UAE (ACN) – SPE (Florisil)	MDLs: 0.13–0.16 ng g^{-1} dw 0.14–2.1 ng g^{-1} dw	74.1– 98.5% (Absolute recovery) 104–136% (relative recovery)??	Suspended solid particles and sludge (China), 2014	0.40– 5.82 ng g^{-1} dw (OOPEs) 1.0–90.5 ng g^{-1} dw (MOPEs)	[88]
PPCPs	Anti-cancer drugs	– PLE (ASE 200, MeOH-H_2O, (65:35, v/v), 100 °C, 4 cycles) – SPE (Oasis MAX) – SPE (Oasis MCX)	MDLs: 3.9–74 µg kg^{-1} dm (Ifosfamide) 2.5–51 µg kg^{-1} dm (Cyclophosphamide)	4–167% (IFO) 8–155% (CP)	Sewage sludge (France), 2009–2011	11.4–42.5 µg kg^{-1} dw (IFO) 12.6 µg kg^{-1} (CP)	[130]
	Pharmaceuticals: fluoroquinolones, tetracyclines, sulfonamides, macrolides	– Freeze-dried, homogenized and sieved – UAE (3 times) – SPE (Oasis HLB)	MDLs: 0.01–0.50 µg kg^{-1}	61–130%	Sewage sludge (China)	< LOQ – 8546 µg kg^{-1} (Total PPCPs) 231–8546 µg kg^{-1} (Fluoroquinolones) 16–7106 µg kg^{-1}(TCs) < LOQ – 15.51 µg kg^{-1} (Sulfonamides) 0.25–28.31 µg kg^{-1} (Macrolides)	[166]

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Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
UHPLC-MS/MS (ESI+/-)							
EDCs	PFCs, natural and synthetic estrogenic compounds; TCS, TCEP, BPA, TCPP, OP, 4-MBC, NP	– UAE (H_2O-MeOH-acetone, (1:2:1, v/v/v)) – SPE (Carbograph-4)	MDLs: 0.04–6 ng g^{-1}	19–93%	Sediments from lakes and two rives (Italy), 2015	< LOQ – 0.5 ng g^{-1} (Bracciano and Martignano lakes) < LOQ – 32 ng g^{-1} (Tiber and Liri river)	[26]
	PBs, UV-filters, TCS and TCC	– UAE (MeOH)	0.03–0.40 ng g^{-1}	83–107%	Compost from WWTPs sewage sludge (Spain)	< LOD – 26.7 ng g^{-1}	[23]
	Hormonal steroid	– MAE (PTFE vessels, MeOH, 500 W, 4 min at 65 °C, 5 min cooling and 10 min at RT) – Filtered (0.20 µm syringe PET)	2.1–192.8 ng L^{-1} MDLs: 1.11–7.90 ng g $^{-1}$	> 60%	Sludge samples (Spain), 2015–2016	< LOQ – 1440 ng g^{-1}	[62]
	Hormonal steroids, NP, OP, BPA	– MAE (PTFE vessels, MeOH, 200 W, 16 min) – Filtered (0.45-µm syringe) – On-line SPE (Oasis HLB)	0.1–0.7 ng g^{-1}	> 77%	Wastewater sludge (Spain), 2010–2012	0.3–473 ng g^{-1}	[150]
PPCPs	Pharmaceuticals and illicit drugs	– Freeze-dried – UAE (MeOH-H_2O, (50:50, v/v)) – Filtered (0.2 µm syringe filter)	0.8–19.9 ng g^{-1} dw (pharmaceuticals) 0.6–14.3 ng g^{-1} dw (illicit drugs)	50–110% (for more than 77% of compounds)	Sewage sludge (Greece), 2013	< LOQ – 267 ng g^{-1} dw < LOQ – 77.3 ng g^{-1} dw	[51]
	Pharmaceuticals and PCPs (PBs, BzPs, TCS)	– QuEChERS (NaCl, $MgSO_4$ and PSA)	MDLs: 0.15–3.0 ng g^{-1}	50–93%	Sludge sams (Brazil), 2012	13 ng g^{-1} (benzophenone-3) Other compounds not detected	[27]
ECs	PFOA, PFOS, BPA	– UAE (100 mM sodium hydroxide, MeOH-H_2O, (80:20, v/v), MeOH) – SPE (ENVI-Carb) – SPE (Oasis WAX) – SPE (C18, only for BPA)	No data	80.9% (PFOA, PFOS) 68.4% (BPA)	Sewage sludge (Hong Kong, China), 2012–2013	1.80–2.67 ng g^{-1} dw (PFOA) 10.5–10.7 ng g^{-1} dw (PFOS) 155–142 ng g^{-1} dw (BPA)	[100]
	UV-Filters, PBs, estrogenic compounds, BPA, antibacterials/antibiotics, NSAIDS and other pharmaceuticals	– Freeze-dried – MAE (H_2O-MeOH, (50:50, v/v), pH(2), 800W, 30 min) – SPE (Oasis MCX) ● Acidic analytes (0.6% HCOOH in MeOH) ● Basic analytes (7% NH_4OH in MeOH)	MDLs: 0.03–4.81 ng g^{-1}	40.8–165.4%	Digested sludge (England)	0.3–5800 ng g^{-1} (PPCPs)	[120]
LC-HRMS UHPLC-Orbitrab-MS (HESI-II+/-)							
EDCs	BTHs, BTRs and BSAs,	– QuEChERs (NaCl, $MgSO_4$, citric acid disodium salt and trisodium salt dihydrate and Z-sep + dSPE	0.5–10 ng g^{-1} dw	> 80%	Sewage sludge (Spain)	< LOQ – 181.2 ng g^{-1}	[67]

(*continued on next page*)

Table 2 (*continued*)

Compound	Analyte	Sample preparation (Sample)	LODs	Analyte's relative recoveries	Solid waste origin	Amounts detected	Ref.
LC-QTOF-MS (ESI+/-)							
PPCPs	Chlorinated azoles (antimycotics)	– MSPD (Florisil and PSA sorbents) – SCX cartridge (neutral and acid species) – SAX (neutral and basic compounds)	LOQ: 2 ng g^{-1}	75–124%	Sludge/biosolid (Spain), 2014–2015	2–295 ng g^{-1} (sludge) 5–152 ng g^{-1} (biosolid)	[25]
	Pharmaceuticals and estrogenic compounds	– QuEChERS ($MgSO_4$ and PSA)	1–2500 ng g^{-1}	15–131%	Sewage sludge (France), 2009	< LOD – 5957 ng g^{-1}	[119]
LC-QTOF-MS (ESI+)							
PPCPs	Non-steroidals	– MSPD – Clean-up with silica cartridges	LOQ: 0.005–0.05 ng g^{-1}	84–105%	Sewage sludge (Spain)	1.8–21.6 ng g^{-1}	[144]
LC-QqLIT-MS/MS (ESI+)							
Emerging BFRs	HBCDs, TBBPA, BPA, MonoBBPA, DiBBPA, TriBBPA	– UAE (DCM-MeOH, (1:9, v/v)) – SPE (C18 cartridges)	1.40–66 ng g^{-1} dw (HBCDs, TBBPA) 66–200 ng g^{-1} dw (BPA and TriBPA)	39–120%	Sewage sludge (Catalonia, Spain)	97.5 ng g^{-1} dw (HBCDs) 472 ng g^{-1} dw (TBBPA) 55.6–2595 ng g^{-1} (BPA) 886 ng g^{-1} dw (MonoBBPA) 807 ng g^{-1} dw (TriBBPA)	[58]
PPCPs	Illicit drugs and their metabolites	– PLE (ASE 200, MeOH-H_2O, (9:1, v/v), 50 °C, one cycle) – SPE (Evolute ABN)	0.1–6.4 ng g^{-1} dw	89–130%	Sewage sludge (Spain), 2010	0.5–479.0 ng g^{-1} dw > 100 ng g^{-1} dw (Cannabinoids, methadone and its metabolite)	[102]
TFC-LC-MS/MS (ESI+/-)							
EDCs	Synthetic estrogenic compounds and conjugates, antimicrobials, PBs, BPA, APs, BTRs, and OPFRs	– PLE (ASE 200, H_2O-MeOH-acetone, (1:2:1, v/v/v), 50 °C, 3 cycles) – SPE (Oasis HLB)	0.031–38 ng g^{-1} 321 ng g^{-1} (OP1EO) 125 ng g^{-1} (NP1EO)	40–115% (on-line method) 33–127% (off-line method)	Sewage Sludge (Ebro river, Spain)	2.6–29,416 ng g^{-1}	[59]

Abbreviations: ACN, acetonitrile; APs, alkylphenols; APCI, atmospheric pressure chemical ionization; APEOs, alkylphenol ethoxylates; BA, benzoic acid; BFRs, brominated flame retardants; BBPA, bromobisphenol A; BHT, 2,6-di-tert-butyl-4-methylphenol; BPs, bisphenols; BPA, bisphenol A; BSAs, benzenesulfonamides; BTHs, benzothiazoles; BTRs, benzotriazoles; BzPs, benzophenones; CP, cyclophosphamide; DAD, diode array detector; DCM, dichloromethane; d-SPE, dispersive solid-phase extraction; E2, 17β-estradiol; ECs, emerging contaminants; EDCs, endocrine disrupting chemicals; EE2, 17α-ethinylestradiol; EPA, Environmental Protection Agency; ESI, electrospray ionization; EtAc, ethyl acetate; Fl, fluorescence detector; FRs, flame retardants; HBCDs, hexabromocyclododecanes; HESI, heated electrospray ionization; HIS, high intensity sweeteners; HPLC, high-performance liquid chromatography; IBF, ibuprofen; IFO, ifosfamide; LC-TOF-MS, liquid chromatography–time-of-flight-mass spectrometry; LC-HRMS, liquid chromatography/high resolution mass spectrometry; LLE, liquid-liquid extraction; LOD, limit of detection; LOQ, limit of quantification; LSE, liquid-solid extraction; 4-MBC, 4-Methylbenzylidene camphor; MAE, microwave-assisted extraction; MDL, method detection limit; MeOH, methanol; MOPEs, monomeric organophosphate esters; MPB, methyl paraben; MQL, Method quantification limits; MSPD, matrix solid-phase dispersion; NP, 4-nonylphenol; NP1EO, nonylphenol monoethoxylate; NSAIDs, non-steroidal anti-inflammatory drugs; OP, 4-octylphenol;OP1EO, octylphenol monoethoxylate; OOPEs, oligomeric organophosphate esters; OPs, organophosphorous compounds; OPEs, organophosphate esters; OPFRs, organophosphorous flame retardants; PAEs, phthalic acid esters; PBs, parabens; PCPs, personal care products; PFC, perfluorinated compounds; PFCAs, perfluoroalkyl carboxylates; PFOA, perfluorooctanoate; PFOS, perfluorooctane sulfonate; PFSAs, perfluoroalkyl sulfonates; PLE, pressurized liquid extraction; PPCPs, pharmaceuticals and personal care products; QqLIT, hybrid triple quadrupole/linear ion trap; QTOF, Quadrupole Time-of-flight; RT, room temperature; SAs, sulfonamides; SLE, solid-liquid extraction; SPAs, synthetic phenolic antioxidants; SPE, solid-phase extraction; TBBPA, tetrabromobisphenol A; TCs, tetracyclines; TCC, triclocarban; TCEP, Tris(2-chloroethyl) phosphate; TCPP, Tris(chloroisopropyl) phosphate; TCS, triclosan; TFC, turbulent flow chromatography; UAE, ultrasound-assisted extraction; UHPLC, ultra high performance liquid cromatography; WWTPs, wastewater treatment plants.

Table 3
Methods for the determination of nanoparticles in solid waste/sewage sludge samples.

Analytical technique	Compound	Sample preparation	LODs	Solid waste/sewage sludge origin	Amounts detected	Ref.
APPI-MS	Organic nanoparticles	– Freeze-dried – UAE (toluene) – LSE (toluene; by orbital shaking, twice) – Centrifugation – Twice filtration	No data	Sludge sample (Netherlands)	32 ng kg^{-1}	[16]
ICP-MS	Ag	– Digestion tube Kjeldahl – Concentrated HCl and HNO_3 – Filtration (copper nitrate filter paper)	0.14 µg L^{-1}	Sewage sludge solids (England)	3–14 mg kg^{-1} dw	[73]
ICP-AES TEM	α-Ag_2S-NPs	– Freeze-dried and ground – UAE (H_2Od; soticated in a water bath) – 1 mL slurry was diluted with MeOH	No data	Sewage sludge (Midwest, U.S)	856 mg kg^{-1} (Ag) 12.0 g kg $^{-1}$ (S)	[77]
ICP-MS XANES	ZnO-NPs	– Benchtop anaerobic digesters – Freeze-dried – Microwave-assisted reverse aqua regia digestion (HCl-HNO_3, 1:3, v/v)	421 mg kg^{-1} (Zn on control treatment)	Sewage sludge (South Australia)	890–939 mg kg^{-1}	[95]
SP-ICP-MS	Ti-, Fe-, Zn-, Sn-, and Pb-Containing NPs)	– Freeze-dried and homogenized – LSE (modified BCR sequential extraction procedure, by end-over-end shaking): 1. Extracted with acetic acid; 2. Extracted with hydroxylamnonium chloride with HNO_3 to pH1.5; 3. Treated with hydrogen peroxide and extracted with ammonium acetate with HNO_3 to pH 2.0; – EPA-approved, microwave-assisted nitric acid digestion	No data	Sewage sludge (China)	ND – 12,965.05 g kg^{-1}	[143]
ICP-AES	Nano- and larger TiO_2 particles	– Freeze-dried and ground – UAE (H_2O) – Diluted with MeOH – EPA-approved, microwave-assisted nitric acid digestion using a MARS system (for class A Biosolid)	No data	Sewage sludge (Midwest and west of USA)	96.9–4510 mg kg^{-1} dw (sludge) 810 mg kg^{-1} dw (class A Biosolid)	[78]
ICP-XAS	Ag-NPs, AgCl-NPs	– Benchtop anaerobic digesters – Freeze-dried – Microwave digestion in HNO_3	No data	Sewage sludge (Australia)	< 7 mg kg^{-1} (control samples)	[114]
ICP-OES	Ag	– Microwave-assisted acid-digestion (65% HNO_3, 35% H_2O_2 and 48% HF) using an UltraClave 3, MLS GmbH system	No data	Sewage sludge (Switzerland)	393 mg kg^{-1} (sludge mean) 1431 mg kg^{-1} (ash samples)	[108]
ICP-OES	Heavy metals: Cu, Ni, Pb, Zn, Cr	– Liquid–solid ratio of 10 mL g^{-1} (double deionised water) – LSE (H_2Od, by end-over-end shaking (60 rpm) in the dark for 24 h – Centrifuged (30 min, 450 g) – Filtered	0.01–0.2 mg L^{-1}	Dried and fresh sewage sludge (north-eastern Spain)	0.15–73 mg kg^{-1} (dried sludge) 0.2–20 mg kg^{-1} (fresh sludge)	[109]
AAS	ZnO-NPs	– Microwave-assisted acid-digestion (HNO_3, HF and double-deionised H_2O, (1:1:1, v/v/v), twice) using a MARS system	No data	Sewage sludge (North of Spain)	83.88 mg kg^{-1} (sludge) 82.62 mg kg^{-1} (sludge)	[54]

Abbreviations: AAS, atomic absorption spectrometry APPI, atmospheric pressure photo ionization; EPA, Environmental Protection Agency; HF, hydrofluoric acid; IPC-AES, inductively coupled plasma atomic emission spectroscopy; IPC-MS, inductively coupled plasma mass spectrometer; IPC-OES, inductively coupled plasma optical emission spectrometry; LSE, liquid-solid extraction; MeOH, methanol; NPs, nanoparticles; o.n, overnight; SP-IPC-MS, single particle inductively coupled plasma mass spectrometry; TEM, transmission electron microscopy; UAE, ultrasound assisted extraction; XANES, X-ray absorption near-edge structure; XAS, X-ray absorption spectroscopy.

While classical techniques such as mechanical shaking or Soxhlet extraction are still employed as extraction techniques in some publications, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and pressurized-liquid extraction (PLE) are the preferred options for sample treatment in many cases. In addition, other extraction techniques which require lower amount of solvents have been increasingly used in the determination of emerging contaminants from sewage sludge samples. These include matrix solid phase dispersion (MSPD); Quick, Easy, Cheap, Effective, Rugged & Safe (QuEChERS); pressurized hot water extraction (PHWE) or micro-extraction by packed sorbent (MEPS). For instrumental techniques, the most common choices for detection and quantification of the compounds studied in sludge samples remain gas chromatography (GC) and liquid chromatography (LC) coupled to mass spectrometry, single or tandem (MS, MS/MS).

3.1. Sample preparation

3.1.1. Sample collection

Sampling sludge locations within WWTPs depend largely on the type of sewage sludge sample required for the following analysis. While most authors opt for sampling sludge after the final dewatering step (press or centrifuge) in order to obtain a representation of the total biosolid product removed from the WWTPs; [3,10,40,52,55,67,79,86,87,93,98,99,102,117,118,148,158,159] others prefer sampling after the anaerobic digestion step in which most of the organic matter is removed [10,27,33,59,95,99,136,158]. However, the underflow of the primary and secondary tanks (clarifiers) has also been chosen as sampling sites [10,17,29,79,95,98,99,158].

Long-term composite sampling achieves a greater representation of the total sewage sludge, accurately showing the fluctuations and average performance of the production batch over an extended period of time. This type of sampling is a tedious process and hence, it is not the most used option [3,16,93,98,159]. Grab on samples, however, require less manual operation and can be considered comparable to a 20–30 day composite sample, since the clarifier underflow and the digester detention times diminish the variability in sludge properties and produce a homogenous mixture [145]. Hence, grab on samples are the preferred alternative for sample collection of sewage sludge [16,23,46,52,79,102,119,130,139].

A sufficient amount of sludge - often ranging from 500 mL to 5 L – is retrieved from the chosen sampling location. Amber bottles and jars [3,4,13,17,29,33,41,44,45,52,77,79,98,99,102,117–119,158,159] or stainless steel buckets [27,79] are normally the common choice for sample collection, as it avoids interference of oligo phenylene ethynylene molecules (OPEs) and protects the compounds contained within the sample from photodegradation, humidity and other external factors. Other alternatives for sampling include using aluminum foil [26,59,93,159,167] and/or polyethylene bags or containers [16,23,44,93,130,136], which are adequate for analysis of metals. After sampling, the samples are usually transported to the laboratory under refrigeration and later stored at −20 °C until sample extraction and analysis.

Before sampling, glassware is usually cleaned with ultrapure water and an organic solvent such as acetone and hexane [52,116], or most commonly methanol (MeOH) [46,92,93]. Moreover, in order to reduce or inhibit microbial activity, certain chemicals are sometimes added to the sample. Formaldehyde 1% (v/v) [17–19,44,45]; formaldehyde 3% (v/v) with water [23]; NaN_3 [29]; sodium azide [170]; NaN_3 $g_{SS(dw)}{}^{-1}$ sodium azide [147]; or MeOH 1% (v/v) [68] has been traditionally used.

3.1.2. Sample pre-treatment

Before analysis, sewage sludge samples are subjected to a pre-treatment process. This necessary step facilitates the following extraction and removes matrix constituents that would interfere with the instrumental determination [149]. The first step prior to extraction is water removal, as it assures proper contact between the solvent and the matrix in the extraction process [114]. There are several strategies used to eliminate water from sludge samples, depending on the compounds that need to be analyzed. Centrifugation and decantation is employed by some authors as an alternative for separation of suspended solids from wastewater and before further water removal by air-drying or heating [17,20,44,98,130]. While air-drying is fairly uncommon [23], heating the samples in an oven is also used [44]. Analytes prone to degrade at certain temperatures would require lower temperature, which would imply a greater period of time to eliminate the water from the sludge [114]. Hence, most authors opt for lyophilizing the samples, as it is a simple, time-effective method in which analytes are not evaporated or degraded [3,13,20,29,52,55,59,86,87,93,99,119,148].

After obtaining the dried sludge, the samples are normally homogenized by grinding with a mortar and pestle. In order to ensure similar particle size, the final pre-treatment step consists of sieving. Depending on the following extraction method, a certain particle size is desired, ranging from 425 µm [117], 125 µm [59,148], 2 mm [13,32], < 100 mm [99], 250 µm [130], 1.41 mm [23,44], < 100 µm [98], 0.5 mm [164] to 0.2 mm [55], for example.

3.1.3. Sample treatment

The complexity of sewage sludge samples requires some kind of preparation prior to their analysis by most analytical techniques. An efficient extraction is important in order to get a good purification and isolation of the target analytes from the matrix. The extraction techniques used in the methods published in literature are summarized in Tables 1–3 and are briefly discussed below.

3.1.3.1. Mechanical shaking. Classical techniques such as stirring and mechanical shaking (either by hand-agitation, vortex or orbital shaker) have been reported for the extraction of EDCs from sludge samples in a few publications. PBDE congeners [116], APs [109], benzotriazoles UV-filters [169], BPs [30,74], PBs and their metabolites [28,75,89,154], antibiotics [81], emerging compounds such as benzothiazoles and benzophenones [74], among others PCPs [28] are examples of analytes extracted by mechanical shaking. The most used extraction solvent is MeOH, pure [81,116,133] or mixed with water (5:3, v/v) [56,74,75,89,154]. On the other hand, cyclohexane, acetone-hexane (1:1, v/v) and acetonitrile (ACN) with 1% of acetic acid have also been applied for the determination of APs [109], benzotriazoles UV-filters [169] and some PCPs (triclocarban (TCC), non-steroidal anti-inflammatory drugs (NSAIDs), PBs and BPA) [28], respectively. Two or three consecutive extractions are generally performed. It should be noted that in most methods using agitation, extraction is commonly followed by a SPE clean-up step. For example, SPE cartridges such as Oasis MCX [74,75,89,154], C18 [81] or silica [169] have all been used after mechanical shaking extraction. Mechanical shaking was also reported to be used in some works for nanoparticle determination. For example, orbital shaking with toluene was implemented during extraction of organic particles [16] and end-over-end shaking with H_2O (for 24 h in the dark) during the analysis of some heavy metals [109]. For Ti-, Fe-, Zn-, Sn, and Pb- containing NPs, a modified BCR sequential extraction procedure also applying end-over-end shaking was performed [143].

3.1.3.2. Soxhlet extraction. Although Soxhlet is highly efficient for extraction of these type of compounds from solid matrices, it employs long extraction times and the use of large volumes of solvents [171]. Despite these disadvantages, some EDCs (mostly flame retardants) have been extracted from sewage sludge. For example, it has been applied for the determination of organophosphorus compounds with dichloromethane-ethyl acetate (DCM-EtAc, (1:1, v/v)) and LC analysis [158]. PBDEs congeners [32,79,159], other HFRs such as BTBPE and DBDPE [159], and some EDCs including PBs, phenylphenols, triclosan

(TCS), APs and BPA [14] have all been favorably extracted with Soxhlet as well, and later analyzed with GC. DCM, [32,79] acetone-hexane (1:1, v/v) [159] and MeOH [14] were employed as solvents in these cases. Solvent volumes reported were 100 mL and 200 mL respectively [14,32,159], and extraction times ranged from 16 to 48 h. Before Soxhlet extraction, it is usual to homogenize and dry the solid sample with anhydrous sodium sulfate (Na_2SO_4) [14,79,158,159]. A clean-up treatment such as alumina and silica gel SPE is habitually required as a result of the extraction. Nevertheless, in the last years Soxhlet extraction has been gradually replaced by other equally effective techniques, such as UAE and PLE, which require less time and quantity of extracting solvents.

3.1.3.3. Solid-phase extraction. SPE sample preparation allows multiresidue analysis for compounds with a wide range of physicochemical properties and polarities, while allowing their good storage. Although SPE is considered an extraction technique, in this type of complex matrices it is commonly used as a subsequent treatment for clean-up purposes. Consistently, SPE combined with a previous extraction step, has become the most widely used choice to clean-up a variety of EDCs, PBDEs and PPCPs. The three classes of sorbents available (reverse phase, normal phase or mixed-mode sorbents) have been applied in column or cartridges for clean-up of sewage sludge extracts. Oasis® HLB (divinylbenzene/N-vinylpyrrolidone copolymer) has been the common choice for the purification of PPCPs and EDCs using SPE in the off-line and on-line modes [90,150] from sludge matrices. This sorbent is the most versatile and displays the best overall recoveries for the extraction of analytes of a wide range of polarities [162]. According to these authors, Oasis HLB showed the best recoveries (85.4–105.8%) for the extraction of seven bisphenols in a single extraction step. In contrast, GCB cartridge resulted in relatively poor recoveries (< 60%) of BPS, TCBPA and TBBPA (analytes with stronger acidity) and C18 had the lowest recoveries rates (< 20%) of BPS and BPF (analytes relatively polars). This could be attributed to the strong bonding to the sorbent (GCB) and the weak absorbance and losses occurred during the clean-up step (C18). Li et al. [85] also evidenced good recoveries for parabens in the sludge samples extracted by HLB SPE (from 86.8% to 99.2%) with relative standard deviations (RSD = 5) from 1.1% to 8.6%. On-line SPE mode with HLB sorbent was also used for the determination of antibiotics [90] and hormonal steroids, NP, OP, BPA, coupled to LC-MS/MS analysis with moderate to good sensitivity [29,53, 85,118,140,150,162,170]. SPE (HLB) has been commonly used as a clean-up step of PLE and UAE extracts for a wide variety of EDCs because of its versatility [10,17,18,53,117,162]. A disadvantage of using Oasis HLB SPE cartridge is that it is non-selective and co-extraction of non-target compounds can cause significant signal suppression. Despite this, a further clean-up procedure (e.g. by using MAX cartridges) can decrease matrix suppression, getting an effective and selective purification of all target analytes [120,162].

Octadecyl silica sorbents (C18), Florisil, silica and alumina have also been used to analyze EDCs. C18 has been employed for cleaning of endogenous steroid hormones, alkylphenol ethoxylates, bisphenol A and phthalates [159], BPs analogues [133], pharmaceuticals [136], antibiotics [81] and emerging BFRs [58]. LC-MS/MS was used as the analytical technique in all cases, except for the determination of antibiotics and BFRs, where LC with ultraviolet detection (LC-UV) and LC-QqLIT-MS/MS were used. Florisil was applied in the extraction of PBDEs [52,79] and UV-filters [79] for GC analysis, and in the clean-up of flame retardants, hexabromocyclododecanes (HBCDs) [52] and organophosphorus flame retardants (OPFRs) [88] by LC analysis. Silica gel sorbent has been used to analyze halogenated flame retardants by HR-GC; and an automated purification Power Prep System including silica gel, basic alumina and carbon columns for BFRs with HRGC-TQMS-MS analysis was used [41].

Mixed-mode SPE sorbents are becoming increasingly popular in pharmaceutical applications due to their unique selectivity and retention of a wide variety of compounds [168]. These types of sorbents are chemically designed to have multiple retentive sites on an individual particle by allowing the interaction with different functional groups [156]. Solutes interact with the stationary phase through more than one interaction mode, employing the combination of hydrophobic, hydrophilic and/or ionic interactions [69]. Mixed-mode sorbents can be used as an alternative or complementary clean-up procedure to traditional reversed phase, ion exchange and normal phase SPE [168]. An example is Oasis® MCX (Mixed-mode, strong Cation-eXchange) that has been mostly used for cleaning PBs and their metabolites [30,75,88,89,154] although it has also been applied in the case of other EDCs (such as BPs, benzophenones, UV-filters, among others) [74,120,165]. Considerable sensitivity for PBs was achieved after extraction and clean-up with MCX, with LODs ranging from 0.01 to 10.0 ng g^{-1} [154], 0.01–5 ng L^{-1} [75] and 0.2–0.5 ng L^{-1} [30]. Another example of mixed-mode sorbent is Oasis® WAX (mixed-mode, Weak Anion-eXchange) preferably used for extraction of perfluorooctanoate, perfluorooctane sulfonate and perfluoroalkyl compounds [100,132]. Although less common, a wide variety of sorbents have been used for the clean-up of emerging contaminants in sewage sludge samples. These include Phenomenex® Strata X (polymer-based) [127], Evolute® ABN (polystyrene-divinylbenzene incorporating non-ionisable hydroxyl groups) [5,102], Carbograph-4 [26], Lichrolut® EN sorbent (ethylvinylbenzene-divinylbenzene polymer) [14], among other summarized in Tables 1–3.

3.1.3.4. Ultrasound assisted extraction. The greater impact of ultrasound energy in liquid media is attributed to acoustic cavitation, effect that generates numerous bubbles, leading to mechanical erosion of solids and particle rupture. UAE has been increasingly used as an alternative to Soxhlet extraction. Although similar solvents are used in both techniques, the volume of the extraction solvent as well as the extraction time are considered to be reduced using UAE. Ultrasonic bath is the most available and cheapest source of ultrasound irradiation. Despite that, a more efficient system is now used: a cylindrical powerful probe for the sonication of samples [141].

This technique has been applied in the study of a wide range of EDCs. Among the compounds extracted with this technique are natural and synthetic estrogenic compounds [5,18,26,142,147,159], antimicrobials such as TCS [23,26,138,147] and TCC [23], antibiotics such as quinolones [45] and tetracyclines [166], PPCPs [20,51,55,98,99,136,138,164], BPA and/or BPs analogues [26, 58,100,140,147,162], PBs [19,23,30], phthalate esters [159] and UV-filters [23,138], some flame retardants (PBDEs, HBCDDs, OPFRs and BRFs) [101,134,157,158,163] and OPEs [39] and other compounds such as alkylphenols and alkylphenols ethoxylates [33,159], per- and polyfluorinated compounds [26,132], PAHs, PCBs [142] and chlorophenols [162]. UAE has also been successfully applied for extraction of organic [16], α-Ag2S [77] as well as Nano- and larger TiO_2 particles [78]. Regarding the solvents employed during UAE, mixes with H_2O and MeOH (1:1, v/v) are the most used for pharmaceuticals extraction followed by LC analysis, as reported by several authors [20,51, 55,100,136,138]. Although less common, mixes of MeOH with ACN, DCM, acetone and hexane solvents, or combinations of both, have also been utilized. For example, ACN and MeOH-ACN (1:1, v/v) (after a previous extraction with 1% acetic acid in MeOH) were used for extraction of OPFRs [88] and perfluoroalkylcarboxilates, perfluoroalkylsulfonates [132] and OPEs [118], respectively. Acetone combined with MeOH and H_2O or DCM was also applied in the determination of several EDCs [26,159]. Hexane-acetone (4:1, v/v) mixture was used for the extraction of alkylphenol ethoxylates and BRFs [33]; and MeOH followed by a second extraction with DCM-hexane (1:1, v/v) was used for steroid hormones and phthalates determination [159] from sludge samples, along with PBDE congeners and HBCDs from biosolids [52]. In GC analysis, in addition to the organic solvents used in LC, EtAc and cyclohexane were also reported as solvents for estrogenic compounds

[18], flame retardants [35], PAHs and PCBs [142] extractions. In the case of organic α-Ag2S and TiO_2 particles, toluene [16] and distilled H_2O [77,78] were employed before analysis by APPI-MS, ICP-AES-TEM and ICP-ES, respectively. In general, the required volume of extractant and the extraction time are reduced in comparison with those of the Soxhlet extraction. An advantage of UAE is that the amount of extraction solvent required as well as the extraction time are considerably reduced compared to Sohxlet extraction. The volume is around ten times less (e.g.100 mL required in Sohxlet and 10 mL in UAE) and the time is shortened from hours to half an hour on average, according to the literature [14].

3.1.3.5. Pressurized liquid extraction. PLE uses conventional liquid solvents at elevated pressures to achieve temperatures higher than their normal boiling point. Thereby, solubility and mass transfer rate of the analytes are increased, obtaining shorter extraction times with a lower amount of solvent [171]. In the past few decades, PLE became a popular strategy to sample preparation as it is an extraction technique capable of extracting EDCs in solid matrices. Compared to traditional extraction methods, such as Soxhlet, it uses less solvent and takes less time per sample [137]. Volume of extraction solvent (in the range of 4–100 mL) is comparable with that required in UAE, but the extraction time is shorter, generally below 30 min [137]. In addition, PLE exhibits a high level of automation and the ability to perform multiple extractions simultaneously [44]. A wide variety of target EDCs have been determined from sludge samples by using PLE as the extraction technique. Among these, BPs congeners and BPA [29,44,59], APs [59], hormonal steroids [29,59,66], flame retardants such as BFRs [40,41,59,167] and chlorinated flame retardants [167], PBs [19,58,85] and some pharmaceuticals [8], antibiotics [45,53,117] and antimicrobials [40,59] are included. PLE has also been performed using different types of solvents or mixtures. Flame retardants have been determined by GC using DCM, hexane and acetone as solvents. For example, for the extraction of PBDE congeners, HBB, PBEB and BBDPE, hexane-DCM (1:1, v/v) mixture was used at 100 °C and 1500 psi in two cycles [58]; for BDE congeners hexane-DCM (1:1, v/v) was used as well, at 40 °C in one static extraction [97]. Many of the extracting mixtures combine water or MeOH with other solvents for further LC analysis, such as MeOH-acetone (1:1, v/v), followed by an H_2O-MeOH cycle for the extraction of estrogenic compounds and BPA [29], H_2O-isopropyl alcohol (1:4, v/v) for the antimicrobials TCS and TCC [10]; and ACN-H_2O (1:3, v/v) for SAs antibiotics [53]. In some methods, MeOH was applied as the only extraction solvent for the analysis of PBs and metabolites [19,85] and pharmaceuticals [8], or mixed with water in different proportions for illicit drugs [102] and anticancer drugs [130]. Other solvents were also employed, such as EtAc at 100 °C and 1000 psi for BPA and their chlorine derivatives [44], and DCM-hexane (3:1, v/v) at 90 °C and 1500 psi for SPAs [92,93]. In PLE, other parameters to take into consideration are temperature, pressure, extraction time and number of cycles. Regarding temperature, it normally ranges from 40 °C to 120 °C. High temperature (120 °C) was used for PBs [19] and TCC and TCS [10] extractions with MeOH and H_2O-isopropyl alcohol, respectively. Extraction pressure in almost all cases was fixed in 1500 psi (10.34 MPa), even though 1000 psi [44], 1250 psi [102] and 2001 psi [10] have also been reported. In the case of static extraction time, it is usually set within 2–16 min. The most used extraction time is of 10 min [10,41,58,66,85,92,93]. The number of cycles studied was found to be in the range of 1–4 cycles, although the most frequently used was 3 cycles [40,41,44,53,59,92,93,167]. Only one method reported using 4 extraction cycles for the analysis of anticancer drugs [130]. After PLE extraction, it is usual to apply a SPE clean-up step using different types of cartridges [117], since it improves pre-concentration of the sample and reduces the matrix effect [44]. As with other solvent-based extraction techniques, non-target analytes that can interfere with detection and quantification are often co-extracted from the sample matrix. This is the reason why a post-extraction clean-up (e.g. SPE, GPC or packed chromatographic columns) is generally needed before the analysis of the resulting extract from PLE [137]. In general terms, PLE provided acceptable recoveries for the extraction of EDCs in sewage sludge samples similar to those obtained with techniques such as UAE and MAE, with some occasional exceptions. For example, Benítez-Villalba et al. [19] compared both extraction techniques (UAE and PLE) for PBs extraction and, although PLE provided the highest recoveries (especially for methyl-, ethyl-, and propylparaben), both methods exhibited good analytical parameters and no statistically significant differences regarding accuracy and sensibility. Pang et al. [118] had shown that PLE is a more suitable extraction method for OPEs. While recoveries ranged from 24% to 58% by using UAE, results gave recoveries in the range of 56–119% with PLE – almost 2–4 times higher than those obtained with UAE.

3.1.3.6. Microwave assisted extraction. MAE offers several advantages over other techniques such as small quantities of samples, lower solvent consumption, shorter extraction times and the ability to extract a large number of samples simultaneously [62,82]. The extraction solvents required for MAE have to absorb microwaves (solvents with permanent dipole leading), hence, they are limited. In spite of that, the mix of solvents with and without dipoles opens up a wide variety of solvent mixtures [171]. The use of MAE to extract different families of EDCs from solid sludge matrices has been developed. Methods in literature have reported the successful extraction of hormonal steroids [62,150], quinolone antibiotics [45], TCS [19], chlorobromo derivatives [83], PBDEs [116], some pharmaceuticals [13,120] and other EDCs such as BPA [13,14,120,150], UV-filters [120], PBs [14,120], NP, OP and their corresponding ethoxylates [14,68]. An *in situ* acetylation was carried out with the presence of acetic anhydride during the MAE process for the extraction of TCS and its derivatives [83]. The extracts are usually diluted with water to $<$ 5% organic solvent content. Then, resultant solutions are treated as a liquid sample and are subject to a clean-up step before analysis. MAE in combination with SPE for clean-up is the most widely used choice to prepare solid samples according to the bibliography described above. Concerning microwave power, it covers a wide range from 200 W to 1200 W. For example, 1000 W was used during determination of quinolone antibiotics [45], 500 W for the analysis of EDCs [13,62] and 1200 W, the strongest irradiation, was reported during the determination of PBDEs congeners [116]. On the other hand, sample digestion is necessary before determining metal concentrations in complex matrices. Thus, an acid digestion using MAE is commonly used in methods for determination of nanoparticles in sewage sludge samples. Acid digestion is performed in most cases with HNO_3, pure or mixed with H_2O_2, H_2O or HF, as described in published literature [54,78,96,108,143]. Some examples are applied in the case of Ag/AgCl-NPs [96] and ZnO-NPs. Analysis were carried out with microwave digestion for Ag-NPs and using HNO_3, HF and double-deionised H_2O, in proportion 1:1:1 (v/v/v), employing a MARS system, for ZnO-NPs [54]. In contrast, Lombi et al. [95] used a microwave reverse aqua regia digestion procedure (HCl-HNO_3, (1:3, v/v)) for ZnO-NPs determination. Aqua regia digestion is an adequate method for analyzing total-recoverable metals in complex matrices; therefore it was successfully applied in sewage sludge [95]. Azzouz and Ballesteros [14] compared MAE, UAE and Sohxlet extraction techniques under optimal variables for the simultaneous determination of 13 EDCs in environmental solid samples. The best results were obtained with MAE, with recoveries of 93–99%. In contrast, UAE was somewhat less efficient (recoveries of 81–95%) followed by Soxhlet extraction (recoveries of 70–89%). MAE was the best choice on the basis of the amount of organic solvent and extraction time used (10 min and 3 min, respectively).

3.1.3.7. Pressurized hot water extraction. PHWE is an organic solvent free technique in which water is used as the extraction solvent at high temperature and pressure. The basis of this extraction technique is the same as PLE [94]. In PHWE, variables such as temperature of extraction, pressure, number of cycles and the flush volume likewise that in PLE are also studied. pH of the water is also a factor that affects extraction efficiency when analytes exhibit acid-based properties [171]. PHWE was applied for the extraction of N-nitrosamines in sewage sludge samples at pH 7.5, 125 ºC and 1500 psi. Preheating and static extraction periods were 6 and 5 min, respectively, with a flush volume of 60%. Two extraction cycles were performed. A previous headspace solid-phase microextraction (HS-SPME) was carried out before analysis of N-nitrosamines by GC-MS, obtaining considerably sensitivity with LODs ranging from 0.03 to 0.15 ng g^{-1} [94].

3.1.3.8. Matrix solid-phase dispersion. Although it is not a commonly used extraction technique, MSPD is a technique very suitable for the treatment of complex matrices [4,15]. MSPD with complex matrices, as sewage sludge, not only ensures an efficient extraction of the target analytes similar to UAE and PLE but also prevents the increase of potential interferences. It allows the simultaneous extraction and clean-up of compounds with a notable reduction in solvent consumption, does not require expensive instrumentation and is simple to use [3]. MSPD has been used for the determination of EDCs and PPCPs [19,62,89,150,154] in sewage sludge. MSPD has also been successfully applied to the extraction of synthetic and natural estrogenic compounds [4], PBs [49,61], TCS, TCC, BPA and some pharmaceuticals [86,87,139] including NSAIDs [46], UV-filters [139] and chlorinated azoles [25]. Among the most important variables during MSPD extraction process are the extractive solvent (used as dispersant) and the elution solvent. These conditions are normally the main focus. For example, for the extraction of PBs and chlorinated by-products in sewage sludge, several extraction solvents such as DCM, MeOH, EtAc, and a mixture EtAc-MeOH (9:1, v/v) has been tested. EtAc mixed with MeOH provided the best recoveries ($> 80\%$), so this mixture was selected as the extraction solvent. Among all clean-up sorbents assayed (Florisil, alumina and PSA), Florisil provided, in general, the best results for all PBs studied and, therefore, it was selected as clean-up sorbent [3]. This method obtained recovery results for parabens between 85% and 125%, in general similar to those described using liquid solid extraction, UAE or PLE for soil and sediment samples [19,85,89]. For the extraction of estrogenic compounds for soil amended with sludge different extraction solvents, ethyl acetate, ACN and MeOH were tested. ACN-MeOH (9:1, v/v) with C18 as the clean-up solvent showed the best recoveries and therefore, this mixture was chosen for the extraction procedure [4].

3.1.3.9. Microextraction by packed sorbent. MEPS is a new miniaturized form of the SPE that can be connected on-line to GC or LC [110]. Ever since this technique was introduced in 2004, it has been widely accepted as an alternative to other sorptive microextraction techniques [1]. It is fully automated and faster, simpler and consumes less volume of solvents than the classical sample preparation techniques (SPE, liquid extraction, etc.). The packing is inserted directly into the syringe and not into a separate column. MEPS can also be used several times, up to more than 400 times for water samples. It is other advantage over the conventional SPE column that is only used once [97]. It can handle small volumes of sample (10 µL) as well as large volumes (1000 µL). In spite of being more commonly applied for the analysis of compounds in biological fluids, such as plasma, blood and urine, MEPS can be also used for sludge samples. For example, Martínez-Moral and Tena [97] applied MEPS for the clean-up of PLE extracts for BDE congeners determination by GC-MS/MS. The optimized combined method provided LODs in the range of 0.01 and 0.04 ng g^{-1} and good relative recoveries (92–102%) compared with other methods used for determination of PBDEs (BDEs congeners) by GC-MS/MS – using classical techniques such as Sohxlet, UAE and PLE followed with conventional SPE.

3.1.3.10. Solid-phase microextraction and headspace solid-phase microextraction (SPME and HS-SPME). SPME is a fast, simple, efficient adsorption and desorption extraction procedure, which eliminates the need for solvent for concentrating volatile or nonvolatile analytes in liquid matrices. In this technique a very small amount of the extracting phase is placed on a thin rod made of fused-silica. The small geometry of the device allows rapid mass transfer during extraction and desorption, prevents plugging and overcomes SPE limitations [6]. SPME has been successfully applied to determine a wide range of compounds from EDCs such as chlorophenols, estrogenic compounds, androsterone, DHT, 19- norethindrone, TCS and BPA [147], N-nitrosamines [94] to PCPs such as macrocyclic musk fragrances [148] in sewage sludge samples coupled to GC. Samples were diluted with ultrapure water and efficiently extracted by polydimethylsiloxane-divinylbenzene [148], divinylbenzene-carboxen-polydimethysiloxane [94] or fiber of polycrylate [147].

3.1.3.11. Quick, easy, cheap, effective, rugged, and safe. QuEChERS is an alternative to traditional liquid-liquid and solid phase extraction [7]. Although less frequently reported, few applications using QuEChERS have also been applied for sewage sludge samples. It has been successfully used for the determination of pharmaceuticals [27,119] including NSAIDs [28,127], benzenesulfonamines, benzothiazoles and benzotriazoles [67], natural and synthetic hormonal steroids (estrogenic and androgenic compounds) [5,119], and other classes of PCPs such as PBs, TCC, BPA and benzophenones [27,28]. In addition, QuEChERS extraction can be combined with on-line SPE, getting a remarkable decrease in total analysis time together with a significant increase of pre-concentration. Automatically coupling with LC-MS/MS was investigated in one work for the determination of selected pharmaceutical compounds in sewage sludge [127]. As we can observe in tables, ChEchERS is, in general terms, the least efficient method since it gives recoveries that vary from 15 to $>$ 100%, as in the extraction of estrogenic compounds and pharmaceuticals [119].

3.2. Instrumental measurement

The most common techniques employed for the detection and quantification of emerging contaminants in sewage sludge samples are summarized in Tables 1–3. GC or LC coupled to MS or MS/MS have been usually applied. Volatile or volatizable organic compounds are often separated by GC, while LC is generally applied for polar and less volatile compounds. Moreover, analytical determinations involving trace quantities of pharmaceuticals would usually employ LC-MS/MS. In this case, the matrix effect can become an inconvenient in the analysis of EDCs and PPCPs involving electrospray ionization (ESI) as the source. However, GC, in combination with electron impact ionization (EI) mass spectrometry (GC-MS), can be applicable for analysis of these compounds with no apparent matrix effect. Furthermore, it is less costly and requires less operation than LC-MS/MS.

GC habitually demands the inclusion of a derivatization reaction with the purpose of improving the chromatographic behavior of the analytes while increasing the sensitivity, selectivity and peak separation as a result [93]. Thus, most EDCs require derivatization due to their polar nature. This step reduces adsorption of the analyte onto the chromatographic column and prevents thermal decomposition at the injector port [14]. This additional step presents several disadvantages in the treatment of the sample, such as an increase on the complexity of the treatment and the total analysis time and more chances of error. In this sense, GC has been used to analyze PAHs and PCBs [142], phenolic substances [14,68,93,109,147], UV-filters [169], macrocyclic musk fragances [148], N-nitrosamines [94], PBDEs congeners [32,35,40,41,52,58,97,116] and other halogenated flame retardants [40,159,167] in sewage sludge samples. BPA, PBs, TCS and pharmaceuticals have also been quantified by this instrumental technique. While some of these compounds have been determined using GC without a previous derivatization step, most are frequently derived before their analysis due to their low volatility and presence of polar functional groups with active hydrogens. This is the case of hydroxyl, phenolic EDCs, amines and amides. Different strategies for derivatization usually involve the use of acylation (usually acetylation), alkylation or silylating reagents [3,4,164]. The majority of the methods reported for flame retardants involving PBDE congeners do not require a derivatization reaction. In contrast, synthetic and natural hormones, phenolic substances and pharmaceuticals have been commonly analyzed using GC after silylation with N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) or N-methyl-N-(trimethylsilyl)-trifluoroacetamide (MSTFA) to form methoximated trimethylsilyl derivatives (TMS). The derivatization of estrogenic hormones and some anti-inflammatory compounds was usually carried out using BSTFA with pyridine (1:1) [4,17,18], BSTFA with 1% of trimethylchlorosilane (TMCS) [13] or BSTFA mixed with both [68]; while progesterone and androgens, such as testosterone, were derived using MSTFA-TMIS-DTE (1000:2:5, v/v/v) [5,68]. Likewise, phenyl- and alkylphenols involving NP1EO, NP2EO, 4tOP and NP, BPA and PBs have all been analyzed using GC-MS in sewage sludge directly [109,147] or after derivatization with BSTFA [14,68]. Other derivatization agents (MTBSTFA and HFBA + triethylamine) were also applied to these compounds [33,58]. TCS has also been determined using GC-MS after derivatization with BSTFA 1%TMCS [13,14], MTBSTFA [58] or with MAE in situ acetylation technique using acetic anhydride [83].

As the analysis of emerging contaminants requires high selectivity and low LODs, the most usual technique reported for sludge samples is gas chromatography coupled to MS and MS/MS as they fit the requirements for the determination of these compounds (Table 1). MS detector can provide great selectivity and sensitivity, depending on the type of ionization mode selected. EI ionization mode was one of the first ionization techniques developed for mass spectrometry and the most used option for the detection of EDCs in sludge samples using a coupling to GC (see Table 1). Negative chemical ionization (NCI) mode [32,58,83,52,107] has been used for PBDEs as well, as it often offers greater sensitivity than EI. GC, in combination with electron capture negative ion mass spectrometry (ECNI), is a versatile tool for the determination of trace amounts of brominated compounds in environmental samples [126]. This method has utility because it only sees organohalogens and renders co-extracted compounds invisible to the analytical tool. Thus, it was a sensitive method for determination of polybrominated compounds such as PBDE congeners, brominated alkylbenzenes and polybrominated biphenyls [40,159] via detection of the bromide ion isotopes m/z 79 and 81. On the other hand, collision-induced dissociation (CID) with GC-MS/MS was reported to be used for the analysis of nitrosamines [94].

Inductively coupled plasma mass spectrometry (ICP-MS) has been usually involved with the detection of NPs in sewage sludge matrices. The main advantages of this technique lie in the high precision, low detection limits, low economic cost and multi-element and simultaneous analysis of most elements and isotopes present in the periodic table in few minutes. In such a way, Ag, Ti, Fe, Sn, and Pb containing NPs were examples of elements determined by using this tool [73,95,143]. Combination of ICP with other types of detectors was also typically employed for nanoparticles analysis (Table 3) [77,78,96,108].

LC coupled to MS or MS/MS is usually the best choice to analyze a wide number of EDCs present in sewage sludge samples (Table 2), although LC with other detectors have also been reported for the detection of EDCs in sludge matrices. LC-MS allows a successful detection with high sensibility and selectivity of extremely polar, thermally unstable and large molecular weight compounds, as is the case of acidic compounds, steroids and antibiotics, respectively. Other detectors for LC, such as UV or DAD together with FLD were also chosen to analyze antibiotics [81] and several PPCPs, including anti-inflammatory drugs, estrogens, antibiotics, lipid regulators, β-blockers, antiepileptic and stimulant drugs, respectively [98,99]. In many cases, UHPLC has been selected instead of HPLC, since these LC techniques show better resolution and a shorter analysis time [10,19,23,26,27,30,51,62,65,66,88,100,118,120,150,162,166]. Regarding ionization mode, ESI, in both positive and negative mode, was chosen as the most sensitive interface for ionizing the target compounds before MS/MS. Only in one reported work, ionization was carried out by atmospheric pressure chemical ionization (APCI) during the detection of BPA and its chlorinated derivatives [44]. APCI supplies more ionization options for low polar compounds and in some measure, suppresses the matrix effect; while ESI can lead to background interferences. On the other hand, electrospray interface heated electrospray ionization source (HESI-II) was used in LC-(Orbitrap)-MS analysis for the detection of steroid hormones [67]. HESI-II offers better desolvation and needle performance to improve sensitivity.

The triple quadrupole (QqQ) is widely considered as the most sensitive and selective tool for EDCs determination in sewage sludge samples. Nevertheless, recent advances in LC-MS have shown that time of flight (TOF) [119,144] or orbitrap [67] analyzers are a very suitable alternative to QqQ. These instruments allow screening of targeted and untargeted analytes due to their mass accuracy (< 5 ppm) and high-resolution power. Hybrid triple quadrupole/linear ion trap (QqLIT) was also applied in two works for the analysis of emerging BFRs [58] and PPCPs [67]. In most cases, the best option for EDCs analysis is the MS system operating in ESI and multiple reactions monitoring (MRM) mode. MRM allows monitoring two transitions between precursor and product ions. For each compound, the optimum collision energies were usually selected to get two, three or several characteristic MRM transitions with the best signal intensity. The one with the best signal intensity is chosen for quantification, and the other best transitions are used to confirm the compound [27]. Therefore, the identification of the compounds from sludge samples at very low concentrations is possible.

4. Conclusions

The present work provides a review of the main extraction techniques and instrumental techniques used for the determination of emerging contaminants in sewage sludge samples originating from different WWTP locations as well as their surroundings. Conventional treatment techniques (mechanical shaking, stirring, Soxhlet), although still applied for extraction, present several disadvantages such as manual manipulation, long analytical times and large volumes of solvents. PLE, UAE or MAE have been adopted extensively in the last 5 years for the extraction of several classes of emerging contaminants from solid and semi-solid sewage sludge samples. SPE has also been widely used as an extraction technique, as well as a clean-up step for extracts after undergoing other extraction procedures. The ability to extract a great variety of compounds with diverse physicochemical properties makes SPE the most preferred option to analyze EDCs and PPCPs, as it allows multi-residue analysis of compounds off-line or on the on-line mode. In the recent years, novel microextraction techniques such as MEPS, SPME, HS-SPME or QuEChERS have also become an option for the analysis of emerging contaminants from sludge samples, though the number of publications employing these techniques is not as extensive. As can be seen, recovery results varied greatly due to the diversity of chemical classes among the selected EDCs and to the differences among the extraction methods used. In general terms, the range of recoveries provided by the majority of the techniques studied was relatively good ($> 60\%$) but with some exceptional cases. Recoveries over 100% could be explained by contributions of intrinsic heterogeneity and complexity of solid matrices, or by method errors. QuEChERS showed to be the least efficient method for the extraction of EDCs.

The main instrumental techniques selected for analysis of sewage sludge samples are liquid and gas chromatography coupled to mass spectrometry. Although different classes of detectors (LC-DAD-FLD, LC-UV, TFC-LC-MS/MS, etc) have been used to determine EDCs, PPCPs and PBDEs, the most used remains tandem mass spectrometry coupled to LC due to its high sensitivity. PLE followed by LC-MS/MS measurement is the most common choice for many authors for the detection of EDCs and PPCPs, given their polar nature. Alternative methods such as QuEChERS, MSPD or MEPS have also been employed, most commonly before LC-HRMS analysis. Though, the amount of published papers focused on alternative and novel microextraction methods is scarce. For PBDEs determination in sludge samples, GC-MS is the most used instrumental technique. GC-MS has also been employed for determination of EDCs and PPCPs, usually requiring a previous derivatization step. The number of publications regarding to analysis of nanoparticles from sludge samples is significantly lower in comparison to the rest of the studied compounds. The most used technique, however, is ICP coupled to a variety of detectors, including MS, AES, XAS or OES.

To conclude, a remarkable increase in the number of publications employing novel extraction and chromatographic techniques for the determination of emerging contaminants in sewage sludge samples has been noted in the last years. This suggests that these methods are quickly replacing conventional treatment processes developed over the last years.

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Conflict of interest

The authors declare no conflicts of interest.

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