Phthalate Esters (PAEs): Emerging Organic Pollutant in Aquatic Ecosystems

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Abstract

One of the most produced organic chemicals is known as Phthalate esters (PAEs) which are also excessively used with huge applications in industrial procedures as well as in packaging, medical centers, cosmetics, painting, agriculture, and consumer product uses. These organic pollutants are ubiquitous in the environment, mostly due to uncontrolled urbanization and are a cause of adverse impacts on humans and other living organisms. They even possess carcinogenicity characteristics and endocrine disrupting properties in the aquatic environment through their metabolites. Several studies were found to report the disrupting impacts these compounds make with their prevalence, toxicity, and exposure paths in the aquatic system, including humans. Waters are specifically vulnerable to PAEs because of the various sources of input through land runoff, agriculture, urban households, leaching of wastes etc., thus making it an emerging pollutant in the water. However, modern methodologies and instrumentations have been successful to measure even small amounts of PAEs in lakes, rivers, oceans, and other samples of aquatic systems. This study aims to *provide a thorough study of the distribution and characteristics of phthalate esters and their effects on aquatic ecosystems including aquatic organisms and humans all over the world. These data will be beneficial for understanding the overall distribution of PAEs in the aquatic environment and reducing their ecological footprint.*

Keywords: PAEs, Aquatic ecosystem, Endocrine disruptor, Drinking water, Surface water, Wastewater.

1. Introduction

Phthalate esters (PAEs) are organic micro pollutants which have great public concern due to their serious ecological and human health effects. Phthalate Esters are used in industries that have a common chemical structure of dialkyl or alkyl/aryl esters of 1,2-benzenedicarboxylic acid (Annamalai and Vasudevan, 2020; Giuliani et al., 2020). Phthalic anhydride and suitable alcohol produce phthalic acid's easters which are known as PAEs (Howdeshell et al., 2008; Vats et

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al., 2020; Giuliani et al., 2020). Phthalic anhydride and suitable alcohol produce phthalic acid's easters which are known as PAEs (Howdeshell et al., 2008; Vats et al., 2013). The polar carboxyl group only provides some characteristics of PAEs if the small alkyl groups, generally presented by R and R' such as methyl or ethyl are present.

Some of the PAEs that are used on a daily basis in usable products include (DMP), benzylbutyl phthalate (BBP), diisobutyl phthalate (DIP), di-n-butyl phthalate (DBP), diethyl phthalate (DEP), di-n-octyl phthalate (DOP), dicyclohexyl phthalate (DCHP), bis (2-ethylhexyl) phthalate (DEHP), diisodecyl phthalate (DiDP), di-n-hexyl phthalate (DHP), and diisononyl phthalate (DiNP) (Wang et al., 2019; Dutta et al., 2020; Zhang et al., 2021).

PAEs also show a lower melting point and greater boiling points which contributes to their heat-transfer abilities (Giuliani et al., 2020). PAEs can be linear and branched types, both of which are used in plastic production. Less volatilities are the reason for linear structures to have extraordinary flexibilities, and volatility being a concern, lower alkyl chain containing PAEs are not often used to produce plastics. Many daily activity items can contain PAEs including paint, vinyl flooring, printing ink, adhesive, packaging materials, capsules for medicine, cosmetics, packaging etc (Giuliani et al., 2020; Zhang et al., 2021).

PAEs are increasing their commercial needs, as a result, they are being used at a great amount since the 1930s (Wang et al., 2018; Heo et al., 2020) with an estimated global production of 6-8 million tons annually (Seyoum and Pradhan, 2019). The primary use of the PAE compounds can be found in enteric coatings, pills, stabilizer film, lubricants, emulsifying agents, suspending agents, dispersants, viscosity controlling agents and many more; mainly they are utilized as plasticizer (Ji et al., 2014; Wang et al., 2015; Wang et al., 2018; Heo et al., 2020; USEPA, 2021). PAEs are used by adding these substances to different plastic materials. Some of the plastic materials that contain at best 60% of PAEs are polyvinyl chloride (PVC), polyethylene terephthalate, polyethylene, polyvinyl acetate, etc. They are beneficial to increase the plasticity and extensibility of plastic polymers (Giuliani et al., 2020). Some other uses of PAEs are in building equipment, agricultural products, medical instruments, toys for children, personal and health care products, waxes, textiles, glues and adhesives, etc. (Ling et al., 2007; Gao and Wen, 2016). Modern electronic devices like blood transfer and catheters were also reported to contain PAE's in some research (Chakraborty et al., 2019, Malarvannan et al., 2019). As the usage of PAE is increasing in different segments of the consumer cycle, it has gained the spotlight in research and studies have confirmed the presence of PAEs in different environments (Salaudeen et al., 2018; Ai et al., 2021; Li et al., 2021).

In this paper, the main focus is on the presence and effects of PAEs in aquatic environments. These compounds are known for their bioavailability, and they possess degradable nature, as a result, there are great possibilities of PAE accumulation in higher organisms as well as aquatic life (Arambourou et al., 2019; He et al., 2020; Zhang et al., 2021). Several secondary sources were used to conduct this review. Most recent reports and research covering the prevalence of PAEs and their adverse impacts as well as historical studies were analyzed to compile this review. Worldwide impacts of PAEs on the aquatic ecosystems were studied. Majority of the scientific journal articles and reports were taken from time between 2006 and 2022, but the recent (within 5 years) articles were prioritized. More than 2000 journal articles and reports were found using some keywords such as phthalate esters, phthalate esters in water, phthalate esters toxicity, treatment of phthalate esters, phthalate esters in aquatic ecosystems, phthalate esters bioaccumulation, phthalate esters in sediments, phthalate esters biodegradation, etc. Although not all the articles were directly relevant to the study, thus, around 79 articles were thoroughly read and used in the study. This study has highlighted the current knowledge of PAEs occurrence, ubiquity to identify impacts and toxicity of PAEs in aquatic ecosystems and human health. The aim of this research is to provide better knowledge and understanding toward the effects and distributions of PAEs as emerging organic pollutant in the aquatic environment.

2. Methodology

2.1 Data collection strategies

To reflect the overall condition of PAEs in the aquatic ecosystem a systematic literature review was conducted using the electronic search of Google scholar, ScienceDirect, and PubMed.

In addition, international monitoring organizations such as United Nations Environmental Program (UNEP), United States Environmental Protection Agency (USEPA), and World Health Organization (WHO) reported data was analyzed to know PAEs prevalence, impacts, reduction, and regulation strategies of different countries. From the large number of literatures, this review focused on studies from 2006 to 2022 but priorities in recent five years on aquatic ecosystem in different countries around the world. To exhibit the ubiquity of PAEs in aquatic ecosystem

18 countries PAEs level has studied and most of them was from Asia where 16 literatures was about China and 9 was from France which was shown in the map (Figure 1). Furthermore, the effects and toxicity of PAEs in environment and human health studied from several literatures were reported.

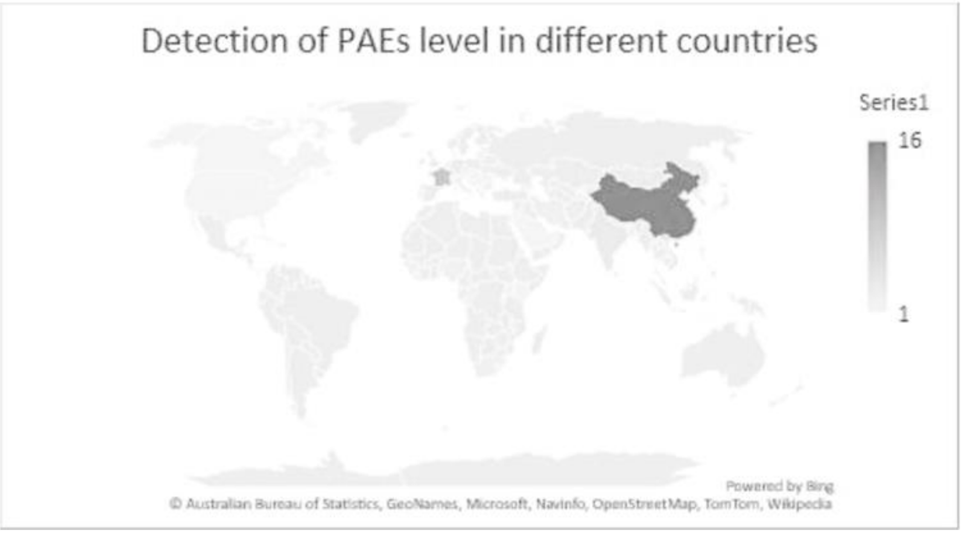
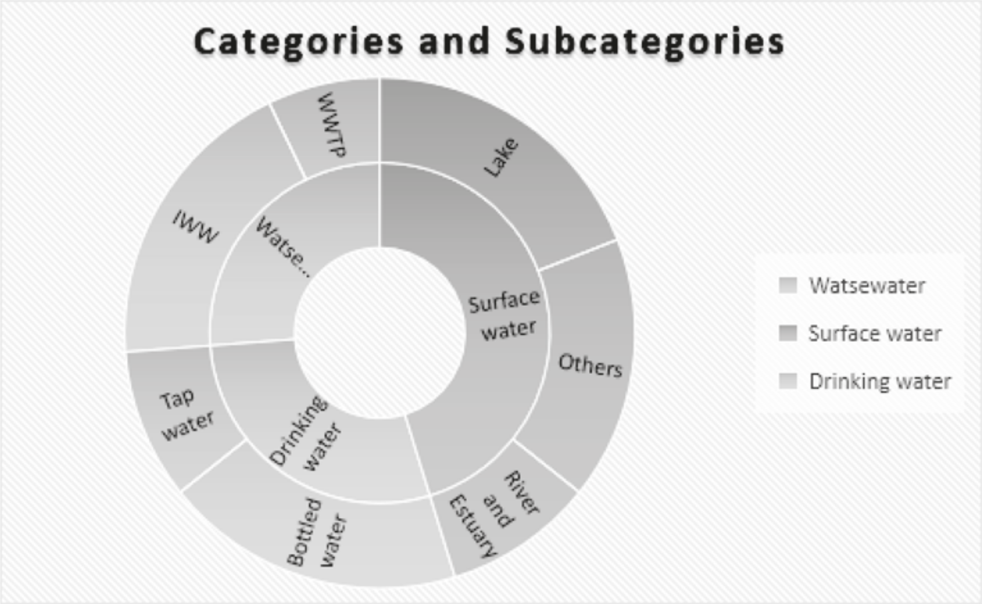


Figure 1: Geographic Locations of Detected Paes Level from Selected Literature



IWW=Industrial Wastewater; WWTP= Wastewater Treatment Plant

Figure 2: Category and Subcategory of Publications

The literature was screened with three categories which divided into seven subcategories (Figure 2). The selection criteria of the literature focused on those publications which was followed by authentic analytical methods and determined the concentration of PAEs individually. Literature on the concentration of PAEs was found by searching keywords as "Phthalates in Wastewater", "Phthalates in Surface, river and lake water", and "Phthalates in drinking water". Furthermore, impacts and toxicity of PAEs was studied by searching "Impacts and toxicity of PAEs in aquatic Ecosystem", "Impact and toxicity of PAEs in human health". The data collection strategies are depicted in Figure 3.

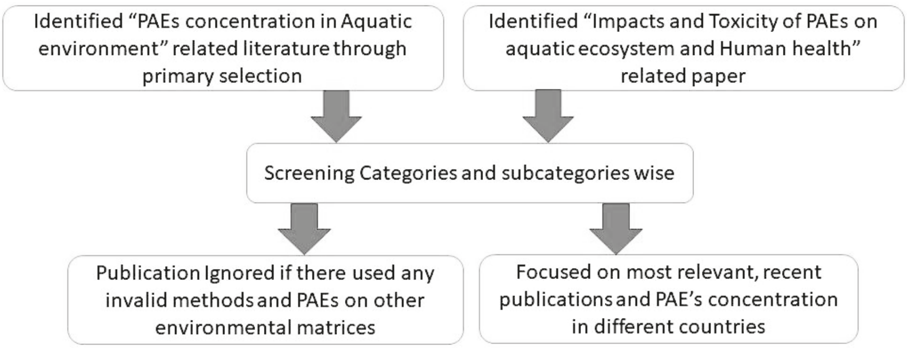


Figure 3: Data Collection Strategies on PAEs

3. Results and Discussion

3.1 Phthalate Esters

Phthalates are synthetic organic chemicals which consists of chemical structure with di alkyl or alkyl/ aryl esters of phthalic acid (Figure 4). Phthalates have low melting point (<-25°C) and it's an odorless chemical which make them a suitable compound as plasticizer (Stales et al., 1997). Therefore, it's not surprising that phthalate esters are ubiquitous compound in aquatic environmental matrices due to their widespread uses in industrial and domestic products.

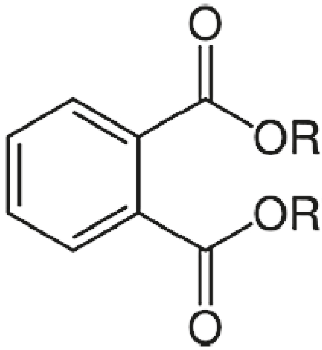


Figure 4: Phthalate esters general structure

This endocrine disruptor released into the aquatic environment via waste disposal, production, use and can easily leached out into water (Salaudeen et al., 2018; Henkel et al., 2019). As plastics is everywhere, plastic aged and degrades which increases the release of PAEs in the environment. Chinese Environmental Agency and United States Environmental Protection Agency selected six targeted PAEs as priority pollutant which included di-(2-ethylhexyl) phthalate (DEHP), dimethyl phthalate (DMP), diethyl phthalate (DEP), dibutyl phthalate (DBP), di-n-octyl phthalate (DnOP), butyl benzyl phthalate (BBP) (Wang et al., 2021). Table-1 depicted the potential application, properties, and toxicity parameters of six targeted phthalate.

Table-1: Physicochemical properties and potential application of six targeted phthalate (Wang et al., 2021, Baloyi et al., 2021)

PAEs	CAS	Molecular mass (g/mol)	RfD (mg/ kg/day)	Carcinogenic grade	Potential application
DEHP	117-81-7	390.56	0.02	B2	Medical devices, Tubing, blood storage bag, plastic toy, wall tiles, baby pants, dolls, food packaging, wire, cables, furniture materials.
DMP	131−11−3	194.18	10	D	Insecticides, adhesive, shampoo, air freshener, hair styling products.
DEP	84−66−2	222.24	0.8	D	Cosmetics, perfumes, deodorant, nail polish, pill coating,

					pharmaceuticals, Aftershave, makeup, lotion.
DBP	84−74−2	278.34	0.1	D	Nitrocellulose lacquers, explosives, nail polish, textile lubricating agent, printing ink.
BBP	85−68−7	312.36	0.2	C	Adhesive, vinyl flooring, carpet tiles, food packaging, and artificial leather.
DnOP	117−84−0	390.56	0.02	-	Mostly used in Children's toy. Other uses as dye carrier, plastisol, colourants.

RfD= reference dose for oral exposure; CAS= chemical abstracts service

Like other organic compounds, PAEs also lipophilic and extracted with lipid soluble chemicals. To detect PAEs in the aquatic environment EPA has provided standard methods (Table 2). Liquid Liquid Extraction (LLE) and Solid Phase Extraction (SPE) is the part of this method as sample preparation process. In SPE process, analytes are isolated from mixture in response to its physicochemical properties (Falenas, 2019). On Contrary, LLE is a basic technique uses two different immiscible liquids such as water and organic solvent according to the preference. Moreover, SPE technique uses in extraction process is increasing because of its easy application, ability to save solvent and time (Net et al., 2015). After extracting the analytes, GC method combined with mass spectroscopy (MS)/ flame ionization detectors (FID)/ Electron capture detector (ECD) used as a main tool for the identification and quantification of PAEs (Yang et al., 2015; Salaudeen et al., 2018; Weizhen et al., 2020)

Table-2: Standard method of detection PAEs level by EPA

Water Matrices	Extraction	Solvent	Quantification	EPA method No
Drinking water	LLE, SPE	Dichloromethane (DCM)	GC-MS	506, 525.2
Municipal and industrial wastewater	LLE	Dichloromethane (DCM)	GC-MS, GC-ECD	606, 625

3.2 Ubiquity of phthalate esters in aquatic ecosystem

In aquatic environment, PAEs concentration found trace μg/L to mg/L varying on their degree of uses in products all over the world. Also, the large variety and abundance of PAEs have been observed. However, the pollution and occurrence level mostly were mild to moderate. Furthermore, Previous studies indicate that most dominant PAEs in the aquasphere are DEHP, DBP, DMP, DEP, and BBP (Baloyi et. 2021; Luo et al., 2021; Zhao et al., 2020; Zheng et al., 2014).

3.2.1 Wastewater

Wastewater is one of the main hotspots of contamination of PAEs as industrial and domestic uses of PAEs in products end up in wastewater and transferred into different water matrices. Several literatures measured the concentration of PAEs in domestic and industrial wastewater (Table 3). Among all studied literatures, it has been observed that DEHP is higher in concentration in both wastewater where the highest amount found in Paris conurbation catchment WWTP (39.4-160 μg/L) and in Textile (38.8-248 μg/L). In Ikeja WWTP, Nigeria found greater level of PAEs including DEHP (15.7-43.5 μg/L), DMP (10.8- 24.9 μg/L), DEP (9.86- 16.6 μg/L), DBP (17.7- 25.3 μg/L), and BBP (0.52- 10.8 μg/L). PAEs were found in textile, pharmaceuticals, Aerospace, and cosmetic industries. PAEs in wastewater were found in several countries like India, France, China, Vietnam, Saudi Arab, South Africa, and Vietnam (Table 3). However, numerous countries didn't study the PAEs level in their wastewater yet.

Table-3: Concentration of PAEs in Wastewater in different countries

Matrices	Concentration in μg/L						Country	Ref
	DEHP	DMP	DEP	DBP	DnOP	BBP		
Wastewater Treatment Plants (WWTP)								
North Indian WWTP	n.d.-132	-	n.d.-20	0.8-90	-	n.d.-9	India	Gani et al., 2016
Paris conurbation catchment WWTP	39.4-160	-	5.23-17.7	0.60-3.31	-	0.46-3.91	France	Bergé et al., 2014
Harbin WWTP	1.7-25.4	n.d.-1.52	n.d.-1.37	3.47-4.13	1.11-14.15	n.d.-17.03	China	Gao et al., 2014
Fontenay-lesBriis WWTP	2.0 ± 1.2	0.03 ± 0.03	0.04 ± 0.05	0.14 ± 0.10	0.01 ± 0.01	0.16 ± 0.15	France	Tran et al., 2015

Riyadh WWTP	0.11-2.85	0-0.81	0-0.63	0.045-3.02	0-0.58	0-1.04	Saudi Arab	Al-Saleh et al., 2017
Ikeja WWTP	15.7-43.5	10.8-24.9	9.86-16.6	17.7-25.3	-	0.52-10.8	Nigeria	Olujimi et al., 2017
Adelaide WWTP	3.44–48.16	1.35-12.07	2.53-24.42	nd–451.48	nd–21.75	2.38–80.70	South Africa	Salaudeen et al., 2018
Hanoi WWTP	2.84-42.4	0.22-1.87	1.26–7.04	1.58–9.45	0.53-2.73	0.380–8.97	Vietnam	Le et al., 2021
Industrial Wastewater								
Textile	38.8-248	-	2.87-76.3	2.26-14.9	-	0.44-6.08	France	Bergé et al., 2014
Pharmaceutical	0.60-386	-	0.47-137	0.48-6.96	-	0.13-2.90	France	Bergé et al., 2014
Aerospace industries	0.80-33.3	-	0.22-4.85	0.44-1.19	-	0.03-2.21	France	Bergé et al., 2014
Cosmetic industries	6.04-85.2	-	112-120	0.37-1.19	-	0.04-0.04	France	Bergé et al., 2014
Domestic and industrial	4.1-13	0.26-0.81	n.d.-2.7	<0.1-0.47	n.d.-< 0.1	n.d.-0.11	Austria	Clara et al., 2010

3.2.2 Surface water

The level of PAEs was detected in surface water among different countries (Table-4). Unlike the concentration in wastewater the level of PAEs is lower in surface water. Adeniyi et al. (2011) detected greater level of PAEs (255-2705 µg/L) in Ogun River, Nigeria among all other studies. On contrary, Chepchirchir et al. (2017) found mild level of PAEs (0.001-0.1 µg/L) in Sosiani River, Kenya. Studies showed that frequently the standard level of annual DEHP (1.3 µg/L) in surface water exceeded (EU directive 2008/105/EC) (UNEP, 2020). PAEs detection and studies rate is higher in Asia due to not having restrictions in using PAEs unlike in developed countries such as USA and Europe (UNEP, 2020; Das et al., 2021; Li et al., 2021). Surface water is more contaminated with PAEs which are adjacent to industries and other notable anthropogenic activities such as manufacturing, Agriculture, solid waste disposal and wastewater treatment plants (Zhu et al., 2019).

Table-4: Concentration of PAEs in Surface water in various countries

Matrices	Concentration in µg/L						Country	Reference
	DEHP	DMP	DEP	DBP	DOP	BBP		
River water								
Hanjiang River	0.36-0.42	0.02-0.04	0.13-0.25	0.001-0.59	0.01-0.05	0.003-0.02	China	Dong et al., 2022
Yellow River	0.43-0.83	0.38-0.64	0.31-0.45	0.78-0.80	0.002-0.004	0	China	Zhao et al., 2020
Rhone River, France	0.4068	0.0057	0.0305	0.0405	n.d.	-	France	Paluselli et al., 2018
Jiulong River estuary	0.57-3.66	0.03-0.12	0.03-0.05	0.37-0.67	-	-	China	Li et al., 2017
Sosiani River	0.001-0.010	-	-	n.d.-0.140	-	0.002-0.008	Kenya	Chepchirchir et al., 2017
Huai River	0.08-1.52	0.02-0.19	0.02-0.92	2.17-21.98	-	0.02-2.16	China	Shi et al., 2016
Songhua River	2.26-11.55	0.98-4.12	1.33-6.67	1.69-11.81	0.69-6.14	nd-4.39	China	Gao and Wen, 2016
Kaveri River	0.51	0.02	0.24	0.03	0.25	0.04	India	Selvaraj et al., 2015
Pearl River	0.57	0.57	0.22	0.41	0.03	0.19	China	Li et al., 2014
Somme River	5.16-20.80	0.02-0.25	0.26-6.98	0.22-3.86	-	-	France	Net et al., 2014
Jukskei River	0.49-5.58	0.04-0.56	0.08-0.39	-	0.79-3.65	-	South Africa	Sibali et al., 2013
Selangor River	0.39	0.01	0.04	0.21	0.009	0.01	Malaysia	Santhi and Mustafa, 2013
Ogun river	255-480	n.d.	1480-1755	2025-2705	-	-	Nigeria	Adeniyi et al., 2011
Seine River Estuary	0.16-0.31	0.03-0.18	0.07-0.18	0.07-0.32	-	-	France	Dargnat et al., 2009
Lake and other surface water								
Hanoi Lake Water	1-48.7	0.11-2.95	0.64-14	0.78-34	n.d. – 7.31	0.18-21.1	Vietnam	Le et al., 2021
Taihu Lake	0.14-0.83	0.05-0.1	0.02-0.09	0.03-1.31	n.d.-0.10	0.04-0.16	China	Luo et al., 2021

Small Xingkai Lake	0.12-3.25	0.001-0.011	0.002-0.007	0.10-0.53	n.d.-0.004	0.001-0.005	China	Yang et al., 2021
Large Xingkai Lake	0.22–3.46	0.003-0.026	0.003-0.018	0.11–1.52	n.d.-0.007	0–0.002	China	Yang et al., 2021
Poyang Lake	0.023-0.896	n.d.-0.253	n.d.-0.127	0.121-1.297	nd-0.018	-	China	Ai et al., 2021
Lake Victoria	0.21−23	0.07−0.4	0.04−1.1	0.35−16	-	-	Uganda	Nantaba et al., 2021
U-Tapao canal	1.28-5.28	-	-	nd-3.36	-	-	Thailand	Kingsley and Witthayawirasak, 2020
Asan Lake	n.d.-1.34	n.d.-0.18	n.d.-0.05	n.d.-0.34	n.d.-0.02	n.d.	Korea	Lee et al., 2019
Lakes Shichaha	0.140-0.519	0.047-0.143	0.006-0.013	0.009-0.157	0.015-0.022	n.d.- 0.512	China	Zheng et al., 2014
Guanting Reservoir	0.043-0.149	0.023-0.084	n.d.-0.006	n.d.-0.594	0.013 0.029	n.d.- 1.246	China	Zheng et al., 2014
Lake Chaohu	n.d.-0.58	0.015-3.67	0.006-0.28	0.070-17.53	n.d.-0.045	n.d.-0.11	China	He et al., 2013
False Creek Harbor	0.17-0.44	0.002-0.005	0.05-0.35	0.05-0.244	0.005-0.04	0.002-0.006	Canada	Mackintosh et al., 2006

3.2.3 Drinking water

It’s a concerning issue that several studies found hazardous phthalates in drinking water (Table 5). Yousefi et al. (2019) measured that greater concentration of PAEs in bottled water in Iran and Abdolahnejad et al, (2019) found mild concentration in tap water in Isfahan, Iran. Bottled water contains higher concentration of PAEs than tap water (Table 5). Recent studies on PAEs in bottled water is increasing due to have high exposure especially DEHP is continuously exceeding its RfD value (Baloyi et. al., 2021; Abdolahnejad et al., 2019; Wang and Qian, 2021). DBP and DEHP are the most dominant compounds in drinking water among other phthalate esters (Yousefi et al., 2019). Loraine and Pettigrove (2006) and Liu et al. (2015) investigated PAEs concentration from the source of drinking water and found higher amount of DEHP and DBP.

Table-5: Concentration of PAEs in drinking water of different countries

Matrices	Concentration in µg/L						Location,Country	Ref
	DEHP	DMP	DEP	DBP	DnOP	BBP		
Bottled Water	0.257	0.38	0.198	0.317	0.248	0.633	South Delhi, India	Das et al., 2014
water filtration plants	2.67-5.94	0.098-0.78	0.899-1.49	1.44-8.34	-	0.053-1.19	San Diego, USA	Loraine and Pettigrove, 2006
Tap water	1.01–14.5	n.d. – 0.54	n.d. – 2.57	0.014–2.56	n.d. – 1.93	0.197–4.21	Hanoi, Vietnam	Le et al., 2021)
Bottled water	0.23-1.95	n.d. - 0.17	n.d. - 0.99	0.14-3.07	n.d. - 0.94	0.25-4.37	Hanoi, Vietnam	Le et al., 2021
Tap water	0.002-6	-	N.d-0.11	n.d.-0.07		n.d-0.1	Isfahan, Iran	Abdolahnejad et al., 2019
Bottled water	0.24-0.73	-	-	8.98-11.5	n.d-1.60	n.d.-0.69	Chengdu, China	Yin et al., 2019
Tap water	1.84-2.68	-	-	n.d.-2.04	-	-	Sadao, Thailand	Okpara et al., 2022
Bottled water	6.93	2.23	5.92	6.53	-	-	Sari, Iran	Yousefi et al., 2019
Bottled Water	2.18	-	-	3.23	-	-	Cluj-Napoca, Romania	Wang and Qian, 2021)
Waterworks	5.51	0.76	0.19	1.56	0.24	0.35	Qingdao, China	Liu et al., 2015

3.3 Impact on Aquatic Ecosystem

PAEs are currently discovering as a threat to aquatic habitats. The key attributes of effects on ecosystems are continuous inputs and intrinsic toxicity. Anthropogenic activities can contribute huge number of PAEs to the adjacent aquatic ecosystems like lakes, rivers, canals etc. that are situated or crosses agricultural and industrial areas, as well as urban residents (Salaudeen et al., 2018; Ai et al., 2021; Li et al., 2021). Certain anthropogenic activities act as the primary source of PAEs on aquatic ecosystem by releasing phthalate due to industrial activities, landfills, wastewaters, household wastes regardless of some freshwater algae and cyanobacteria being able to produce monoethylhexyl phthalate under natural states (Zhang et al., 2019; Zhang et al., 2021). PAEs generally possess high octanol-water partition (K_{ow}/log K_{ow}25) (1.61–9.46) and low vapor pressures (Pa25) (1.84 × 10−6–0.263), as a result, they are less volatile which makes them flexible to enter different water bodies and ecosystems (Net et al., 2015; Das et al., 2021; Zhang et al., 2021). The higher molecular weight PAE's tend to show higher sorption to organic matter, which is a result of increased hydrophobicity. The escalation of hydrophobicity happens due to rising alkyl chain length which increases the Kow value (Das et al., 2021; Zhang et al., 2021).

Aquatic organisms are exposed to PAEs followed by their entrance into the system. High nutrient-grade organisms may get exposed to PAEs by ingestion, afterwards they are moved up the food chain; the system is affected my PAEs in several manners. The effects are dependent on their capability to show toxicity to aquatic organisms and ecosystems. Some of the most toxic PAEs are BBP, DEHP, and DBP (Staples et al., 1997; Aarab et al., 2006; European Commission, 2008; Arambourou et al., 2019; Zhang et al., 2021); as a result, they pose the most toxic effects to aquatic organisms (Crafford and Avenant-Oldewage, 2010). A study by Staples et al. (1997) showed that the exposure of these compounds as well as DMP, DEP, DIBP, DAP were responsible to create both acute and chronic effects in organisms including fish, invertebrates and algae. The fact is also supported by Zhang et al. (2021) who showed such effects with symptoms of necrosis, cardiac edema, crooked tails, lack of tactile response etc. More harmful effects such as liver, kidney damage, effects on reproduction etc. were observed on adult life forms (Gao et al., 2018).

PAEs containing lower molecular weight are only toxic in concentrations that are lower than their aqueous solubilities. As the alkyl chain length increases, the toxicity also follows up to 4 atoms of carbon (Staples et al., 1997). Unfavorable effects on aquatic life forms were seen from some studies of ecotoxicity that showed broad range of endpoints which were at much decreased level (ng/L to μg/L) than the recent ones (Oehlmann et al., 2009; Zhang et al., 2021).

The LC50, also known as the median lethal concentration, is the determinant of chemical substance toxicity in organisms (Huang et al., 2020; Zhang et al., 2021). Moreover, Zhang et al. (2021) studied a dose of 96h LC50 range on common carp for the PAEs DEP, DBP, DOP, and DEHP and found similarities with marine flounder and Nile tilapia in the DEP and DBP lethal concentrations. Microalgae possess the ability to degrade PAEs, so as a result some benthic diatom such as *Cylindrotheca closteriums* were found to catalyze the deconstruction of DEP and DBP instead of being affected by those (Li et al., 2015) Although some short chained PAEs have a tendency to bioaccumulate, studies found them to be decomposable in nature (He et al., 2020; UNEP, 2020).

Despite of the PAE's ubiquitousness, studies about those including their exposure route to human and behavior of bioaccumulation failed to gather much information. Although their accumulation rate in biota was explored by eco-toxicological research. A study by Net et al. (2015) presented their results on how larger bioaccumulation factor (BAFs) values can cause the accumulation of PAEs in different species at a higher capacity. Variances of the values were also reported in several studies which directs toward a more detailed and improved system of monitoring of PAEs in the aquatic system (Baloyi et. al, 202). Most vulnerable are those communities who benefit from the waters for fishing, personal use, irrigation use etc. and needs more research and continuous monitoring. The fact was supported by He et al. (2020) in his study about a Chinese river-water dependent village when PAEs were found in livestock meat samples. An important relationship between the biota of the area and adjacent river water was also noted by the research team which points to the possibility of river water influencing PAEs uptake and bioaccumulation (He et al., 2020). PAEs containing molecular weights that are higher than usual have showed extraordinary capability of accumulation in sediments (UNEP, 2020).

3.4 Phthalate Toxicity, Exposure and Effects on Human Health

Humans are continuously exposed to endocrine and metabolic disruptor phthalate esters from different compounds in small quantities from thousands of industrial and household products including cosmetics, toys, foods, packaging materials, beverage and drinking water (He et al., 2020; Abtahi et al., 2019; Gong et al., 2018). Humans are exposed from aquatic ecosystem to this chemical through different routes such dermal skin, inhalation, ingestion, and absorption by consuming foods and drinking water (Giuliani et al., 2020; Abtahi et al., 2019; Paluselli et al., 2018). PAEs arises as global concern due to their toxicity, mutagenic and carcinogenic characteristics to humans on exposure (Gao and Wen, 2016; Li et al., 2020; USEPA, 2021). Exposure to PAEs varying different levels by acting as an endocrine disruptor. Endocrine disruptor referred as active hormone agent that act like hormone in the endocrine system and causes physiological dysfunction (Talia et al., 2021; You and Song, 2021; Darbre, 2019). Most concerning issues about this endocrine disruptor posits that low dose of this chemical can interfere with reproduction, growth and other hormonal mediated process (Zoeller et al., 2014; Gore et al., 2015). Though endogenous hormones are typically present in human body, tiny amount of exogenous hormonal active substances can cause severe impacts. Several studies showed some other effects of PAEs on human exposure which listed in (Table 6).

Table-6: Summarized health effects of PAEs from different studies

Exposure measure	Health effects	Ref	Sex	Age
Urine	Atopic dermatitis	Blakeway et al., 2020	All	All
Urine	Endometriosis	Cai et al., 2019	Female	Adult
Urine	Breast Cancer	Fu et al., 2017	Female	Adult
Multiple	Cardiometabolic risk factors, and Obesity	Golestanzadeh et al., 2019	all	Children
Multiple	Semen quality and sperm DNA damage	Høyer et al., 2018	M	Adult
Multiple	Autism	Jeddi et al., 2016	all	children
Urine	Neurodevelopment disorders	Lee et al., 2018	all	children
NR	Early onset puberty	Poursafa et al., 2015	all	children
Urine	Fertility	Vabre et al., 2017	Female	Adult
Blood	Fetal sex hormone changes, Anogenital distance, hypospadias, cryptorchidism; other congenital malformations	Marie et al., 2015	all	Infant
Indoor Air	Asthma	Li et al., 2017	all	children

Human biomonitoring studies shows that the half-life of PAEs on urine and/or blood plasma of human and rodents is less than 24h (Wang et al., 2019; Giuliani et al., 2020). While DEHP binds with blood plasma protein, biliary excretion, and enterohepatic circulation in humans have been indicated that major elimination pathway of PAE is urinary excretion (Frederiksen et al., 2007; Wang et al., 2019). Jiang et al. (2018) investigated that high urinary phthalate metabolites in pregnant women have experienced lower hemoglobin concentrations, increased blood clotting time, and increased likelihood of anemia (Jiang et al., 2018). Also, PAEs have serious adverse effects on development and functioning of male reproductive organs (Xie et al., 2019).

There are several available literatures based on occurrence and levels of PAEs for suggestions to avoid or minimize the exposure to PAEs. Suggestion to minimize the effects of PAEs with limited evidence are- minimal use of personal care products, using alternative of plastics and can for packaging foods, avoiding nutritional supplement, no micro waved foods, frequent handwash and balanced diet (Koniecki et al., 2011; Braun, 2017; Wang et al., 2019). A study by Chen et al. (2015) explored these PAEs exposure minimizing strategies among 30 young girls and post inventory results found that Phthalate metabolites significantly reduced within one-week intervention period. Frequent hand wash ($P = 0.009$) and avoiding uses of plastic cups (*P* = 0.016) were most significant among all strategies to reduce phthalate metabolites in urine, particularly, DEHP and mono-n-butyl phthalate (MBP) (Chen et al., 2015). It is also recommended to avoid using untreated river and lake water as those could be major source of exposure to phthalate, especially in rural areas where clean water is limited. Another study in China by He et al. (2020) found that using untreated river water is responsible for 79, 83, and 88% of the estimated PAEs daily intake in toddler, children and adults and revealed an increasing trend with age (He et al., 2020). It's also notable that consuming meats, some vegetables (He et al., 2020) and some corns (Rice, and wheat) (Sun et al., 2015; Xu et al., 2020) serve as a source of PAEs exposure. Therefore, consuming organic farm foods which contains no synthetic products would be the best suggestion to avoid PAEs exposure **through ingestion.**

Table-7: Toxicity of PAEs

Phthalates	MRLs/TDI	Toxicity	Citation
DEHP	100 (MRL-Chronic)	Reproduction	ATSDR 2021
	60 (MRL-Intermediate)		
	50 (TDI)		
DBP	500 (MRL- Acute)	Reproduction, Development	ATSDR 2021, European Food Safety Authority 2019
	10 (TDI)		
DEP	7,000 (MRL-Acute)	Reproduction	ATSDR 2021
	6000 (MRL-Intermediate)	Hepatic	
BBP	500 (TDI)	Reproduction	European Food Safety Authority 2019

UNEP (2020) published an assessment report on chemical and wastes issues on posing human health and environmental risk and reviewed that several countries have taken measures to reduce the PAEs exposure. Denmark has successfully reduced the risk of PAEs exposure by imposing tax on using PVC and PAEs and repealed the enforce in 2019 as part of successful reduction of overall PAEs utilization. The Korean Ministry of Food and Drug Safety and though National Food Safety Standard in China prohibited usages of DBP, BBP, and DEHP. China also banned the use of DBP, BBP, DEHP, DOP, DiNP, and DiDP in textile products. Canadian Government banned in using DEHP in cosmetics and BBP, DBP, DEHP, DOP, DiNP, and DiDP restricted in using (below 1 mg/kg). Other countries like Peru and Columbia prohibited using BBP, DBP, DOP, DEHP, DiNP, and DiDP in plastics for children (UNEP 2020). To minimize the widespread effects of PAEs on health and environment, the concerned world leading international organizations need to monitor and regulate the PAEs level. Several international organizations like Agency for Toxic Substances and Disease Registry (ATSDR) and European Food Safety Authority EFSA regulated PAEs toxicity by setting limit in the form of Minimal Risk Levels (MRLs) and Tolerable Daily Intake (TDI) (Table-7). United States National Academies of Sciences, Engineering and Medicine (2017) obtained that current toxicity method can identify DEHP hazard but cannot determine the level at which human can be affected. In addition, some references doses and safe limits are set by regulating agency based on animal testing which couldn't be safe limit for human (UNEP, 2020). It's high time to discover methods for monitoring studies on human samples. A survey conducted in 2015–2016 by National Health and Nutrition Examination Survey (NHANES) and found that mostly affected community to high concentration PAEs are people living under the poverty line (USCDC, 2018; USEPA, 2018). Another similar trend found in children who lives under low socio-economic income household (Navaranjan et al., 2019; UNEP, 2020). Now the concerning issue that there is not identified limits of daily intake or minimum risk level for most of the PAE compounds. Another worrying and notable fact that these compounds are not regulated in most of the developing countries; hence their impacts could be catastrophic and they are not measuring the level PAEs in their environmental matrices and no epidemiological report has published yet (Baloyi et al., 2021).

4. Conclusion

Presence and distribution of PAEs in environment, specifically in aquatic systems, is one of the most significant issues which needs instant attention. Various point and non-point sources are responsible to contribute the pollutants in the water, thus making it a great concern and several studies supported the fact by showing the exposure of PAEs on aquatic life as well as humans. Studies have focused on the toxicity and its effects of PAEs on aquatic organisms' organs, tissues, and other parts, which have demonstrated a clear need of protection of the water resources and monitoring. Although the various exposure sources have been brought under light by many researchers, studies on integrated and mixed exposures, effects of different sources were limited. This review was done to gather information about the research that focused on the monitoring and characterization of PAEs, while highlighting their adverse effects on humans and other aquatic organisms in aquatic system. However, it is also observed that implementation of strict regulations on PAE supplies in the aquatic systems of developing countries were very limited. The effort of some countries to regulate and monitor the spread of PAEs by various measures were seen to be ineffective. It is the result of burgeoning population of humans that have caused excessive production of PAE as well as its ubiquitous applications. Thus, more focused research in this area is a matter of great concern.

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