Insights Into the Prevalence and Impacts of Phthalate Esters in Aquatic Ecosystems

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Phthalate esters (PEs) are by far the most produced and extensively used synthetic organic chemicals with notable applications in many industrial products such as vinyl upholstery, adhesives, food containers, packaging materials, printing inks, adhesives, cosmetics, paints, pharmaceuticals munitions, and insecticides among other. PEs have long been recognised as ubiquitous organic pollutants of prime environmental concern, with urbanisation amongst the main cause and source of these compounds. Due to their notoriety, these compounds are known to pose devastating effects to living organisms including humans. The presence of PEs and their metabolites in the aquatic ecosystems is of concern primarily due to their endocrine disrupting and carcinogenicity properties. Several research studies have reported prevalence, exposure pathways, toxicity, and impacts of PEs in aquatic ecosystems and humans. Their principal routes of exposure could be direct or indirect, of which the direct route include contact, eating, and drinking contaminated foods, and the indirect route constitute aerosols, leaching and other forms of environmental contamination. PEs find way into water systems through means such as effluent discharges, urban and agricultural land runoff, leaching from waste dumps and other diffuse sources. High-end instrumentation and improved methodologies on the other hand have resulted in increased ability to measure trace levels (μg/L) of PEs and their metabolites in different matrices and ecological compartments of water or aquatic ecosystems such as lakes, oceans, rivers, sediments, wetlands and drinking water samples. In light of the above, this article provides an informed and focused information on the prevalence of phthalate esters in aquatic systems and related effects on living organisms and humans. Furthermore, techniques that have enabled the extraction and analysis of these PEs in aquatic samples are also explained. Future research outlooks and needs are also highlighted in this manuscript. This information will be used to better understand their temporal and spatial distributions in the aquatic systems and aid in devising prudent means to curtail their ecological footprints.

Keywords: aquatic ecosystem, aquatic organisms, carcinogenic, endocrine disruptor, health risks, phthalate esters, phthalate esters toxicity

INTRODUCTION

Phthalate esters (PEs) belong to a group of industrial organic compounds with a common chemical structure, dialkyl or alkyl/aryl esters of 1,2-benzenedicarboxylic acid (Annamalai and Vasudevan, 2020; Giuliani et al., 2020). They are esters of phthalic acid produced by reacting phthalic anhydride with an appropriate alcohol (Howdeshell et al., 2008; Vats et al., 2013; Annamalai and Vasudevan, 2020). The polar carboxyl group contributes little to the physical properties of PEs, except when R and R' are very small alkyl groups (such as methyl and ethyl). The general chemical structure of PEs is shown in **Figure 1**, where R and R' represents alkyl groups. The most commonly utilized PEs in consumer products are dimethyl phthalate (DMP), diethyl phthalate (DEP), diisobutyl phthalate (DIP), di-n-butyl phthalate (DBP), benzylbutyl phthalate (BBP), dicyclohexyl phthalate (DCHP), di-n-hexyl phthalate (DHP), bis (2-ethylhexyl) phthalate (DEHP), di-n-octyl phthalate (DOP), diisodecyl phthalate (DiDP) and diisononyl phthalate (DiNP) (Wang Y. et al., 2019; Dutta et al., 2020; Zhang et al., 2021). **Table 1** highlights the chemical structures and uses of some of the most commonly used PEs.

PEs' different chemical and physical properties account for many of their potential individual applications (Wang Y. et al., 2019). Their general low melting and high boiling points give them applications as heat-transfer fluids and carriers (Giuliani et al., 2020). Both linear and branched PEs are utilized in the production of plastics; with linear esters having outstanding flexibilities at low temperatures as they are less volatile. PEs with alkyl side chains lower than six carbons are not often used as plasticizers because volatility is a concern. PEs can be found in printing ink, paint, adhesives, vinyl flooring, and even in most food packaging materials, cosmetics, and pharmaceuticals products (Giuliani et al., 2020; Zhang et al., 2021).
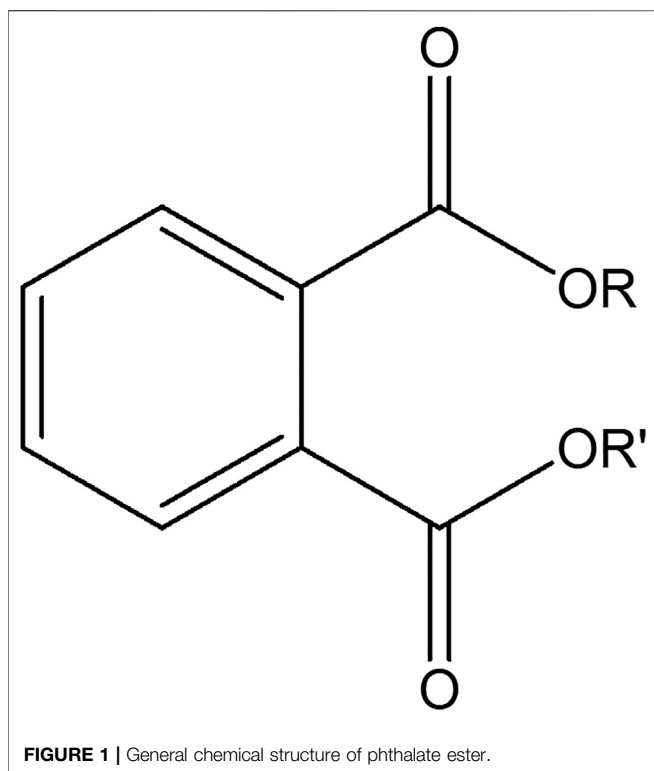
Owing to their growing economic and commercial interest, PEs are by far the most used synthetic organic chemicals in a large variety of products since 1930s (Wang et al., 2018; Heo et al., 2020). Global production of PEs is estimated at 6 to 8 million tons per annum (Seyoum and Pradhan, 2019) with utilization by various industrial companies sitting at more than 3 million tons (Zhang et al., 2021). These compounds are mainly used for enteric coatings of nutritional supplements and pharmaceutical pills, as viscosity controlling agents, emulsifying agents, lubricants, binders, gelling agents, stabilizers film formers, dispersants, and suspending agents but primarily as plasticizers (Ji et al., 2014; Wang B. et al., 2015; Wang et al., 2018; Heo et al., 2020; USEPA, 2021). They are generally added to plastic materials such as polyethylene, polyethylene terephthalate, polyvinyl acetate and polyvinyl chloride (PVC), at the composition of up to 60% by weight of the PEs, to improve the elasticity and extensibility of the polymers (Giuliani et al., 2020). End applications comprise food products, building materials, children's toys, medical devices, agricultural adjuvants, adhesives and glues, personal care products, detergents and surfactants, modeling clay, waxes, printing inks and coatings, paints, and textiles (Ling et al., 2007; Huang et al., 2008; Gao and Wen, 2016). A large variety of household applications, for example, vinyl upholstery, adhesives, shower curtains, floor tiles, cleaning materials, food holders and coverings contain PEs. PEs are also found in modern electronics (Chakraborty et al., 2019; Zhang et al., 2019) and clinical applications, for example, catheters and blood transfusion devices (Chiellini et al., 2013; Malarvannan et al., 2019). In light of their extensive uses and diverse applications, different studies have reported the presence of PEs residues in different receiving ecosystems (Salaudeen et al., 2018; Ai et al., 2021; Li et al., 2021), though here the aquatic ecosystems are reviewed. Furthermore, their magnificent bio-availability and degradability nature would indispensably foster high possibility for these compounds to accumulate in aquatic organisms and humans (Arambourou et al., 2019; He et al., 2020; Zhang et al., 2021).

This review was conducted through an exhaustive online database literature search from ScienceDirect (https://www.sciencedirect.com/), Google Scholar (https://scholar.google.com), international monitoring bodies databases such as World Health Organization (WHO), United States Environmental Protection Agency (USEPA) and United Nations Environmental Program (UNEP) to identify relevant and most recent articles and reports of PEs prevalence and their impacts on aquatic ecosystems worldwide. Studies considered were those published in accredited scientific journals and reports from recognized international bodies and majority of them were limited to a decade old (2011–2021), with preference given to those that are not older than 5 years. The following set of keywords were used to search and select the most suitable studies; phthalate esters, phthalate ester metabolites, phthalate esters in water, phthalate esters in sediments, phthalate esters in aquatic ecosystems, phthalate esters toxicity, phthalate esters bioaccumulation, phthalate esters biodegradation, health impacts of phthalate esters, treatment of phthalate esters. Based on the above criteria, more than 4,000 articles were found of which 184 articles deemed more relevant (including scientific reports) were used in the current article. The current state of knowledge regarding the occurrence, different extraction and analytical techniques and impacts of PEs in aquatic ecosystems is highlighted so as to provide a better understanding of their temporal and spatial distributions in aquatic systems and to aid in devising prudent means to curtail their ecological footprints.

PREVALENCE OF PHTHALATE ESTERS IN AQUATIC ECOSYSTEMS

Due to their widespread domestic and industrial applications, it is not surprising that ubiquity of PE contaminants is noted in different aquatic ecosystem compartments such as: marine water, sediments, rivers, lakes, and wetlands, and from wastewater treatment plants (Gao and Wen, 2016; Al-Saleh et al., 2017; Wang et al., 2017; Salaudeen et al., 2018; Arfaeinia et al., 2019; Zhu Q. et al., 2019; Cheng et al., 2019; Zacharia, 2019; WHO, 2021). PEs are readily released during production, use and waste disposal, and can easily leach out into water (Vats et al., 2013; Salaudeen et al., 2018; Henkel et al., 2019). Specifically, they

FIGURE 1 | General chemical structure of phthalate ester.

are easily released into the environment because there is no covalent bond between them and polymers in which they are

mixed in (Koniecki et al., 2011; Zheng et al., 2014; Wang X. et al., 2015; Chi and Gao, 2015; Gao L. et al., 2019). Furthermore, as plastics age and breakdown, the release of PEs into the environment gets accelerated. Since PEs plasticizers are not chemically bound to PVC, they also easily filter into aquatic ecosystems among others (Olkowska et al., 2017; Chen et al., 2018; Kashyap and Agarwal, 2018). PEs enter the environment through several pathways including losses during manufacturing processes and weathering, leaching or volatilization from final products (Kashyap and Agarwal, 2018; Das et al., 2021). Several aquatic ecosystems such as lakes (Lee Y.-M. et al., 2019; Gao X. et al., 2019), wetlands (Gao and Wen, 2016; Wang et al., 2017), marine environments and rivers (Arfaeinia et al., 2019; Zacharia, 2019; Ai et al., 2021; WHO, 2021) have been characterized as highly polluted by PEs among other organic pollutants.

In the aquasphere, PEs occur at wide concentration range from trace (μg/L) to mg/L depending on the degree of PEs application and products. Large variety and abundance of PEs can be observed in aquatic ecosystems in different countries; however, the pollution levels and occurrences are mild to moderate. Adeniyi et al. (2011) reported the presence of up to 2,705 μg/L of PEs from river water in Nigeria, while Liu et al. (2015) reported between 0.02 and 0.77 μg/L in waterworks from China, from undetectable to 0.43 μg/L on surface water in Iran by Abtahi et al. (2019). Specifically, communities which are located adjacent to industries that use or produce these compounds tend to be greatly exposed to the PEs. Eventually, these compounds will find their way into the waterways since they are receptors of all effluents and pollutants in runoff. With PEs containing
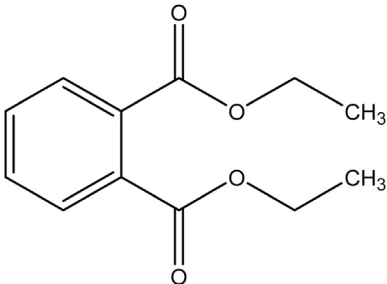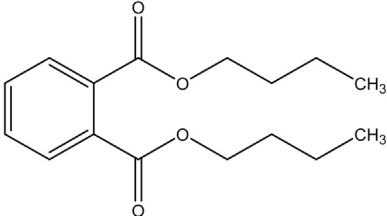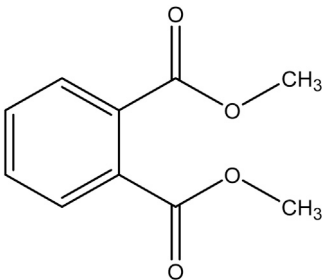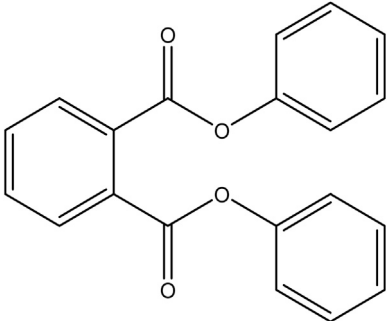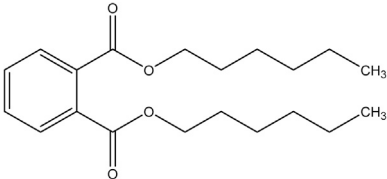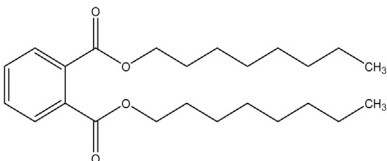
TABLE 1 | Applications and potential sources of exposure for some of the most commonly used PEs.

Phthalate ester	CAS number	Chemical structure	Application/potential sources of exposure
Bis-(2-ethylhexyl) phthalate	117–81–7		Medical tubing, blood storage bags, medical devices, indoor air, table cloths, food packaging, plastic toys, floor tiles, wall coverings, furniture upholstery, shower curtains, garden hoses, rainwear, baby pants, dolls, swimming pool liners, some toys, shoes, automobile upholstery and tops, packaging film and sheets, and sheathing for wire and cable Swan et al. (2005); Rudel and Perovich (2009); Olujimi et al. (2010); USEPA (2018); Wang Y. et al. (2019)
Benzyl butyl phthalate	85–68–7		Vinyl flooring, adhesives, sealants, food packaging, furniture upholstery, carpet tiles, and artificial leather; also used in certain adhesives (Olujimi et al. (2010); Dominguez-Morueco et al. (2014); Liu et al. (2015); Wang Y. et al. (2019)

(Continued on following page)

TABLE 1 | (Continued) Applications and potential sources of exposure for some of the most commonly used PEs.

Phthalate ester	CAS number	Chemical structure	Application/potential sources of exposure
Diethyl phthalate	84–66–2		Cosmetics, nail polish, aftershave, body lotions, deodorants, perfumes/cologne, pharmaceuticals, herbal coating, insecticide Cartwright et al. (2000); Jianlong et al. (2004); Wang X. et al. (2019)
Di-n-butyl phthalate	84–74–2		Cosmetics, aftershave, nail polish, make-up, perfumes, pharmaceuticals, herbal coating, chemiluminescent glow sticks Olujimi et al. (2010); Mankidy et al. (2013); Wang Y. et al. (2019)
Dimethyl phthalate	131–11–3		Hairstyling products, indoor air freshner, shampoo, aftershave, adhesives and insecticides Swan et al. (2005); Rudel and Perovich (2009); Olujimi et al. (2010); USEPA (2018); Wang Y. et al. 2019
Diphenyl phthalate	84–62–8		Flooring, automotive, construction, medical, clothes, households, wire and cables Swan et al. (2005); Rudel and Perovich (2009); Olujimi et al. (2010)
Di-n-hexyl phthalate	84–75–3		Toys and children's cosmetics, food packaging, small appliances, rubber products, plastic additives as well as inert ingredients in pesticides (Wang Y. et al., 2019)
Di-n-octyl phthalate	117–84–0		Medical tubing and blood storage bags, wire and cables, carpet back coating, floor tile, and adhesives, cosmetics and pesticides. Its major usage is in children's toys Rudel and Perovich (2009); Olujimi et al. (2010)

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TABLE 1 | (*Continued*) Applications and potential sources of exposure for some of the most commonly used PEs.

Phthalate ester	CAS number	Chemical structure	Application/potential sources of exposure
Diisodecyl phthalate	26,761–40–0		Construction materials, PVC sheet and coating products, packaging materials, children's toys, artificial leathers NICNAS (2008); Koniecki et al. (2011)
Diisononyl phthalate	28,553–12–0		Construction materials, electrical wires and cables, automotive care, clothing, paint, coatings, electrical and electronic products and furniture Koniecki et al. (2011)

products and effluents being anthropogenically exorbitant in the aquatic ecosystems, it is also essential to understand the extent of occurrence and fate, biodegradation, bioaccumulation, and persistence.

In light of the above, an array of literature has investigated the temporal and spatial distribution of these compounds in different aquatic ecosystems to demonstrate the presence and distribution of these compounds in different countries globally (Paluselli et al., 2018; Abtahi et al., 2019; Mi et al., 2019; He et al., 2020; Ai et al., 2021). Furthermore, studies in the past decade that have reported the presence of PEs in aqueous and edaphic matrices including their concentration levels as reported in **Tables 2**, **3**. DMP, DEP, DBP, BBP, and DEHP are the most dominant PEs in both aquatic sediments and waters with some DEHP concentrations frequently exceeding the annual average environmental water (freshwater and marine) quality standard of 1.3 μg/L (EU directive 2008/105/EC) (UNEP, 2020). The high number of recent PEs studies and PEs detection rate in Asia could probably be attributed to the higher volume of PEs produced and used in these environments, because of the absence of stricter regulations on usage of the PEs designated as priority pollutants unlike in developed countries of Europe and United States of America (UNEP, 2020; Das et al., 2021; Li et al., 2021). However, most values do not exceed the trigger threshold values of 5,100, 1,300, and 64.6 μg/L for DMP, DEP, and BBP respectively for protection of about 80% of aquatic species proposed by Australian and New Zealand guidelines (Net et al., 2015a). Ground and surface water bodies receive notable levels of PEs from different human activities such as agriculture, solid waste disposal, manufacturing industries and wastewater treatment plants (WWTPs) among others (Liu et al., 2015; Gao and Wen, 2016; Al-Saleh et al., 2017; Zhu Q. et al., 2019). A recent South African study by Salaudeen et al. (2018), revealed gross water pollution by PEs in the wastewater treatment plants (WWTPs) of Amathole Municipality in Eastern Cape province. In this study, the authors reported the presence of DMP, DEP, DBP, BBP, DEHP, and DOP of with DBP and DEHP

as the most abundant PEs. The reported concentration in the influents were in the range of 2.7–2,488 μg/L and 130–1,094 μg/g dry weight in the sludge which exceeded acceptable limits of 100 μg/g for dry weight as recommended by the European Union for agriculture use (EU legislation 86/278/EEC). Furthermore, Salaudeen et al. (2018) reported the levels of PEs to be much higher in the WWTP unit processes than upstream of the WWTP and the effluents discharging point hence suggesting that the WWTPs are among the key source of anthropogenic PEs in the environment and they could be identified as one of the hotspots and source for PEs in aquatic ecosystems. In particular, the concentration of PEs ranged from undetectable to 17 μg/L upstream, 2.7–2,488 μg/L in the WWTPs, and undetectable to 25 μg/L in the effluent (Salaudeen et al., 2018). Considering the magnitude of their toxicity and impacts thereof, these compounds will drastically affect the receiving aquatic ecosystem and its integrity to foster life. Moreover, their composition could grossly be attributed to the level of anthropogenic activities, such as industries, that discharge their effluents to different handling facilities such as domestic and industrial WWTPs (Olijimi et al., 2012; Liu et al., 2015; Gao and Wen, 2016; Al-Saleh et al., 2017; Zhu Q. et al., 2019).

In aquatic ecosystem, some PEs are stable, persistent, and resistant to natural degradation, hence previous studies demonstrated the feasibility of PEs from contaminated water to bio-accumulate and bio-magnify in the food chain (Ma et al., 2013; Sun et al., 2015). Albeit, biodegradation is the dominant route for PEs degradation in the environment (Staples et al., 1997a; Chang et al., 2004; Xu et al., 2020; Das et al., 2021). Documented studies have reported that marine microalgal (Gao and Chi, 2015) and some microbial species possess the capability to degrade PEs (Ren et al., 2018; Yu et al., 2020), with microbial degradation considered the main route of PEs transformation (Yu et al., 2020). Microbial degradation is however, generally affected by external environmental factors and typical lack of specific degrading bacteria in the aquatic ecosystem, which in turn makes PEs degradation difficult under natural conditions, hence their

TABLE 2 | Mean (RSD)/range concentrations of some PEs in environmental water samples (µg/L).

Locations	Phthalate ester compounds										References
	DMP	**DEP**	**DIP**	**DBP**	**DHP**	**BBP**	**DEHP**	**DCHP**	**DOP**	**DiDP**	
Ogun river, Nigeria	nd	1,480–1,755	—	2,080–2,705	—	—	255–480	—	—	—	Adeniyi et al. (2011)
Chaohu lake, China	0.015–3.670	0.006–0.283	—	0.070–17.53	—	nd–0.107	nd–0.576	—	nd–0.045	—	He et al. (2013)
Selangor river, Malaysia	0.002–0.028	0.006–0.113	—	0.028–0.306	—	0.002–0.021	0.051–0.507	—	0.0002–0.014	—	Santhi and Mustafa (2013)
Songhua river, China	0.98–4.12	1.33–6.67	—	1.69–11.81	—	nd–4.39	2.26–11.55	—	0.69–6.14	—	Gao et al. (2014)
Somme river, France	0.01–0.25	0.26–6.98	—	nd	—	nd	5.16–20.80	—	0.22–3.386	—	Net et al. (2014)
Waterworks, China	0.071	0.035	—	0.35	—	0.026	0.77	—	0.026	—	Liu et al. (2015)
Kaveri river, India	nd–0.094	0.036–0.52	—	nd–0.372	—	0.0054–0.145	nd–0.822	—	nd–0.085	—	Selvaraj et al. (2015)
WWTPs, S. Arabia	0.228(0.188)	0.182(0.134)	—	0.748(0.577)	—	0.388(0.278)	0.468(0.495)	—	0.195(0.209)	—	Al-Saleh et al. (2017)
Jiulong river, China	0.34–0.15	0.014–0.51	—	0.31–0.51	—	—	0.12–1.76	—	—	—	Li et al. (2017)
Changjiang river, China	0.65–0.311	nd–0.181	0.028–0.469	0.53–2.41	nd–0.011	nd–0.001	nd–0.008	nd–0.151	nd–0.011	nd–0.018	Zhang et al. (2017)
Adelaide WWTP, S.A	1.35–12.07	2.53–24.42	—	nd–451.48	—	2.38–80.70	3.44–48.16	—	nd–21.75	—	Salaudeen et al. (2018)
Rhone river, France	0.0057	0.0305	—	0.0405	—	—	0.407	—	nd	—	Paluselli et al. (2018)
Songhua river, China	0.065–0.208	0.14–0.334	—	0.190–4.762	—	—	0.364–2.682	—	nd–0.621	—	Wen et al. (2018)
Surface water, Iran	0.26(0.23)	0.04(0.23)	—	0.2(0.23)	—	0.05(0.23)	0.43(0.23)	—	nd	—	Abtahi et al. (2019)
Pearl river, China	0.052(0.035)	1.62(1.09)	0.397(0.293)	0.176(0.141)	0.553(0.549)	0.834(0.850)	8.88(11.1)	0.092(0.096)	0.472(0.536)	0.018(0.014)	Cheng et al. (2019)
Taihu lake, China	nd–1.32	0.08–4.79	—	nd–2.54	—	0.08–4.72	nd–1.41	—	0.07–0.59	—	Gao X. et al. (2019)
Asan lake, Korea	nd–0.18	nd–0.05	nd–0.07	nd–0.34	nd–0.07	nd	nd–1.34	nd–0.07	nd–0.02	—	Lee Y.-M. et al. (2019)
Liao river, China	—	nd–1.75	—	1.43–16.6	—	nd–6.55	nd–37.3	—	—	—	Zheng et al. (2019)
Yangtze river, China	0.017–0.035	0.009–0.057	0.077–0.205	0.135–0.801	—	0.001–0.0014	0.073–0.261	—	0.0005–0.001	—	He et al. (2020)
Poyang lake, China	nd–0.253	nd–0.127	—	0.121–1.297	—	nd	0.023–0.896	—	nd–0.018	—	Ai et al. (2021)
Baoding lake, China	0.086–2.20	nd–2.04	0.079–1.48	nd–2.14	—	nd–1.51	—	nd–1.91	—	—	Li et al. (2021)
Baoding pond, China	nd–2.32	nd–1.68	nd–1.52	nd–1.68	—	nd–1.92	—	nd–1.93	—	—	Li et al. (2021)
Lake Victoria, Uganda	0.07–0.4	0.04–1.1	—	0.35–16	—	—	0.21–23	—	—	—	Nantaba et al. (2021)

"RSD" = relative standard deviation"—" = not analyzed; "nd" = not detected; "WWTPs" = wastewater treatment plants; "S.A" = South Africa; "S. Arabia" = Saudi Arabia.

TABLE 3 | Mean (RSD)/range concentrations of some PEs in sediments samples (μg/g dry weight) and standard deviations.

Locations	Phthalate ester compounds											References
	DMP	DEP	DIP	DBP	DHP	BBP	DEHP	DCHP	DOP	DiDP	DiNP	
Ogun river, Nigeria	nd–0.85	0.08–0.35	—	0.19–1.42	—	—	0.02–0.82	—	—	—	—	Adeniyi et al. (2011)
Jukskei river, S.A	0.0002–0.006	0.003–0.005	—	0.006–0.057	—	nd	0.017–3.66	—	—	—	—	Sibali et al. (2013)
Qiantang river, China	nd–0.179	nd–0.218	0.019–0.769	0.034–0.241	nd–0.0094	nd–0.021	0.365–6.24	nd–0.0035	nd–0.019	—	—	Sun et al. (2013)
Songhua river, China	0.03–0.09	0.04–0.04	—	0.60–0.88	—	nd–0.10	0.23–0.57	—	nd–0.38	—	—	Gao et al. (2014)
Pearl river, China	0.001–0.019	0.001–0.091	0.108–12.4	0.042–5.03	nd	nd–0.113	0.415–29.5	nd–0.011	nd–0.181	—	—	Liu et al. (2014)
Suburban rivers, China	0.02(0.05)	0.09(0.27)	—	1.55(2.56)	—	0.50(1.22)	10.52(14.30)	—	0.49(1.37)	—	—	Wang J. et al. (2014)
Kaveri river, India	nd–0.0037	nd–0.185	—	nd–0.664	—	nd–0.0078	nd–1.40	—	nd–0.0085	—	—	Selvaraj et al. (2015)
Wetland, China	nd–0.012	nd–0.029	—	nd–0.039	—	nd–0.020	0.136	—	nd–0.027	—	—	Gao and Wen (2016)
Costal/Harbor, Taiwan	nd–0.021	0.0014–0.072	0.002–0.11	nd–0.20	—	—	0.0–36.7	—	nd	0.024–5.28	nd–40.31	Chen et al. (2017)
Juilong river, China	nd–0.004	nd–0.002	—	0.003–0.23	—	—	0.033–1.28	—	—	—	—	Li et al. (2017)
Qixinghe wetland, China	nd–0.036	nd–0.060	0.01–0.049	0.018–0.071	nd–0.0071	nd–0.028	0.038–0.295	nd	nd-0.0464	—	—	Wang et al. (2017)
Changjiang river, China	0.001–0.0004	nd–0.0002	nd–0.0068	nd–0.0073	—	—	nd–0.0046	—	—	—	—	Zhang et al. (2017)
Changjiang river, China	0.622	0.265	4.41	3.05	—	—	5.08	—	—	—	—	Zhang et al. (2018)
Persian gulf, Iran	5.68(0.99)	5.83(0.53)	2.50(0.20)	11.9(0.68)	—	9.19(0.52)	30.25(4.75)	—	6.35(0.83)	—	—	Arfaeinia et al. (2019)
Pearl river, China	0.007(0.004)	0.083(0.031)	0.867(0.478)	1.84(1.33)	0.058(0.033)	0.08(0.044)	7.61(7.50)	0.25(0.179)	0.133(0.096)	0.157(0.115)	—	Cheng et al. (2019)
Taihu lake, China	0.950–3.50	0.590–2.29	—	0.500-1.75	—	0.420–1.30	0.550–4.77	—	0.480–16.2	—	—	Gao X. et al. (2019)
Asan lake, Korea	nd–0.006	nd–0.004	nd–43.2	nd–0.535	nd–0.028	nd	0.007–8.33	nd–0.019	nd	—	—	Lee Y.-M. et al. (2019)
Marine, China	—	nd–0.0025	nd–0.0064	nd–0.0068	—	nd–0.0016	nd–0.016	nd	—	—	—	Mi et al. (2019)
Sludge, China	0.195	0.053	0.440	0.957	0.001	0.005	14.7	—	0.018	—	—	Zhu Q. et al. (2019)

"RSD" = relative standard deviation"—" = not analyzed; "nd" = not detected; "S.A" = South Africa.

long half-life, that range from a few years to several hundred years (Fang et al., 2018; Das et al., 2021; Zhang et al., 2021).

Interestingly, recent studies confirmed the ability of *Bacillus mojavensis* B1811 (Zhang et al., 2018a) and *Paracoccus kondratievae* BJQ0001 bacterium (Xu et al., 2020) to have high efficiency for the degradation of PEs. The results of the study by Zhang et al. (2018a), showed that at 0.5 μg/L; DEHP, DBP, BBP, and DPP could almost be completely degraded by strain B1811 within 4 days in mineral salt medium under shaking conditions, while only 5.9% of the DMP and 42.9% of DEP present with short alkyl chains, were degraded by strain B1811 under the same conditions with DMP and DEP degraded to 0.471 and 0.285 μg/L respectively. Xu et al. (2020), also found that strain BJQ0001 is also capable of successfully degrading substrates DMP, DEP, DBP, DIBP, and DEHP simultaneously when they are coexisting in the fermentation system at 0.2 μg/L of the PEs mixture, but with slightly reduced degradation rates. He et al. (2020), studied bioaccumulation of PEs in muscle tissues of domestic livestock (pig, cattle and chicken) and fish in China. In their study, the authors reported that most PEs congeners are not likely to accumulate in organisms due to their bioaccumulation factors being ≤2 except for DEP, DMP and BBP which were reported to comprise the BAFs values of ≥2, with the pig showing more capacity to accumulate PEs than the other animals' tissues. This could be attributed to the fact that the pig generally has more fat contents than both the cattle and chicken and PEs are lipophilic.

ENVIRONMENTAL AND HUMAN HEALTH RISKS ASSOCIATED WITH PHTHALATE ESTERS

Phthalate Esters Impacts on Aquatic Ecosystems

Aquatic ecosystems such as rivers, dams, lakes and wetlands that are located within or passes through agricultural, industrial, residential and urban environments are exposed to a lot of different types of PEs from various anthropogenic inputs (Salaudeen et al., 2018; Ai et al., 2021; Li et al., 2021). Although both the cyanobacteria and freshwater algae are capable of producing DBP or monoethylhexyl phthalate (MEHP) under natural conditions, which can then be released to aquatic ecosystem, anthropogenic activities pollution such as agricultural pesticides, industrial effluents, commercial wastewaters, landfills (Zhang et al., 2021) and household-electronic and solid wastes (Zhang et al., 2019) all act as the main avenues of PEs into these aquatic ecosystems. Due to their high octanol-water partition (K_{ow}/logK_{ow}^{25}) (1.61–9.46) and low vapor pressures (Pa^{25}) (1.84×10^{-6}–0.263), most PEs entering the water environment have extremely low volatility hence can easily migrate into various water bodies and enter aquatic organisms (Net et al., 2015a; Das et al., 2021; Zhang et al., 2021). Since the value of K_{OW} increases with increasing alkyl chain length, this results in increased hydrophobicity for the higher molecular weight PEs, hence their higher sorption to organic matter (Das et al., 2021; Zhang et al., 2021).

Upon entering the aquatic ecosystem, PEs directly come into contact with aquatic organisms. PEs can enter high-nutrient-grade aquatic organisms through ingestion and pass along the food chain (Zhang et al., 2021). PEs affect the aquatic ecosystem in diverse ways. Such is demonstrated by their ability to elicit their toxicity (immunotoxin, neurotoxic, genotoxic, endocrine, metabolic, and developmental toxicities) to fish and aquatic invertebrates with BBP, DEHP, and DBP eliciting the most effects (Staples et al., 1997b; Aarab et al., 2006; European Commission, 2008; Arambourou et al., 2019; Zhang et al., 2021). Thenceforth, the introduction of these compounds poses massive toxicity problem for the aquatic ecosystems and living organisms in there (Crafford and Avenant-Oldewage, 2010). As reviewed by Staples et al. (1997b), DMP, DEP, DAP, DBP, DIBP, and BBP exposure were found to have acute or chronic effects across, algae, invertebrates, and fish species. A recent review by Zhang et al. (2021) also noted acute and chronic toxic effects on aquatic organisms, with symptoms such as crooked tails, necrosis, cardiac edema, lack of tactile response and death on aquatic animal embryos, while on adult organisms, PEs exposure could lead to adverse effects on reproduction, damage to the liver, kidney, and other organs (Gao et al., 2018). It was noted that lower molecular weight PEs were acutely and chronically toxic at concentrations below their aqueous solubilities and that toxicity increased with increasing alkyl chain length up to and including four carbon atoms (Staples et al., 1997b). Reviewed ecotoxicity studies for these PEs showed adverse effects to aquatic organisms with broad range of endpoints and at much lower concentration levels (ng/L to μg/L) than that are being obtained in recent environmental studies (Oehlmann et al., 2009; Zhang et al., 2021).

Toxicity of chemical substances to aquatic organisms is determined by the median lethal concentration (LC$_{50}$) (Huang et al., 2020; Zhang et al., 2021). As reviewed by Zhang et al. (2021), the common carp 96 h LC$_{50}$ ranges for DEP, DBP, DOP, and DEHP are 34.8–53, 16.30–35, 7.95, and 37.95 mg/L respectively, while the lethal concentrations of DEP and DBP in marine flounder and Nile tilapia are also similar to those of carp. Contrary to this, lethal concentration of other small-sized fish such as juvenile triangular Bream (*Magalobrame tarminalis*) is significantly lower, with 96 h LC$_{50}$ values for DMP, DEP, DBP, and DEHP as low as 3.29, 6.60, 2.08, and 5.41 mg/L respectively. They are also toxic for many other aquatic species with DEP's LC$_{50}$/EC$_{50}$ values of 3 and 132 mg/L for marine algae and protozoan respectively, with the lowest NOECs (1.7–4 mg/L) for algae, fish and invertebrates (Staples et al., 1997b; Net et al., 2015a). Some of these toxicity studies on aquatic organisms are listed in **Table 4** with their health effects. However, some aquatic organisms like micro-algae have PEs degradation capabilities. Instead of being toxicologically affected, benthic diatom (*Cylindrotheca closterium*) demonstrated the ability to accelerate degradation of DEP and DBP (Li et al., 2015). Research indicate that most PEs (with short carbon-chains) are degradable in the environment, however some tend to bioaccumulate in biological samples (He et al., 2020; UNEP, 2020).

TABLE 4 | Toxic effects of some PEs on aquatic organisms.

Organisms	PEs	Test concentration levels	Toxicity	References
Estuarine copepod (*Eurytemora affinis*)	DEHP	109 µg/L, 10 days	Exposure to DEHP, especially from embryonic development could results in endocrine disruption	Forget-Leray et al. (2005)
Murray river rainbowfish (*Melanotaenia fluviatilis*)	DBP	125, 250, 500, and 1,000 µg/L, 7 days	Increased spermatogonia, liver choriogenin and an induction in brain aromatase suggest continuous exposure for 7 days can adversely affect both male and female reproductive system	Bhatia et al. (2013); Bhatia et al. (2014)
Marine medaka (*Oryzias melastigma*)	DEHP	0.1 and 0.5 mg/L, 6 months	Continuous exposure results in accelerated start of spawning, production in females, reduced oocytes fertilization rate in untreated females paired with treated males	Ye et al. (2014)
Larvae midge (*Chironomus riparius*)	BBP	10^{-3}, 10^{-2}, 10^{-1}, 1, and 10 µg/L, 48 h	Novel and significant dose and time-dependent alterations in expression profile of genes involved in cell processes such as energy metabolism, stress response, hormone pathways and detoxication activities even at lower concentrations	Herrero et al. (2015)
Abalone (*Haliotis diversicolor upertexta*)	DBP	2, 10, and 50 µg/L, 30 days	Major metabolite changes related to metabolic energy, environmental stress and osmotic regulation, with increase in intracellular metabolites the most obvious change	Zhou et al. (2015)
Mature goldfish (*Carassius auratus*)	DEHP	1, 10, and 100 µg/L, 30 days	Decreased sperm production, motility and velocity after the 30 days test period	Golshan et al. (2015)
African sharptooth catfish (*Clarias gariepinus*)	DEHP	0, 10, 100, 200, and 400 µg/L, 14 days	Consistent and unique pattern of biphasic effect on steroidogenic enzyme genes, which increases at low concentration (10 µg/L), and affects the brain and head kidney	Arukwe et al. (2017)
Zebrafish embryos (*Danio rerio*)	DEP, BBP, DBP	DEP: 0.08, 0.4, 2, and 10 mg/L; BBP: 0.02, 0.1, 0.5, and 2.5 mg/L; DBP: 0.0008, 0.004, 0.02, 0.1 mg/L, 14 days	Disruption of sex hormones through modulating key steroidogenic genes in male zebrafish over 14 days exposure period to DEP, BBP, and DBP.	Sohn et al. (2016)
	DMP, DEP, DEHP, DOP, DiNP, DiDP	0, 0.01, 0.1, 1.0, 10 and 100 mg/L, 6 h - 7 days	Exposure DMP, DEP, DEHP, and DOP significantly increased E2/T ratio in H295R cells while DEHP influenced the expression of *vtg1, esr1,* and *cyp19a1b* genes in zebrafish larvae. In zebrafish, DMP, DEP, DiNP, DiDP exposure showed significant transcriptional alteration of steroid hormones genes even at lower concentrations suggesting great endocrine disrupting potencythan DEHP. Generally, PEs reduced heart rate and body length of developing zebrafish embryos	Lee H. et al. (2019)
Daphnia magna	DEP, DBP, DEHP	1 and 10 µmol/L, 14 days	Enhanced fat accumulation upon exposure to all the tested PEs, analysis of genes involved in fat metabolism suggests the increase in fat content could be due to inhibition of absorption and catabolism of fatty acids, reduced body size. While DEP and DBP decrease lifespan, DEHP results in increased reproduction output	Seyoum and Pradhan (2019)

While PEs tend to be ubiquitous in the biosphere, there is limited information about their route of exposure, bioaccumulation behavior, and human exposure. Furthermore, eco-toxicological studies have played a pivotal role in determining the degree at which these compounds accumulate in biota, specifically the plants and animals. Net et al. (2015a), indicated that a high capacity to accumulate the PEs by species could be obtained when the BAFs values are larger than 1,000 [log (BAFs) > 3]. In their study, the authors reported the mean log (BAFs) values which ranged between 0.91 and 2.96, thus implying that most PEs congeners are not likely to be accumulative in organisms. It is worth noting that large variances of BAFs values of individual PEs can also be found in other studies as reported by Net et al. (2015a), and for this, the explanation could be based on the discrepancies between the physicochemical properties of individual PEs, variances in temporal bioavailability, and species-specific in metabolic capability, resulting in individually and/or jointly impacting on the bioaccumulation of PEs in the biota (Adeogun et al., 2015; Net et al., 2015a). This further necessitates the need for improved and continual monitoring of PEs in aquatic ecosystems, especially those being utilized by communities for various basic functions such as fishing, irrigation, drinking and bathing. Such is evidenced by the recent study by He et al. (2020), in a rural agricultural area of western China where people are dependent on river water for domestic and household uses and found that their pigs, cattle and chicken meat samples all contained PEs. A significant correlation was also observed between the biota and river water samples, indicating that river water heavily influenced PEs uptake and accumulation in the biological samples (He et al., 2020). PEs, notably high molecular weight ones, have exceptional ability to accumulate in sediments; where sorption to particles and the low-oxygen conditions slows PEs degradation process by reducing their degradation rates (UNEP, 2020).

Phthalate Esters Exposure, Toxicity and Human Health Effects

Humans are continually exposed to PEs daily as these compounds are found in little quantities in literally thousands of industrial and household products ranging from cosmetics, toys, curtains, electrical appliances, food, packaging materials, beverages and

drinking water (Baloyi, 2012; Gong et al., 2018; Luo et al., 2018; Abtahi et al., 2019; He et al., 2020). Humans are exposed to PEs from aquatic ecosystems via different routes, namely; dermal skin absorption, inhalation, and ingestion from food and drinking water (Alharbi et al., 2018; Paluselli et al., 2018; Abtahi et al., 2019; Giuliani et al., 2020). Upon exposure or uptake, effects exerted range from mutagenicity, teratogenicity, and carcinogenicity. In fact, global concern about PEs arise due to their hazardous, toxicity, mutagenic, teratogenic and carcinogenic characteristics to humans on exposure (Gao and Wen, 2016; Zarean et al., 2016; Zacharia, 2019; Li et al., 2020; USEPA, 2021). PEs at varying levels of exposure may adversely affect human health by acting as endocrine disruptors (Zarean et al., 2016; De Toni et al., 2017; Jiang et al., 2018; Ren et al., 2018; Zhu M. et al., 2019; Zhang et al., 2021). Endocrine disruptors are sometimes also referred to as hormonally active agents that act like hormones in the endocrine system, disrupting the physiological functioning of endogenous hormones (Balaguer et al., 2019; Darbre, 2019; Xu and Yin, 2019; Talia et al., 2021; You and Song, 2021). The endocrine system in humans and most groups of animal life, including aquatic organisms, consists of glands that secrete hormones, and receptors that detect and react to the hormones (Hiller-Sturmhöfel and Bartke, 1998). Studies have associated endocrine disruptors to severe biological effects in animals, giving rise to concerns that low-level exposure to PEs might cause similar effects in human beings (Krimsky, 2001; Lin et al., 2018; Balaguer et al., 2019; USEPA, 2021) since PEs have similar effects on the endocrine system (WHO/UNEP, 2013).

The theory of endocrine disruption posits that low-dose exposure to chemicals that interact with hormone receptors can interfere with reproduction, development, and other hormonally mediated processes (Zoeller et al., 2014; Gore et al., 2015; Xu and Yin, 2019). Furthermore, since endogenous hormones are typically present in the body in relatively tiny concentrations, the theory also holds that exposure to relatively small amounts of exogenous hormonally active substances such as PEs could disrupt proper functioning of the body's endocrine system (Diamanti-Kandarakis et al., 2009; Marty et al., 2011). Thus, endocrine disruptors such as PEs elicit adverse effects at much lower doses than a toxicant acting through a different mechanism. The half-life of PEs diesters in

TABLE 5 | Recommended toxicity uptake limits of some PEs in humans.

Phthalates	MRLs/TDI (µg/kg/day)	Toxicity endpoint	References
DEP	7,000 (MRL-Acute)	Reproduction	ATSDR (2021)
	6,000 (MRL-Intermediate)	Hepatic	ATSDR (2021)
DBP	500 (MRL-Acute)	Developmental	ATSDR (2021)
	10 (TDI)	Reproduction	European Food Safety Authority (2019)
BBP	500 (TDI)	Reproduction	European Food Safety Authority (2019)
DEHP	100 (MRL-Intermediate)	Reproduction	ATSDR (2019)
	60 (MRL-Chronic)	Reproduction	ATSDR (2019)
	50 (TDI)	Reproduction	European Food Safety Authority (2019)
DOP	3,000 (MRL-Acute)	Hepatic	ATSDR (2021)
	400 (MRL-Intermediate)	Hepatic	ATSDR (2021)
DiDP	150 (TDI)	Hepatic, reproduction	European Food Safety Authority (2019)
DiNP	150 (TDI)	Hepatic, reproduction	European Food Safety Authority (2019)

"Acute'' = 1–14 days; "Intermediate" = 15–364 days; "Chronic" = 1 year and longer.

human biomonitoring studies in blood plasma and/or urine of humans and rodents is less than 24 h (Wang Y. et al., 2019; Zhang et al., 2019; Giuliani et al., 2020; Shin et al., 2020). Other studies have reviewed pharmacokinetics of PEs and found that diesters are rapidly hydrolyzed to monoesters in the gastrointestinal tract (Latini, 2005; Frederiksen et al., 2007; Dodson et al., 2014; Cequier et al., 2015). While binding of DEHP metabolites to blood plasma proteins, biliary excretion, and enterohepatic circulation in humans have been suggested (Frederiksen et al., 2007), urinary excretion remains the major elimination pathway of PEs (Wang Y. et al., 2019). In one study by Jiang et al. (2018), prolonged blood clotting time, decreased hemoglobin concentrations, and increased likelihood of anemia were all associated with high urinary phthalate metabolites in pregnant women on their late third trimester.

PEs exposure timing is presumed to be critical, since different hormone pathways are active during different stages of development (WHO/UNEP, 2013). High doses of certain PEs have shown hormonal activity in rodents' studies with reported liver and testicles damages and birth defects. Exposure to PEs during pregnancy could result in birth defects such as venereal enlargement of the male offspring and various forms of altered genitals developments, low sperm count and quality (Swan et al., 2005; Philippat et al., 2012; Sathyanarayana et al., 2014; Qureshi et al., 2016; Huang et al., 2017; Hoffman et al., 2018; Rehman et al., 2018; Xie et al., 2019). A study by Colon et al. (2000), found that Puerto Rican girls with premature breast development had higher levels of PEs in their blood compared to other girls, suggesting an association between PEs exposure and abnormal reproductive organs development. Swan et al. (2005) also found that baby boys born to mothers with highest levels of PEs were seven times more likely to have a shortened anogenital distance. This authenticates that one way or another, prenatal PEs exposure could and could've played a role in most cases of abnormal reproductive organs development, miscarriage and adverse birth outcomes (Toppari et al., 2006; Tilson, 2008; Mu et al., 2015; Hoffman et al., 2018). Therefore, it is very important not to only screen and monitor but also put preventative measures in place to limit exposure to such important endocrine disruptors as this could influence the fetal health (Chen et al., 2019).

PEs have also been linked with endometriosis and reduced female fertility (Cobellis et al., 2003; Reddy et al., 2006), obesity, preterm birth and low birth weight (Mu et al., 2015; Stojanoska et al., 2017; Hoffman et al., 2018), diabetes in adults (Svensson et al., 2011; Stojanoska et al., 2017), autism spectrum disorders (Jeddi et al., 2016), changes in sex hormone levels, breast cancer and prostate cancer (Lopez-Carrillo et al., 2010; Zhu M. et al., 2019), adverse effects on immune system, bronchial obstruction and asthma symptoms and neuropsychological development (Cho et al., 2010; Tellez-Rojo et al., 2013; Wang I.-J. et al., 2014; Kim et al., 2018; Zhang et al., 2019). PEs exposure could also interfere with production of the male sex hormones and testosterone, which is necessary for proper development and functioning of the male reproductive organs (Xie et al., 2019). Interference with testosterone activity, especially early in life, can have irreversible undesirable effects on male reproduction organs.

Some of the suggestions on avoiding and/or minimizing exposure to PEs for concerned people, are based on the available literature on occurrence and levels of PEs. Although with limited evidence that this will positively affect one's health, suggestions to minimize effects include among other strategies; eating a balanced diet, reduced consumption of canned and plastic packaged food, no nutritional supplements, no microwaved food, frequent hand washing, minimal application of personal care products such as cosmetics, moisturizers and perfumes that contains PEs (Koniecki et al., 2011; Chen et al., 2015; Braun, 2017; Wang Y. et al., 2019). In Taiwan, Chen et al. (2015) explored these PEs exposure reduction strategies in 30 (4–13 years old) young girls and found that pre-intervention dominant urinary PEs metabolites were significantly lower post the one-week intervention period. The study found that frequent hand washing ($p = 0.009$) and reduced intake of beverages in plastic cups ($p = 0.016$) were the most effective ways to reduce PEs metabolites in urine, particularly DEHP and mono-n-butyl phthalate (MBP) metabolites (Chen et al., 2015). However, avoiding personal care products containing PEs can be tricky and impossible as countries such as the United States do not require that PEs be disclosed on the list of the ingredients (Dodson et al., 2012). It is also recommended to avoid and minimize utilization of untreated water from the rivers as they can act as a major source of exposure to human by PEs, especially in rural areas where access to clean water is limited. A study by He et al. (2020), in China, found that untreated river water accounted for 79, 83, and 88% of the estimated PEs (DMP, DEP, BBP, DIBP, DNBP, DEHP, and DOP) daily intakes in toddlers, children and adults respectively, which exhibited an increasing trend with age, and this agreed with another study, also in China by Ji et al. (2014), where water ingestion and/or absorption was the major source of exposure to DBP, DEHP, and DOP. It is also worth noting that domestic animal meat can also serve as another route of PEs exposure, especially pork, beef, chicken and some vegetables (He et al., 2020) and some crops producing eaten grains such as rice, maize and wheat (Sun et al., 2015; Xu et al., 2020), so it is befitting to suggest and recommend consumption of organic farm produces which contain no synthetic products.

An assessment report by UNEP (2020) on chemicals and waste issues posing risks to human health and the environment has reviewed measures taken by several countries to reduce the use and exposure of PEs through various means. Among these measures, Denmark successfully reduced the use and exposure to PEs by introducing tax on products containing PVC and phthalates, although the tax was then repealed in 2019, in part due to reductions in the overall utilization of PEs. The Korean Ministry of Food and Drug Safety adopted and prohibited the production, import sale or use medical devices containing DBP, BBP, and DEHP. China, through National Food Safety Standard prohibited the use of DMP, DBP, DOP, and DiDP as additives in food contact materials, and banned the use of DBP, BBP, DEHP, DOP, DiNP, and DiDP in infants and children's textile products. Canadian government has already banned the use of DEHP in cosmetics and medical devices and restricts concentrations of BBP, DBP, DEHP, DOP, DiNP, and DiDP to below 1 mg/kg in childcare articles. Columbia and Peru also restrict contents of

BBP, DBP, DOP, DEHP, DiNP, and DiDP in flexible plastic for children (UNEP, 2020). The widespread utilization, potential exposure and effects of PEs also necessitated the need for monitoring by international agencies such as the United Nations Environmental Program (UNEP), International POPs Elimination Network (IPEN), United States National Health and Nutrition Examination Survey (NHANES), United States Centers for Disease Control and prevention (USCDC), United States Environmental Protection Agency (USEPA) and Stockholm Convention, and for the Agency for Toxic Substances and Disease Registry (ATSDR) and European Food Safety Authority (EFSA) to regulate and recommend toxicity limits for some of the most utilized PEs. **Table 5** lists recommended levels of some individual PEs as set out by ATSDR (2021), EFSA (2019), with regulated concentration in the form of Minimal Risk Levels (MRLs) and Tolerable Daily Intake (TDI). A study by the United States National Academies of Sciences, Engineering and Medicine (2017) found that although the current toxicity test methods can identify DEHP hazard, they may not accurately and conclusively be able to predict the levels at which humans are affected, implying that some of the reference doses and other "safe" limits established by regulatory agencies based on animal testing, may in fact be not safe to humans (UNEP, 2020). Such discovery calls urgently for improved and reliable methods for PEs biomonitoring studies on human samples. Statistically representative sample of United States population in a 2015–2016 NHANES survey revealed that high concentration of PEs was prevalent among people living below the poverty line (USCDC, 2018; USEPA, 2018). Similar trend of high exposure to PEs among children of low socio-economic income household was also found to be prevalent in Canada (Navaranjan et al., 2019; UNEP, 2020). It is worth noting that there are no known or documented MRLs/DTI and/or toxicity endpoints for majority of the PE compounds yet. Worryingly, these compounds are not regulated in most developing countries, specifically the low-and middle-income countries (LMIC) hence their impacts might be catastrophic, yet they are not captured in any epidemiological report or assay.

EXTRACTION AND ANALYSIS OF PHTHALATE ESTERS IN AQUATIC ECOSYSTEMS

Extraction of PEs

Like most organic compounds contaminants that are of environmental concern, PEs are also lipophilic, and thus typically extract into lipid soluble compounds. These esters have been detected in very low ranges of parts per billions (ppb) and parts per million (ppm) in different environmental samples (Sibali et al., 2013; Lee Y.-M. et al., 2019; Arfaeinia et al., 2019; Dong et al., 2019; Zhang et al., 2019; Annamalai and Vasudevan, 2020; He et al., 2020). Reliable and sensitive analytical methods for trace detection are therefore paramount. PEs analysis procedure generally involve a three-step process; extraction, column clean-up and chromatographic determination and/or quantification. Different methods and procedures for PEs determination have been reviewed and findings are well documented (Arfaeinia et al., 2019; Annamalai

and Vasudevan, 2020; He et al., 2020). All these studies employed a typical separation approach comprising of sample collection, extraction of target compounds from the samples and extracts clean-up process, then qualitative/quantitative analysis. The most common and basic methods are briefly explained below.

Solid Phase Extraction

SPE is a sample preparation process by which analytes are isolated from wide variety of matrices (compounds) in the mixture according to their physical and chemical properties (Falenas, 2019). SPE is advocated for due to its ease of implementation, ability to save time and solvent (Net et al., 2015b). SPE has been used to isolate PEs with great success from river and tap waters (Dominguez-Morueco et al., 2014; Selvaraj et al., 2015; Wang R. et al., 2019). Advances have been made recently to improve applicability and reliability of SPE by utilizing different covalent organic framework (COF) adsorbents (Santana-Mayor et al., 2018; Tong et al., 2019; Pang et al., 2020). Examples of such are the successful development and applications among others of fabricated COF-(TpBD)/Fe$_3$O$_4$ (rapid magnetic separation and reusable after washing with methanol) to magnetic solid phase extraction of 15 PEs with detection limit as low as 0.005 µg/L and good recoveries of 79.3–121.8% (Pang et al., 2020); 0.01–0.28 µg/L detection limit and recoveries of 80–112.8% with fabricated core-shelled Fe$_3$O$_4$ graphitic carbon sub-microcube (Tong et al., 2019); 0.006–0.178 µg/L detection limit and recoveries of 70–120% with Fe$_3$O$_4$ nanoparticles coated with reduced-graphene oxide (Santana-Mayor et al., 2018). However, the downsides to these advances are that they are delicate and expensive therefore they are not practical especially for developing countries.

Solid Phase Micro-Extraction

SPME employs a miniature automatic device to integrate sampling, enrichment and separation, purification, concentration and injection into one simple procedure which is more sensitive and environmentally friendly (Yang et al., 2015). Introduction of modulating agent into the synthesis fibers enhances PEs extraction efficiency significantly which is evident achieved satisfactory recoveries (Wang X. et al., 2019; Guo et al., 2019). In early 21st century, novel SPME systems with new selective coatings received much attention in the development of SPME (Mehdinia and Aziz-Zanjani, 2013). In 2010, a headspace SPME approach was established and optimized for analysis of sixteen PEs compounds in oil matrices with a special fiber as sorbent. This approach had the major advantage of not requiring any sample manipulation thereby minimizing cross contamination from glassware, solvents and samples. With minor modifications to the method, it has been employed by several other researchers in China for PEs analysis in marine water samples with relative standard deviations of less than 10% and different satisfactory recoveries; 68–114% (Zhang et al., 2017), 55.4–110.9% (Zhang et al., 2018b), in South Africa for WWTPs effluents; 75–116% (Salaudeen et al., 2018). However, the method's main drawbacks are that the fibers are rather expensive and tend to break (Yang et al., 2015).

Soxhlet Extraction

This method is applicable to the extraction of non-volatile and semi volatile organic compounds from solids such as sediments,

sludges, soils and solid wastes (Sibali, 2008). Soxhlet extraction uses relatively affordable glassware and organic solvents. Once loaded it requires no hands-on manipulation and provides efficient extraction. In one study by Liu et al. (2014), SE was used for sixteen PEs analysis from urban lakes and rivers in China, with reported recoveries of 61–112% and average relative standard deviations of less than 10% for water and sediments samples. In South Africa, SE optimized and applied for PEs extraction on soil and sediments samples from Muledane open dump, Thohoyandou, Limpopo province, with recoveries of between 88–90% (Adeniyi et al., 2008; Fatoki et al., 2010). Also, in Venda, Limpopo province, South Africa, Fatoki et al. (2010). With minor modifications and recoveries of 90–122%, SE was also optimized and applied for PEs extraction from sediments samples in Jukskei river catchment in Gauteng province of South Africa (Sibali et al., 2013).

Liquid-Liquid Extraction

LLE, also known as solvent extraction is a basic technique in the laboratory and a traditional method used to separate compounds based on their preferences for two different immiscible liquids, usually water and an organic solvent. It is an extraction of lipophilic compounds from aquatic medium which results in the water rich and the organic rich phases (Cai et al., 2007). LLE has been used in a couple of environmental studies involving the analysis of PEs in aquatic ecosystems (Cai et al., 2007; Fatoki et al., 2010; Hadjmohammadi and Ranbari, 2011; Sibali et al., 2013). Fatoki et al. (2010), optimized and applied LLE for PEs analysis from Venda, Limpopo province, South Africa, with recoveries of 81–90% and relative standard deviation of less than 5%. In Africa,

with minor modifications, Sibali et al. (2013) also successfully optimized and utilized the LLE method to extract PEs from water samples collected in Jukskei river catchment in Gauteng province of South Africa with recoveries of 95–122% and relative standard deviation of less than 10% while Nantaba et al. (2021) obtained recoveries of 83–115% in Lake Victoria of Uganda. Some of the benefits for LLE are the easy phase separation, rapid partition equilibrium, less toxicity and good compatibility for the subsequent determination (Cai et al., 2007).

Ultra-Sonication Extraction

Selvaraj et al. (2015), utilized the method to extract PEs from the sediments with good recoveries of 79–121% in India. With minor modifications, USE method was also applied to extract PEs from sediments in China, recoveries of 69–123% and relative standard deviations of less than 10% were reported (Wang et al., 2017; Zhang et al., 2017; Zhang et al., 2018b; Weizhen et al., 2020). Li et al. (2015), also employed the method on biodegradation of both diethyl phthalate and dibutyl phthalate esters from marine sediments albeit with no percentage recovery reported, this demonstrate the applicability of the method.

Sample Clean-Up and PEs Analysis

Extracts from environmental samples usually contain large amount of other potential interfering organic compounds which could give rise to high background during instrumental analysis, hence a clean-up process is necessary before analysis. More often, this is done by adsorption chromatography in the form of aluminum oxide, florosil or silica gel columns which traps unwanted compounds. Should the clean-up step be omitted the

TABLE 6 | Some of the recent extraction and analysis methods applied on environmental matrices.

Country	Extraction method	Environmental matrix	Recovery rate (%)	Detection limit (µg/L)	Instrumental analysis	References
India	SPE	Water (river)	33–121	0.47–1.22	GC-MS	Selvaraj et al. (2015)
Spain	SPE	Water (wastewater/pond)	70–120	0.006–0.178	HPLC-MS/MS	Santana-Mayor et al. (2018)
Korea	SPE	Water (lake)	77–112	0.001–0.021	GC-MS	Lee Y.-M. et al. (2019)
China	SPE	Water (lake)	79–91	0.009–0.078	GC-MS	Ai et al. (2021)
China	SPE	Water (river)	76–110	0.008 (LOQ)	GC-MS	Cheng et al. (2019)
China	SPE	Water (river)	71–130	0.0001–0.075	GC-ECD	Weizhen et al. (2020)
China	SPME	Water (marine)	68–114	0.0004–0.00032	GC-MS	Zhang et al. (2017)
Iran	SPME	Water (surface/river)	98–102	0.017–0.035	GC-FID	Abtahi et al. (2019)
China	SPME	Water (lake)	66–122	0.003–0.033	GC-MS	Li et al. (2021)
South Africa	SE	Water (river)	90–122	0.027–0.056	GC-FID	Sibali et al. (2013)
China	SE	Sediments (river)	68–119	0.00044–0.055	GC-MS	Sun et al. (2013)
China	SE	Sediments (river)	61–112	0.00112–0.00859	GC-MS	Liu et al. (2014)
China	SE	Sediments (river)	76–110	0.008 (LOQ)	GC-MS	Cheng et al. (2019)
China	SE	Sediments (marine)	94–141	0.00005–0.00132	GC-MS	Mi et al. (2019)
Iran	LLE	Water (river/marine)	92–102	0.9976–0.9993	HPLC-UV	Hadjmohammadi and Ranbari (2011)
South Africa	LLE	Water (river)	81–122	0.027–0.056	GC-FID	Sibali et al. (2013)
Uganda	LLE	Water (lake)	83–115	0.0002–0.001	GC-MS	Nantaba et al. (2021)
China	USE	Sediments (river)	71–125	0.0008–0.00038	GC-MS	Wang J. et al. (2014)
India	USE	Sediments (river)	79–108	0.47–1.22	GC-MS	Selvaraj et al. (2015)
Taiwan	USE	Sediments (marine)	83–107	0.0033–0.0432	GC-MS	Chen et al. (2017)
China	USE	Sediments (wetlands)	84–110	0.35–0.78	GC-MS	Wang et al. (2017)
China	USE	Sediments (marine)	76–105	0.00012–0.0016	GC-MS	Zhang et al. (2018c)
Iran	USE	Sediments (marine)	68–111	0.007–0.027	GC-MS	Arfaeinia et al. (2019)
Korea	USE	Sediments (lake)	89–118	0.104–1.32	GC-MS	Lee Y.-M. et al. (2019)
China	USE	Sediments (river)	75–123	0.0001–0.075	GC-ECD	Weizhen et al. (2020)

crude extracts are likely to contaminate the capillary column during instrumental analysis. Generally, the glass column is prepared by packing it with glass wool at its base and about 1–5 g of silica gel/florisil/aluminum oxide slurry in extracting solvent, anhydrous sodium sulfate is added above the column packing material (about 1 cm) to dehydrate the extracts. The column is saturated with extracting solvent, extract loaded on to the column and eluted with enough extracting solvent to ensure that all target compounds are eluted. The final eluate is concentrated to about 1 ml before Gas chromatography (GC) analysis (Fatoki et al., 2010; Sibali et al., 2013; Liu et al., 2014; Lee Y.-M. et al., 2019) or liquid chromatography (LC) such as high performance or Ultra performance coupled with mass spectroscopy (MS) (Santana-Mayor et al., 2018; He et al., 2020).

Development of gas chromatograph fused-silica capillary columns has resulted in an increased separation powers for PEs (Liu et al., 2013; Yang et al., 2015). This is greatly due to the general low molecular weight, relatively low polarity and thermal stability of PEs. GC methods combined with mass spectroscopy (MS), MS/MS, Electron capture detector (ECD) or flame ionization detectors (FID) have steadily become the main tool for identification and quantification of PEs in the 21st century (Yang et al., 2015; Salaudeen et al., 2018; Weizhen et al., 2020), and to some extent, LC coupled to MS detector (He et al., 2020). Common methods used for determination and analysis of PEs from different environmental matrices are based on GC-MS/FID (Sibali et al., 2013; Qureshi et al., 2016; De Toni et al., 2017; Zhang et al., 2018c; Salaudeen et al., 2018; Li et al., 2020), GC-ECD (Weizhen et al., 2020), Stir-Bar Sorptive Extraction-Thermal Desorption (SBSE-TD)-GC/MS (Heo et al., 2020), Ultra Performance Liquid Chromatography (UPLC) coupled to a Quadrupole Time of Flight Mass Spectrometer (TOF-MS) (He et al., 2020), ultra-high-performance liquid chromatography coupled to triple quadrupole tandem mass spectrometry (UHPLC-QqQ-MS/MS) (Santana-Mayor et al., 2018). Quantification of PEs is generally performed using internal standard calibration method (Liu et al., 2014; Lee Y.-M. et al., 2019; He et al., 2020; Li et al., 2020; Weizhen et al., 2020). **Table 6** gives a summary of various extraction methods used on different environmental matrices, percentage recovery rate, detection limits and analytical instrument used.

All methods discussed demonstrate their fair share in terms of applicability and reliability for PEs extractions from different environmental matrices by yielding good and acceptable recoveries, especially the solid phase extraction. However, development of covalent organic framework absorbents for solid phase extraction is a delicate and time-consuming process. USE has also yielded great recoveries, but the downside is the need for hands-on and multiple extraction processes to concentrate the extracts. Although solid phase micro-extraction is regarded as an innovative solvent free extraction method with satisfactory recoveries, it is very technological which limits the applicability of the method, especially to under-developed and developing countries

without access to state-of-the-art instrumentations. It was also noted from the reviewed research that LLE was barely utilized in the last decade, instead SPE and SPME have become the most preferred methods for PEs extraction from aquatic water matrices.

CONCLUSION

Occurrence of PEs in the environment is undoubtedly of great concern and more so in aquatic ecosystem where diverse sources are responsible for input of these toxic pollutants into the water and sediments. Biomonitoring studies elsewhere have clearly demonstrated that both human and aquatic life exposure from PEs polluted water is ubiquitous. PEs toxicity in aquatic ecosystems has been shown to affect biota therein and is also associated with human exposure and health risks that result from human contact, ingestion of contaminated food (e.g. fish and crops irrigated with PEs polluted water), and inhalation. Different toxicity studies have characterized the adverse effects (hatchability, embryonic development, and sex ratio) of PEs on different tissues, organs, and systems of aquatic organisms. The need to protect water resources and the aquatic ecosystem is well demonstrated through the multitude monitoring and toxicity data availed from various researches. Different sources of exposure to PEs are well documented but several questions about cumulative exposures, contributions of various sources in toxicity and mixed exposures remain partially answered. While the review here has demonstrated that there has been a lot of research characterizing and monitoring PEs in aquatic ecosystems and their effects on humans and other living organisms, very limited action has been implemented toward strict regulation and regulatory enforcement for these compounds in many developing countries. Although several countries have made efforts to regulate and limit the distribution and application of PEs by various industrial fields, through the establishment of various policy thresholds that restrict and limit the amount of PEs on certain products, and tolerable intake through MRLs and TDI for individual PEs per person. However, these efforts seem to be ineffective as exposure to PEs is exacerbated by the expanding human population and increasing PEs production and widespread application in various industries. There is ongoing need for regulatory agencies to put in place more research informed environmental, health-protective and legally binding regulations as well as enforcing them.

AUTHOR CONTRIBUTIONS

All the authors contributed to the drafting, revision and approved the submitted article version. NB took responsibility of handling the compilation of article as first author while MT took the lead role on submission and revision of the article as corresponding senior author.

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