



# A critical review on extraction and analytical methods of phthalates in water and beverages

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## ABSTRACT

Phthalates (PAEs) are the class of lipophilic chemicals, which are used as additives in the manufacturing of plastics. It results in presence of PAEs in water and beverages because of their migration capacity. Their presence has attracted considerable attention due to their potential impacts on ecosystem functioning and public health. In addition, an enormous number of research articles have been published between 2000 and 2020, which have been identified and their results have been tabulated displaying PAEs analyzed, matrices, sample preparation, analytical method used, the limit of detection (LOD), and recovery percentages. Numerous sample preparation and analytical methods are found which are suitable for the reliable determination of the PAEs. The analysis of the PAEs is difficult due to their ubiquitous presence and their complexity, therefore suitable precautions, should be taken into account. In this review, we provide an overview of various pre-treatment measures and detection methods for PAEs in several types of water and beverages, mainly focusing on the last 20 years published works have been discussed. Pre-treatment methods mainly include liquid-liquid extraction (LLE), solid-phase extraction (SPE), solid-phase microextraction (SPME), liquid-phase microextraction (LPME), and many more rare techniques. Chromatographic and non-chromatographic techniques coupled with or without diodes, spectrophotometers, and detectors, have been described. The concept of "green analytical chemistry" for PAE determination has also been discussed. Hereby, the limitations and challenges in these applications are also included.

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## 1. Introduction

Since the dawn of history, humans have endeavored for the development of many materials with benefits that are not found naturally. One such was the invention of plastic in the early 20<sup>th</sup> century reaching its peak within the next 100 years. The Discovery of Plastic was revolutionary because for the first-time human manufacturing was not constrained by the limits of nature [1]. In 1855, Alexander Parkes established the foundation for the "plastic era" when Parkesine (celluloid) was invented from cellulose. Followed by the discovery of the first polymerized plastic, Polyvinyl chloride (PVC) was discovered between 1838 and 1872. Later on, a key breakthrough occurred in 1907, when the first real synthetic plastic Bakelite was manufactured by the Belgian American chemist Leo Baekeland [2]. According to EPA in 2018, about 380 million tons of plastic are annually produced, of which only 19% are recycled and only 12% are incinerated. It is believed that humans consume

at least 50,000 microplastic particles through food and water in a year.

Phthalates, or phthalic acid esters (PAEs) are a class of lipophilic chemicals that are added as additives during manufacturing to soften the plastics. In the 1920s, as an alternative to camphor phthalates were first introduced. They are well known for their durability, stability, and flexibility to soften plastics, they were known as plasticizers. Pieces of evidence show that microplastics have the great potential to act as a carrier as well as a transporter of chemicals into the organisms [3]. These plastics were coated with toxic chemicals like phthalates when metabolized on exposure, these leach off and incorporates into the animal tissue, inducing serious health risks [4]. Mainly, these are released from a product by heat, agitation, or prolonged storage during any stage of the product life-cycle from production via usage to disposal.

Monitoring of PAEs in beverages and water has become a necessity because ingestion, inhalation, skin absorption, and intravenous injection are the potential pathways for exposure. They are readily absorbed into the human body and are converted into their respective metabolites and they tend to pass out of the body through urine and feces [5]. PAEs are ubiquitous – air (atmospheric aerosols and indoor air), rivers, marine, sediments, soils, samples,

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**Table 1**  
Physico-chemical properties of phthalates.

PAEs	CAS Registration number	Molecular Formula	Molecular Weight	Specify gravity (20 °C)	Water solubility (mg/L)	Melting point (°C)	Boiling point (°C)	No. of carbon atoms per chain
Dimethyl phthalate (DMP)	131-11-3	C <sub>10</sub> H <sub>10</sub> O <sub>4</sub>	194.18	1.19	4000	5.5	283.7	1
Di-ethyl phthalate (DEP)	84-66-2	C <sub>12</sub> H <sub>14</sub> O <sub>4</sub>	222.24	1.12	1000	-40	298	2
Di-n-butyl phthalate (DBP)	84-74-2	C <sub>14</sub> H <sub>38</sub> O <sub>4</sub>	278.35	1.05	11.2	-35	340	4
Butyl benzyl phthalate (BBP)	85-68-7	C <sub>19</sub> H <sub>20</sub> O <sub>4</sub>	302.39	1.11	2.7	-35	370	4,6
Di-2-ethyl hexyl phthalate (DEHP)	117-81-7	C <sub>24</sub> H <sub>38</sub> O <sub>4</sub>	390.62	0.99	0.003	-40	384	8

instruments, and even in chemicals and biota, therefore, there is a difficulty in analysis of real samples with low concentrations [6]. The analysis of PAEs in beverages or water is a big challenge due to their intricacy as well as the presence of a mixture of contaminants.

This review article aims at providing a general overview of phthalates, physio-chemical properties, toxic effects, and different analytical methods both sample preparations along with detection methods which are currently being applied for analysis of PAEs from 2000. This article also discusses challenges encountered in any analytical laboratory, which helps in solving them to guarantee a reliable analysis.

### 1.1. Physicochemical properties of PAEs

Phthalates or Phthalic acid esters usually called PAEs are the compounds that are synthesized by double esterification from phthalic anhydride and specific alcohols [7]. The general structure of phthalate ester mainly consists of a planar aromatic benzene ring attached with two carboxyl groups at R and R' positions and its chemical formula is C<sub>6</sub>H<sub>4</sub>(CO<sub>2</sub>H)<sub>2</sub>. Commonly, at room temperature phthalates are colorless, odorless oily liquids in nature with the high boiling point, low melting points, low volatility, and poor solubility in water influencing their high solubility, presence in the environment as well as making them very useful as plasticizer [8].

Depending on the molecular weight, phthalates can be divided into two: Low Molecular Weight Phthalates (LMWP) and High Molecular Weight Phthalates (HMWP). Compounds with low molecular weight are those with 1-4 carbon atoms in their side chains which include DMP (Dimethyl phthalate), DEP (diethyl phthalate), DBP (dibutyl phthalate), and DIBP (di-isobutyl phthalate) [9]. While on the other hand, compounds with high molecular weight are those with 5 or more carbon atoms on their side chains which consist of mainly DEHP (di-(2- Ethylhexyl) phthalate), DIDP (di-isodecyl phthalate), and DINP (di-isononyl phthalate) (Phthalates, 2008). Fig. 1 shows major applications of PAEs as they are the major component in the plasticized products that are used all over the world such as flooring tiles, wires and cables, wall coverings, self-adhesive films or labels, roofing membranes, automobile applications, building materials, tarps, toys, and mainly for manufacturing of PVC [11].

Owing to the widespread of phthalates in the biosphere, the most commonly used 5 types of PAEs are discussed in this article: DEP, DEHP, DINP, BBP, and DBP. The main physicochemical properties are molecular weight, specific gravity, melting point, boiling point, water solubility (S<sub>W</sub>), vapor pressure (V<sub>P</sub>), Henry's constant (H), air-water partitioning (K<sub>AW</sub>), octanol-air partition (K<sub>OA</sub>), octanol-water partitioning (K<sub>OW</sub>), and organic carbon partitioning (K<sub>OC</sub>) [12]. Table 1 shows the general physicochemical properties of PAEs. Generally, PAEs are oily liquids at optimum temperatures since they have low melting and high boiling points. Water sol-

ubility influences the PAE's biodegradation, bioaccumulation, bio-magnification potential, and aquatic toxicity and also controls the distribution between water, soil/sediment, and atmosphere [13].

### 1.2. Sources and fate of phthalates

Food and water are the major sources of phthalates for human exposure. Phthalates are not intentionally added ingredients but rather "indirect" food additives. Because, they are prone to migrating out of the plastic polymer matrix into the surroundings, due to the inability of covalent bonding with the polymer matrix. Leaching and migration of the PAEs in the environment occur due to the non-chemical bonding with plastic polymer. Exposure can occur during any stage of manufacturing, disposal of products, and even during their usage [12]. Nowadays, Food is the leading source of exposure to Phthalate. They are omnipresent in our daily life – especially in drinking water, soft drinks, sports drinks, dairy products, meats, fish, oils and fats, baked goods, infant formula, processed foods, and fast foods [14]. Fig. 2 depicts the sources of PAEs found in food products stored in plastic containers, through packing materials, processing equipment in the food industry, plastic wrapping covers, and films. PVC tubing, PVC gaskets in metallic caps for glass jars, printing inks, paper, and board packaging are also major sources of phthalate [15].

The abiotic degradation of PAEs occurs by two different processes: Hydrolysis and Photo-degradation. Hydrolysis is a slow process and the products include acid and alcohol. Aqueous hydrolysis is insignificant, whereas hydrolysis under acidic or alkaline conditions has been reported to be significant. Photodegradation occurs through the absorption of UV light from sunlight, which is mediated by either direct or indirect mechanisms. Biodegradation is considered the major route of degradation of PAEs using microorganisms (Fig. 3). Research has shown microbes from diverse habitats have shown to degrade phthalate esters [16].

### 1.3. Toxic effects of phthalates on human exposure

Phthalates are extremely dangerous to human life. These are considered endocrine disrupting chemicals as they are well known for their toxicity even at low concentrations. These can mimic or block the hormonal actions affecting the normal metabolic activities of living beings, especially animals and humans [17]. PAEs accumulate in the body and cause chronic intoxication mainly affecting the liver and reproductive system. Humans are exposed to PAEs mainly through four routes:

- 1 Ingestion - mainly through PAE plasticizing, food contamination during the preparation or packaging process, drugs, and nutritional preparations, baby toys, etc.
- 2 Inhalation - mainly through indoor dust and from medical devices.

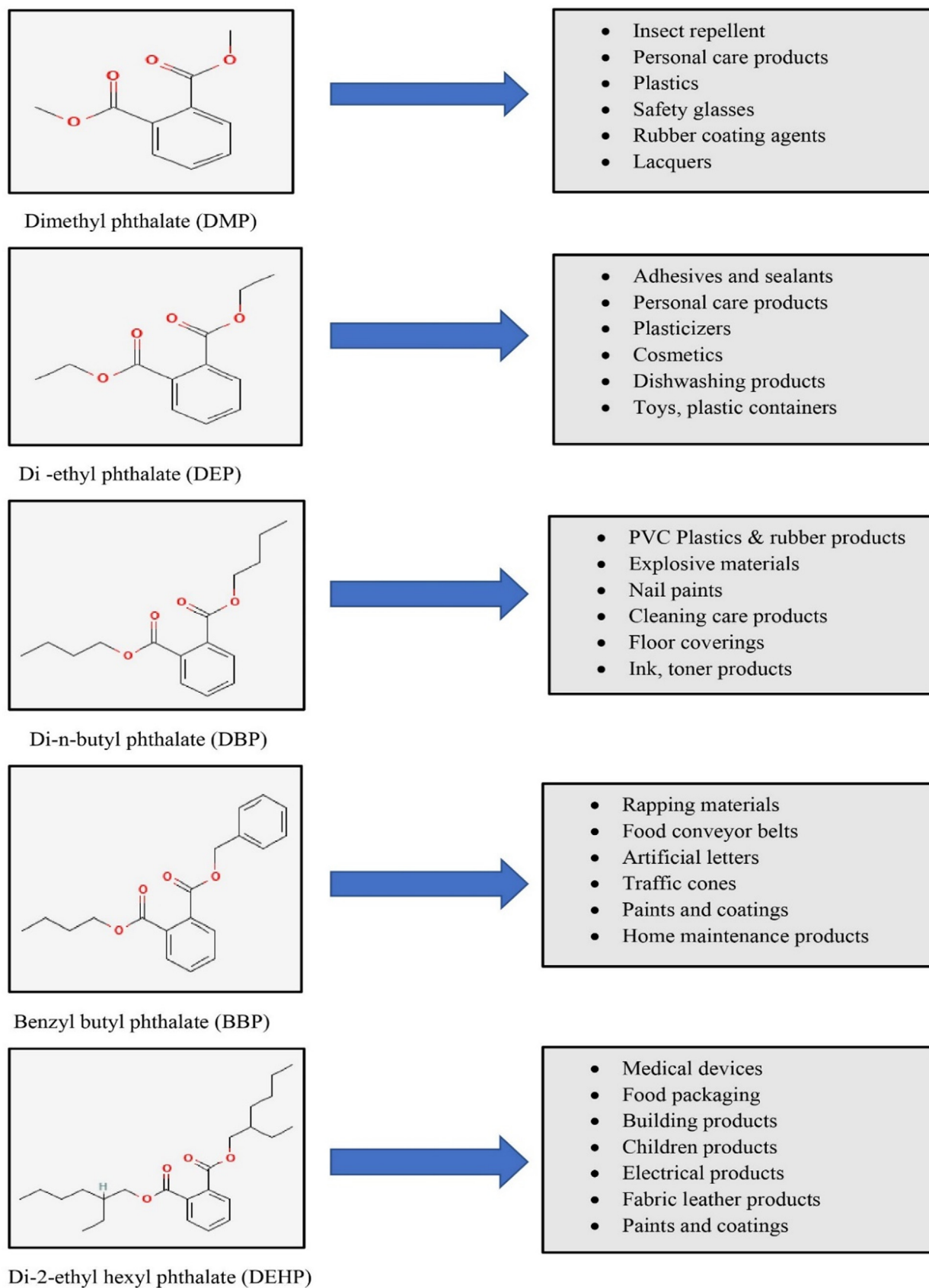


Fig. 1. Chemical structures of PAEs and their application.

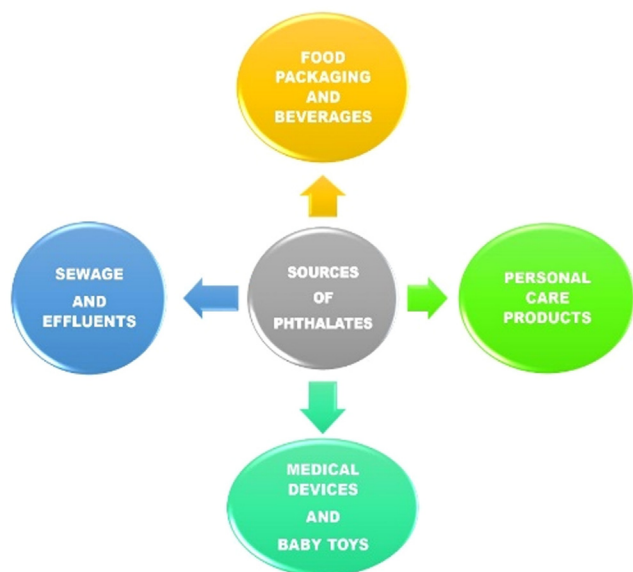


Fig. 2. Sources of phthalates.

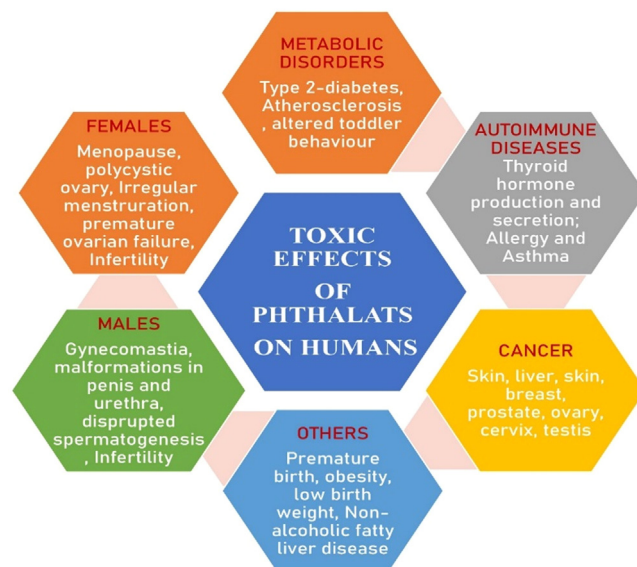


Fig. 4. Health effects of phthalates.

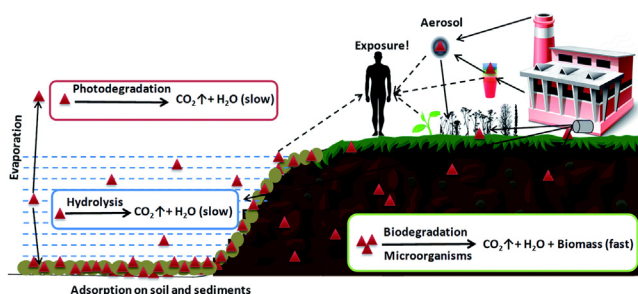


Fig. 3. Proposed pathway denoting the fate of PAEs in environment, transport, and human exposure Source: [15].

- 3 Intravenous – mainly from medicinal PVC devices transporting intravenous fluids, nutritional formulas, blood, etc.
- 4 Dermal contact – contamination mainly through the usage of cosmetics, clothes, footwear, gloves, insecticides, paints, toys, etc [10].

Phthalate exposure has been correlated to several health issues, as they interfere with the production of the sex hormones, seminiferous tubules, and ovaries that are necessary for the proper development and functioning of the male and female reproductive organs. When this interference occurs in early life stages, it can have an irreversible effect on male and female reproduction [18]. Other health effects mainly include cancer, metabolic, autoimmune, reproductive [19], and neurological disorders [20] (Fig. 4).

#### 1.4. Permissible levels of phthalates

WHO produces international norms on water quality and human health in the form of guidelines for the basic regulation and standard-setting, in developed and developing countries worldwide. The overall health is dependent on the quality of drinking water. According to WHO, the standard limit of DEHP in drinking water is 0.8 µg/L. Similarly, Consumer Products Safety Commission (CPSC) has banned the use of 6 phthalates (DEHP, DBP, BBP, DINP, DIDP, and DNOP) on toys and child care products, not more than 0.1 percent.

According to regulation No. 10/2011 EC of 14 January 2011 of European Union established standard limits of many compounds

used in packaging and set regulations specifying the migration tests using food stimulants to determine their probable migration into food. Specific Migration Limit (SML) is the maximum accepted concentrations of a given substance released from a material/article into food/food stimulants.

According to US EPA (Environment Protection Agency) and FDA (Food and Drug Administration) in food/ food stimulants are given below. The overall migration limit in food is not more than 10 µg in dm<sup>2</sup> of contact surfaces (Table 2).

## 2. Extraction or pre-treatment methods

In the last 15-20 years it was found that the number of PAE analyses went up from the commonly analyzed 8 PAEs, namely DMP, DEP, DIBP, DBP, dicyclohexyl phthalate (DCHP), di-*n*-octyl phthalate (DNOP), and DEHP to almost 23 PAEs. With time the sample preparation has also progressed from liquid phase extraction using organic solvents to solid-phase microextraction techniques to their most recent modifications. Among the extraction methods gas chromatography and liquid chromatography are still the favored methods with ameliorating LODs of analysis of a wide range of samples.

Sample preparation can be mainly divided into three types i.e., Solid-phase, liquid phase, and others. Let us briefly discuss the extraction methods involved in these three phases.

### 2.1. Solid phase extraction (SPE)

Solid-phase extraction has always been the center of attraction due to its ease of operation, its ability to save time and solvent, and also works in a semi-automation method [21]. It can also eliminate emulsions. Other than this, high enrichment factors are also obtained through SPE. SPE has proved to be a dominant method for the extraction and sample preparation of water samples. SPE can also be operated online by directly connecting it to the chromatograph allowing its full automation [22]. Activated solid phase is used to extract PAE's from water samples and eluted using organic solvent [23]. The SPE types of equipment can either be discs or cartridges [24] and this has been used in France as a standard extraction method NF EN ISO 18856 [25]. A typical cartridge device consists of short columns; an open syringe barrel containing the sorbent with different particulate sizes (50-60µm). The cartridges

that efficiently removed PAEs include C18, Octadecylsilane (ODS), HLB, and a mixture of LiChrolut RP18 and LiChrolut EN (2.5/1 by weight) [26].

It is to be noted that PAEs in water can be extracted directly without filtration if SSM  $\leq 1$  g/L [27], but to avoid clogging whenever the sample contains a high level of SSM ( $>1$  g/L) filtration with GF/F is quintessential. The particulate phase is reduced when water is filtered through GF/F, leading to a 20% inclination of the total concentration [28]. The commonly used eluting solvents include MeOH, DCM, hexane, and acetone. Almost all SPE cartridges are built of polyethylene (PE) or polypropylene (PP), having the capacity to release 3-14 ng of DBP, DnBP, and DEHP for 500 mg ODS sorbent [29].

## 2.2. Magnetic SPE (MSPE) and dispersive SPE (DSPE)

MSPE is considered green analytical chemistry (GAC) technique due to the minimization of the negative environmental impact of chemical laboratories that perform environmental or food analyses. A good sensitivity is displayed by a solution of a dispersed iron-based magnetic carbon nanotube, as an alternative to SPE. GC/MS- SIM when combined with MPSE facilitates low LOQs in a wide range of 3.1-37 ng/L for 16 PAEs [30]. The multi-walled carbon nanomaterial when incorporated into the cartridges is also an efficient method [31]. Lately, two new procedures have been laid out based on graphene-dispersive SPE (DSPE) for the extraction of PAEs from water and beverages packed in plastic bottles [32]. The former method employs graphene as a carbon sourced nanomaterial because of its ultra-high specific surface area (about 2630 m<sup>2</sup>/g), whereas latter method consists of a fake magnetic molecularly imprinted microsphere (MAG-MIM) adsorbent [32]. Most often desorption organic solvents like ACN, acetone, ethyl acetate, and n-hexane are used. When compared with the traditional method graphene-DSPE is a simple, expeditious, and worthwhile method, with less sensitivity when GC/MS-SIM analysis is conducted for PAE extraction from water samples [33].

## 2.3. Solid-phase microextraction (SPME)

Solid-phase microextraction (SPME) is also considered as a GAC technique [34]. It requires the use of a fiber coat made of either liquid polymer or solid sorbent with an extracting phase can be used for the extraction of PAEs from water. After extraction, the SPME fiber could be transferred to the GC injection port where thermal desorption of PAEs takes place along with the analysis. The extraction process includes the sorption of analytes onto a microfiber coated with a hydrophilic polymer [35]. Based on solid sorbents, a large number of fiber coatings such as polydimethylsiloxane and divinylbenzene (PDMS-DVB), handmade polyaniline, and polyacrylate fibers are available which could be successfully employed for the analysis of the 6 main PAEs listed in the precedence list of the US-EPA [36]. The known advantage of SPME is an organic solvent-free technique, which reduces the risk of secondary contamination that occurs during the pretreatment stage. This fiber can be reused further for 100-300 cycles. But still, the quantification of PAEs using SPME method remains under development. The literature concerning this technique is very scanty and most of them were less efficient for all the selected PAEs. It is very difficult to quantify PAEs when solids are utilized because of the adsorption efficacies. Under optimal conditions, for some of the PAEs, SPME allows obtaining lower LODs than other extraction methods [37]. Liu [38], stated that SPME protocol can also be automated by using an autosampler like CombipAL.

Similarly, Ion trap mass analyzers use a combination of electric or magnetic fields to capture or trap ions inside the mass analyzer which are used widely for the determination of the PAEs

[17]. Rios et al., [39] used a solvent-free analytical approach based on headspace SPME of the oil matrices heated at a high temperature coupled with the GC with the mass spectroscopy detector mainly the GC-ion trap which was developed for the determination of PAEs in oil matrices. In-tube solid phase micro extraction (IT-SPME) has been used in the extraction process of different types of phthalates. Chafer *et al.*, 2008 [165] used a commercially available capillary tube of 80cm length coated with polydimethylsiloxane of 95% and 5% of polydiphenylsiloxane (TBR-5) to carry out the on-line extraction and preconcentration of the DBP and DEHP. In another study, authors proposed a cost-effective method which combines on-line, (IT-SPME) in in-valve configuration and capillary liquid chromatography with UV diode array detection of different types of phthalates (DEHP, MEHP, DEP, DBP) [166]. The in-tube SPME-HPLC is a simple and rapid method which provides a useful tool for the screening and determination of phthalate contamination in infusion solutions [167].

## 2.4. Stir-bar sorptive extraction (SBSE)

SBSE is also a GAC extraction method employed for PAE extraction [40]. It is based on the adsorption of dissolved PAEs on a 20 mm magnetic stirrer coated glass covered with an adsorbent phase of PDMS polymer of minimum thickness. Later on, directly immersed and then introduced into the analytical instrument for PAE desorption. It is understood that extraction yields of PAEs depend on their  $K_{ow}$ . SBSE might be used at room temperature, for more than one hour at a stirring of 500-1000 rpm, or with higher temperature and agitation of about 50 °C and 1200 rpm respectively [41]. The factors which affect the efficiency are temperature, agitation speed [42], NaCl addition (5%), and MeOH content (0%).

### 2.4.1. Liquid phase extraction (LLE)

LLE can be defined as the method which uses 50-500 mL of organic solvent added into the aqueous sample of 500-1000 mL. With the vigorous shaking the contents inside, PAEs in its organic phase after decantation could be obtained [43]. When compared with water, propanol is a good solvent for PAE extraction. Propanol is miscible in water and organic solvents therefore; ammonium sulphate is used to separate the two phases [44]. Non-miscible solvents such as hexane and DCM with water shows a good efficiency [45]. With the addition of an organic modifier such as 50% methanol, the extraction of most non-polar PAEs like DEHP and DNOP can be greatly improved [46]. 80% recovery could be achieved when successive extractions of the sample are done. Significantly, analysis of the water samples using LLE without the separation of SSM from water could be done. By employing various methods like EPA-Method 506, centrifugation, addition of 20-150 g/L of NaCl addition, ultrasound, freezing, or vigorous stirring the eventual emulsion involving water can help in SSM separation [47]. The presence of emulsions can affect the extraction efficiency of PAEs in the SSM and the addition of NaCl is not always a permanent solution to improve the condition [48].

The addition of organic salts could be avoided by the use of non-miscible organic solvents which saves time and involve less preparatory steps, thereby reducing the source of contaminations. In this context, EPA method 8061 [49] is the most commonly used. The initial step of this technique is the filtration of the 2 L of water with 0.7  $\mu$ m GF/F, which is later on spiked with the IS, and extracted with 3  $\times$  100 mL of DCM. Sodium sulfate could be used for the elimination of the trace amounts of water and can be replaced by 1 mL hexane before GC-MS analysis [50]. The LLE procedure is easy to employ but requires the large quantity of organic solvents and is considered to be expensive. Moreover, it is a labor-intensive and time-consuming process.

#### 2.4.2. Solid supported LLE (SLE)

As an alternate to LLE, a few techniques have been developed. Solid supported LLE (SLE) is one such method, which uses inert support which is packed into a disk or cartridge, similar to solid-phase extraction. According to a literature study, SLE is a technique where a water samples with PAEs is delivered through a cartridge which is pure, inert, finely divided with a sorbent made of diatomaceous earth. The PAEs are then dissolved in an immiscible organic solvent. SLE allows minimizing the interference of the matrices. Generally, SLE utilizes the inert material which retains in the entire sample – both analytes and matrix components. The analytes are then selectively eluted off the material using an immiscible organic solvent, leaving the matrix components on the media. Here the samples are loaded onto the column and flow through the sorbent to waste, the entire sample is loaded onto the extraction bed in SLE [51].

#### 2.4.3. Liquid-phase microextraction (LPME)

LPME is a miniaturized form of the traditional liquid-liquid extraction in which the extracting organic phase is limited to a few microliters for the extraction of the target analytes. LPME is characterized by the usage of the low volumes of the immiscible solvents which acts as the acceptor phase for the extraction of compounds from aqueous phase which is the donor phase [52]. LPME can be distinguished into three categories [53]:

- 1 Single drop microextraction (SDME) – A drop suspended from the tip of a syringe is the extractant phase of SDME.
- 2 Hollow-fibre-LPME (HF-LPME) – The extraction is carried out using hydrophobic porous hollow fiber that consists of liquid membrane, and the acceptor phase is introduced to the fiber.
- 3 Dispersive liquid-liquid microextraction (DLLME) – The extracted solution is added to disperser solvent which rapidly infuses into the aqueous phase resulting in cloudy solution with increased surface of contact between sample and extractant, followed by centrifugation to obtain the analyte [54]. The different forms of DLLME are Ultrasound-assisted dispersive liquid-liquid extraction (UA-DLLME); Ultrasound-vortex-assisted dispersive liquid-liquid microextraction (USVA-DLLME); Magnetic stirring-assisted dispersive liquid-liquid microextraction (MSA-DLLME).

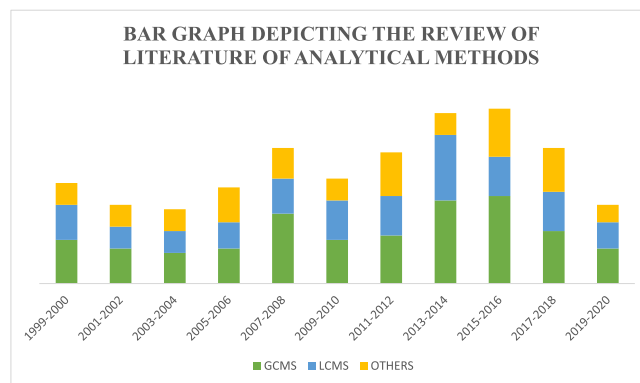
#### 2.4.4. Microporous membrane LLE (MMLLE) and Homogeneous liquid-liquid extraction (HLLLE)

MMLLE is a developed method of sample extraction that allows automation of the micro-LLE process to a blank card. This card contains the PP membrane that is grooved twice for the entry of the aqueous phase along with the organic solvent. The extraction process is based on the partition coefficient between the two phases and the diffusion of analytes in the samples [46].

HLLLE is an outstanding method that extracts the desired solutes existing in a homogenous solution into a water-immiscible phase by a phase separation phenomenon. The procedure of HLLLE is very simple, rapid, and requires many additional reagents. In HLLLE, the contact area between two phases (water and organic) is extremely large and the equilibrium state could be obtained rapidly, therefore there is no need for vigorous mechanical shaking. To the best of our knowledge alone, one work has been carried out for the extraction and determination of PAEs using the HLLLE-HPLC-UV [55]. The results exhibit that it is a reliable technique for the detection of trace amounts in water samples. Similarly, cold-induced aggregation microextraction (CIA-ME) uses ILs for HLLME. The mechanism is similar to DLLME, but its dispersion is based on temperature-dependent dissolution instead of dissolution [56]. Low consumption of toxic solvents and time are the main advantages of the HLLLE Table 2.

**Table 2**  
showing the permissible levels of PAEs in water as per EPA and FDA.

Type of Phthalate	Permissible level
DBP	0.3 µg/L
DEHP	1.5 µg/L
DEHP (Bottled water)	0.006 µg/L
BBP	60 µg/L
DIDP	9 µg/L
DIBP	Not allowed in food contact materials



**Fig. 5.** Bar graph showing the literature review of analytical studies carried in last 20 years.

The main advantages and disadvantages of the above-mentioned pre-treatment measures are given in Table 3.

### 3. Analytical determination of phthalates

The identification, and quantification of PAEs in the environment requires pre-treatment (sample preparation) followed by determination techniques. The selection of an appropriate instrumental technique for this process mainly depends on the physicochemical characteristics of the target analytes and their sensitivity levels. The analytical methods are categorized broadly into two based on the literature study, they are as follows:

- (1) Direct analytical methods
- (2) Non-Chromatographic methods

Fig. 5 shows the analytical works for PAE detection performed in the last 20 years.

#### 3.1. Direct analytical methods

Several direct analytical methods have been reported for the determination of PAEs in drinking water, drinks, oils, and fats. Some of them are Gas chromatography, Liquid chromatography, Micellar electrokinetic capillary chromatography, Fourier transform infrared spectroscopy, UV spectrophotometry, Nuclear Magnetic resonance (NMR) methods. GC/LC are different separation techniques that are usually coupled with different kinds of detectors to selectively and specifically identify target compounds from the mixture. PAEs in food, beverages, and other polymers are also detected using the LC/GC coupled with a mass spectrometer (MS). A mass spectrometer is an effective analytical tool used for measuring the mass-to-charge ratio ( $m/z$ ) for the identification and quantification of the compounds with low LOD (ng/L or <ng/g) [146].

##### 3.1.1. Gas chromatography (GC) Analysis

Table 4, proves that the most frequently used separation technique for the analysis of PAEs is Gas chromatography, due to the thermal stability and volatile nature of the PAEs [146].

**Table 3**  
Advantages and Disadvantages of different sample preparation methods.

Sample preparation methods	Advantages	Disadvantages
Solid-phase extraction (SPE)	<ul style="list-style-type: none"> <li>➤ Reduces the use of solvents</li> <li>➤ More purified extracts produced</li> <li>➤ Excellent extraction efficiency</li> </ul>	<ul style="list-style-type: none"> <li>➤ Necessitates extensive sample handling and treatment measures</li> <li>➤ Requires clean-up using Florisil</li> <li>➤ High blank values</li> <li>➤ Use of fibre is limited.</li> <li>➤ Batch -to-batch variation, low repeatability</li> <li>➤ Low capacity</li> </ul>
Solid -phase microextraction (SPME)	<ul style="list-style-type: none"> <li>➤ Simple and efficient</li> <li>➤ Low cost</li> <li>➤ Extraction process is solvent free</li> <li>➤ High sensitivity</li> </ul>	<ul style="list-style-type: none"> <li>➤ Limited to PDMS (extractants) sufficiently enriched substances</li> <li>➤ Batch-to-batch variation</li> <li>➤ Low repeatability</li> <li>➤ Clean-up required for oils and fatty extracts</li> <li>➤ Additional steps required for fatty acid separation</li> </ul>
Stir bar sorptive extraction (SBSE)	<ul style="list-style-type: none"> <li>➤ High sample capacity</li> <li>➤ High recovery and sensitivity</li> <li>➤ Low detection limits – ng/L</li> <li>➤ Cleaning not compulsory for liquid samples</li> <li>➤ Cleaning is not necessary for non-fatty liquid samples</li> <li>➤ Low cost</li> <li>➤ Reduced extraction time</li> </ul>	<ul style="list-style-type: none"> <li>➤ Environmental contamination more</li> </ul>
Liquid-liquid phase extraction (LLE)	<ul style="list-style-type: none"> <li>➤ Simple, rapid, and better efficiency</li> <li>➤ Inexpensive</li> <li>➤ Simple, inexpensive</li> <li>➤ More reliable than DLLME</li> </ul>	<ul style="list-style-type: none"> <li>➤ Ionic liquids are unstable</li> <li>➤ Tendency to decompose when exposed to metallic catalysts</li> <li>➤ High cost</li> <li>➤ Limited wide application</li> <li>➤ Samples will not be separated properly</li> <li>➤ Requires centrifugation for separation process</li> <li>➤ Use of dodecane, which results in poor response to phthalates</li> </ul>
Dispersive liquid-liquid microextraction (DLLME)	<ul style="list-style-type: none"> <li>➤ Simple, rapid, and better efficiency</li> <li>➤ Inexpensive</li> <li>➤ Simple, inexpensive</li> <li>➤ More reliable than DLLME</li> </ul>	<ul style="list-style-type: none"> <li>➤ Environmental contamination more</li> </ul>
Ultrasound-assisted dispersive liquid-liquid microextraction (UA-DLLME)	<ul style="list-style-type: none"> <li>➤ Simple, rapid, and better efficiency</li> <li>➤ Inexpensive</li> <li>➤ Simple, inexpensive</li> <li>➤ More reliable than DLLME</li> </ul>	<ul style="list-style-type: none"> <li>➤ Environmental contamination more</li> </ul>
Ultrasound-vortex-assisted dispersive liquid-liquid microextraction (USVA-DLLME)	<ul style="list-style-type: none"> <li>➤ Improved extraction efficiency</li> <li>➤ Able to analyze matrices with large alcohol content</li> <li>➤ Trace and ultra-trace amounts could be detected.</li> </ul>	<ul style="list-style-type: none"> <li>➤ Limited wide application</li> <li>➤ Samples will not be separated properly</li> <li>➤ Requires centrifugation for separation process</li> <li>➤ Use of dodecane, which results in poor response to phthalates</li> </ul>
Magnetic stirring-assisted dispersive liquid-liquid microextraction (MSA-DLLME)	<ul style="list-style-type: none"> <li>➤ Simple, fast, and efficient</li> <li>➤ No dispenser solvent is required which increases extraction recovery</li> </ul>	<ul style="list-style-type: none"> <li>➤ Limited wide application</li> <li>➤ Samples will not be separated properly</li> <li>➤ Requires centrifugation for separation process</li> <li>➤ Use of dodecane, which results in poor response to phthalates</li> </ul>

Generally, GC is conducted using nonpolar gas chromatographic columns and Helium as the mobile phase. A split/splitless injector in splitless mode with or without pulsed mode along with capillary gas chromatography (CGC) is used for the analysis of the volatile and thermostable PAEs. Similarly, many researchers have tested programmable temperature vaporizing (PTV) injection in the splitless mode, which rises the amount of sample introduced into the column, thus obtaining good sensitivity and better LODs than in the split mode [147]. Conventional GC separation methods have also been used frequently [82]. PAEs like DBP, BBP, and DEHP in non-carbonated mineral water are determined by GC-MS with the LOD between 0.002 and 0.05 µg/L [89]. Another method executed by Ustun *et al.*, [94] depicts the analysis of some PAEs in bottled lemonade by GC-MS using the fused silica capillary column, where the LOQ was greater (16-52 µg/L) than the former one.

Generally, GC-MS is a coupled process because of its specificity and high sensitivity of MS, allowing the detection of several types of PAEs at low levels in beverages and food matrices [146], using the electron impact ionization (EI) [108]. Coupling of GC with the Flame ion detector (FID) has been extensively applied, although GC-MS will be used for the confirmation process [107], whereas in some other experiments confirmation was carried out using GC-MS with ion trap (IT) as an analyzer. In MS detection, ITs [92], simple (Q), and triple Q/Q quadrupoles were used as analyzers most usually applied [148], using the full scan [111], single ion monitoring (SIM) [63], or a combination of both monitoring modes, multiple reaction monitoring (MRM) is also used to a little extent for the detection and quantification.

Another alternative is the use of two-dimensional GC (GC x GC), *i.e.* a combination of polar and non-polar columns are used for the analysis of large number of compounds including PAEs in alcoholic distilled beverages [149]. Another method is the use of small-diameter columns to reduce the run times for the GC, popularly known as the Fast- GC (FGC), where 10 PAEs can be analyzed by FGC- triple quadrupole, after SPME [104]. PAEs can be detected with the electron capture (ECD), which are relatively sensitive for

PAEs. The specificity of ECD is restricted as they respond more towards halogenated compounds [150].

Gas Chromatography coupled with MS has many advantages such as limited time for analysis, providing high resolution and sensitivity [102] and disadvantages such as cost of analysis are very high and is a destructive technique [151].

### 3.1.2. Liquid chromatography (LC) analysis

Table 5 shows that LC analysis stands apart as a dependable option in contrast to GC analysis for PAEs, providing a greater selectivity. PAEs are dissolved in a mobile phase, then passed through the stationary phase where they get separated. Generally, C<sub>18</sub> ODS analytical column is the most commonly used stationary phase than shorter chain columns such as C<sub>8</sub> due to the non-polar nature of PAEs. A mixture of ACN/Milli-Q water is the most suitable mobile phase for the separation of the analytes than MeOH/water which is also applied so far [137] without any other additives. Generally, both types of mobile phases are buffered or acidified. Better separation can be obtained when the columns are thermostated between room temperature to 80 °C.

LC could be combined with mass spectrometry (LC-MS/MS) which is an option in contrast to GC-MS, because of the easy sample preparation, lack of derivatization steps, lower sensitivity is obtained by LC-MS. Determination of different PAEs in carbonated cola by LC-MS/MS utilizing the XDB-C8 column and a combination of water/acetic acid as mobile phase with an angle elution brought about LOD of 0.013 µg/L [123]. Though, High-pressure liquid chromatography (HPLC) or ultra HPLC (UHPLC) is the most commonly used technique for the determination of the PAEs that could not be sufficiently separated by GC. According to a literature study, HPLC utilizing C18 columns running in isocratic or gradient elution has been broadly used for the detection of PAEs in food and beverages, especially because of the presence in trace amounts and its ability in analyzing thermally temperamental and non-volatile organic chemicals [152]. Detectors such as Diode-Array-Detector (DAD) or UV coupled with LCs are more affordable techniques with good

**Table 4**  
Shows the gas chromatography-based analytical methods carried out from 2000 – 2020.

Matrix	Analyte	Extraction technique(Sorbent)	Analytical technique	LOD/LOQ	Recovery %	Reference
Water	DMP, DEP, DBP, BBP, etc	SPME (Polyacrylate fiber)	GC-MS	0.007-0.17 µg/L	-	[57]
Drinking water	DEP, DBP, BBP, DEHP	SPME (Carbowax-divinylbenzene)	GC-MS	0.005-0.04 µg/L	-	[58]
Water	DMP, DEP, DBP, DEHP, etc	SPME (PDMS-DVB)	GC-MS	2-27 ng/L	-	[59]
Beverages	DEP, DBP, BBP, DEHP, etc	Steam distillation and extraction	GC-MS	2-5 ng/mL	-	[60]
Water	DMP, DEP, DBP, BBP, DEHP	SPME-TD (Polyacrylate fiber)	GC-MS	50-200	0-116	[61]
Mineral water	DEP, DBP, DEHP	SPME (PDMS-DVB)	GC-MS	0.01	-	[62]
Milk	DMP, DEP, DBP, BBP, DEHP	SPE (C18)	GC-MS	0.06-0.36 µg/kg	73-119	[63]
Milk	DMP, DEP, DBP, BBP, DEHP, etc	Headspace SPME (10 SPME fibers compared)	GC-MS	0.12-1.8 ng/g	-	[64]
Water	DMP, DEP, DBP, BBP, DEHP	SPME (PDMS, PDMS-DVB, PA, CAR-PDMS, CW-DVB)	GC-MS	2-103 pg/mL	-	[65]
Drinking water	DMP, DEP, DBP, BBP, DEHP, etc	Stir bar sorptive extraction	GC-MS	3-40 ng/L	-	[66]
Mineral water	DMP, DEP, DBP	LPME	GC-MS	0.43-4.30	95-97	[67]
Wine	DMP, DEP, DBP, DEHP	Headspace SPME (CW-DVB, PA, PDMS-DVB)	GC-MS	0.15-2.2 µg/L	-	[68]
Vegetable oil	DMP, DEP, DBP, BBP, DEHP	Headspace SPME (PDMS, CX/PDMS, PDMS/DVB)	GC-ECD	0.2-0.5 mg/kg	-	[69]
Drinking water	DMP, DBP, BBP	DLLME	GC-MS	2-8	68.1-88.9	[70]
Bottled water	DMP, DEP, DBP, DEHP	SPME (PDMS/DVB)	GC-MS	0.02 µg/L	-	[71]
Bottled water	DMP, DEP, DIBP, DBP, BBP, etc	Headspace SPME (PDMS/DVB, PDMS, DVB/CAR/PDMS)	GC-MS	0.003-0.085 µg/L	-	[72]
Mineral water	DMP, DEP, DBP, BBP, DEHP	LPME	GC-MS	0.02-0.05	-	[48]
Drinking water	DBP, DEHP	LLE	GC-ECD	-	-	[73]
Ultrapure water	DEP, DBP, BBP, DEHP	SPE-ATD	GC-MS	36-95	15-101	[74]
Water	DMP	SBSE-TD	GC-MS	150	29	[75]
Alcoholic beverages	9PAEs	LLE	GC-(EI)-MS(IT)	0.7 mg/L	104-110	[76]
Soybean milk	DMP, DEP, DBP, etc	MIPSE	GC-MS	0.013-0.022 µg/g	75.8-107.5	[77]
Olive oil	DMP, DEP, BBP, DIBP, DEHP, etc	Headspace SPME (DVB/CAR/PDMS, PDMS, PA)	Ion - trap (IT)-MS	0.02-0.05 mg/kg	-/ <20	[39]
Water	DMP, DEP, DBP, BBP, DEHP, etc	LLE	GC-MS	2-30 ng/L	70-94	[79]
Water	DMP, DEP, DiBP, DBP, BBP, etc	SPME (Polypyrrole coated magnetic particles)	GC-MS	0.006-0.068 µg/L	91.9-113.4	[80]
Bottled milk	DMP, DEP, DBP, BBP, etc	UA-DLLME	GC-FID	0.64-0.79 ng/g	93.2-105.7	[81]
Water, Vinegar	DMP, DEP, DiBP, DBP, DEHP	Air-assisted LLME	GC-FID	-	-	[82]
Water, beverages	DMP, DEP, DiBP, DBP, BBP, DCHP, etc	SPME (Magnetic multi-walled carbon nanotubules)	GC-MS	4.9-38 ng/L	64.6-125.6	[83]
Cow milk	5 PAEs	DLLME	GC-FID	1.5-3 µg/L	20-102	[84]
Wine	DMP, DEP, DBP, BBP, DEHP, etc	USVA-DLLME	GC-FID	≥0.22 µg/L	85-100.5	[85]
Water	DBP, DEHP	SPE (Polythiophene-coated Fe <sub>3</sub> O <sub>4</sub> nanoparticles)	GC-FID	0.2-0.4 µg/L	85-92	[86]
Water	DMP, DEP, DBP, BBP, DEHP, etc	LLE	GC-MS	8-25 ng/L	73.5-106.6	[87]
Vegetable juice	DMP, DEP, DCHP, DBP, DEHP, DIBP, BBP	HF-LPME	GC-MS	0.0001-0.01 mg/L	71.8-90.1	[88]
Mineral water	DiBP, DBP, BBP, DEHP	LLE	GC-MS	0.001-0.052	-	[89]
Carbonated water	DMP, DEP, DBP, DEHP	SPE	GC-MS	-	60-114	[90]
Mineral water	DBP, BBP, DEHP	SPME (PEDOT-TiO <sub>2</sub> nanocomposite fiber, PDMS)	GC-FID	0.05-12	86-107	[91]
Mineral water, cola, vinegar	DMP, DEP, DBP, DEHP	HLLE	GC-FID	0.02-0.71	81.3-110.0	[78]
Hydro-alcoholic food beverages	DMP, DEP, DBP, DIBP, DEHP	SPE	GC-FID	1.21-2.51 pg/µL	94-103	[92]
Plastic bottled beverages	BBP, DEP, DBP, DNOP, etc	MAG-MIM-dSPE	GC-FID	0.53-1.2 µg/L	89.5-101.3	[32]
Bottled water	DMP, DEP, DBP, BBP etc	LLE	GC-MS	20-80	84-96	[93]
Cola, Lemonade	DMP, DEP, BBP, DSP, DEHP, DNOP	LLE	GC-MS	2-7	-	[94]

(continued on next page)



Table 4 (continued)

Matrix	Analyte	Extraction technique(Sorbent)	Analytical technique	LOD/LOQ	Recovery %	Reference
Tap water	DMP, DEP, DBP, DEHP, BBP	SPE	GC-MS	0.010-0.46	77-94	[95]
Bottled water	DMP, DEP, DBP, BBP, DEHP, DOP	DLLME	GC-MS	5-22	-	[96]
Alocoholic water	DMP, DEP, DBP, DEHP	USVADLLME	GC-MS	30-100	91.5-100.5	[97]
Chinese liquor	DBP, BBP, DEHP, DNOP	VSLLE	GC-MS	4.9-13	81.2-93.7	[98]
Mineral water, lemon, juice, cola, vinegar	DMP, DEP, DiBP, DBP, DEHP	SB-DLLME	GC-MS	90-250	49-100	[99]
Water	DBP, DEP, DEHP	Magnetic SPE	GC-MS	0.01-0.025 µg/L	-	[100]
Milk	DMP, DEP, DiBP, DBP, DEHP, etc	Extraction with ethyl acetate	GC-MS	0.09-0.36 ng/g	79.1 -110.3	[101]
Bottled water	DMP, DEP, DBP, DBEP, DHP, BBP, etc	LLE	GC-MS	16-14 µg/L	84-91	[102]
Wine	DEHP	DI-SPME (Graphene (G) and graphene oxide (GO) coated segmented fibers)	GC-(EI)-MS(Q)	0.3 ng/L	98	[103]
Vegetable oil	10 PAEs	DI-SPME (PDMS and Carboxpack Z/PDMS fiber)	GC-(EI)-MS(QpQ)	0.015-0.144 mg/kg	-	[104]
Drinking water, vegetable oil	DBP, DEHP, etc	Head space SPME	GC-FID	0.06-0.08 µg/L	87-112	[105]
Tea	DMP, DEP, DBP, DiBP, DEHP	SDE	GC-MS	0.24-3.72 µg/kg	79.83-116.67	[106]
Water	DBP, BBP, DEHP, DNOP, etc	UA-DLLME	GC-FID	0.64-2.82 µg/L	-	[107]
Cow milk	16 PAEs	SDME	GC-(EI)-MS	0.001-0.2 µg/L	70-108	[108]
Tea	5 PAEs	DI-SPME	GC-(EI)-MS(Q)	2-3 ng/L	82-106	[109]
Milk	13 PAEs	µ-SPME	GC-(EI)-MS(Q)	0.01-0.20 µg/L	77-103	[110]
Brandy	3 PAEs	USVA-DLLME	GC-(EI)-MS	3-300 µg/kg	99-101	[111]
Water	4 PAEs	Dispersive magnetic SPE	GC-MS	0.08-0.15 µg/L	-	[112]
Carbonated soft drinks	DEHP, others	Magnetic SPE	GC-MS	6766.6 - 14,008 ng/L	-	[113]
Water	4PAEs	Solvent based dispersive LLME	GC-IT/MS	1.0-8.0 µg/L	98-102%	[17]

PDMS-DVB – Polydimethylsiloxane-divinylbenzene; CW-DVB – Carbowax-divinylbenzene; PA- Polyacrylate; PDMS- Polydimethylsiloxane; CAR-PDMS – Carboxen - polydimethylsiloxane

performance. A study conducted in red wine using LC-DAD, with a C18 column and combination of methanol/water as mobile phase with angle elution, give rise to LODs from 2.0 to 2.2 µg/L [129]. Another type of LC analysis is the LC-UV, where the use of a C<sub>8</sub> column with a blend of the aqueous acetonitrile containing 1% of methanol as mobile phase with gradient elution. In a study conducted by Zaater *et al.*, [93] in mineral water observed LODs in between 0.12 and 0.50 µg/L.

The dissolved analytes can be easily recuperated and can be completely automated as well as easy to operate are the main advantages of the LC analysis. The drawbacks of LC are they display a lower efficacy than GC, which can occur a co-elution when samples separate, which are functionally and chemically identical, and they lack high solvent consumption [153].

### 3.1.3. Micellar electrokinetic capillary chromatography (MEKC)

MEKC can be used as a substitute to HPLC, GC for PAE analyses due to its high efficacy, rapid analyzing capacity, and lesser utilization of reagents. MEKC is one of the various capillary electrophoresis methods. The separation principle of MEKC is based on the addition to the buffer solution of a micellar "pseudo stationary" phase, which interacts with the differential partition of the analytes between micelles and water.

According to a literature study, MEKC has been used in the determination of PAEs from landfills and water samples, soils, etc. Based on the MEKC principle, only two works have been published to date. Sun *et al.*, [154] established a new method analysis for 4 PAEs. The target analytes were detected by utilizing the sweeping β-cyclodextrin modified micellar electrokinetic chromatography coupling with diode-array detection (MEKC-DAD), where electropherograms could be obtained. The analysis time is very less, approximately less than 14 min, with good resolution between the

peaks. When this online preconcentration is coupled with DLLME, the LOQs result in between 1.4 and 2.7 µg/L. In another study conducted by Yue and co-workers, [143] in which the capillary was loaded with running buffer and utilizing as an acceptor phase for the headspace in tube microextraction of DEP, DBP, and DEHP from various water samples and beverages. Using the reverse flow micellar electrokinetic capillary chromatography, the capillary ends were placed in vials with a running solution for the separation after the abstraction process. In this technique, the analysis time is about 14 min and LODs are just a few µg/L.

### 3.1.4. Fourier transform infrared spectroscopy (FTIR)

FTIR is a simple preferred method of infrared spectroscopy, in which the IR radiation is passed through the samples. Some of the infrared radiation is absorbed by the sample whereas some of it is transmitted. The resulting spectrum represents the molecular absorption and transmission, thus creating a molecular fingerprint of the sample, and thus helpful in qualitative analysis. This technique is based on a simple optical device called an interferometer, which can produce a unique type of signal which contains all the infrared frequencies encoded into it. The main advantages of this technique are its high speed, less time-consuming, high sensitivity, internal calibration, and mechanical simplicity. FTIR was developed to overcome the limitations encountered with dispersive spectrometers.

Phthalate analysis could be performed by FTIR based on their state of matrix. If the samples are in liquid or solid forms, an internal reflection accessory called the universal attenuated total reflectance (UATR) can be employed for the estimation and a cuvette is utilized or a drop is placed on a handmade crystal. A study was conducted for the detection of 15 types of PAEs from tea drinks and other milk-related drinks. The samples were direct analyzed in real-time (DART) Fourier transform-ion cyclotron resonance-MS

**Table 5**

Shows the liquid chromatography-based analytical methods carried out from 2000 – 2020.

Matrix	Analyte	Extraction technique(Sorbent)	Analytical technique	LOD/LOQ	Recovery %	Reference
Wastewater	DEP, DEHP	SSPE (octadecylsilica C18)	LC-MS	-	69-71	[114]
Water samples	BBP, DEHP	SPE (Polystyrene columns)	LC-UV	1-200 µg/L	99-104	[115]
Water samples	DnBP	Without pre-treatment	LC-UV	500 µg/L	-	[36]
Seawater samples	10 MPEs	SPE	LC-UV	0.19-3.98 ng/L	50-72	[116]
Seawater sample	DEHP	SPE (Pinnacle™ II Phenyl column)	LC-UV	-	70	[117]
Cooking oil, water	DMP, DEP, DBP, BBP, DEHP, etc	SPE (Nylon 6 nanofibers mat)	HPLC (C18)	0.001 µg/L; 0.020 µg/L	85.92-88.9	[118]
Orange juice	DMP, DEP, DBP, BBP, DEHP, DNOP	SPE (C18 column)	LC-UV	2-14	76-112	[119]
Chinese white spirit	4 PAEs	DLLME	MECK-DAD	0.4-0.8 µg/L	90-106	[120]
Wastewater	5 PAEs	LLE	LC-UV	0.60-1.23 µg/L	57-97	[47]
Water	DMP, DEP, BBP, DBP	MSA- DLLME	HPLC-UV	0.13-0.38µh/L	82-98.2	[121]
Chilli, sweet sauce, ketchup	16PAEs	DLLME	HPLC-DAD	0.09-1.01 µg/L	70-120	[122]
Soft drinks	DEHP	SPE (Silica gel RP-2, C18, and C8 column)	HPLC-ESI-MS/MS	13 ng/L	97.0- 1102.8	[123]
Soybean milk	BBP, DEHP	Magnetic SPE	HPLC-UV/VIS	0.52-50.9 ng/mL	87.2-103.4	[124]
Edible oil	DMP, DEP, DBP, DEHP, DOP	Solid membrane extraction	HPLC-UV/VIS	0.02-0.15 ng/mL	85.92-101.03	[125]
Mineral water, juice, milk	DNOP	HF-LPME	LC-UV	0.2-2.5	81-108.0	[126]
Water sample	8PAEs	SPE	UHPLC-ESI-MS/MS	1-30 ng/L	65-135	[127]
Water samples	8PAEs	SPE (Nylon 6 nanofibrous membrane)	LC-ESI-MS/MS	-	-	[128]
Alcoholic beverages	DIBP, DBP, BBP, DEHP	Conventional ionic DLLME	HPLC-DAD	1.5-4.2 ng/mL	88.5-104.6	[129]
Wine	DMP, DEP, DIBP, DNBP, BBP, DEHP, DOP	Filter (0.2µm)	HPLC-MS/MS	1.6-26.6 µg/L	94.6 – 105.7	[130]
Milk, liquor, wine, and others	DMP, DEP, DBP, BBP, DEHP, DNOP	Glass based SPE	HPLC-MS/MS	0.8-15 µg/kg	75.7-115.2	[131]
Juice	DMP, DBP, BBP, DEHP, DNOP	LLE	LC-MS/MS	-	-	[132]
Mineral bottle	DMP, DEP, DBP, DEHP, DNOP	LLE	LC-UV	0.12-0.5	80-95	[93]
Alcoholic beverages, juices, soft drinks, water	7PAEs	USVA-DLLME	HPLC-UV	0.019-0.208 µg/L	55-118	[133]
Energy drink	DMP, DEP	LPME	LC-UV	0.3-0.5	90-92	[134]
Edible oils	The total content of PAEs	DLLME	HPLC-DAD	0.11 µmol/kg	82-99	[135]
Bottled water	DMP, DEP, DBP	SPE (C18-bonded silica membrane)	LC-UV	0.7-2.4	80-112	[136]
Raw and tea infusions	6 PAEs	QuEChERS	HPLC-PDA	73 µg/kg	70-101	[137]
Water	8PAEs	dSPE (Basolite® F300 metal-organic framework)	HPLC-MS	22-69 ng/L	70-118%	[138]

(FT-ICR-MS) obtaining LODs between 0.1 to 1.0 µg/L [142]. This technique helps in the determination of the target analytes from complex matrices due to its ultrahigh resolving power and accurate mass measurement capacity. Lower LODs can be obtained despite the higher number of the analytes present in the sample, without the use of any separation techniques. In another study, the leaching of the PAEs from the plasticizer polymers could be detected by FTIR [155]. Similarly, work has been conducted recently by a group of researchers using FTIR and GC-MS. The FTIR technique showed a rapid determination method of phthalate content in PVC articles. When compared with the GC-MS, the FTIR method is rapid, less expensive, and fewer steps are required for sample preparation and also showed the quantification of the total amount of phthalate content instead of simple phthalate amount [156]. Thus, depicting FTIR could be used for pre-screening analysis. FTIR applications are limited but coupling could be performed with separation techniques like GC/LC because of the less sensitivity of FTIR alone.

### 3.1.5. Colorimetric analysis

The colorimetric analysis is a quantitative technique used to measure the concentration of a given chemical element or any compound in a solution with the aid of a color reagent. This could be used for organic or inorganic compounds and can be used with or without an enzymatic stage. Colorimetric methods could be widely used in medical laboratories and for industrial purposes mainly in the analysis of water samples related to industrial water treatment. Table 6 proves that PAEs could be detected easily.

Recently, a study was conducted describing the usage of simple colorimetric analysis for the determination of Phthalates by the conversion of anhydrous phthalates to a dye. Here, the phthalates were hydrolyzed with the sodium hydroxide and dehydrated to form phthalic anhydride, which was later converted into a marker called fluorescein when reacted with resorcinol, with the help of concentrated sulphuric acid as a catalyst. Later the presence was detected using absorbance spectrometry. The detection limits vary from phthalate to phthalate. The LODs for DEHP is 0.1 µmol. This

**Table 6**

Shows the other analytical methods (except GC &amp; LC) carried out from 2000 – 2020.

Matrix	Analyte	Extraction technique	Analytical technique	LOD/LOQ	Recovery %	Reference
Water samples	3 PAEs	-	UTP- modified gold nanoparticles- colorimetric analysis	0.5 ppm	-	[139]
Surrogate alcohol	DEHP	Sample added to NMR buffer – volume adjusted to Ethanol	NMR-UV Spectroscopy	90 mg/L	95-105%	[140]
Drink	DEHP	Membrane Filtration	Diffuse Reflectance UV spectroscopy (DRUV)	7.9 µg/L	99-105%	[141]
Tea drinks, milk	15 PAEs	-	DART- MS (FT-IC-MS)	0.1-1.0 µg/L	-	[142]
Water and Beverages	DEP, DBP, DEHP	-	MEKC-DAD	1.4-2.7 µg/L	-	[143]
Water	DEHP, DISP, DBP, BBP, etc	Ultra-sonication extraction process	UV-spectrophotometry	0.1 µmol	-	[144]
Water samples	DEP, DBP, DEHP	-	DNA modified gold nanoparticles – colorimetric analysis	0.026 – 0.144 ppm	-	[145]

method could be used for the detection of the total amount of phthalates in real samples at the submicromolar levels, by converting the phthalates into dyes [144]. Some studies demonstrate the usage of diffused reflectance UV spectrometry coupled with membrane filtration. According to the study, the DEHP in the drinks is passed through the membrane and then directly quantified on the membrane surface using an integrating sphere accessory of the UV spectrophotometer. The LODs were 0.0079 mg/L with the recoveries between 99% to 105% when the real samples are analyzed [141].

Colorimetric detection of PAEs could be conducted more accurately and easily with the help of nanoparticles. Gold is the most preferred nanoparticle for the detection process. Recently, colorimetric detection of phthalates was done using the DNA-modified gold nanoparticles (AuNPs). When phthalates are present in the samples, AuNPs forms the aggregates and observe a visible color change from red to blue with an increase in the absorption ratio when the concentration of phthalates increases. The LODs of DEP, DBP, and DEHP were 0.026 ppm, 0.077 ppm and 0.144 ppm respectively. This method depicts high sensitivity and selectivity [145]. A similar study was conducted for the determination of phthalates using Uridine-5-triphosphate (UTP)- modified gold nanoparticles as a color indicator and Cu<sup>2+</sup> as a crosslinker. The method demonstrates high sensitivity and their detection limit is about 0.5 ppm [157]. The advantages of the colorimetric method include its simplicity of preparation and manipulation, cost-efficient, high sensitivity, and less time-consuming.

### 3.1.6. Nuclear magnetic resonance (NMR) analysis

NMR spectroscopy is an indispensable tool that applies a magnetic field to an atomic nucleus and radiofrequency pulses to characterize the resonant frequency of that atomic nucleus according to its chemical or environmental surroundings. NMR spectroscopy could be used to study the physical, chemical, and biological properties of a matter including the determination of molecular identity and structure. Generally, NMR relies on the chemical shift difference between water and solvent peaks in NMR spectroscopy, leading to the detection of water content in organic solvents. Table 6 shows research was conducted in 2011 by a group of researchers on the determination of the diethyl phthalate and polyhexamethyl guanidine in surrogate alcohol using H-NMR coupled with the advanced chemometric methods (MCR-ALS, and ICA) as a reliable tool in routine analysis of the alcoholic beverages. The samples were mixed with the NMR buffer and made up the volume by adding 70% ethanol. Then the mixture was directly poured into the NMR tube and measured directly. The LOD was 90 mg/L and their recovery was 95-105% [158].

Conventional NMR equipment is expensive superconductive magnets, benchtop NMR equipment uses compact permanent magnets. Nowadays, the lower price and smaller size of these units have opened the opportunity to count on mobile equipment that can be installed in production for online analysis.

### 3.2. Non-chromatographic methods

Innumerable works have been reported for PAE determination in beverages and food through analytical methods mainly GC and LC. These methods do have disadvantages such as high blank values and significant expense of instrumentation [159]. According to the literature review, some simple and technically advanced methods have been established by researchers for the detection of PAEs. They are Molecular imprinting technology and Immunoassay-based techniques.

#### 3.2.1. Molecular imprinting technology (MIP)

It is a newly developed procedure used to design artificial receptors with foreordained target selectivity and specificity as ideal materials to be used in various application. Years back, a group of scientists developed a magnetic MIP sensor coupled with magnetic molecularly imprinted SPE for the determination of the phthalates in soya bean milk and other milk samples. None of the samples detected the phthalates, but the recovery was between 98 to 102%. The LOD was reported to be 0.052 ng/L. The coupling of both magnetic molecularly imprinted polymer sensors and the SPE has resulted in good reproducibility, sensitivity, and satisfactory stability [21]. Similar work was done by Li *et al.*, [160] in wine drinks using the molecularly imprinted polymer synthesized using the magnetic graphene oxide and gold nanoparticles, for molecular recognition of elements and development of the phthalate electrochemical sensor. The sensor exhibited a LOD of 222.6 ng/L, exhibiting outstanding repeatability, with recovery percentages between 97 and 104%.

The main advantages of Molecular imprinting technology include its robustness and storage endurance, whereas their disadvantages include a complicated preparation process accompanied by a longer duration of the process, low binding capacity, and poor site accessibility [161].

#### 3.2.2. Immunoassay-based techniques

Immunoassay sensors are solid-state devices, which work on the principle of immunochemical reaction coupled with a transducer. These form one of the important classes of biosensors based on the specific recognition of antigens by antibodies for the formation of a stable complex. Immunoassay-based techniques are

technologically advanced for the detection of PAEs in plastics. A fluorescence immunoassay was developed for the quantification of phthalates in water samples particularly tap water, river water, and leachate from the plastic bottles used for drinking water. An antibody-coated plate was used and each plate was read at different wavelengths for excitation (485 nm) and emission (528 nm) using an automatic detection microplate reader. The LOD obtained through this assay was 20 ng/L and their recovery percentage was between 91 and 109%. Targeted analytes could be detected and interference of other phthalates is very limited in this assay [162]. A similar study was conducted by Sun and Zhuang, [159] developed a biotin-streptavidin enzyme-linked immunosorbent assay (BA-ELISA) for the detection of DBP in beverages and drinking water. The resulted LOD was 5 ng/L with a satisfactory recovery of about 89.5% to 109.5%. This technique showed excellent selectivity with lower cross-reactivity values with DBP analogs.

The advantages of the Immunoassay-based technique include cost-effective, rapid assessment, handling comfortability, and portability.

#### 4. Precautionary measures during assessment of phthalate

Phthalates are omnipresent in the environment as well as in the laboratories. The difficulty in effective measurement of PAE's is due to the presence of their trace amounts in food and beverages, and by the contamination within the laboratory environment and accessories [152].

Laboratory materials such as pipette tips and plastic containers, solvents, sorbents, analytical instruments, gloves, plastic tubing, and even the air and dust present increases the contamination level. Studies prove the presence of these compounds in low concentrations even in high quality reagents usually used for the extraction process [163]. A similar study has reported the presence of PAES found due to the contamination from ambient air in levels between 0.37 and 3.0  $\mu\text{g}/\text{m}^3$ , which leads to further contamination of the glassware and solvents [164]. In addition, even in Milli-Q water PAEs are found in trace amounts [138], thus recommending a separate zone for PAE analysis in different air filters.

To avoid contamination, certain measures should be adopted to decrease the external contamination during the analysis. All the materials used during the extraction, preparation methods should be made up of glass, teflon, polytetrafluoroethylene (PTFE), aluminium, or stainless steel. Similarly, meticulous procedures will be essential for the minimization of the sample contamination and the maintenance of low background concentration mainly sterilization of the laboratory materials and equipments. All laboratory glassware should be washed or cleaned with oxidizing agents, organic solvents such as cyclohexane, n-hexane, isooctane, methanol, or 2,2,4-trimethylpentane [138], whereas nonvolumetric glassware should be exposed to high temperature of 450-550 °C for the removal of volatile substances, after rinsing with water and organic solvents, leading to the reduction of contamination to an extent [164]. All the laboratory apparatus should be washed and stored in suitable boxes covered with lids or aluminium foils to evade PAE adsorption with ambient air [29].

Use of PAE free gloves and pipette tips, periodic assessment of contamination in the inlets and caps of vials in detection equipments. Similarly, use of PAE rich personal care products such as creams, lotions, perfumes, or any cosmetic products by laboratory staff should be strictly prevented [152]. To trace the source of contamination, analytical blanks should be maintained at each step or for the entire analytical procedure. The blanks should be free from any targeted phthalates to minimize the error of quantification. Therefore, it is necessary to raise the number of procedural blanks to avoid contamination [164].

#### 5. Conclusion

Plastics are the most commonly used food packaging materials due to their versatility and phthalates are the most common chemical among them that affects humans on daily basis. These compounds leach from plastic containers to food, beverages leading to health risks. This gave rise to researches in the development of sample extraction and quantitative determination of different types of phthalates in the last few decades. This review communicates about the effects of phthalates on humans, sample preparation methods, and popular analytical methods put forward by different researchers in food and beverages during the last 20 years. To minimize the use of organic solvents, the green extractants mainly the solid and liquid extractions are adopted, helping in environmental pollution control. Among the analytical methods, GC, LC, FTIR, and UV spectroscopy with various detectors are still widely used along with the other non- chromatographic methods for detection of PAEs.

Since it is proven that phthalates can migrate from polymers to beverages and food, necessary steps and regulations should be established. Permissible migration level should be maintained for the evaluation of the potential risk to human health and environment.

#### Author contributions

Dr. P. B. Harathi had the conceptualization and supervision. Amritha P S performed the investigation, visualization, data curation, and writing original draft. Veena Vinod had done the review and editing of the manuscript.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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