Environment International 123 (2019) 543–557

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Review article

Beyond the obvious: Environmental health implications of polar polycyclic aromatic hydrocarbons

Oluyoye Idowu[a], Kirk T. Semple[b], Kavitha Ramadass[c], Wayne O'Connor[d], Phil Hansbro[e,f], Palanisami Thavamani[a,*]

[a] Global Centre for Environmental Remediation (GCER), University of Newcastle, Callaghan, NSW 2308, Australia
[b] Lancaster Environment Centre, Lancaster University, Lancaster LA1 4YQ, United Kingdom
[c] Global Innovative Centre for Advanced Nanomaterials (GICAN), University of Newcastle, Callaghan, NSW 2308, Australia
[d] Port Stephens Fisheries Institute, NSW Department of Primary Industries, Port Stephens, Australia
[e] Centre for Inflammation, Centenary Institute, Sydney, NSW 2050, Australia
[f] University of Technology Sydney, Faculty of Science, Ultimo, NSW 2007, Australia

ARTICLE INFO

Handling editor: Robert Letcher

Keywords:
Polar polycyclic aromatic hydrocarbons
Environmental health
Mutagenesis
Carcinogenesis
Human health

ABSTRACT

The genotoxic, mutagenic and carcinogenic effects of polar polycyclic aromatic hydrocarbons (polar PAHs) are believed to surpass those of their parent PAHs; however, their environmental and human health implications have been largely unexplored. Oxygenated PAHs (oxy-PAHs) is a critical class of polar PAHs associated with carcinogenic effects without enzymatic activation. They also cause an upsurge in reactive oxygen species (ROS) in living cells. This results in oxidative stress and other consequences, such as abnormal gene expressions, altered protein activities, mutagenesis, and carcinogenesis. Similarly, some nitrated PAHs (N-PAHs) are probable human carcinogens as classified by the International Agency for Research on Cancer (IARC). Heterocyclic PAHs (polar PAHs containing nitrogen, sulphur and oxygen atoms within the aromatic rings) have been shown to be potent endocrine disruptors, primarily through their estrogenic activities. Despite the high toxicity and enhanced environmental mobility of many polar PAHs, they have attracted only a little attention in risk assessment of contaminated sites. This may lead to underestimation of potential risks, and remediation end points. In this review, the toxicity of polar PAHs and their associated mechanisms of action, including their role in mutagenic, carcinogenic, developmental and teratogenic effects are critically discussed. This review suggests that polar PAHs could have serious toxicological effects on human health and should be considered during risk assessment of PAH-contaminated sites. The implications of not doing so were argued and critical knowledge gaps and future research requirements discussed.

1. Introduction

It has been more than four decades since the US Environmental Protection Agency (EPA) released a list of 16 representative polycyclic aromatic hydrocarbons (PAHs). This list, popularly known as 16 US EPA PAHs, has over the years gained tremendous recognition as a representative for all non-polar (homocyclic) and polar (heterocyclic/substituted) PAHs. This group of compounds has subsequently played a unique and vital role in environmental and analytical sciences (Andersson and Achten, 2015). However, PAHs comprise several thousand molecules (Achten and Andersson, 2015) that are not being considered. The continuous focus on the 16 US EPA PAHs implies the non-inclusion of many likely toxic compounds (Andersson and Achten, 2015). Importantly, more hydrophilic and mobile polar PAHs such as oxygenated PAHs (oxy-PAHs), nitrated PAHs (N-PAHs) and N/S/O-heterocyclic PAHs are also not included in the list. This trend implies that the toxicological effects of PAHs in most contaminated sites are underestimated (Andersson and Achten, 2015), raising the question on the effectiveness of current global risk assessment and remediation of PAH-contaminated sites (Witter and Nguyen, 2016).

Polar PAHs are of global concern due to their toxicity, persistence, and mobility in the environment (Achten and Andersson, 2015; Wang et al., 2011). Also, the presence of electronegative atoms makes them more reactive and potentially more toxic compared to homocyclic PAHs (Achten and Andersson, 2015). For instance, some oxy-PAHs and N-PAHs do not require enzymatic activation to exert toxic effects, whereas related homocyclic/parent PAHs, such as B[*a*]P, require activation (Debajyoti Ghosal et al., 2016). In addition, N/S/O-heterocycles and

* Corresponding author at: Global Centre for Environmental Remediation, the University of Newcastle, 2258, NSW, Australia.
E-mail address: thava.palanisami@newcastle.edu.au (P. Thavamani).

https://doi.org/10.1016/j.envint.2018.12.051
Received 11 October 2018; Received in revised form 2 December 2018; Accepted 21 December 2018

their metabolites have been linked to endocrine disruption, e.g. with 7-ethoxyresorufin O-deethylase (EROD) induction and estrogenic activities (Brinkmann et al., 2014; Kuch et al., 2010). In most assays, these groups of polar PAHs with nitrogen, oxygen, or sulphur substituted atoms have caused similar or even higher toxicity compared to homocyclic PAHs (Wang et al., 2011; Brinkmann et al., 2014; Chibwe et al., 2015; Wincent et al., 2015).

The toxic properties, as well as the lack of monitoring and control, of polar PAHs by regulatory authorities in risk assessment is a significant cause of concern (Wincent et al., 2015). Therefore, this review aims to describe the mechanism of toxicity of polar and non-polar PAHs and their potential risks to human and environmental health. Specifically, this review will: a. Utilise the physicochemical characteristics of polar and non-polar PAHs to explain the differences in their mobility, bioavailability, and toxicity behaviours; b. Explain the possible impacts of polar PAHs toxicity on human health; and c. Suggest efficient remediation approaches for polar PAHs.

1.1. Sources and types of PAHs

Polycyclic aromatic hydrocarbons are produced from both natural and anthropogenic sources with the latter constituting the significant sources. While natural sources include forest or bushfires, diagenesis, and volcanic eruptions, anthropogenic sources consist of various pyrolytic processes during industrial operations, incineration, vehicular emissions and power generation among others (Wei et al., 2015a). Pyrolytic PAHs are released into the atmosphere in smoke, leading to their deposition on water and in soil (Vignet et al., 2014). Smoke, especially from tobacco, is primarily composed of PAHs and more importantly, polar PAHs. Many studies have confirmed the presence of > 500 types of PAHs in cigarette smoke (St Helen et al., 2012; Roemer et al., 2004; Hang, 2010). Both active smoking and second-hand smoke (SHS) exposure are important sources of toxic PAHs (St Helen et al., 2012). Petrogenic PAHs and their derivatives are present in crude oil and petroleum products often introduced into environmental media as a result of oil spills (Wei et al., 2015a; Bandowe et al., 2014). Polycyclic aromatic hydrocarbons can also be biogenic, resulting from certain terrestrial and aquatic microorganisms (Achten and Hofmann, 2009).

In addition to these primary sources, polar PAHs could indirectly result from homocyclic PAHs through different secondary processes such as (photo) chemical degradation (i.e. reaction with O_3, OH and NO_x) (Bamforth and Singleton, 2005; Lundstedt et al., 2007; Vione et al., 2006). Polar PAHs include oxygenated PAHs (oxy-PAHs), nitrated PAHs (N-PAHs) and, nitrogen, sulphur and oxygen (N/S/O)-Heterocyclic PAHs (Fig. 1).

1.2. Substituted PAHs

1.2.1. Oxygenated PAHs (oxy-PAHs)

Oxygenated (oxy-)PAHs are ketone and quinone substituted PAHs, that result directly from incomplete atmospheric combustion or tropospheric conversion of PAHs (Albinet et al., 2006; Shen et al., 2011) and other precursor molecules (Webb et al., 2006). Tropospheric conversion occurs from atmospheric reactions of PAHs with oxidative species such as ozone, hydroxyl, and nitrate radicals as well as UV-induced photoreactions (Vione et al., 2006). Incomplete metabolism of PAHs in contaminated soil during bioremediation can also yield oxy-PAHs (Lemieux et al., 2008). Oxygenated PAHs are regarded as dead-end products due to the numerous processes through which they are formed (Layshock et al., 2010). Based on functional groups, they have been classified into two major types: carbonyl and hydroxylated PAHs (Lundstedt et al., 2007). Carbonyl PAHs contain one or more carbonylic oxygen atoms attached to the aromatic ring structure, while hydro- hydroxyl groups (Fig. 1). Oxy-PAHs in the environment as their parent

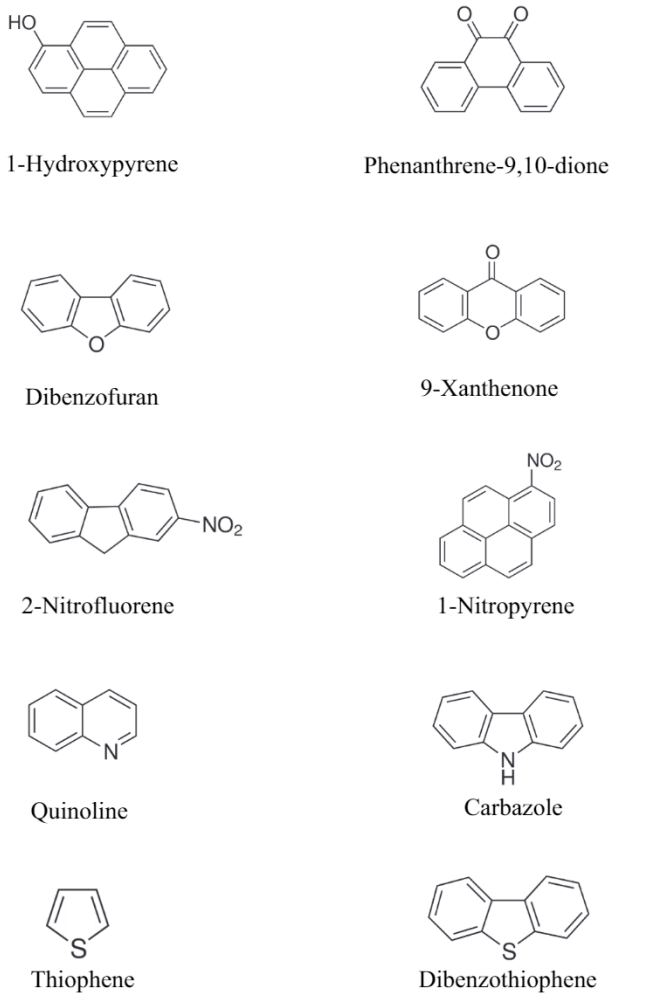

Fig. 1. Structural formulae of representative polar polycyclic aromatic hydrocarbons.

PAHs (Lundstedt et al., 2007).

Studies, which investigated the abundance of oxy-PAHs in soil and atmospheric particulate matter, showed a close correlation between oxy-PAHs and PAHs (Walgraeve et al., 2010; Bandowe and Wilcke, 2010). Higher concentrations of individual oxy-PAHs compared to corresponding parent-PAHs have been reported in contaminated sites undergoing bioremediation (Lundstedt et al., 2007). It could be due to the accumulation of oxy-PAHs at PAH-contaminated sites since most bioremediation methods promote PAH degradation/transformation (Palanisami et al., 2018) Worse still, these transformation products are not routinely monitored (Bamforth and Singleton, 2005).

1.2.2. Nitrated PAHs

These are nitro-functional group-containing derivatives of PAHs (Fig. 1). Nitrated PAHs could result from PAH degradation, pyrolysis or incomplete combustion of fossil fuels and biomass from industries, household stoves and heaters, waste incinerators and natural fires and vehicles (Bandowe and Meusel, 2017). As transformation products of PAHs, they are formed through reactions of particulate-bound PAHs with N_2O_5, NO_2, and NO_3 radicals during atmospheric transport (Jariyasopit et al., 2014; Zimmermann et al., 2013). Nitrated PAHs are generated as waste products of industrial and pharmaceutical processes because of their usage during the production process, as solvents, corrosion inhibitors, etc. (Padoley et al., 2008). They are also common pollutants in diesel vehicle exhaust (Bamford and Baker, 2003). Along with heterocyclic aromatic hydrocarbons, N-PAHs are known

constituents of petroleum-based products such as seal coat pavement sealant (Titaley et al., 2016; Wei et al., 2015b). The concentrations of N-PAHs compared to other PAHs are usually lower (about 1–2 orders of magnitude) with diesel engines emitting greater concentrations of N-PAHs than gasoline engines (Pham et al., 2013). Combustion temperature is an important determinant of N-PAH/PAH ratio (Deng and Chan, 2017) and it is useful in identifying emission sources (Pham et al., 2013). Although the concentrations of N-PAHs in the environment are smaller compared to other PAHs, they are nonetheless of great concern to human health due to their potent mutagenic and carcinogenic properties (Bandowe and Meusel, 2017). Like oxy-PAHs they might not require enzymatic activation to express toxicity. 1-Nitropyrene, for example, is classified as a probable human carcinogen by the International Agency for Research on Cancer (IARC) (Alves et al., 2016).

1.2.3. Nitrogen, sulphur and oxygen-heterocyclic PAHs

Nitrogen, sulphur and oxygen-heterocyclic PAHs contain nitrogen, sulphur and oxygen atoms within the aromatic rings (Fig. 1). About two-thirds of existing aromatic compounds are heterocycles (Bleeker et al., 2001), emphasizing the importance of these compounds in the environment. Heterocyclic PAHs are different in origin, chemical and biological properties from N-PAHs, S-PAHs and oxy-PAHs, which have their heteroatoms as substituents (Andersson and Achten, 2015). Nitrogen, sulphur and oxygen-heterocyclic PAHs can also be referred to as polycyclic aromatic nitrogen heterocycles (PANHs, e.g. indole, acridine); polycyclic aromatic sulphur heterocycles (PASHs, e.g. dibenzothiophene); and polycyclic aromatic oxygen heterocycles (PAOHs, e.g. benzonaphthofuran) (Andersson and Achten, 2015).

These compounds are introduced into the environment from sources similar to other PAHs as well as pharmaceutical and pesticide production, among others (Alves et al., 2016). Nitrogen, sulphur and oxygen-heterocyclic PAHs are significant constituents of bitumen and bitumen emissions (IARC, 2013) and may also originate from natural sources, such as alkaloids, mycotoxins, or nucleotides (Feldmannova et al., 2006). However, they are released predominantly as anthropogenic contaminants through incomplete combustion of fossil fuels, spills or industrial effluents or as a result of oil drilling and refining, wood preservation, and tobacco smoking (Bleeker et al., 2002). In some toxicity assays, N/S/O-heterocyclic PAHs displayed similar or even greater toxicity compared to their homocyclic analogues (Brinkmann et al., 2014).

2. Physico-chemical properties of homocyclic, heterocyclic and substituted PAHs

The physicochemical properties of polar PAHs determine their fate, transport, partitioning and movement within and between environmental compartments as well as toxicological attributes. Variation in physicochemical characteristics of PAHs is related to the functional group polarities and number of rings (Achten and Andersson, 2015). Generally, the boiling point (BP) and the octanol-water partition coefficient (K_{OW}) increase with the number of aromatic rings in the PAH structure, while vapour pressure (Vp) and aqueous solubility decrease with a number of rings (Achten and Andersson, 2015) (Table 1). The presence of polar functional groups impacts higher aqueous solubility and lower K_{OW} to polar PAHs compared to parent PAHs with a similar ring number (Table 1). There is, therefore, potential greater mobility of polar PAHs in environmental media such as soil and sediment compared to parent PAHs. Hydrophilicity, have been shown to, increase in the order NO_2 < COOH < OH < CN < NH_2 < dione (Achten and Andersson, 2015) resulting in greater mobility of oxy-PAHs compared to other substituted PAHs. The substitution of a carbon atom by a nitrogen or oxygen atom in N/O heterocyclic PAHs makes these substances relatively more polar. Sulphur-heterocycles, compared to other [illegible]lar implying a similar environmental [illegible]eeker et al., 2002).

Furthermore, differences in the structure and size of individual PAHs may result in substantial variability in their toxicological properties (Larcher et al., 2014). Higher molecular weight compounds, for example, exhibit greater toxicities than the lower molecular weight ones (Bamforth and Singleton, 2005; Larcher et al., 2014). This could be as a result of their comparatively greater hydrophobicity and tissue partitioning (Bandowe and Meusel, 2017). Also, compounds with oxygen and nitrogen heteroatoms are more toxic than homocyclic hydrocarbons probably because of their higher reactivity (Achten and Andersson, 2015).

Regarding Vp, polar PAHs are typically characterised by lower values compared to their parent PAHs (Table 1). Lower Vp values partly explain greater partitioning into atmospheric particulate phase compared to the gaseous phase and affinity for finer particulate matter (Lui et al., 2016). They can, therefore, enter human lungs and even blood through the particulate matter ($PM_{2.5}$ and PM_1) which have been shown to have the ability to permeate various tissues and organs thereby exerting greater toxic effects (Lui et al., 2017; Ringuet et al., 2012; Agudelo-Castañeda et al., 2017). For highly soluble carcinogens, such as N-heterocyclic PAHs, the associated adverse effects could be more deleterious than other PAHs (Chen and Preston, 2004), as their dissolution occurs more readily in the lungs.

2.1. Fate and behaviour of polar PAHs

2.1.1. Polar PAHs in soil

The fate and behaviour of PAHs in soil could be determined by factors such as the rate of sorption and sequestration, volatilisation, leaching, degradation and uptake by plants (Srogi, 2007). The hydrophobic nature (high K_{ow} values) of homocyclic PAHs makes them relatively less soluble in water (Han et al., 2015). In soil, they tend to sorb strongly to soil surfaces through hydrophobic interactions, especially with time (Chiou et al., 1998).

The mechanism of polar PAHs sorption to soils and sediments varies depending on their individual physicochemical properties. In addition to non-specific hydrophobic interaction with soil organic matter, N-PAHs partition extensively and predominantly to solid phases of the soil through strong π-π interactions, and complexation between nitro-groups and cations or surface oxygen in clay (Bandowe and Meusel, 2017). The strong interaction and relatively lower solubility of N-PAHs make them less mobile and leachable in soils (Bandowe and Meusel, 2017) compared to other polar PAHs. Also, the rate of volatilisation of N-PAHs from soil is very low as a result of low Vp and Henry's Constant (H), and high octanol-air partition coefficient (K_{OA}). In contrast, oxy-PAHs and the N/O-heterocyclic PAHs are highly leachable and partition more readily into the aqueous phase due to their lower K_{ow} and organic carbon-water partition coefficient (K_{oc}) values, thereby sorbing less to organic matter and other carbonaceous materials in soils (Achten and Andersson, 2015).

Investigation of the concentrations of polar PAHs in soils are scarce. However environmentally relevant concentrations have been reported in a few studies (Table 2).

The reported concentrations of oxy-PAHs were higher than those of N-PAHs and heterocyclic PAHs (Table 2). The comparatively lower concentrations of N-PAH to the concentrations of oxy-PAHs may be due to their susceptibility to degradation (Bandowe and Meusel, 2017). Also, gas works and coking plants are likely more viable sources of polar PAHs compared to agricultural and urban activities (Table 2).

2.1.2. Polar PAHs in air

As with soil, the fate and behaviour of polar PAHs in the air, particularly gaseous or particulate phase partitioning, varies with their physicochemical properties. Molecular weight and Vp play important roles in particulate matter (PM) partitioning (Alves et al., 2017). Chemicals with Vp < 1.3×10^{-3} Pa partition almost entirely into the PM and low-molecular-weight compounds (≤202 g/mol) partition more

Table 1
Physico-chemical Properties of Polar and Non-Polar Polycyclic Aromatic Hydrocarbons (PAHs).

PAHs	Molecular Formula	Molecular Weight MW	Boiling Point Bp	Vapour pressure Vp	Water solubility S	Henry's constant H	Log Kow	TEF	LD_{50} (Rat)
Indene	C_9H_8	116.0626	182	1.47E + 02	3.32E + 02	6.50E − 02	2.92	na	na
1-Indanone[a]	C_9H_8O	132.0575	243	3.90E + 00	1.43E + 03	3.20E − 05	2.11	na	Na
Benzofuran[c]	C_8H_6O	118.0419	174	5.87E + 01	6.78E + 02	4.13E − 03	2.67	na	na
Indole[e]	C_8H_7N	117.0579	254	1.63E + 00	3.56E + 03	2.16E − 05	2.14	na	1000
Benzothiophene[f]	C_8H_6S	134.0190	221	2.20E + 01	1.30E + 02	1.17E − 02	3.12	na	1260–1700
Naphthalene	$C_{10}H_8$	128.0626	218	1.13E + 01	3.10E + 01	1.80E − 02	3.35	0.001	1110;1780
Naphthalene-1,4-dione[a]	$C_{10}H_6O_2$	158.0368	301	2.40E − 02	6.68E + 02	8.06E − 08	1.71	na	190
1-Hydroxynaphthalene[b]	$C_{10}H_8O$	144.0575	288	3.70E − 02	8.66E + 02	2.33E − 06	2.85	na	1870,2600
2-Hydroxynaphthalene[b]	$C_{10}H_8O$	144.0575	285	4.30E − 02	7.55E + 02	1.12E − 06	2.70	na	1320–2400
1-Nitronaphthalene[d]	$C_{10}H_7NO_2$	173.0477	304	2.49E − 09	9.18E + 00	7.20E − 05	3.19	na	120
2-Nitronaphthalene[d]	$C_{10}H_7NO_2$	173.0477	314	3.44E − 02	9.24E + 00	8.51E − 05	3.24	na	4400
Quinoline[e]	C_9H_7N	129.0579	237	8.00E + 00	6.11E + 03	6.83E − 05	2.03	na	330–460
Isoquinoline[e]	C_9H_7N	129.0579	243	5.00E + 00	4.52E + 03	2.81E − 05	2.08	na	350–360
Acenaphthylene	$C_{12}H_8$	152.0626	280	8.90E − 01	1.61E + 01	4.66E − 03	3.94	na	na
Acenaphthylene-1,2-dione[a]	$C_{12}H_6O_2$	182.0368	350	2.09E − 03	9.01E + 01	1.40E − 07	1.95	na	na
Acenaphthene	$C_{12}H_{10}$	154.0783	279	2.87E − 01	3.90E + 00	7.53E − 03	3.92	na	10,000; > 16,000
1-Acenaphthenone[a]	$C_{12}H_8O$	168.0575	315	1.30E − 02	2.00E + 01	1.44E − 05	2.79	na	na
3-Nitroacenaphthene[d]	$C_{12}H_9NO_2$	199.0633	500	2.57E − 10	1.05E + 02	1.26E − 14	1.77	na	na
Fluorene	$C_{13}H_{10}$	166.0783	295	8.00E − 02	1.69E + 00	3.93E − 03	4.18	na	LDo: > 16,000
Fluorene-9-one[a]	$C_{13}H_8O$	180.0575	342	7.62E − 03	2.53E + 01	2.77E − 05	3.58	na	na
Benzo[*a*]fluorenone[a]	$C_{17}H_{10}O$	230.0732	403	5.16E − 05	2.16E − 01	2.70E − 06	4.73	na	na
2-Hydroxyfluorene[b]	$C_{13}H_{10}O$	182.0732	333	3.95E − 04	9.60E + 01	1.50E − 05	3.22	na	na
Dibenzofuran[c]	$C_{12}H_8O$	168.0575	287	3.31E − 01	3.10E + 00	8.71E − 03	4.12	na	> 16,000
2-Nitrofluorene[d]	$C_{13}H_9NO_2$	211.0633	496	1.27E − 03	2.16E − 01	2.70E − 05	3.37	0.01	na
Carbazole[e]	$C_{12}H_9N$	167.0735	355	1.83E − 04	1.80E + 00	3.54E − 06	3.72	na	500 − > 16,000
Phenanthrene	$C_{14}H_{10}$	178.0783	340	1.61E − 02	1.15E + 00	1.73E − 03	4.46	0.001	700
Phenanthrene-9,10-dione[a]	$C_{14}H_8O_2$	208.0524	360	3.11E − 04	7.50E + 00	1.10E − 07	2.52	na	na
Cyclopenta[def]phenanthrene-4-one[a]	$C_{15}H_8O$	204.0575	360	1.03E − 03	1.80E + 00	1.08E − 06	3.81	na	na
2-Hydroxyphenanthrene[b]	$C_{14}H_{10}O$	194.0732	363	2.37E − 04	6.90E + 00	2.18E − 07	3.86	na	na
3-Hydroxybenzo[c] phenanthrene[b]	$C_{18}H_{12}O$	244.0888	434	9.77E − 07	3.72E − 01	2.14E − 08	5.04	na	na
3-Nitrophenanthrene[d]	$C_{14}H_9NO_2$	223.0633	543	6.78E − 12	1.67E + 00	2.29E − 15	1.96	na	na
Phenanthridine[e]	$C_{13}H_9N$	179.0735	349	2.77E − 03	3.00E + 02	6.71E − 07	3.48	na	na
Phenanthro[4,5-bcd]thiophene[f]	$C_{14}H_8S$	208.0347	364	8.14E − 04	1.82E − 01		4.95	na	na
Anthracene	$C_{14}H_{10}$	178.0783	340	1.07E − 03	4.34E − 02	2.27E − 033	4.45	0.000	3200
Benzo[*de*]anthracene-7-one[a]	$C_{17}H_{10}O$	230.0732	403	2.95E − 05	2.40E − 01	2.70E − 06	4.81	na	na
Benzo[*a*]anthrancene-7,12-dione[a]	$C_{18}H_{10}O_2$	258.0681	435	4.67E − 06	2.89E − 01	1.27E − 08	4.40	na	na
1-Hydroxybenzo[*a*]anthracene[b]	$C_{18}H_{12}O$	244.0888	434	9.77E − 07	3.72E − 01	2.14E − 08	5.04	na	na
Xanthene[c]	$C_{13}H_{10}O$	182.0732	311	1.13E − 01	1.02E + 00	1.95E − 03	4.23	na	na
Xanthenone[c]	$C_{13}H_8O_2$	196.0524	351	7.80E − 03	4.52E + 00	7.89E − 06	3.39	na	> 500
9-Nitroanthracene[d]	$C_{14}H_9NO_2$	223.0633	543	1.80E − 04	1.14E − 01	8.30E − 06	4.78	na	na
Acridine[e]	$C_{13}H_9N$	179.0735	346	1.80E − 02	3.84E + 01	1.62E − 05	3.40	na	2100
Acridone[e]	$C_{13}H_9NO$	195.0684	368	1.30E − 04	1.40E + 00	7.30E − 06	2.96	na	na
Thioxanthene[f]	$C_{13}H_{10}S$	198.0503	341	2.65E − 03	1.75E + 00	na	3.86	na	na
Thianthrene[f]	$C_{12}H_8S_2$	216.0067	365	4.13E − 03	4.26E − 01	3.39E − 05	4.47	na	na
Pyrene	$C_{16}H_{10}$	202.0783	404	6.00E − 04	1.35E − 01	4.87E − 04	4.88	0.001	2700
Pyrene-1,6-dione[a]	$C_{16}H_8O_2$	232.0524	384	3.69E − 04	6.94E + 01	2.01E − 08	3.08	na	na
1-Hydroxypyrene[b]	$C_{16}H_{10}O$	218.0732	407	3.80E − 06	1.64E + 00	na	4.45	na	na
1-Nitropyrene[d]	$C_{16}H_9NO_2$	247.0633	587	7.36E − 06	1.18E − 02	1.34E − 06	5.06	0.1	na
2-Nitropyrene[d]	$C_{16}H_9NO_2$	247.0633	587	1.68E − 13	1.25E + 01	3.71E − 16	2.55	na	na
1,6-Dinitropyrene[d]	$C_{16}H_8N_2O_4$	292.0484	642	1.39E − 15	4.04E + 00	1.46E − 18	2.37	10	na
Fluoranthene	$C_{16}H_{10}$	202.0783	384	1.23E − 03	2.60E − 01	3.62E − 04	5.16	0.08	10–30
2-Nitrofluoranthene[d]	$C_{16}H_9NO_2$	247.0633	587	1.68E − 13	1.25E + 01	3.71E − 16	2.55	na	na
3,7-Dinitrofluoranthene[d]	$C_{16}H_8N_2O_4$	292.0484	610	2.31E − 14	5.39E + 00	4.70E − 18	2.22	na	na
Benzo[*a*]fluorene	$C_{17}H_{12}$	216.0939	405	6.24E − 04	4.54E − 02	1.09E − 03	5.40	na	na
Benzo[*a*]fluorenone[a]	$C_{17}H_{10}O$	230.0732	403	5.16E − 05	2.16E − 01	2.70E − 06	4.73	na	na
Benzo[*a*]anthracene	$C_{18}H_{12}$	228.0939	438	2.80E − 05	9.40E − 03	4.91E − 04	5.76	0.2	na
Benzo[*de*]anthracene-7-one[a]	$C_{17}H_{10}O$	230.0732	403	2.95E − 05	2.40E − 01	2.70E − 06	4.81	na	na
Benzo[a]anthrancene-7,12-dione[a]	$C_{18}H_{10}O_2$	258.0681	435	4.67E − 06	2.89E − 01	1.27E − 08	4.40	na	na
Chrysene	$C_{18}H_{12}$	228.0939	448	8.30E − 07	2.00E − 03	2.14E − 04	5.81	0.01;0.1	na
1-Hydroxychrysene[b]	$C_{18}H_{12}O$	244.0888	434	9.77E − 07	3.72E − 01	2.14E − 08	5.04	na	na
Benzo[*b*]fluoranthene	$C_{20}H_{12}$	252.0939	443	6.67E − 05	1.50E − 03	2.69E − 05	5.78	0.1;0.8	na
6-Nitrochrysene[d]	$C_{18}H_{11}NO_2$	273.0789	614	1.60E − 14	2.80E + 00	2.24E − 16	3.14	10	na
Benzo[*a*]pyrene	$C_{20}H_{12}$	252.0939	496	1.03E − 04	1.62E − 03	1.87E − 05	6.13	1	na
Benzo[*a*]pyrene-1,6-quinone[a]	$C_{20}H_{10}O_2$	282.0681	441	2.33E − 06	1.25E + 00	3.06E − 09	4.80	na	na
3-Hydroxybenzo[*a*]pyrene[b]	$C_{20}H_{12}O$	268.0888	478	2.61E − 08	8.60E − 02	3.45E − 09	5.63	na	na

Adapted from: Achten and Andersson, 2015.
[a] Keto/Carbonyl-PAH.
[b] Hydroxyl-PAH.

Table 2
Mean concentrations of ΣPolar PAHs in PAH-impacted soils of selected countries.

Country	City/region	Source	Number of sites considered	(ug/g/dw)	References
Oxy-PAHs					
Australia	South Australia	Gasworks	10	161.01	(Palanisami et al., 2018)
		Creosote site	10	53.3	
		Wood preservation	10	29.81	
	Victoria	Gasworks	10	118.28	
		Creosote site	10	58.27	
		Wood preservation	10	37	
	New South Wales	Gasworks	10	326.5	
		Creosote site	10	55.02	
	Western Australia	Oil industry site	10	16.04	
Sweden	Husarviken	Gas works	16	426.66	(Lundstedt et al., 2007)
	Lulea	Coking plant	16	106.76	
	Holmsund	Wood preservation	16	252.88	
	Boden	Wood preservation	14	9.38	
Germany	Berlin	Gas works	18	16.21	(Bandowe and Wilcke, 2010)
	Mainz	Urban	18	0.206	
	North Region	Coking plant	6	57.6	(Susanne et al., 1999)
	North Region	Wood preservation	6	39.1	
France	Homecourt	Coking plant	8	113.12	(Biache et al., 2008)
	Neuver-Maisons	Coking plant	8	543.36	(Agudelo-Castañeda et al., 2017)
Slovakia	Bratislava	Chemical waste dump	14	2.69	(Bandowe et al., 2011)
Czech Republic	Tyn-Lipnik	Urban site	3	35.96	(Zdráhal et al., 2000)
Uzbekistan	Angren	Agricultural soils	12	1.9	(Musa Bandowe et al., 2010)
N-PAHs					
Italy	Catania	Urban soil	1	0.00014	(De Guidi et al., 2016)
China	Eastern China	Agricultural soils	82	0.05	(Sun et al., 2017)
Heterocyclic PAHs					
Dibenzothiophene Dibenzofuran	Beijing, China	Agricultural soils	8	0.06	(Zhihuan et al., 2008)
Dibenzothiophene and Dibenzofuran		Industrial soils	1	0.068	
Dibenzothiophene and Dibenzofuran		Urban grassland	1	0.78	

into the gaseous phase (Walgraeve et al., 2010). Nitrated PAHs exhibit lower Vp compared to other PAHs of similar ring numbers (Bandowe and Meusel, 2017). Greater partitioning of high molecular weight polar PAHs into the PM compared to the low molecular weight polar PAHs have been reported (Yebra-Pimentel et al., 2015).

Parameters such as K_{OA} and gas-particle partition coefficient (K_p) are also important factors in PAHs gas-PM partitioning. Higher K_{OA} and K_p values imply greater partitioning into PM and vice-versa. In addition to higher Mw and lower Vp, N-PAHs, for example, are prevalent in PM due to greater K_{OA} and K_p compared to other polar PAHs (Alves et al., 2017). N-PAHs concentrations, during winter, was about 0.2–100 pg/m^3 and 0.0–20.0 pg/m^3 in particulate and gaseous phase respectively, in a French rural site study (Albinet et al., 2006).

Varying chemical properties results in varying bonding strength between polar PAHs and PM. Nitrated heterocyclic PAHs, because of their ionic properties, sorb to atmospheric PM through ionic and polar intermolecular forces (Arp et al., 2008). Hydrophobic and weak van der Waal forces are prevalent in other related PAHs (Arp et al., 2008; Bandowe et al., 2016). The strength of interaction between the compound and PM plays a vital role in contaminant concentration and persistence. Polar PAHs concentration in the atmospheric PM and gaseous phases have been reported in many studies (Table 3).

2.1.3. Polar PAHs in water

Polar PAHs could be deposited in aquatic ecosystems directly from atmospheric particulate matter or as fallout from rain (Uno et al., 2017). Nitrated-PAHs exhibit lower K_{ow}, Koc and H values, implying their ready partitioning into the aqueous phase (Bandowe and Meusel, 2017). However, despite this, solubility (S) of N-PAHs have been reported to be low compared to other polar PAHs (Bandowe and Meusel, 2017). Oxy-PAHs partition better into the aqueous phase and demonstrates higher solubility and lower lipophilicity (Adrion et al., 2016; Lundstedt et al., 2014). The aqueous solubilities of N/S/O-heterocyclic than other PAHs due to the presence and low K_{ow}. The water-soluble fraction of coal tar consists of about 40% of N/S/O heterocycles (Blum et al., 2011). N-heterocyclic PAHs can exist in ionic form due to the presence of an unpaired electron in their structure. This acid/base characteristic has the potential of improving their dissolution in water during precipitation and in water bodies (Alves et al., 2016; Bandowe et al., 2016). The aqueous solubility of a quinolone, for example, is more than two orders of magnitude higher than, the most soluble homocyclic PAH, naphthalene (Blum et al., 2011).

High solubilities of polar PAHs makes them of priority importance in the pollution of water bodies and aquifers. Persistent N/S/O heterocyclic PAHs contaminant plumes have been reported in coal tar underground water pollution (Blum et al., 2011). Relatively high concentrations, persistence and toxicity of polar PAHs in water bodies have important ecological health implications.

2.2. Comparison of non-polar and polar PAH bioavailability in soil

Most substituted and heterocyclic PAHs are more bioavailable than their parent PAHs, as they are more polar (Alves et al., 2017). A bioavailable compound is freely available to cross an organism's cellular membrane for assimilation, transformation and degradation (Semple et al., 2004). Contaminant bioavailability and the associated risks to biota is closely related to their partitioning behaviour in environmental media. Homocyclic (non-polar) and polar PAHs partition differently in the soil, air and water thereby exerting varying bioavailability and risks to living organisms (Srogi, 2007; Tsibart and Gennadiev, 2013).

In soil, contaminant bioavailability is influenced by environmental conditions, such as soil aggregation, wetness, dryness and aeration. Environmental loss processes, including but not limited to, volatilisation, biodegradation, transformation, leaching, uptake by biota, and physical mass transport also influence contaminant bioavailability (Fig. 2). Importantly, sequestration of contaminants in soil reduces their bioavailability, and may result from contaminant incorporation into natural organic matter, diffusion into soil mesopores and intra-particle

Table 3
Atmospheric Concentrations of some Environmentally-Relevant Polar PAHs.

Compound	Location	Sampling season	Concentration Pg/m^3	Phase	References
Naphthalene-1,4-dione	Athens, Greece	Winter	150	TSP	(Chung et al., 2006)
		Spring	60	TSP	
	Santiago, Chile	Winter	14.4	$PM_{2.5}$	(Tsapakis et al., 2002)
		Spring	61.6		
	San Dimas, CA, USA	Summer	60–140	$PM_{2.5}$	(Cho et al., 2004)
9H-fluorene-9-one	Birmingham, UK	All	4600–5800	TSP and gas	(Harrad et al., 2003)
	Munich, Germany	All	220–460	TSP	(Schnelle-Kreis et al., 2005)
	Marseille area, France	Summer	190–6908	PM_{10}	(Albinet et al., 2007)
Anthracene-9,10-dione	Fresno, CA, USA	Winter	470	TSP	(Chung et al., 2006)
		Spring	10		
		Summer	210		
	Maurienne valleys, France	Winter	1770–2360	PM_{10} and gas	(Albinet et al., 2007)
		Summer	130–470		
Chrysene-5,6-dione	Munich, Germany	All	1.4–82	$PM_{2.5}$	(Lintelmann et al., 2006)
Benzo[*a*]pyrene-1,6-dione	Munich, Germany	All	1.4–82	$PM_{2.5}$	(Lintelmann et al., 2006)
1-Nitropyrene	Baltimore, MD, USA	Winter	27	TSP and gas	(Bamford and Baker, 2003)
		Summer	8.1		
	Forte Meade, MD, USA	Winter	21	TSP and gas	(Bamford and Baker, 2003)
		Summer	1.4		
	Bologna, Italy	Winter	5–32	PM_1 and $PM_{2.5}$	(Sarti et al., 2017)
		Summer	10–330		
9-Nitrophenanthrene	Bologna, Italy	Winter	1–15.6	PM_1 and $PM_{2.5}$	(Sarti et al., 2017)
		Summer	0.5–68		
Quinoline		Winter	bdl-357	$PM_{2.5}$	(Alves et al., 2017)
		Summer	bdl-90		
Acridine		Winter	bdl-373	$PM_{2.5}$	(Alves et al., 2017)
		Summer	bdl-102		
Carbazole		Winter	bdl-97	$PM_{2.5}$	(Alves et al., 2017)
		Summer	bdl-103		
Benzo(*h*)quinolone		Winter	bdl-129	$PM_{2.5}$	(Alves et al., 2017)
		Summer	bdl-136		

Notes: TSP indicates - Total Suspended Particle. bdl indicates - below the detection limit.

micro- or nano-pores, adsorption into rubbery or glassy solid organic matter, aging, and microbial recalcitrance (Doick et al., 2005). These processes influence contaminant bioavailability; however, the influences on bioavailability will also be dependent on contaminant physicochemical properties.

With increasing soil-contaminant contact time, homocyclic PAHs are expected to be more highly sequestered and less bioavailable than polar PAHs (Lundstedt et al., 2007; Bleeker et al., 2001; Enell et al., 2016). As a result of higher mobility and bioavailability, toxicity effects of polar PAHs may be more acute compared to the non-polar PAHs which are more likely to exhibit chronic effects (Lui et al., 2017).

3. Toxicity of PAHs

3.1. Routes of exposure of polar PAHs

The routes of exposure of polar PAHs are not different from the non-polar PAHs. Polar PAHs exposure could be through water, air, soil and food sources. Routes of exposure, therefore, include ingestion, inhalation and dermal/eye absorption. Polycyclic aromatic hydrocarbons' routes of exposure have been well discussed elsewhere (Rengarajan et al., 2015).

3.2. Aryl hydrocarbon receptor (AhR) activation by PAHs

Exposure to PAHs presents a significant human health risk due to their mutagenic and carcinogenic properties (Lemieux et al., 2015a; Lemieux et al., 2015b). Polycyclic Aromatic Hydrocarbons are unique because they do not directly induce DNA damage. Toxicity is derived from the detoxification mechanisms of cells or organisms (Martins et al., 2013). In an attempt to eliminate PAHs from the organism, an [illegible]d to increase water solubility and fa[illegible]016). This is a microsomal CYP monooxygenase-catalysed reaction often referred to as “activation” (Bleeker et al., 2002). The PAH-ligand/AhR activation usually results in the formation of highly reactive genotoxic metabolites, such as diol epoxides and quinones (Bleeker et al., 2002; Baird et al., 2005). These reactive intermediate compounds have the potential to form adducts with DNA (Baird et al., 2005; Moorthy et al., 2015).

The AhR plays important roles in detoxification of PAHs (Fig. 3) through the regulation of bioactivating and detoxifying (CYP) enzymes (Baird et al., 2005; Nebert et al., 2004). Furthermore, PAH carcinogenicity as well as some other toxic effects, are strongly linked to their capacity to activate the AhR (Vondráček et al., 2017). The AhR-inducing potencies of PAHs are believed to contribute to their tumour-promoting activities (Safe et al., 2013) due to the AhR's role in the regulation of cell proliferation, migration, invasion or survival of neoplastic cells (Safe et al., 2013; Dever and Opanashuk, 2012; Dietrich and Kaina, 2010). However, ligands exhibit varying levels of AhR activation, and the correlation between the AhR-inducing capacity and carcinogenicity of PAHs is not direct for some compounds (Larsson et al., 2012). Oxy-PAHs, for example, have been shown to be weak AhR activators (Lui et al., 2017); however, they remain one of the most toxic PAHs known. This is because they generate OH radical directly or through activation, causing fatal damages to biological molecules as a result of oxidative stress (Fig. 3). These include DNA, proteins and lipids damage leading to increased genetic instability, inflammation, proliferation, reduction of antioxidants, apoptosis and angiogenesis (Dasgupta et al., 2014).

3.3. Mechanism of activation of genotoxic PAHs

The process of AhR activation begins when polar and non-polar PAHs bind to the ligand-dependent transcription factor. This results in the activation of a battery of genes including cytochrome P450 (CYP1A1, CYP1A2 and CYP1B1). Three pathways exist according to

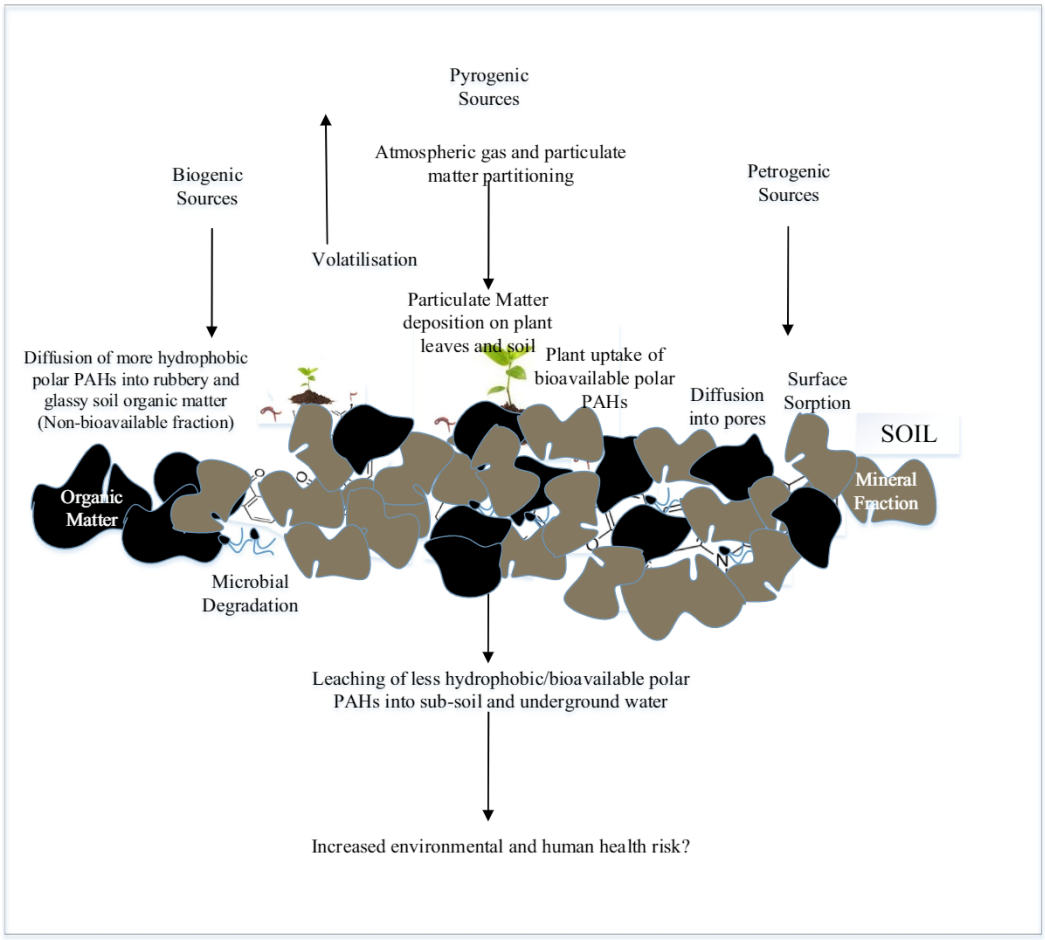

Fig. 2. Conceptiual fate of polar PAHs in soil.

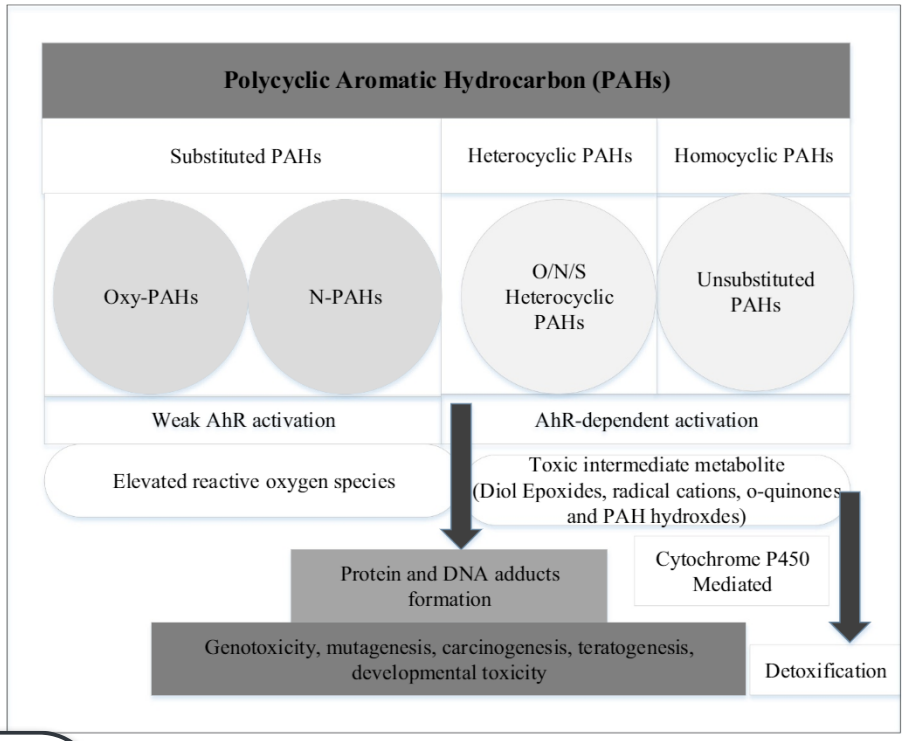

Fig. 3. Mechanism of homocyclic, heterocyclic and substituted-PAH toxicity.

(Moorthy et al., 2015). The CYP1A1/1B1 and epoxide hydrolase pathway (CYP/EH pathway) (Fig. 3) is the most common pathway, occurring mostly in homocyclic and heterocyclic PAHs (Benigni and Bossa, 2011) and resulting in the production of catechols, quinones and diol epoxides which interact with tissue nucleophiles (Fig. 3). The activation pathways were stated in (Benigni and Bossa, 2011) to include: initial epoxidation by cytochrome P450 monooxygenases; epoxide hydrolase (EH) enzyme-controlled hydrolysis to trans-diol and epoxidation of the terminal ring adjacent to a 'bay' or 'fjord' region which produces highly mutagenic and carcinogenic compounds. The other two existing pathways are CYP peroxidase, and dihydrodiol dehydrogenases (DDs) catalysed aldo-keto reductases pathway (AKR pathway). These result in the formation of unstable radical cations and redox-active o-quinones, respectively (Dasgupta et al., 2014; Benigni and Bossa, 2011). Unstable radical cations react with DNA to form adducts while redox cycling of o-quinones could lead to the formation of reactive oxygen species (ROS) and ultimately carcinogenesis.

Carcinogenicity and mutagenicity of polar PAHs, in most cases, follow similar mechanisms as the non-polar PAHs with many of them requiring metabolic activation (Fig. 3). However, the presence of heteroatoms in polar PAHs may influence the process. For example, in the radical cation pathway, the presence of heteroatoms may influence the ionisation potential of the molecules and hence the possibility of forming a stable radical cation (Xue and Warshawsky, 2005). The mechanism of N-PAHs toxicity follows the AhR activation process resulting in DNA damage, DNA adduct formation, changes in gene and protein expression, cell cycle alternations, increased levels of ROS and pro-inflammation (Andersson et al., 2009; Park and Park, 2009). However, N-PAHs can form covalently bonded DNA adducts through ring oxidation or nitro reduction pathways (Watt et al., 2007), while homocyclic PAHs utilise a single pathway of hepatic oxidative activation. The ability to produce covalently bonded DNA adducts through two pathways makes N-PAHs more potent carcinogens than homocyclic PAHs (Deng and Chan, 2017). Biotransformation of N/S/O-heterocyclic PAHs can alter their toxicity. Genotoxicity of acridine was significantly enhanced when it was biotransformed to acridone (Bleeker et al., 1999). N/S/O-heterocycles, including dinaphthofurans, 2-(2-naphthalenyl) benzothiophene, are major cytochrome P4501A (CYP1A)-inducing compounds. In one study, the identified non-priority N/S/O-heterocycles were found to be significantly more potent than the reference compound, benzo[*a*]pyrene (Brack and Schirmer, 2003). Oxy-PAHs are believed to be less potent activators of AhR (Wincent et al., 2015; Wincent et al., 2016). They exert toxicity directly or indirectly (Fig. 4) through the stimulation of oxidative stress and alkylation of cellular nucleophiles, respectively (Benigni and Bossa, 2011).

3.4. Oxidative stress and oxy-PAH toxicity

Oxidative stress is an important consequence of oxy-PAH toxicity. Oxidative stress results from a disturbance in the balance between the production of reactive oxygen species (ROS) and antioxidant defences. It is a state of imbalance between oxidants and antioxidants in the body that favours oxidants (e.g. superoxide, hydrogen peroxide and hydroxyl radical), potentially leading to cell damage as a result of severe oxidative stress and resulting in the formation of oxidised cellular macromolecules. This damage induces and activates biological responses such as inflammation and apoptosis (Fig. 4).

Many studies confirm the higher toxicity of oxy-PAHs (e.g. quinones) compared to parent PAHs, due to oxidative stress (Benigni and Bossa, 2011). Toxicity of some oxy-PAHs resulted in the induction and expression of antioxidant genes in zebra fish (Timme-Laragy et al., 2009; Van Tiem and Di Giulio, 2011) because of the upsurge in ROS. Redox-responsive genes (gst, gpx, gclc and sod) were observed at 48 h post-fertilisation (hpf) in zebra fish embryos exposed to benz(*a*)an- al., 2013). Oxy-PAH toxicity may nalformation and dysfunction, DNA breakdown, apoptosis and protein and lipid degradation (Dranka et al., 2011) as well as mutation and cancer. Phenanthrenequinone, 1, 9-benz-10-anthrone and xanthone exposures increased expression of several oxidative stress-related genes and decreased oxygen consumption rate (OCR) which is a measurement of mitochondrial respiration (Knecht et al., 2013). Some oxy-PAHs are considered extremely toxic compared to others, producing harmful superoxides and killing the majority of cells in a human cell mutagenicity assay (Durant et al., 1996). Reactive oxygen species also affect signal transduction pathways and the regulation of gene expression, thereby playing important roles in the tumour-promoting stage of carcinogenesis (Benigni and Bossa, 2011).

3.5. Comparison of non-polar and polar PAHs toxicity

3.5.1. Genotoxicity

The genotoxicity of polar PAHs has been compared to homocyclic PAHs in many studies. They all show comparable or higher genotoxic effects in polar PAHs. In one of such studies, the genotoxicity of acenaphthenequinone, 7,12-benz[*a*]anthracenquinone, acenaphthene, benz[*a*]anthracene and benzo[*a*]pyrene on Japanese Medaka embryo were investigated using a Comet assay (Dasgupta et al., 2014). It was found that oxy-PAHs caused significant increases in DNA damage after 48 h at the lowest tested concentration of 5 μg/L (Dasgupta et al., 2014). Nitrogen heterocycles were significantly more genotoxic and more potent inducers of AhR than their unsubstituted analogues in a study that investigated cytotoxicity and potential to activate AhR, utilising an in-vitro H4IIEluc transactivation cell assay (Iva Sovadinova et al., 2006). In the same way, a statistically significant increase in genotoxicity, after bioremediation, was reported in a study examining the genotoxic effect of post-remediation soil sample extracts, using the DT_{40} chicken lymphocyte bioassay. Bioreactor treatment of a PAH-contaminated soil resulted in increased genotoxicity throughout the treatment cycle (Hu et al., 2012). The increased genotoxicity was attributed to polar products resulting from bioremediation (Chibwe et al., 2015; Hu et al., 2012).

3.5.2. Mutagenicity

Polar PAHs are more mutagenic than homocyclic PAHs. Despite their relatively smaller concentration in the environment, polar PAHs exert greater mutagenic effects on organisms (Wang et al., 2011). In an assay investigating the direct and indirect-acting mutagenicity of $PM_{2.5}$ and the potential for DNA damage to human lung cells, ΣN-PAH and Σoxy-PAH concentrations, which were just 8% of the Σ parent PAH concentrations, exhibited direct-acting mutagenicity which was 200% higher than the indirect-acting mutagenicity of the homocyclic PAHs (Wang et al., 2011). In another study, organic extracts from ambient air particles showed higher direct mutagenic potency on two strains of Salmonella (Bocchi et al., 2017). The mutagenic potencies of acenaphthenequinone and 7,12-benz[*a*]anthracenquinone were comparable to that of acenaphthene, benz[*a*]anthracene and benzo[*a*]pyrene, especially during more extended periods of exposure (7 days) of Medaka fish embryos (Dasgupta et al., 2014). Increased mutagenicity was observed after aerobic bioremediation of PAH-contaminated soil as a result of the production oxy-PAHs and other polar and toxic PAH transformation products (Chibwe et al., 2015). Working with air particulate samples, oxy-PAH and N-PAH fractions from Beijing, China were shown to be twice as mutagenic as the parent fraction (Wang et al., 2011).

Some oxy-PAHs that have demonstrated their potential for mutagenicity include perinaphthenone, benzanthrone, acenaphthenequinone, 7,12-benz[*a*]anthracenquinone and benzo[*cd*]pyrenone (Dasgupta et al., 2014; Durant et al., 1996). Diesel exhaust particulate-1, 8-dinitropyrene had the strongest direct-acting mutagenicity in an Ames test using strains of *Salmonella typhymurium* (*Hayakawa et al., 1997*). The mutagenicity of 1-nitropyrene, 1, 8-dinitropyrene and 3-nitrofluoranthene could be up to 2×10^5 times greater than those of

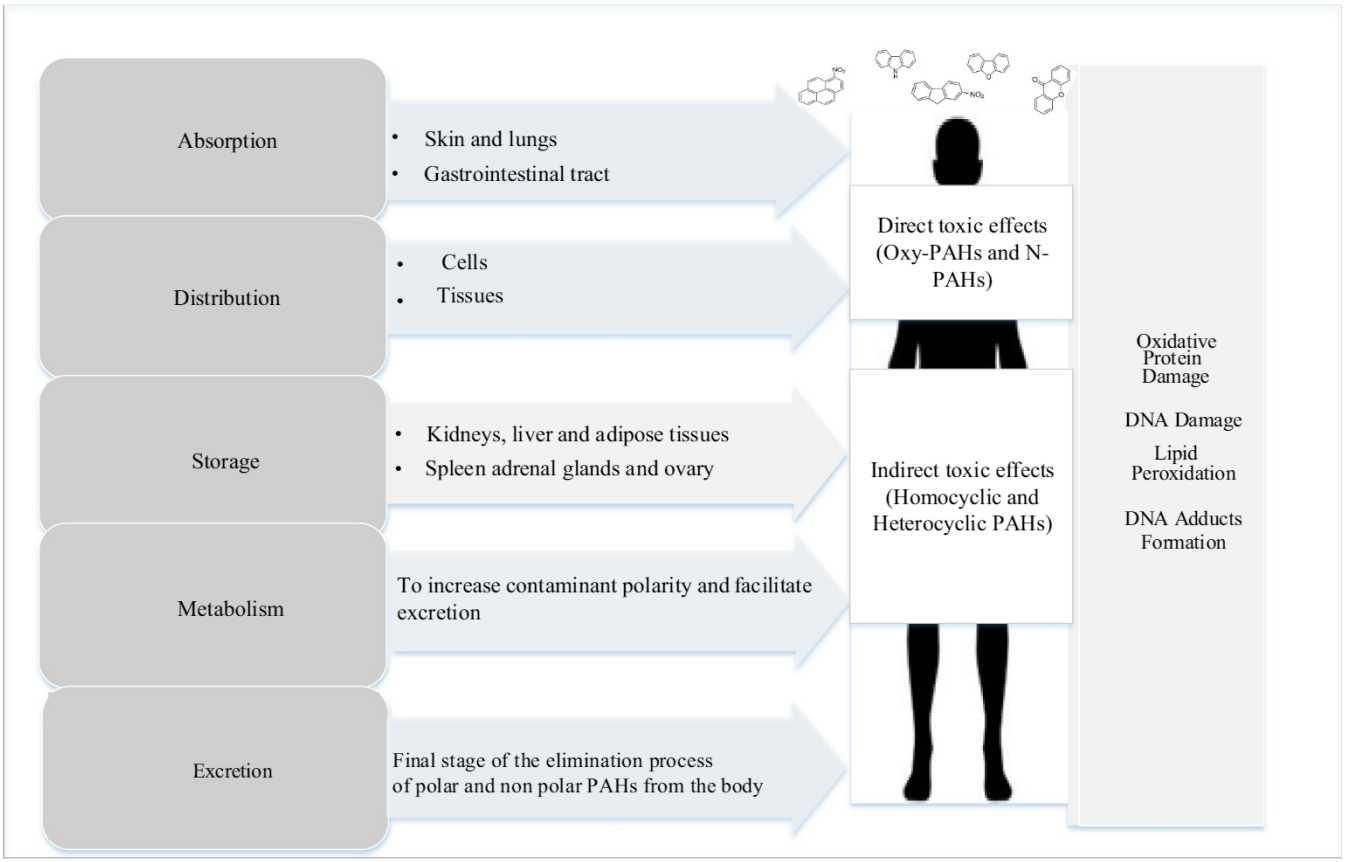

Fig. 4. Polar and non-polar PAH toxicokinetics.

the parent PAHs, even at low concentrations (Durant et al., 1996; Zhang et al., 2014).

3.5.3. Carcinogenicity

Carcinogenic effects of PAHs can be direct or indirect. For direct-acting carcinogens, the compound in question exerts a direct effect and requires no activation. This is the case with oxy-PAHs and some N-PAHs (Fig. 4). Direct acting carcinogenicity of 1-nitropyrene, 1, 8-dinitropyrene and 3-nitrofluoranthene, at low concentration, was ten times greater than that of homocyclic PAHs (Zhang et al., 2014). Unlike N-PAHs and oxy-PAHs, homocyclic PAHs including B[*a*]P and 7,12-dimethylbenzoanthracene are indirect-acting, requiring activation to exert their toxic effects (Rengarajan et al., 2015) Some N-PAHs and several N-heterocyclic PAHs are classified as probable or possible human carcinogens (IARC, 2013).

3.5.4. Developmental toxicity

The developmental toxicity malformation profile in zebrafish embryos for oxy-PAHs, N-PAHs and homocyclic PAHs, have been shown to be similar or higher in the transformation products (Chlebowski et al., 2017). In a study on the effect of coal tar and asphalt-based pavement sealcoat products, zebrafish developmental toxicity test suggested that fractions, where N-PAHs and oxy-PAHs eluted, had the most significant adverse effects (Titaley et al., 2016). Similarly, oxy-PAHs proved to be potent AhR activators and of comparable developmental toxicity as homocyclic PAHs in a study researching the effects of soil extracts from three contaminated industrial sites (Wincent et al., 2015).

The investigation carried out on the developmental toxicity of oxy-PAHs on zebrafish embryos showed adverse effects on the observed ecially yolk sac edema and body axis roupings of compounds based on toxicity to zebrafish embryos exposed to N-PAHs and heterocyclic PAHs as well as oxy-PAHs (Knecht et al., 2013; Chlebowski et al., 2017) as indicated by least effect levels at smallest concentrations are presented in Table 4. It can be observed that regarding developmental toxicity, heterocyclic PAHs were less toxic compared to N-PAHs. All the heterocyclic PAHs are grouped in the least toxic group G except acridine which appears in group B.

3.5.5. Teratogenicity

Polycyclic aromatic hydrocarbons' teratogenic effects such as embryotoxicity (including cancers), congenital disabilities, low weight, premature delivery, delayed child development and low IQ have been well described elsewhere (Wassenberg and Di Giulio, 2004; Frederica Perera et al., 2005). Polar PAHs are believed to exhibit greater reproductive toxicities than non-polar PAHs because of their polar nature (Lubcke-von Varel et al., 2011). For example, in an in-vitro study, N-PAHs were said to disrupt the signalling pathways of retinoids; an important non-steroidal dietary hormone essential for regulation of embryonic development and homeostasis of all vertebrate tissues (Benisek et al., 2008). The investigation of some N-heterocycles' teratogenic effects on survival of first instar larvae of the midge (*Chironomus riparius*) showed that acridone was the most genotoxic of all the N-heterocycles tested in the Mutatox™ test.

Polar PAHs were shown to induce greater estrogenic effects in mixtures of PAHs in road dust, diesel exhaust particulate and sediment extracts (Lubcke-von Varel et al., 2011; Misaki et al., 2016). Specifically, heterocyclic PAHs, including carbazole, induced estrogenic activity upon metabolism using a chemically activated luciferase expression (ER-CALUX) assay (Brinkmann et al., 2014). In an ER-CALUX assay to investigate the estrogenic activities of 12 heterocyclic compounds, acridine, xanthene, indole, 2-methyl benzofuran, 2, 3-

Table 4
Polar PAH toxicity on zebra fish embryo development.

	Toxicity class	N-PAHs and heterocycles	Oxy-PAHs
1.	A (MOST TOXIC)	3-Nitrobenzanthrone, 1,6-dinitropyrene, and 1,3-dinitropyrene	1–4-Naphthoquinone 9-Hydroxybenzo[*a*]pyrene 1–4-Anthraquinone 1–4-Benzoquinone-D4 Phenanthrene-1-4-dione Pyrene-4-5-dione 1–2-Naphthoquinone Phenanthrene-quinone 1–4-Dihydroxyanthraquinone
2.	B	1-Aminopyrene, acridine, 5,6-benzoquinoline	1–9-benz-10-anthrone 2-hydroxyanthraquinone benzo[*a*]fluorenone 6 h-benzo[c-d]pyren-6-one;naphthranthrone Perinaphthenone 2–6-dihydroxyanthraquinone benz[*a*]anthracene-7-12-dione benzo[*c*]phenanthrene [1–4]quinone 1–8-dihydroxyanthraquinone
3.	C	5-Nitroacenaphthalene, 9-nitrophenanthrene, 1,8-dinitropyrene	1-Hydroxy-9-fluorenone 1–5-Dihydroxynaphthalene 2–3-Dihydroxynaphthalene 5–12-Naphthacenequinone 2-Hydroxy-9-fluorenone Acenaphthenequinone 2–6-Dihydroxynaphthalene 1–6-Dihydroxynaphthalene
4.	D	9-Aminophenanthrene, 7-nitrobenz[*a*]anthracene, carbazole, and 2-nitroanthracene	9–10-Anthraquinone 10-Hydroxybenzo[*a*] pyrene 1-Hydroxyanthraquinone 2–7-Dihydroxynaphthalene Chromone 9-Fluorenon
5.	E	1-Nitropyrene and 3-nitrofluoranthene	1–3-Dihydroxynaphthalene 4 h-Cyclopenta[*def*] phenanthren-4-one 1–2-Dihydroxyanthraquinone Aceanthrenequinone Xanthone 12-Hydroxybenzo[*a*] pyrene
6.	F	2-Nitropyrene and dibenzofuran	
7.	G (LEAST TOXIC)	2-Methylbenzofuran, 1-nitronaphthalene, 2-nitrobiphenyl, 2-nitrodibenzothiopene, 2-nitrofluoranthene, 2-nitrofluorene, 2-nitronaphthalene, 2,8-dinitrodibenzothiophene, 3-nitrobiphenyl, 3-nitrodibenzofuran, 3-nitrophenanthrene, 3,7-dinitrobenzo[*k*]fluoranthene, 4-nitrobiphenyl, 6-nitrobenzo[*a*] pyrene, 6-nitrochrysene, 7-nitrobenzo[*k*]fluoranthene, 8-methylquinoline, 9-nitroanthracene, Indole, Quinoline, Thianaphthene, Xanthene.	

Source: Knecht et al. (2013) and Chlebowski et al. (2017).

dimethylbenzofuran, dibenzofuran, dibenzothiophene, quinoline, and 6-methyl quinoline were positive in the ER-CALUX. They had estradiol equivalence factors (EEFs) from 2.85×10^{-7} to 3.18×10^{-5} which [illegible] xenoestrogens (e.g. alkylphenols or [illegible]14).

Table 5
Biomarkers of PAH exposure and associated disease conditions in humans.

	PAH source	Region/Country	Target group	Internal dose biomarker	Associated risk/condition	Ref
1.	Kitchen indoor air	North India	Male kitchen workers	Urinary PAH metabolites	Decline in lung function	(Singh et al., 2016)
2.	Urban polluted air	Bangkok, Thailand	Children	Urinary 1-hydroxypyrene; PAH-DNA adducts (5-fold higher than control)	Prone to development of genotoxic diseases in future	(Ruchirawat et al., 2007)
3.	Unknown	Shangai, China	Women with breast cancer	Urinary 1-hydroxypyrene; 2-naphthol and oxidative stress/lipid peroxidation biomarkers (8-hydroxy-2′-deoxyguanosine, malondialdehyde)	Presence of breast cancer in target group	(Lee et al., 2010)
4.	Vehicular emission	Copehagen, Denmark	Non-smoking bus drivers	Repair product of mutagenic oxidation of guanine - (8-oxo-2′-deoxyguanosine	Prone to various genotoxic diseases	(Loft et al., 1999)
5.	Unknown	Iran	Some infertile males	Over expression of AhR; Antagonistic suppression of sex steroid hormones by AhR	Male infertility; Loss of normal ovarian functions.	(Bidgoli et al., 2011)
6.	Marijuana	United State of America	A group of marijauana smokers	Urinary PAH biomarkers (2-, 3-, and 9-hydroxyfluorene; 1-, 2-hyroxynaphthalene; 1-,2-and 3-hydroxyphenanthreene; 1-hydroxypyrene	Prone to lung cancer	(Wei et al., 2016)
7.	Metallurgy	France	Workers involved in metallurgical activities	3-Hydroxybenzo(*a*)pyrene	Prone to the development of various types of cancers	(Barbeau et al., 2014)
8.	Coke-oven activities	Wuhan City, China	Workers exposed to coke-oven	4-Hydroxyphenanthrene	Increased risk of diabetes especially in smokers and overweight individuals	(Yang et al., 2017)
9.	Multiple sources	United State of America	Women with early onset of menopause	1-Hydroxynaphthalene 2-Hydroxynaphthalene 3-Hydroxyfluorene, 9-Hydroxyfluorene,	Early onset of natural menopause	(Huang et al., 2018)

4. Implications of PAH toxicity on human health

Most epidemiological studies focus on homocyclic PAHs. There is inadequate attention to polar PAHs, despite being relatively more toxic than homocyclic PAHs. The findings of some epidemiological investigations on PAHs are further discussed (Table 5). This will allow for a better appreciation of the potential risks of polar PAHs to humans and other living organisms, especially as the toxicity of homocyclic PAHs is often through the effects of highly reactive polar genotoxic metabolites rather than direct effects of homocyclic PAHs (Sen and Field, 2013). In most of the studies, urinary hydroxylated PAHs (OH-PAHs) were the biomarkers used for health risk assessment of PAHs exposure (Table 5). In many case-control studies, there was a strong positive relationship between disease conditions and the presence of biomarkers — male infertility associated positively with the overexpression of AhR, in an Iranian case-control study (Table 5). Loss of ovarian functions, the decline in lung functions, development of cancers, early onset of natural menopause and incidences of diabetes are other health anomalies reported to be associated with PAH exposure in the literature (Table 5).

5. Strategies for remediation of PAH-contaminated environmental media

The presence of polar and non-polar PAHs in the environment can impact adverse effects on living organisms. Effective remediation of polluted environmental media has become very important if PAHs toxic effects are to be curtailed. The aim of remediation and particularly bioremediation is to completely remove pollutants from the environment or degrade them into less harmful forms such as CO_2 and H_2O (Yebra-Pimentel et al., 2015). Current bioremediation of PAH-impacted soils might result in the production of toxic transformation products (usually polar PAHs) and resultant greater toxicity and risk to humans and other living organisms (Lemieux et al., 2015b).

Optimised bioremediation techniques aimed at enhancing the biodegradation processes and ensuring effective and complete pollutant degradation are being developed (Yebra-Pimentel et al., 2015). In contaminated soils, such optimization might focus on improvement of physical and chemical properties as well as the nutrient status of the soil. Effective optimization may provide favourable conditions for microorganisms leading to improved microbial abundance and diversity (Bandowe et al., 2019). Contaminant bioavailability in soils might also improve, due to optimization (Bandowe et al., 2019). Microbial species known to degrade PAHs readily include *Pseudomonas putida* NCIB 9816, *Pseudomonas putida* G7, ND6 and BS202, *Pseudomonas* sp. C18, *Ralstoni* Sp.U2, *Cunninghamella elegans*, *Pleurotus ostreatus*, *Phanerochaete chrysosporium* (*Gaur* et al., *2018*).

Both in situ and ex situ remediation treatments can be used in the remediation of PAH-polluted soils. Bioventing, biostimulation and bioaugmentation in situ processes have been used to introduce aeration systems, nutritive media and microbes into environmental media, respectively (Behera et al., 2018). Ex situ remediation methods include composting and biopiling (Yebra-Pimentel et al., 2015). Both in situ and ex situ approaches are employed in remediation of polar and non-polar PAHs (Table 6).

6. Conclusion: knowledge gaps and future prospects

This review, for the first time, attempted to shed light on, the physicochemical properties, environmental behaviour, bioavailability and toxicity of polar PAHs. We have been able to show, based on the reviewed articles, that most polar PAHs are relatively more mobile and could pose more risk to humans and other living organisms. This should have positive implications for current risk assessment and abatement strategies regarding PAH-contaminated sites.

…wledge about concentration, fate and …in various environmental media.

Table 6
Methods of polar and non-polar PAHs remediation.

Contaminant	Environmental media	Strategy	Mechanism	References
Homocyclic PAHs and high molecular weight oxy-PAHs	Soil	Natural attenuation using species-rich grassland mixtures	PAH degradation due to elevated microbial biomass resulting of diverse species	(Bandowe et al., 2019)
Low and high molecular weight PAHs and oxy-PAHs	Soil	Surfactant-aided soil washing and chemical oxidation by activated persulphate	Surfactant washing to aid mass transfer of PAHs from solid to aqueous phase; PAH degradation by means of chemical oxidation	(Li et al., 2019)
Homocyclic PAHs and oxy-PAHs	Soil	Pre-treatment and ethyl lactated based fenton treatment	Pre-treatment to facilitate desorption of PAHs; fenton treatment for oxidative degradation	
Homocyclic PAHs and N/S/O heterocycles	Groundwater	Activated carbon-permeable reactive barrier	Sub-surface fluid flow management and activated carbon treatment zone	(Palm et al., 2014)
Homocyclic and S-heterocyclic PAHs	Saline soil	Natural attenuation, bioaugmentation and phytoremediation	Bioaugmentation enhances microbial population; phytoremediation utilizes plant and microbes interaction within the rhizosphere to enhance PAH degradation	(Aranda et al., 2017)

Adequate information on their toxicity also exist. This is in contrast to the lack of information on the environmental presence, partitioning dynamics, bioavailability and toxicity of heterocyclic and substituted PAHs. This lack of information limits the recognition of the potential risk polar PAHs could pose to living organisms and particularly humans.

Polar PAHs' fate in the environment could be driven by both hydrophobic and hydrophilic interactions depending on physicochemical properties, unlike non-polar PAHs that exhibit relatively similar behaviours, in environmental media, due to their unique hydrophobic nature. Strong hydrophobic behaviour in polar PAHs might translate to low concentration in environmental media, as it is with N-PAHs which also have high degradation potentials. Oxygenated PAHs, on the other hand, partitions less into organic matter and more into the aqueous phase. They are regarded as 'dead-end products' as they are highly stable in the environment, maintaining concentrations comparable to that of homocyclic PAHs.

The different behaviour and ubiquitous nature of polar PAHs in the environment, influenced by higher bioavailability of most of them, suggest greater risks. Widespread presence in the atmospheric gaseous phase, PM, soil, sediments, groundwater and various aquatic environments might result in increased environmental and human risks. Even at deficient concentrations, some polar PAHs could cause devastating health effects compared to homocyclic PAHs.

It, therefore, implies that remediation of a few targeted PAHs in contaminated sites does not correspond to a reduction in health risk. To ensure real risk abatement, risk assessment of PAHs should be holistic and consider the possible antagonistic and synergistic interactions among mixed contaminants, in contaminated sites. The current trend of individual contaminant assessment is highly deficient. Polar PAHs contribute significantly to risks posed by contaminated sites and should be included in monitoring programs or in current risk assessment models. Their lack of consideration in risk assessment could overwrite the essential objective of risk abatement.

The following research efforts are, therefore, proposed based on the identified knowledge gaps:

- Survey of the environmental abundance of polar PAHs in soils, sediments and air to establish environmental exposure levels.
- Qualitative and quantitative profiling of polar PAHs in contaminated sites to improve risk assessment efforts.
- Polar PAHs bioaccessibility/bioavailability studies to understand the actual proportion that could get into the gastrointestinal tract, blood and other vital tissues and organs of humankind.
- Toxicity studies using various bioassays to understand its genotoxic, mutagenic, carcinogenic and teratogenic effects better.
- Epidemiological studies to establish the link between high incidences of diseases and widespread presence of polar PAHs in the environment.

The ongoing research investigations within our team may address some of these critical knowledge gaps, which will help fellow scientists and regulators to refine the existing risk assessment paradigm.

Declaration of interest

None.

Acknowledgement

The authors acknowledge the support rendered by the Commonwealth of Australia and the University of Newcastle, Australia, through the Australian Government Research Training Program (RTP) Scholarship. P Hansbro is supported by the National Health and Medical Research Council of Australia (grant # 1079187).

References

Achten, C., Andersson, J.T., 2015. Overview of polycyclic aromatic compounds (PAC). Polycycl. Aromat. Compd. 35 (2–4), 177–186.
Achten, C., Hofmann, T., 2009. Native polycyclic aromatic hydrocarbons (PAH) in coals - a hardly recognized source of environmental contamination. Sci. Total Environ. 407 (8), 2461–2473.
Adrion, A.C., Singleton, D.R., Nakamura, J., Shea, D., Aitken, M.D., 2016. Improving polycyclic aromatic hydrocarbon biodegradation in contaminated soil through low-level surfactant addition after conventional bioremediation. Environ. Eng. Sci. 33 (9), 659–670.
Agudelo-Castañeda, D., Teixeira, E., Schneider, I., Lara, S.R., Silva, L.F.O., 2017. Exposure to polycyclic aromatic hydrocarbons in atmospheric PM1.0 of urban environments: Carcinogenic and mutagenic respiratory health risk by age groups. Environ. Pollut. 224, 158–170.
Albinet, A., Leoz-Garziandia, E., Budzinski, H., Viilenave, E., 2006. Simultaneous analysis of oxygenated and nitrated polycyclic aromatic hydrocarbons on standard reference material 1649a (urban dust) and on natural ambient air samples by gas chromatography-mass spectrometry with negative ion chemical ionisation. J. Chromatogr. A 1121 (1), 106–113.
Albinet, A., Leoz-Garziandia, E., Budzinski, H., Viilenave, E., 2007. Polycyclic aromatic hydrocarbons (PAHs), nitrated PAHs and oxygenated PAHs in ambient air of the Marseilles area (South of France): concentrations and sources. Sci. Total Environ. 384 (1–3), 280–292.
Alves, C.A., Vicente, A.M., Custódio, D., Cerqueira, M., Nunes, T., Pio, C., Lucarelli, F., Calzolai, G., Nava, S., Diapouli, E., Eleftheriadis, K., Querol, X., Musa Bandowe, B.A., 2017. Polycyclic aromatic hydrocarbons and their derivatives (nitro-PAHs, oxygenated PAHs, and azaarenes) in PM2.5 from southern European cities. Sci. Total Environ. 595, 494–504.
Alves, C.A., Vicente, A.M.P., Gomes, J., Nunes, T., Duarte, M., Bandowe, B.A.M., 2016. Polycyclic aromatic hydrocarbons (PAHs) and their derivatives (oxygenated-PAHs, nitrated-PAHs and azaarenes) in size-fractionated particles emitted in an urban road tunnel. Atmos. Res. 180, 128–137.
Andersson, H., Piras, E., Demma, J., Hellman, B., Brittebo, E., 2009. Low levels of the air pollutant 1-nitropyrene induce DNA damage, increased levels of reactive oxygen species and endoplasmic reticulum stress in human endothelial cells. Toxicology 262 (1), 57–64.
Andersson, J.T., Achten, C., 2015. Time to say goodbye to the 16 EPA PAHs? Toward an up-to-date use of PACs for environmental purposes. Polycycl. Aromat. Compd. 35 (2–4), 330–354.
Aranda, E., Godoy, P., Reina, R., Badia-Fabregat, M., Rosell, M., Marco-Urrea, E., García-Romera, I., 2017. Isolation of Ascomycota fungi with capability to transform PAHs: insights into the biodegradation mechanisms of *Penicillium oxalicum*. Int. Biodeterior. Biodegrad. 122, 141–150.
Arp, H.P.H., Schwarzenbach, Rene P., Kai-Uwe, Goss, 2008. Ambient gas/particle partitioning. 1. Sorption mechanisms of apolar, polar, and ionizable organic compounds. Environ. Sci. Technol. 42, 5541–5547.
Baird, W.M., Hooven, L.A., Mahadevan, B., 2005. Carcinogenic polycyclic aromatic hydrocarbon-DNA adducts and mechanism of action. Environ. Mol. Mutagen. 45 (2–3), 106–114.
Bamford, H.A., Baker, J.E., 2003. Nitro-polycyclic aromatic hydrocarbon concentrations and sources in urban and suburban atmospheres of the Mid-Atlantic region. Atmos. Environ. 37 (15), 2077–2091.
Bamforth, S.M., Singleton, I., 2005. Bioremediation of polycyclic aromatic hydrocarbons: current knowledge and future directions. J. Chem. Technol. Biotechnol. 80 (7), 723–736.
Bandowe, B.A.M., Leimer, S., Meusel, H., Velescu, A., Dassen, S., Eisenhauer, N., Hoffmann, T., Oelmann, Y., Wilcke, W., 2019. Plant diversity enhances the natural attenuation of polycyclic aromatic compounds (PAHs and oxygenated PAHs) in grassland soils. Soil Biol. Biochem. 129, 60–70.
Bandowe, B.A.M., Meusel, H., 2017. Nitrated polycyclic aromatic hydrocarbons (nitro-PAHs) in the environment – a review. Sci. Total Environ. 581-582, 237–257.
Bandowe, B.A.M., Meusel, H., Huang, R., Hoffmann, T., Cao, J., Ho, K., 2016. Azaarenes in fine particulate matter from the atmosphere of a Chinese megacity. Environ. Sci. Pollut. Res. 23 (16), 16025–16036.
Bandowe, B.A.M., Meusel, H., Huang, R.J., Ho, K., Cao, J., Hoffmann, T., Wilcke, W., 2014. PM2.5-bound oxygenated PAHs, nitro-PAHs and parent-PAHs from the atmosphere of a Chinese megacity: seasonal variation, sources and cancer risk assessment. Sci. Total Environ. 473-474, 77–87.
Bandowe, B.A.M., Sobocka, J., Wilcke, W., 2011. Oxygen-containing polycyclic aromatic hydrocarbons (OPAHs) in urban soils of Bratislava, Slovakia: patterns, relation to PAHs and vertical distribution. Environ. Pollut. 159 (2), 539–549.
Bandowe, B.A.M., Wilcke, W., 2010. Analysis of polycyclic aromatic hydrocarbons and their oxygen-containing derivatives and metabolites in soils. J. Environ. Qual. 39 (4), 1349–1358.
Barbeau, D., Persoons, R., Marques, M., Hervé, C., Laffitte-Rigaud, G., Maitre, A., 2014. Relevance of urinary 3-hydroxybenzo(*a*)pyrene and 1-hydroxypyrene to assess exposure to carcinogenic polycyclic aromatic hydrocarbon mixtures in metallurgy workers. Ann. Occup. Hyg. 58 (5), 579–590.
Behera, B.K., Das, A., Sarkar, D.J., Weerathunge, P., Parida, P.K., Das, B.K., Thavamani,

P., Ramanathan, R., Bansal, V., 2018. Polycyclic Aromatic Hydrocarbons (PAHs) in inland aquatic ecosystems: perils and remedies through biosensors and bioremediation. Environ. Pollut. 241, 212–233.
Benigni, R., Bossa, C., 2011. Mechanisms of chemical carcinogenicity and mutagenicity: a review with implications for predictive toxicology. Chem. Rev. 111 (4), 2507–2536.
Benisek, M., Blaha, L., Hilscherova, K., 2008. Interference of PAHs and their N-heterocyclic analogs with signaling of retinoids in vitro. Toxicol. in Vitro 22 (8), 1909–1917.
Biache, C., Mansuy-Huault, L., Faure, P., Munier-Lamy, C., Leyval, C., 2008. Effects of thermal desorption on the composition of two coking plant soils: impact on solvent extractable organic compounds and metal bioavailability. Environ. Pollut. 156 (3), 671–677.
Bidgoli, S.A., Karimi, M., Asami, Z., Baher, H., Djamali Zavarhei, M., 2011. Association between testicular aryl hydrocarbon receptor levels and idiopathic male infertility: a case-control study in Iran. Sci. Total Environ. 409 (18), 3267–3273.
Bleeker, E.A.J., Noor, L., Kraak, M.H.S., de Voogt, P., Admiraala, W., 2001. Comparative metabolism of phenanthridine by carp (*Cyprinus carpio*) and midge larvae (*Chironomus riparius*). Environ. Pollut. 112, 11–17.
Bleeker, E.A.J., Van Der Geest, H.G., Klamer, H.J.C., De Voogt, P., Wind, E., Kraak, M.H.S., 1999. Toxic and genotoxic effects of azaarenes: isomers and metabolites. Polycycl. Aromat. Compd. 13 (3), 191–203.
Bleeker, Eric A.J., Wiegman, S., de Voogt, Pim, Kraak, Michiel, Leslie, Heather A., de Haas, Elske, Admiraal, Wim, 2002. Toxicity of azaarenes. Rev. Environ. Contam. Toxicol. 173, 39–83.
Blum, P., Sagner, A., Tiehm, A., Martus, P., Wendel, T., Grathwohl, P., 2011. Importance of heterocylic aromatic compounds in monitored natural attenuation for coal tar contaminated aquifers: a review. J. Contam. Hydrol. 126 (3–4), 181–194.
Bocchi, C., Bazzini, C., Fontana, F., Pinto, G., Cassoni, F., 2017. Genotoxicity of airborne PM2.5 assessed by salmonella and comet assays in five cities of the Emilia-Romagna (Italy) mutagenicity monitoring network. Environ. Mol. Mutagen. 58 (9), 719–729.
Brack, W., Schirmer, K., 2003. Effect-directed identification of oxygen and sulfur heterocycles as major polycyclic aromatic cytochrome P4501A-inducers in a contaminated sediment. Environ. Sci. Technol. 37, 3062–3070.
Brinkmann, M., Maletz, S., Krauss, M., Bluhm, K., Schiwy, S., Kuckelkorn, J., Tiehm, A., Brack, W., Hollert, H., 2014. Heterocyclic aromatic hydrocarbons show estrogenic activity upon metabolization in a recombinant transactivation assay. Environ. Sci. Technol. 48 (10), 5892–5901.
Chen, H.-Y., Preston, M.R., 2004. Dissolution of azaarenes from urban aerosols. Atmos. Environ. 38 (7), 1023–1028.
Chibwe, L., Geier, M.C., Nakamura, J., Tanguay, R.L., Aitken, M.D., Simonich, S.L., 2015. Aerobic bioremediation of PAH contaminated soil results in increased genotoxicity and developmental toxicity. Environ. Sci. Technol. 49 (23), 13889–13898.
Chiou, Cary T., Mcgroddy, Susan E., Kile, D.E., 1998. Partition characteristics of polycyclic aromatic hydrocarbons on soils and sediments. Environ. Sci. Technol. 32.
Chlebowski, A.C., Garcia, G.R., La Du, J.K., Bisson, W.H., Truong, L., Massey Simonich, S.L., Tanguay, R.L., 2017. Mechanistic investigations into the developmental toxicity of nitrated and heterocyclic PAHs. Toxicol. Sci. 157 (1), 246–259.
Cho, A.K., Di Stefano, E., You, Y., Rodriguez, C.E., Schmitz, D.A., Kumagai, Y., Miguel, A.H., Eiguren-Fernandez, A., Kobayashi, T., Avol, E., Froines, J.R., 2004. Determination of four quinones in diesel exhaust particles, SRM 1649a, and atmospheric PM2.5 special issue of aerosol science and technology on findings from the fine particulate matter supersites program. Aerosol Sci. Technol. 38 (Supp 1), 68–81.
Chung, Myeong Y., Lazaro, R.A., Lim, Dianne, Jackson, Joscelyne, Lyon, Julie, Rendulic, Dora, Hasson, Alam S., 2006. Aerosol-borne quinones and reactive oxygen species generation by particulate matter extracts. Environ. Sci. Technol. 40, 4880–4886.
Dasgupta, S., Cao, A., Mauer, B., Yan, B., Uno, S., McElroy, A., 2014. Genotoxicity of oxy-PAHs to Japanese medaka (*Oryzias latipes*) embryos assessed using the comet assay. Environ. Sci. Pollut. Res. Int. 21 (24), 13867–13876.
De Guidi, G., Falciglia, P.P., Catalfo, A., De Guidi, G., Fagone, S., Vagliasindi, F.G.A., 2016. Soil contaminated with PAHs and nitro-PAHs: contamination levels in an urban area of Catania (Sicily, southern Italy) and experimental results from simulated decontamination treatment. Clean Techn. Environ. Policy 19 (4), 1121–1132.
Debajyoti Ghosal, S.G., Dutta, Tapan K., Ahn, Youngho, 2016. Current state of knowledge in microbial degradation of polycyclic aromatic hydrocarbons (PAHs): a review. Front. Microbiol. 7 (1369), 1–27.
Deng, K., Chan, W., 2017. Development of a QuEChERS-based method for determination of carcinogenic 2-nitrofluorene and 1-nitropyrene in rice grains and vegetables: a comparative study with benzo[*a*]pyrene. J. Agric. Food Chem. 65 (9), 1992–1999.
Dever, D.P., Opanashuk, L.A., 2012. The aryl hydrocarbon receptor contributes to the proliferation of human medulloblastoma cells. Mol. Pharmacol. 81 (5), 669–678.
Dietrich, C., Kaina, B., 2010. The aryl hydrocarbon receptor (AhR) in the regulation of cell-cell contact and tumor growth. Carcinogenesis 31 (8), 1319–1328.
Doick, K.J., Dew, N.M., Semple, K.T., 2005. Linking catabolism to cyclodextrin extractability: determination of the microbial availability of PAHs in soil. Environ. Sci. Technol. 39 (22), 8858–8864.
Dranka, B.P., Benavides, G.A., Diers, A.R., Giordano, S., Zelickson, B.R., Reily, C., Zou, L., Chatham, J.C., Hill, B.G., Zhang, J., Landar, A., Darley-Usmar, V.M., 2011. Assessing bioenergetic function in response to oxidative stress by metabolic profiling. Free Radic. Biol. Med. 51 (9), 1621–1635.
Durant, John L., Busby Jr., William F., Lafleur, Arthur L., Penman, Bruce W., Crespi, C.L., 1996. Human cell mutagenicity of oxygenated, nitrated and unsubstituted polycyclic aromatic hydrocarbons associated with urban aerosol. Mutat. Res. 371, 123–157.
Enell, A., Lundstedt, S., Arp, H.P., Josefsson, S., Cornelissen, G., Wik, O., Berggren Kleja, D., 2016. Combining leaching and passive sampling to measure the mobility and [illegible] and colloids of native oxy-PAHs, N-PACs, and [illegible] Environ. Sci. Technol. 50 (21), 11797–11805.
Feldmannova, M., Hilscherova, K., Marsalek, B., Blaha, L., 2006. Effects of N-heterocyclic polyaromatic hydrocarbons on survival, reproduction, and biochemical parameters in Daphnia magna. Environ. Toxicol. 21 (4), 425–431.
Frederica Perera, D.T., Whyatt, Robin, Lederman, Sally Ann, Jedrychowski, Wieslaw, 2005. DNA damage from polycyclic aromatic hydrocarbons measured by benzo[a] pyrene-DNA adducts in mothers and newborns from Northern Manhattan, the World Trade Center Area, Poland, and China. Cancer Epidemiol. Biomark. Prev. 14 (3), 709–714.
Gaur, N., Narasimhulu, K., PydiSetty, Y., 2018. Recent advances in the bio-remediation of persistent organic pollutants and its effect on environment. J. Clean. Prod. 198, 1602–1631.
Han, Y.M., Bandowe, B.A.M., Wei, C., Cao, J.J., Wilcke, W., Wang, G.H., Ni, H.Y., Jin, Z.D., An, Z.S., Yan, B.Z., 2015. Stronger association of polycyclic aromatic hydrocarbons with soot than with char in soils and sediments. Chemosphere 119, 1335–1345.
Hang, B., 2010. Formation and repair of tobacco carcinogen-derived bulky DNA adducts. J. Nucleic Acids 2010.
Harrad, S., Hassoun, S., Callén Romero, M.A.S., Harrison, R.M., 2003. Characterisation and source attribution of the semi-volatile organic content of atmospheric particles and associated vapour phase in Birmingham, UK. Atmos. Environ. 37 (35), 4985–4991.
Hayakawa, K., Akio, Nakamura, Nokiro, Terai, Ryoichi, Kizu, Kyoko, Ando, 1997. Nitroarene concentrations and direct-acting mutagenicity of diesel exhaust particulates fractionated by silica-gel. Chem. Pharm. Bull. 45 (11), 1820–1822.
Hu, J., Nakamura, J., Richardson, S.D., Aitken, M.D., 2012. Evaluating the effects of bioremediation on genotoxicity of polycyclic aromatic hydrocarbon-contaminated soil using genetically engineered, higher eukaryotic cell lines. Environ. Sci. Technol. 46 (8), 4607–4613.
Huang, Y., Guo, J., Lv, N., Li, S., Wu, Y., Bai, R., Shen, J., Chen, G., Zhang, D., 2018. Associations of urinary polycyclic aromatic hydrocarbons with age at natural menopause in U.S. women aged 35–65, NHANES 2003–2012. Environ. Pollut. 1878–1886.
IARC, 2013. Bitumens and bitumen emissions, and some *N*- and *S*-heterocyclic polycyclic aromatic hydrocarbons. IARC Monogr. Eval. Carcinog. Risks Hum. 103, 1–360.
Iva Sovadinova, L.B., Janosek, Jaroslav, Hilscherova, Klara, Giesy, John P., Jones, Paul D., Holoubek, Ivan, 2006. Cytotoxicity and aryl hydrocarbon receptor–mediated activity of n-heterocyclic polycyclic aromatic hydrocarbons: structure–activity relationships. Environ. Toxicol. Chem. 25 (5), 1291–1297.
Jariyasopit, N., Zimmermann, K., Schrlau, J., Arey, J., Atkinson, R., Yu, T.W., Dashwood, R.H., Tao, S., Simonich, S.L., 2014. Heterogeneous reactions of particulate matter-bound PAHs and NPAHs with NO_3/N_2O_5, OH radicals, and O_3 under simulated long-range atmospheric transport conditions: reactivity and mutagenicity. Environ. Sci. Technol. 48 (17), 10155–10164.
Knecht, A.L., Goodale, B.C., Truong, L., Simonich, M.T., Swanson, A.J., Matzke, M.M., Anderson, K.A., Waters, K.M., Tanguay, R.L., 2013. Comparative developmental toxicity of environmentally relevant oxygenated PAHs. Toxicol. Appl. Pharmacol. 271 (2), 266–275.
Kuch, B., Kern, F., Metzger, J.W., von der Trenck, K.T., 2010. Effect-related monitoring: estrogen-like substances in groundwater. Environ. Sci. Pollut. Res. Int. 17 (2), 250–260.
Larcher, T., Perrichon, P., Vignet, C., Ledevin, M., Le Menach, K., Lyphout, L., Landi, L., Clerandeau, C., Lebihanic, F., Menard, D., Burgeot, T., Budzinski, H., Akcha, F., Cachot, J., Cousin, X., 2014. Chronic dietary exposure of zebrafish to PAH mixtures results in carcinogenic but not genotoxic effects. Environ. Sci. Pollut. Res. Int. 21 (24), 13833–13849.
Larsson, M., Orbe, D., Engwall, M., 2012. Exposure time-dependent effects on the relative potencies and additivity of PAHs in the Ah receptor-based H4IIE-luc bioassay. Environ. Toxicol. Chem. 31 (5), 1149–1157.
Layshock, J.A., Wilson, Glenn, Anderson, Kim A., 2010. Ketone and quinone-substituted polycyclic aromatic hydrocarbons in mussel tissue, sediment, urban dust, and diesel particulate matter. Environ. Toxicol. Chem. 29, 2450–2460.
Lee, K.H., Shu, X.O., Gao, Y.T., Ji, B.T., Yang, G., Blair, A., Rothman, N., Zheng, W., Chow, W.H., Kang, D., 2010. Breast cancer and urinary biomarkers of polycyclic aromatic hydrocarbon and oxidative stress in the Shanghai Women's Health Study. Cancer Epidemiol. Biomark. Prev. 19 (3), 877–883.
Lemieux, C.L., Lambert, I.B., Lundstedt, S., Tysklind, M., White, P.A., 2008. Mutagenic hazards of complex polycyclic aromatic hydrocarbon mixtures in contaminated soil. Environ. Toxicol. Chem. 27 (4), 978–990.
Lemieux, C.L., Long, A.S., Lambert, I.B., Lundstedt, S., Tysklind, M., White, P.A., 2015a. Cancer risk assessment of polycyclic aromatic hydrocarbon contaminated soils determined using bioassay-derived levels of benzo[a]pyrene equivalents. Environ. Sci. Technol. 49 (3), 1797–1805.
Lemieux, C.L., Long, A.S., Lambert, I.B., Lundstedt, S., Tysklind, M., White, P.A., 2015b. In vitro mammalian mutagenicity of complex polycyclic aromatic hydrocarbon mixtures in contaminated soils. Environ. Sci. Technol. 49 (3), 1787–1796.
Li, Y., Liao, X., Huling, S.G., Xue, T., Liu, Q., Cao, H., Lin, Q., 2019. The combined effects of surfactant solubilization and chemical oxidation on the removal of polycyclic aromatic hydrocarbon from soil. Sci. Total Environ. 647, 1106–1112.
Lintelmann, J., Fischer, K., Matuschek, G., 2006. Determination of oxygenated polycyclic aromatic hydrocarbons in particulate matter using high-performance liquid chromatography–tandem mass spectrometry. J. Chromatogr. A 1133 (1), 241–247.
Loft, S., Poulsen, H.E., Vistisen, K., Knudsen, L.E., 1999. Increased urinary excretion of 8-oxo-2′-deoxyguanosine, a biomarker of oxidative DNA damage, in urban bus drivers. Mutat. Res. Genet. Toxicol. Environ. Mutagen. 441 (1), 11–19.
Lubcke-von Varel, U., Machala, M., Ciganek, M., Neca, J., Pencikova, K., Palkova, L., Vondracek, J., Loffler, I., Streck, G., Reifferscheid, G., Fluckiger-Isler, S., Weiss, J.M.,

Lamoree, M., Brack, W., 2011. Polar compounds dominate in vitro effects of sediment extracts. Environ. Sci. Technol. 45 (6), 2384–2390.
Lui, K.H., Bandowe, B.A.M., Ho, S.S.H., Chuang, H.C., Cao, J.J., Chuang, K.J., Lee, S.C., Hu, D., Ho, K.F., 2016. Characterization of chemical components and bioreactivity of fine particulate matter (PM2.5) during incense burning. Environ. Pollut. 213, 524–532.
Lui, K.H., Bandowe, B.A.M., Tian, L., Chan, C.S., Cao, J.J., Ning, Z., Lee, S.C., Ho, K.F., 2017. Cancer risk from polycyclic aromatic compounds in fine particulate matter generated from household coal combustion in Xuanwei, China. Chemosphere 169, 660–668.
Lundstedt, S., Bandowe, B.A.M., Wilcke, W., Boll, E., Christensen, J.H., Vila, J., Grifoll, M., Faure, P., Biache, C., Lorgeoux, C., Larsson, M., Frech Irgum, K., Ivarsson, P., Ricci, M., 2014. First intercomparison study on the analysis of oxygenated polycyclic aromatic hydrocarbons (oxy-PAHs) and nitrogen heterocyclic polycyclic aromatic compounds (N-PACs) in contaminated soil. TrAC Trends Anal. Chem. 57, 83–92.
Lundstedt, S., White, P.A., Lemieux, Christine L., Lynes, Krista D., Lambert, Lain B., Öberg, Lars, Hagiund, Peter, Tyskiind, Mats, 2007. Sources, fate, and toxic hazards of oxygenated polycyclic aromatic hydrocarbons (PAHs) at PAHcontaminated sites. Ambio Î6, 475–485.
Martins, M., Costa, P.M., Ferreira, A.M., Costa, M.H., 2013. Comparative DNA damage and oxidative effects of carcinogenic and non-carcinogenic sediment-bound PAHs in the gills of a bivalve. Aquat. Toxicol. 142-143, 85–95.
Misaki, K., Takamura-Enya, T., Ogawa, H., Takamori, K., Yanagida, M., 2016. Tumour-promoting activity of polycyclic aromatic hydrocarbons and their oxygenated or nitrated derivatives. Mutagenesis 31 (2), 205–213.
Moorthy, B., Chu, C., Carlin, D.J., 2015. Polycyclic aromatic hydrocarbons: from metabolism to lung cancer. Toxicol. Sci. 145 (1), 5–15.
Musa Bandowe, B.A., Shukurov, N., Kersten, M., Wilcke, W., 2010. Polycyclic aromatic hydrocarbons (PAHs) and their oxygen-containing derivatives (OPAHs) in soils from the Angren industrial area, Uzbekistan. Environ. Pollut. 158 (9), 2888–2899.
Nebert, D.W., Dalton, T.P., Okey, A.B., Gonzalez, F.J., 2004. Role of aryl hydrocarbon receptor-mediated induction of the CYP1 enzymes in environmental toxicity and cancer. J. Biol. Chem. 279 (23), 23847–23850.
Padoley, K.V., Mudliar, S.N., Pandey, R.A., 2008. Heterocyclic nitrogenous pollutants in the environment and their treatment options–an overview. Bioresour. Technol. 99 (10), 4029–4043.
Palanisami, Thavamani, Idowu, Oluyoye, Megharaj, Mallavarapu, Semple, Kirk, Lundstedt, S., 2018. First study on the occurrence and distribution of oxygenated polycyclic aromatic hydrocarbons (oxy PAHs) in contaminated soils in Australia: implications for risk assessment paradigm. Environ. Sci. Technol. Lett (Submitted for publication).
Palm, W.U., Mänz, J.S., Ruck, W., 2014. Remediation of PAHs, NSO-heterocycles, and related aromatic compounds in permeable reactive barriers using activated carbon. In: Permeable Reactive Barrier: Sustainable Groundwater Remediation. CRC Press, pp. 215–248.
Park, E.J., Park, K., 2009. Induction of pro-inflammatory signals by 1-nitropyrene in cultured BEAS-2B cells. Toxicol. Lett. 184 (2), 126–133.
Pham, C.T., Kameda, T., Toriba, A., Hayakawa, K., 2013. Polycyclic aromatic hydrocarbons and nitropolycyclic aromatic hydrocarbons in particulates emitted by motorcycles. Environ. Pollut. 183, 175–183.
Rengarajan, T., Rajendran, P., Nandakumar, N., Lokeshkumar, B., Rajendran, P., Nishigaki, I., 2015. Exposure to polycyclic aromatic hydrocarbons with special focus on cancer. Asian Pacific Journal of Tropical Biomedicine 5 (3), 182–189.
Ringuet, J., Leoz-Garziandia, E., Budzinski, H., Villenave, E., Albinet, A., 2012. Particle size distribution of nitrated and oxygenated polycyclic aromatic hydrocarbons (NPAHs and OPAHs) on traffic and suburban sites of a European megacity: Paris (France). Atmos. Chem. Phys. 12 (18), 8877–8887.
Roemer, E., Stabbert, R., Rustemeier, K., Veltel, D.J., Meisgen, T.J., Reininghaus, W., Carchman, R.A., Gaworski, C.L., Podraza, K.F., 2004. Chemical composition, cytotoxicity and mutagenicity of smoke from US commercial and reference cigarettes smoked under two sets of machine smoking conditions. Toxicology 195 (1), 31–52.
Ruchirawat, M., Settachan, D., Navasumrit, P., Tuntawiroon, J., Autrup, H., 2007. Assessment of potential cancer risk in children exposed to urban air pollution in Bangkok, Thailand. Toxicol. Lett. 168 (3), 200–209.
Safe, S., Lee, S.O., Jin, U.H., 2013. Role of the aryl hydrocarbon receptor in carcinogenesis and potential as a drug target. Toxicol. Sci. 135 (1), 1–16.
Sarti, E., Pasti, L., Scaroni, I., Casali, P., Cavazzini, A., Rossi, M., 2017. Determination of n-alkanes, PAHs and nitro-PAHs in PM2.5 and PM1 sampled in the surroundings of a municipal waste incinerator. Atmos. Environ. 149, 12–23.
Schnelle-Kreis, J., Sklorz, M., Peters, A., Cyrys, J., Zimmermann, R., 2005. Analysis of particle-associated semi-volatile aromatic and aliphatic hydrocarbons in urban particulate matter on a daily basis. Atmos. Environ. 39 (40), 7702–7714.
Semple, K.T., Doick, K.J., Jones, K.C., Burauel, P., Craven, A., Harms, H., 2004. Peer reviewed: defining bioavailability and bioaccessibility of contaminated soil and sediment is complicated. Environ. Sci. Technol. 38 (12), 228A–231A.
Sen, S., Field, J.M., 2013. Genotoxicity of Polycyclic Aromatic Hydrocarbon Metabolites. pp. 83–127.
Shen, et al., 2011. Emission of oxygenated polycyclic aromatic hydrocarbons from indoor solid fuel combustion. Environ. Sci. Technol. 45, 3459–3465.
Singh, A., Chandrasekharan Nair, K., Kamal, R., Bihari, V., Gupta, M.K., Mudiam, M.K.R., Satyanarayana, G.N.V., Raj, A., Haq, I., Shukla, N.K., Khan, A.H., Srivastava, A.K., 2016. Assessing hazardous risks of indoor airborne polycyclic aromatic hydrocarbons in the kitchen and its association with lung functions and urinary PAH metabolites in kitchen workers. Clin. Chim. Acta 452, 204–213.
[illegible]tal exposure to polycyclic aromatic hydro-
[illegible]5 (4), 169–195.
St Helen, G., Goniewicz, M.L., Dempsey, D., Wilson, M., Jacob 3rd, P., Benowitz, N.L., 2012. Exposure and kinetics of polycyclic aromatic hydrocarbons (PAHs) in cigarette smokers. Chem. Res. Toxicol. 25 (4), 952–964.
Sun, Z., Zhu, Y., Zhuo, S., Liu, W., Zeng, E.Y., Wang, X., Xing, B., Tao, S., 2017. Occurrence of nitro- and oxy-PAHs in agricultural soils in eastern China and excess lifetime cancer risks from human exposure through soil ingestion. Environ. Int. 108, 261–270.
Susanne, Meyer, Cartellieri, Simone, Steinhart, H., 1999. Simultaneous determination of PAHs, hetero-PAHs (N, S, O), and their degradation products in creosote-contaminated soils. Method development, validation, and application to hazardous waste sites. Anal. Chem. 71, 4023–4029.
Timme-Laragy, A.R., Van Tiem, L.A., Linney, E.A., Di Giulio, R.T., 2009. Antioxidant responses and NRF2 in synergistic developmental toxicity of PAHs in zebrafish. Toxicol. Sci. 109 (2), 217–227.
Titaley, I.A., Chlebowski, A., Truong, L., Tanguay, R.L., Massey Simonich, S.L., 2016. Identification and toxicological evaluation of unsubstituted PAHs and novel PAH derivatives in pavement sealcoat products. Environ. Sci. Technol. Lett. 3 (6), 234–242.
Tsapakis, M., Lagoudaki, E., Stephanou, E.G., Kavouras, I.G., Koutrakis, P., Oyola, P., von Baer, D., 2002. The composition and sources of PM2.5 organic aerosol in two urban areas of Chile. Atmos. Environ. 36 (23), 3851–3863.
Tsibart, A.S., Gennadiev, A.N., 2013. Polycyclic aromatic hydrocarbons in soils: sources, behavior, and indication significance (a review). Eurasian Soil Sci. 46 (7), 728–741.
Uno, S., Tanaka, H., Kokushi, E., Bacolod, E.T., Koyama, J., 2017. Distributions of nitrated polycyclic aromatic hydrocarbons in the sediment of Osaka Bay, Japan. Mar. Pollut. Bull. 124 (2), 1014–1019.
Van Tiem, L.A., Di Giulio, R.T., 2011. AHR2 knockdown prevents PAH-mediated cardiac toxicity and XRE- and ARE-associated gene induction in zebrafish (*Danio rerio*). Toxicol. Appl. Pharmacol. 254 (3), 280–287.
Vignet, C., Le Menach, K., Lyphout, L., Guionnet, T., Frere, L., Leguay, D., Budzinski, H., Cousin, X., Begout, M.L., 2014. Chronic dietary exposure to pyrolytic and petrogenic mixtures of PAHs causes physiological disruption in zebrafish–part II: behavior. Environ. Sci. Pollut. Res. Int. 21 (24), 13818–13832.
Vione, D., Maurino, V., Minero, C., Pelizzetti, E., Harrison, M.A., Olariu, R.I., Arsene, C., 2006. Photochemical reactions in the tropospheric aqueous phase and on particulate matter. Chem. Soc. Rev. 35 (5), 441–453.
Vondráček, J., Pěnčíková, K., Neča, J., Ciganek, M., Grycová, A., Dvořák, Z., Machala, M., 2017. Assessment of the aryl hydrocarbon receptor-mediated activities of polycyclic aromatic hydrocarbons in a human cell-based reporter gene assay. Environ. Pollut. 220, 307–316.
Walgraeve, C., Demeestere, K., Dewulf, J., Zimmermann, R., Van Langenhove, H., 2010. Oxygenated polycyclic aromatic hydrocarbons in atmospheric particulate matter: molecular characterization and occurrence. Atmos. Environ. 44 (15), 1831–1846.
Wang, W., Jariyasopit, N., Schrlau, J., Jia, Y., Tao, S., Yu, T.W., Dashwood, R.H., Zhang, W., Wang, X., Simonich, S.L., 2011. Concentration and photochemistry of PAHs, NPAHs, and OPAHs and toxicity of PM2.5 during the Beijing Olympic games. Environ. Sci. Technol. 45 (16), 6887–6895.
Wassenberg, D.M., Di Giulio, R.T., 2004. Synergistic embryotoxicity of polycyclic aromatic hydrocarbon aryl hydrocarbon receptor agonists with cytochrome P4501A inhibitors in *Fundulus heteroclitus*. Environ. Health Perspect. 112 (17), 1658–1664.
Watt, Danielle L., Utzat, C.D., Hilario, Pablo, Basu, Ashis K., 2007. Mutagenicity of the 1-nitropyrene-DNA adduct *N*-(deoxyguanosin-8-yl)-1-aminopyrene in mammalian cells. Chem. Res. Toxicol. 20, 1658–1664.
Webb, P.J., Hamilton, Jacqueline F., Lewis, Alastair C., Wirtz, Klaus, 2006. Formation of oxygenated-polycyclic aromatic compounds in aerosol from the photo-oxidation *o*-tolualdehyde. Polycycl. Aromat. Compd. 26 (4), 237–252.
Wei, B., Alwis, K.U., Li, Z., Wang, L., Valentin-Blasini, L., Sosnoff, C.S., Xia, Y., Conway, K.P., Blount, B.C., 2016. Urinary concentrations of PAH and VOC metabolites in marijuana users. Environ. Int. 88, 1–8.
Wei, C., Bandowe, B.A.M., Han, Y., Cao, J., Zhan, C., Wilcke, W., 2015b. Polycyclic aromatic hydrocarbons (PAHs) and their derivatives (alkyl-PAHs, oxygenated-PAHs, nitrated-PAHs and azaarenes) in urban road dusts from Xi'an, Central China. Chemosphere 134, 512–520.
Wei, C., Han, Y., Bandowe, B.A.M., Cao, J., Huang, R.J., Ni, H., Tian, J., Wilcke, W., 2015a. Occurrence, gas/particle partitioning and carcinogenic risk of polycyclic aromatic hydrocarbons and their oxygen and nitrogen containing derivatives in Xi'an, Central China. Sci. Total Environ. 505, 814–822.
Wincent, E., Jonsson, M.E., Bottai, M., Lundstedt, S., Dreij, K., 2015. Aryl hydrocarbon receptor activation and developmental toxicity in zebrafish in response to soil extracts containing unsubstituted and oxygenated PAHs. Environ. Sci. Technol. 49 (6), 3869–3877.
Wincent, E., Le Bihanic, F., Dreij, K., 2016. Induction and inhibition of human cytochrome P4501 by oxygenated polycyclic aromatic hydrocarbons. Toxicol. Res. 5 (3), 788–799.
Witter, A.E., Nguyen, M.H., 2016. Determination of oxygen, nitrogen, and sulfur-containing polycyclic aromatic hydrocarbons (PAHs) in urban stream sediments. Environ. Pollut. 209, 186–196.
Xue, W., Warshawsky, D., 2005. Metabolic activation of polycyclic and heterocyclic aromatic hydrocarbons and DNA damage: a review. Toxicol. Appl. Pharmacol. 206 (1), 73–93.
Yang, J., Zhang, H., Zhang, H., Wang, W., Liu, Y., Fan, Y., 2017. Smoking modify the effects of polycyclic aromatic hydrocarbons exposure on oxidative damage to DNA in coke oven workers. Int. Arch. Occup. Environ. Health 90 (5), 423–431.
Yebra-Pimentel, I., Fernández-González, R., Martínez-Carballo, E., Simal-Gándara, J., 2015. A critical review about the health risk assessment of pahs and their metabolites in foods. Crit. Rev. Food Sci. Nutr. 55 (10), 1383–1405.

Zdráhal, Z., Karásek, P., Lojková, L., Bucková, M., Večeřa, Z., Vejrosta, J., 2000. Pressurised liquid extraction of ketones of polycyclic aromatic hydrocarbons from soil. J. Chromatogr. A 893 (1), 201–206.
Zhang, Q., Gao, R., Xu, F., Zhou, Q., Jiang, G., Wang, T., Chen, J., Hu, J., Jiang, W., Wang, W., 2014. Role of water molecule in the gas-phase formation process of nitrated polycyclic aromatic hydrocarbons in the atmosphere: a computational study. Environ. Sci. Technol. 48 (9), 5051–5057.
Zhihuan, Z., Fengpeng, H., Qingwei, B., Song, L., 2008. Vertical distribution and environmental significance of sulfur and oxygen heterocyclic aromatic hydrocarbons in soil samples collected from Beijing, China. Environ. Pollut. 153 (2), 457–467.
Zimmermann, K., Jariyasopit, N., Massey Simonich, S.L., Tao, S., Atkinson, R., Arey, J., 2013. Formation of nitro-PAHs from the heterogeneous reaction of ambient particle-bound PAHs with $N_2O_5/NO_3/NO_2$. Environ. Sci. Technol. 47 (15), 8434–8442.