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Review

A review of airborne polycyclic aromatic hydrocarbons (PAHs) and their human health effects

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ABSTRACT

Polycyclic aromatic hydrocarbons (PAHs) are a large group of organic compounds comprised of two or more fused benzene rings arranged in various configurations. PAHs are widespread environmental contaminants formed as a result of incomplete combustion of organic materials such as fossil fuels. The occurrence of PAHs in ambient air is an increasing concern because of their carcinogenicity and mutagenicity. Although emissions and allowable concentrations of PAHs in air are now regulated, the health risk posed by PAH exposure suggests a continuing need for their control through air quality management. In light of the environmental significance of PAH exposure, this review offers an overview of PAH properties, fates, transformations, human exposure, and health effects (acute and chronic) associated with their emission to the atmosphere. Biomarkers of PAH exposure and their significance are also discussed.

Contents

1. Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a large group of chemicals with 2 to 7 fused aromatic rings (Arey and Atkinson, 2003; Di-Toro et al., 2000). Some PAHs are well known as carcinogens, mutagens, and teratogens and therefore pose a serious threat to the health

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and the well-being of humans (Boström et al., 2002). The physicochemical properties of PAHs makes them highly mobile in the environment, allowing them to distribute across air, soil, and water bodies where their presence is ubiquitous (Baklanov et al., 2007; Latimer and Zheng, 2003; Sverdrup et al., 2002).

Polycyclic aromatic hydrocarbons are released into the environment from both natural and anthropogenic sources (WHO, 2003). The widespread occurrence of PAHs is due to their production by virtually all types of combustion of organic materials. The anthropogenic sources of PAHs and their derivatives are diverse and include: incomplete burning of fuels, garbage, or other organic substances such as tobacco and plant material. (Zhang and Tao, 2009). Likewise, forest fires and volcanic eruptions can also contribute to the natural budget of the PAH inventory (Zhang and Tao, 2009).

PAHs are widely distributed in the atmosphere and were one of the first atmospheric pollutants designated as a suspected carcinogen. The PAHs entering the atmosphere can be transported over long distances before deposition through atmospheric precipitation onto soils, vegetation or waters (Ravindra et al., 2008). As molecular weight increases, the carcinogenicity of PAHs also increases with reducing acute toxicity. The most potent PAH carcinogens have been identified to include benzo[a] anthracene, benzo[a]pyrene, and dibenz[ah]anthracene (Armstrong et al., 2004; Bach et al., 2003; CCME, 2010). Given the ubiquitous presence of PAHs in the environment and the health risk associated with their exposure, the aim of this paper is to review contemporary information on the properties, fate, and risk associated with the presence of these compounds in the atmosphere.

2. Chemical characteristics of PAHs

PAHs are organic substances made up of carbon and hydrogen atoms grouped into at least two condensed or fused aromatic ring structures (CCME, 2010). They can be divided into two categories: low molecular weight compounds consisting of fewer than four rings and high molecular weight compounds of four or more rings. Pure PAHs are usually colored, crystalline solids at ambient temperature (Masih et al., 2012). The physical properties of PAHs vary with their molecular weight and structure. The vapor pressure of PAHs decreases with increasing molecular weight (Akyuz and Cabuk, 2010). PAHs are highly lipophilic and therefore miscible in organic solvents. In addition, aqueous solubility decreases for each additional ring added to the PAH. PAHs also display other properties such as light sensitivity, heat resistance, conductivity, emittability, corrosion resistance, and physiological action (Masih et al., 2012). PAHs possess very characteristic UV absorbance spectra. As each ring structure has a unique UV spectrum, each isomer exhibits a unique UV absorbance spectrum. This is especially useful in the identification of PAHs. Most PAHs are also fluorescent, emitting characteristic wavelengths of light when they are excited (Masih et al., 2010). Although the health effects of individual PAHs differ, some PAHs have been identified to be of greatest concern due to highly adverse effects on humans. The physicochemical properties of few selected PAHs are shown in Table 1.

3. Fate and transformations of PAHs in atmosphere

The behavior of PAHs in the atmosphere depends on complex physico-chemical reactions, interactions with other pollutants, photochemical transformations, and dry and wet deposition (Delgado Saborit et al., 2010; Zhong and Zhu, 2013; Zhu et al., 2009). PAHs in the ambient air exist in vapor phase or adsorb into airborne particulate matter depending on the atmospheric conditions (ambient temperature, relative humidity, etc.), the nature (i.e., origin and properties) of the aerosol, and the properties of the individual PAH (Lima et al., 2005; Ravindra et al., 2008; Wang et al., 2013; Zhang and Tao, 2009). In general, low-weight PAHs (i.e., with two, three, or four rings) are more volatile (with low temperatures of condensation) and exist mainly in the gas phase (Kameda, 2011). Although the lighter PAH compounds are considered to be less toxic, they are able to react with other pollutants (such as ozone, nitrogen oxides, and sulfur dioxide) to form diones, nitro- and dinitro-PAHs, and sulfuric acids, respectively of which toxicity may be more significant (Park et al., 2001). PAHs with four or more rings show insignificant vaporization under all environmental conditions (Kameda, 2011). Most of the heavier PAHs therefore occur mainly in the particulate phase in the atmosphere due to their low vapor pressure (Kameda et al., 2005). A significant correlation was also found between the amounts of dust in the air and PAH concentrations in the particulate phase (Kuo et al., 2012). Hence, the concentrations of PAHs in the gas phase increase in summer or in general in tropical regions, whereas particulate phase PAHs are dominant during winter or in general in Arctic regions (Lai et al., 2011; Mohanraj et al., 2012). The adsorption of PAHs onto particulate phases can also be affected by the humidity (Li et al., 2011). Moreover, PAH adsorption also depends on the types of suspended particulates (e.g., soot, dust, fly-ash, pyrogenic metal oxides, pollens, etc.) (Zhang and Tao, 2009). A schematic of PAH fate and distribution in atmosphere is shown in Fig. 1.

4. PAH concentration levels in the environment

4.1. Atmosphere

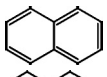
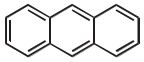
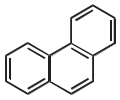
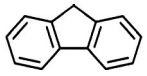
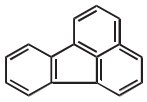
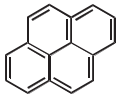
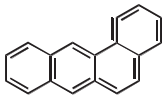
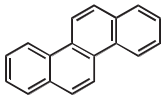
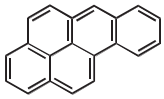
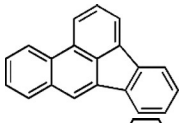
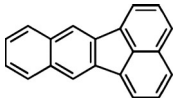
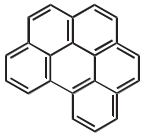
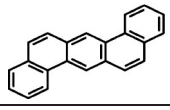
The presence of PAHs in the environment is due primarily to emissions from incomplete combustion of carbon containing fuels from natural, industrial, commercial, vehicular and residential sources. Although low molecular weight PAHs are found more commonly as vapor in the troposphere, they can also exist in the particulate phase through condensation after emission. In contrast, the high molecular weight PAHs are dominantly found in the particulate phase.

Detailed estimates of PAH emissions in the UK are available from the National Atmospheric Emissions Inventory (NAEI, 2013) which shows that in 2010 the total annual anthropogenic emissions of the 16 EPA priority PAHs were 621 tonnes of which 3.23 tonnes were B[a]P. These anthropogenic emissions are similar to natural emissions of B[a]P from episodes such as forest fires, long-range transport from volcanoes, and other natural combustion events, which were estimated to be 2.88 tonnes in 2010. The relative sources of anthropogenic B[a]P in 2010 were: residential and commercial combustion (76%), industrial combustion (6.7%), road transport (4.3%), metal production (3.4%), waste incineration (1.0%), and other sources (8.4%).

Reductions in PAH emissions have occurred consistently since the 1950s following the widespread introduction of the first clean air policies. In more recent times, the introduction of much tighter legislation concerning the allowable concentrations of PAH (especially benzo[a] pyrene — BaP) in air combined with legislation banning the uncontrolled burning of industrial wastes and agricultural stubble has continued to reduce the presence of these compounds in ambient air. Furthermore the decline of the aluminum production industry in much of Western Europe has also contributed to this decrease, although many of these emissions have now moved to Eastern Europe, Asia and the Middle East where production is concentrated. The reduction in primary emissions of PAHs over the years has had a dramatic effect on the observed concentrations of PAHs in ambient air. An example shown in Fig. 2 demonstrates a reduction in ambient BaP concentrations of three orders of magnitude in 60 years in London, UK. However, in developing countries (e.g., China, India, Brazil, and Sudan) where biomass and coal are the dominant energy sources, BaP concentrations are still too high to observe such rapid changes occurring in UK. Fig. 3 shows the relative contributions between various combustion sources of BaP in both the whole world and several important countries.

Because the sources of PAHs are almost always related to combustion, the concentrations of the individual PAHs in air are often highly correlated. Small variations in these correlations can be used to identify

Table 1
Structure and properties of PAHs investigated in this work.

Order	Compound name	Formula	Mol. wt. (g mo l^{-1})	CAS number	Vapor pressure at 25 °C (Pa)	Boiling point (°C)	Structure
1	Naphthalene	$C_{10}H_8$	128	91-20-3	11.9	218	
2	Acenaphthylene	$C_{12}H_8$	152	208-96-8	3.86	280	
3	Acenaphthene	$C_{12}H_{10}$	154	83-32-9	0.50	279	
4	Anthracene	$C_{14}H_{10}$	178	120-12-7	3.4×10^{-3}	340	
5	Phenanthrene	$C_{14}H_{10}$	178	85-01-8	9.07×10^{-2}	339–340	
6	Fluorene	$C_{13}H_{10}$	166	86-73-7	0.432	295	
7	Fluoranthene	$C_{16}H_{10}$	202	206-44-0	1.08×10^{-3}	375–393	
8	Pyrene	$C_{16}H_{10}$	202	129-00-0	5.67×10^{-4}	360–404	
9	Benzo(a)-anthracene	$C_{18}H_{12}$	228	56-55-3	6.52×10^{-7}	435	
10	Chrysene	$C_{18}H_{12}$	228	218-01-9	1.04×10^{-6}	441–448	
11	Benzo(a)-pyrene	$C_{20}H_{12}$	252	50-32-8	6.52×10^{-7}	493–496	
12	Benzo[b]fluoranthene	$C_{20}H_{12}$	252	205-99-2	1.07×10^{-5}	168	
13	Benzo[k]fluoranthene	$C_{20}H_{12}$	252	207-08-9	1.28×10^{-8}	217	
14	Benzo(ghi)-perylene	$C_{22}H_{12}$	276	191-24-2	1.33×10^{-8}	525	
15	Dibenz[a,h]anthracene	$C_{22}H_{14}$	278	3-70-3	2.80×10^{-9}	262	

specific local sources (A.S. Brown and R.J.C. Brown, 2012) and unusual pollution events (R.J.C. Brown and A.S. Brown, 2012). In terms of absolute levels over the last two decades, concentrations of BaP in urban regions can range from 0.3 and 0.6 ng m^{-3} in Houston, USA and London, UK, respectively, to 11 and 9.3 ng m^{-3} in Santiago, Chile and Lahore, Pakistan, respectively (Warneck and Williams, 2012). The highest values are generally found when industrial, rather than traffic or residential, contributions are dominant.

Two other properties of PAH concentrations in air are relevant to consider: seasonality and phase partitioning. In areas where local sources are mostly industrial, PAH concentrations show little seasonality because emissions are constant throughout the year. However in most urban, residential and rural areas where the local sources are related to residential and commercial heating, they show significant seasonality during the year (e.g., relative enhancement during the cold winter). This effect is particularly pronounced when the fuels used for heating exhibit high PAH emissions factors. A clear example of this is found in Northern Ireland, UK where solid fuel sources such as coal and wood are still commonly burnt for heating (Brown, 2013; R.J.C. Brown et al., 2013). For instance, the average BaP concentration during December–January was 3.0 ng m^{-3} compared to 0.19 ng m^{-3} during June–August.

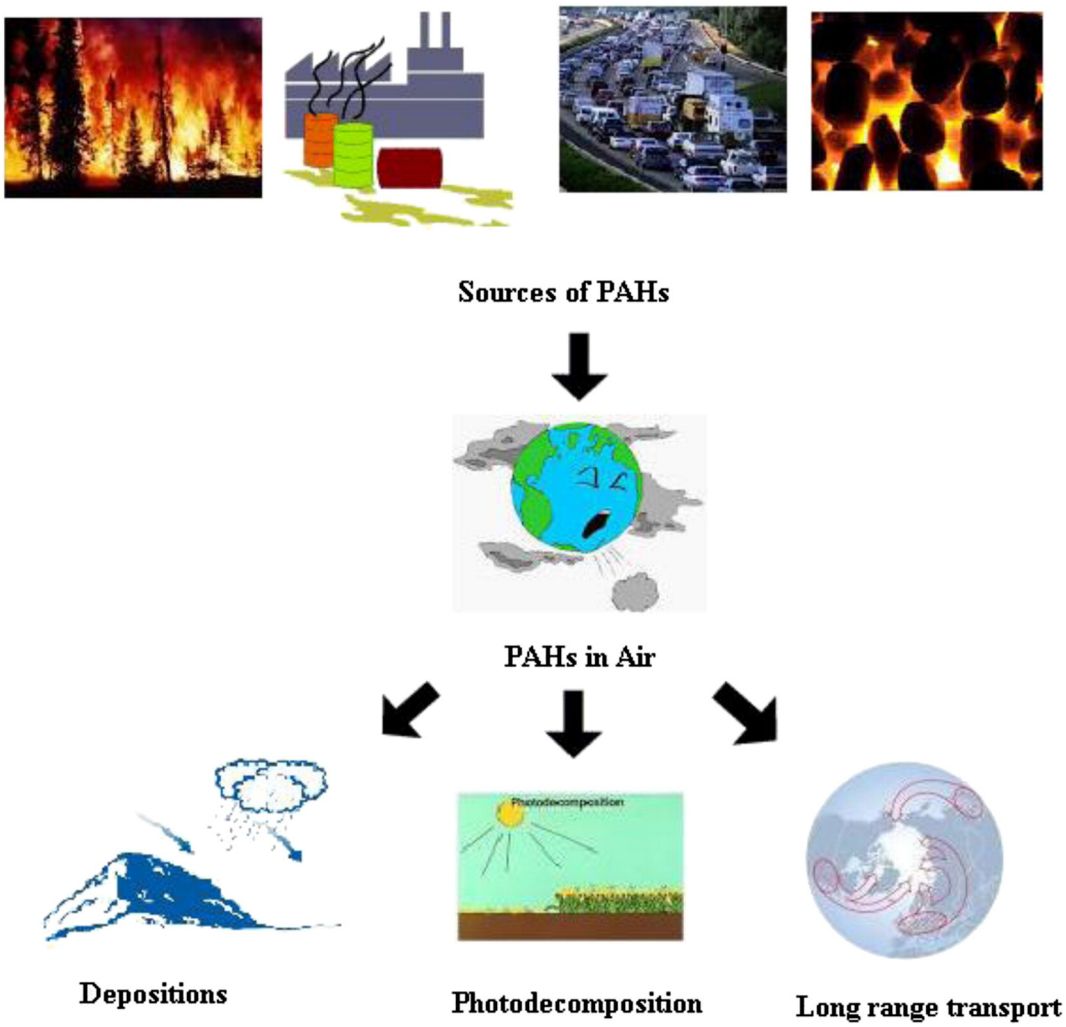


Fig. 1. Schematic of the fate of PAHs in the atmosphere.

The gas to particle phase partitioning of PAHs in air is a function of both ambient temperature and also volatility of the PAH in question. Therefore as ambient temperature increases ,the equilibrium shifts towards PAHs in the vapor phase. There is also some dependence, in the short term at least, of the gas to particle partitioning ratio on the source of emission and other atmospheric chemistry and meteorological considerations. Some exemplar gas to particle PAH ratio measurements are given in Table 2, showing the good correlation between the percentage of the PAH total found in the particulate phase and both molecular weight and vapor pressure.

4.2. Other environmental reservoirs

Just like other pollutants, PAHs bound to particulate matter may be readily deposited from air to the terrestrial biosphere. This is the main route by which PAHs enter other environmental compartments. A recent European field trial of a standard method for PAH measurement in deposition in Austria, Germany, France, and Netherlands recorded BaP deposition rates of 34, 212, 7.7, and 13 ng $m^{-2}d^{-1}$, respectively (CEN, 2011). Because of their lipophilicity, PAHs deposited to terrestrial and aquatic biosystems are found primarily in soil, sediment, and other oily substances, as opposed to in water. Humans and other fauna may be exposed to PAHs through eating plants grown in PAH contaminated soil — BaP concentrations in urban soils in India have been measured at 100 μg/kg (Ray et al, 2012). However, by far the greatest exposure of human to PAHs in food comes through the cooking process both from emissions during cooking and also from the final food product: especially if the food has been grilled or charred (Kim et al., 2011).

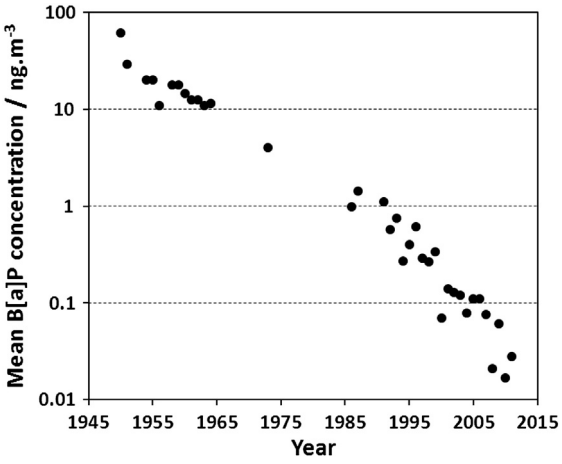


Fig. 2. Annual mean BaP concentrations measured at selected monitoring stations in Central London from 1950 to the present day. Source: A.S. Brown et al., 2013.

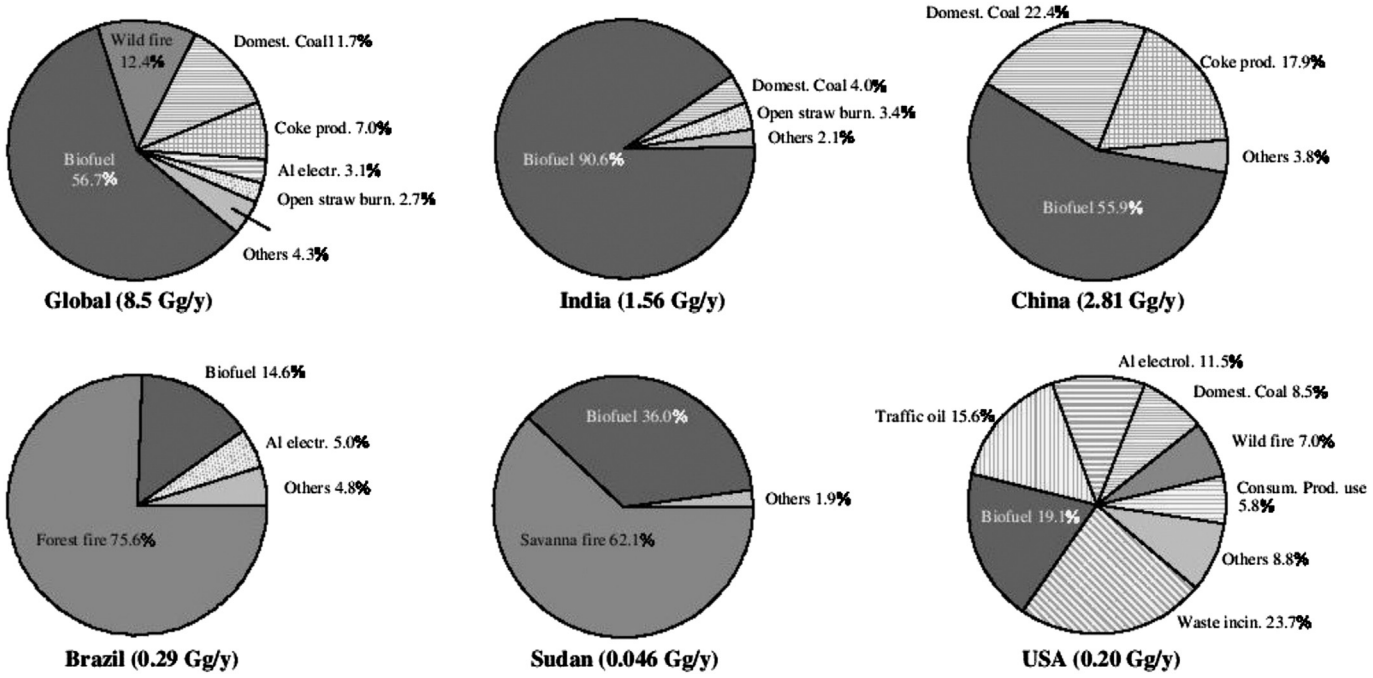


Fig. 3. Relative contributions of various sources to BaP emission (Source: Zhang and Tao, 2009).

5. Human exposure to polycyclic aromatic hydrocarbons

The major route of exposure to PAHs in the general population is from breathing ambient (and indoor) air, eating food containing PAHs, smoking cigarettes, or breathing smoke from open fireplaces (ACGIH, 2005). A variety of PAHs from tobacco smoke are suspected human carcinogens (Lannerö et al., 2008). For non-smokers, the main route of exposure is through food. Processing (such as drying and smoking) and cooking of foods at high temperatures (grilling, roasting, and frying) are major sources of generating PAHs (Chen and Lin, 2001). Some crops (such as wheat, rye, and lentils) may synthesize PAHs or absorb them via water, air, or, soil (Ciecierska and Obiedziński, 2013). Moreover, intake of PAHs may occur from contaminated soil via ingestion, inhalation, or dermal (skin) exposure and from inhalation of PAH vapors (Wang et al., 2012).

Occupational exposure to PAHs may occur from workers breathing exhaust fumes (such as mechanics, street vendors, or motor vehicle drivers) and those involved in mining, metal working, or oil refining (Armstrong et al., 2004; See et al., 2006). Routes of exposure include ingestion, inhalation, and dermal contact in both occupational and non-occupational settings (Ravindra et al., 2008). Some exposures may simultaneously involve multiple routes such as dermal and inhalation exposures from contaminated air, affecting the total dose of absorption.

6. Acute or short-term health effects

The acute effects of PAHs on human health will depend mainly on the extent of exposure (e.g., length of time), the concentration of PAHs during exposure, the toxicity of the PAHs, and the route of exposure, e.g., via inhalation, ingestion, or skin contact (ACGIH, 2005). Many other factors may also affect health impacts. These include factors such as pre-existing health conditions and age. Short-term exposure to PAHs also has been reported to cause impaired lung function in asthmatics and thrombotic effects in people affected by coronary heart disease (ACGIH, 2005). However, it is not known which components of the mixture were responsible for these effects. Currently there is not a full understanding of the ability of PAHs at ambient concentrations to induce human health effects in the short-term. In contrast, occupational exposures to high levels of pollutant mixtures containing PAHs are known to result in symptoms such as eye irritation, nausea, vomiting, diarrhea, etc. (Unwin et al., 2006). Mixtures of PAHs are also known to cause skin irritation and inflammation (Unwin et al., 2006). Anthracene, benzo(a)pyrene, and naphthalene are direct skin irritants, while anthracene and benzo(a)pyrene are reported to be skin sensitizers, i.e. as cause of an allergic skin response in animals and humans (IPCS, 2010).

7. Chronic or long-term health effects

For workers exposed to mixtures of PAHs and other work place chemicals, a series of health problems (an increased risk of skin, lung, bladder, and gastrointestinal cancers) have been reported (Bach et al., 2003; Boffetta et al., 1997; Diggs et al., 2011; Olsson et al., 2010). Long-term exposure to low levels of some PAHs (e.g., pyrene and BaP)

Table 2
Exemplar gas to particulate partitioning data, adapted from Possanzini et al. (2004).

PAH	Percentage of total found in particulate phase
Naphthalene	2%
Fluorene	5%
Acenaphtene	4%
Acenaphtylene	11%
Phenanthrene	9%
Anthracene	8%
Fluoroanthene	16%
Pyrene	55%
Benzo[*a*]anthracene	78%
Chrysene	89%
Benzo[*b*]fluoroanthene	91%
Benzo[*a*]pyrene	89%
Benzo[*e*]pyrene	85%
Perylene	100%
Benzo(*ghi*)perylene	83%
Indeno[1,2,3-*cd*]pyrene	100%
Anthanthrene	100%
Coronene	100%

has been identified as the cause of cancer in laboratory animals (Diggs et al., 2012). Animal studies have also shown adverse reproductive and developmental effects from PAH exposure while such effects have not commonly been detected in humans (Wells et al., 2010). Exposure to PAHs may induce cataracts and cause kidney and liver damage and jaundice (ATSDR, 1995). Repeated skin contact to the PAH naphthalene can result in redness and inflammation of the skin (Srogi, 2007). Breathing or swallowing large amounts of naphthalene can cause the breakdown of red blood cells (Srogi, 2007). The harmful effects of PAHs depend on the mechanism of exposure. Unfortunately in almost none of published studies, is there detailed information of human health effects following oral exposure to PAHs. In the majority of studies humans have been occupationally exposed to PAH via inhalation, while in a few studies the exposure has been via dermal contact. There is little information on human exposure to individual polycyclic aromatic hydrocarbons (PAHs) except for some accidental contact with naphthalene. In addition some data from controlled short-term studies of volunteers are available, but the conclusions are not transferable to the human exposure to PAHs via food. All other reports are on exposure to mixtures of PAHs, which also contained other potentially carcinogenic non-PAH chemicals either in occupational or environmental situations, making it difficult to deconvolve the effect of the PAHs alone. Information on the health effects of these mixtures is in practically all cases confined to their carcinogenic potential, based on evidence from a number of epidemiological studies, especially for lung cancer and in some cases cancers of the skin and of the bladder (Armstrong et al., 2002). Moreover, as PAHs have the potential to interfere with hormone systems, they can exert harmful effects on reproduction and immune function. As such, DNA damage induced by PAH exposure has been demonstrated by numerous authors (Garcia-Suastegui et al., 2011; Gunter et al., 2007; John et al., 2009). Long-term exposure to PAHs is suspected to raise the risks of cell damage via gene mutation and cardiopulmonary mortality (Kuo et al., 2003). Fig. 4 depicts a simple flow chart connecting health effects with short and long term exposure.

7.1. Carcinogenicity

Reactive metabolites (e.g., epoxides and dihydrodiols) of some PAHs have become one of the major health concerns because of their potential to bind to cellular proteins and DNA with toxic effects, despite the presence of some unmetabolized PAHs (Armstrong et al., 2004). The resulting biochemical disruption and cell damage can lead to mutations, developmental malformations, tumors, and cancer (Bach et al., 2003). Evidence indicates that mixtures of PAHs may be more carcinogenic to humans than individual PAHs. The evidence comes primarily from occupational studies of workers exposed to mixtures of PAHs. According to the U.S. Environmental Protection Agency (USEPA, 2008), seven PAH compounds have been classified as probable human carcinogens: benz(a)anthracene, benzo(a)pyrene, benzo(b)fluoranthene, benzo(k)fluoranthene, chrysene, dibenz(ah)anthracene, and indeno(1,2,3-cd)pyrene.

Information on human exposure and associated carcinogenicity has usually been acquired from the occupational exposure of workers to PAHs, e.g., during coke production, roofing using bituminous products, oil refining, and coal gasification (Bach et al., 2003; Zhang and Tao, 2009). In the past, chimney sweeps and workers using tar were dermally exposed to substantial amounts of PAHs. Hence, there is good evidence that skin cancer in many of these workers was caused by PAHs (Boffetta et al., 1997). In one of the previous studies, the relationship between lung cancer and working conditions (e.g., in the gas industry and coal tar industry) was explored (Kennaway, 1995). An increased incidence of cancers, particularly of the lung, was shown in epidemiologic studies of gas workers (Armstrong et al., 2004). An excessively high rate (16-fold higher) of lung cancer was found in coke-oven workers (Armstrong et al., 2002). The increases in lung cancer cases were closely correlated with the time spent for working on top of ovens where the average BaP concentration was about 30 mg m^{-3} (Moolgavkar et al., 1998). A small increased risk of cancer in workers exposed to diesel exhaust has also been suggested by some epidemiologic studies (Boers et al., 2005; Clapp et al., 2008; Travares et al., 2004). However, it should be noted that all these working environments produce, not only PAHs, but also others pollutants with potential carcinogenic effects.

Drinking mate (a traditional South American infused drink prepared from steeping dried leaves of yerba mate) has also been suspected for the association with cancers of the esophagus, oropharynx, larynx, lung, kidney, and bladder. Kamangar et al. (2008) found very high concentrations of carcinogenic PAHs in yerba mate leaves and in hot and cold mate infusions. This finding supported the hypothesis that the carcinogenicity of mate may be related to its PAH content. The carcinogenicity of certain PAHs had been well established in laboratory animals (Samanta et al., 2002). Researchers reported increased incidences of skin, lung, bladder, liver, and stomach cancers as well as injection-site sarcomas in animals (Samanta et al., 2002). Animal studies show that certain PAHs can also affect the hematopoietic and immune systems producing reproductive, neurologic, and developmental effects (Jong et al., 1999; Latif et al., 2010). In laboratory studies, animals exposed to certain levels of some PAHs over long periods have suffered from lung cancer from inhalation, stomach cancer from ingesting PAHs in food, and skin cancer from skin contact (Hecht, 1999; Latif et al., 2010; Lynch and Rebbeck, 2013). Benzo(a)pyrene is the most common PAH to cause cancer in animals and was the first chemical carcinogen to be discovered (Latif et al., 2010). Continued research regarding the mutagenic and carcinogenic effects from chronic exposure to PAHs and metabolites is needed. Table 3 indicates the carcinogenic classifications of selected PAHs by specific agencies.

Exposure to PAHs in air at ambient concentrations close to those specified in regulation is thought to pose a lower risk. A recent study of BaP concentrations in Northern Ireland (Butterfield and Brown, 2012) concluded that, amongst the population of 94,000 exposed to ambient concentration above the 1 ng m^{-3} target value in the province, only an additional 3 incidences of lung cancer over a 70 year period would be expected.

7.2. Teratogenicity

Embryotoxic effects of PAHs have been described in experimental animals exposed to PAH such as benzo(a)anthracene, benzo(a)pyrene, and naphthalene (Wassenberg and Di-Giulio, 2004). Laboratory studies conducted on mice have demonstrated that ingestion of high levels of benzo(a)pyrene during pregnancy resulted in birth defects and decreased body weight in the offspring (Kristensen et al., 1995). Likewise, the studies of the US's Center for Children's Environmental Health (CCEH) demonstrated that exposure to PAH pollution during pregnancy is related to adverse birth outcomes including low birth weight, premature delivery, and delayed child development (Perera et al., 2005). High prenatal exposure to PAHs is also associated with low IQ at age three, increased behavioral problems at ages six to eight, and childhood asthma (Edwards et al., 2010; Perera and Herbstman, 2011).

Lupo et al. (2012) indicated an association between occupational exposure to PAHs among mothers who are over 20 years and occurrence of gastroschisis. Langlois et al. (2013) found a statistically significant relationship between maternal occupational exposure to PAHs for cleft lip with or without cleft palate ($P_{trend} = 0.02$). According to experimental model systems, exposure to PAHs was expected to result in congenital heart defects (CHDs). However, in a case–control study, insignificant associations were observed between estimated maternal occupational exposure to PAHs and CHDs in offspring (Lupo et al., 2012). Ren et al. (2011) investigated placental PAH levels in 80 fetuses or newborns with neural tube defects in China. The results of their study showed that the risk of a defect was 4 to 5 times greater, when the levels of PAHs were above the average of 597 ng g^{-1} of lipids. In

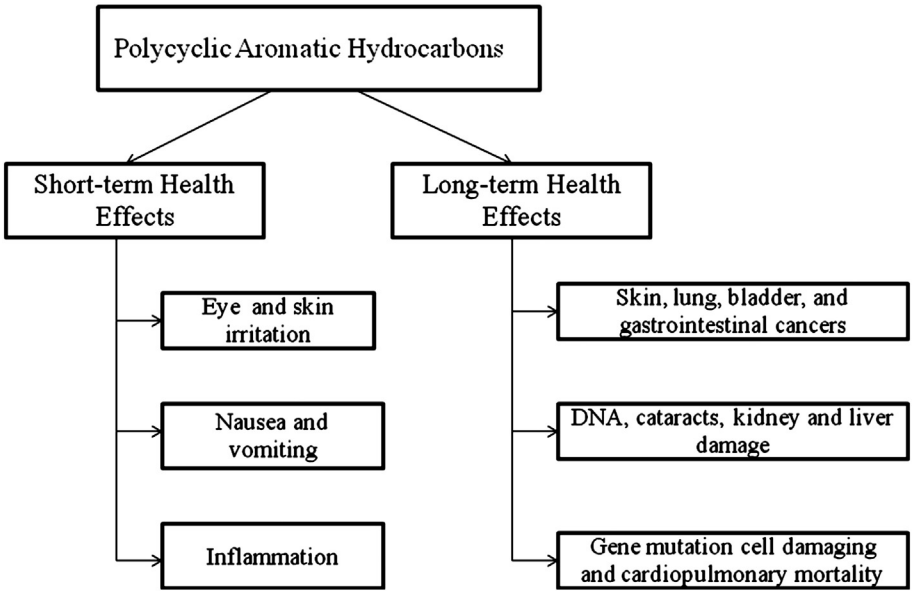


Fig. 4. Flow chart showing short and long term health effects of exposure to PAHs.

one of the recent studies in China, Yuan et al. (2013) reported the association between the low levels of placental PAH-DNA adducts with an increased risk of neural tube defects, especially when a low adduct level was coupled with a high placental PAH concentration. These authors provided a body of evidence to suggest that PAHs may be teratogenic. Because PAHs are lipophilic, they readily penetrate cellular membranes (including the placenta). During PAH metabolism, enzymatic activity can result in the formation of reactive intermediates that can form covalent bonds with DNA (Rice and Baker, 2007). DNA adducts have been demonstrated to result in a spectrum of cellular mutations that may be teratogenic (Wells et al., 2010).

7.3. Genotoxicity

Numerous studies on lymphocytes from workers exposed to PAHs (including BaP) have identified DNA adducts of BaP (mainly the diol epoxide). In one of the previous studies on iron foundry workers, elevated levels of mutations at the hprt locus in lymphocytes were shown approximately to correlate with the levels of DNA adducts (IPCS, 1998). Genotoxicity plays an important role in the carcinogenicity process and may be in some forms of developmental toxicity as well. In one of the previous studies, 32 PAHs were tested for genotoxicity in *Escherichia coli* PQ37 using the standard tube assay of the SOS

Table 3
Carcinogenic classifications of selected PAHs by specific agencies.

Order	Agency	PAH compound(s)	Carcinogenic classification	Reference
1	Agency for Toxic Substances and Disease Registry (ATSDR)	• Benz(a)anthracene, • Benzo(b)fluoranthene, • Benzo(a)pyrene, • Dibenz(a,h)anthracene, and • Indeno(1,2,3-c,d)pyrene	Known animal carcinogens	ATSDR (1995)
		• Benz(a)anthracene and • Benzo(a)pyrene.	Probably carcinogenic to humans	
2	International Agency for Research on Cancer (IARC)	• Benzo(a)fluoranthene, • Benzo(k)fluoranthene, and • Ideno(1,2,3-c,d)pyrene.	Possibly carcinogenic to humans	IARC (2010)
		• Anthracene, • Benzo(g,h,i)perylene, • Benzo(e)pyrene, • Chrysene, • Fluoranthene, • Fluorene, • Phenanthrene, and • Pyrene	Not classifiable as to their carcinogenicity to humans	
3	U.S. Environmental Protection Agency (EPA)	• Benz(a)anthracene, • Benzo(a)pyrene, • Benzo(b)fluoranthene, • Benzo(k)fluoranthene, • Chrysene, • Dibenz(a,h)anthracene, and • Indeno(1,2,3-c,d)pyrene	Probable human carcinogens	USEPA (2008)
		• Acenaphthylene, • Anthracene, • Benzo(g,h,i)perylene, • Fluoranthene	Not classifiable as to human carcinogenicity	

Table 4
Standards and regulation covering Polycyclic Aromatic Hydrocarbons (PAHs) in environmental media.

Order	Agency	Medium	Level	Comments	Reference
1	American Conference of Governmental Industrial Hygienists	Air	0.2 mg m^{-3}	Threshold limit value (TLV) for benzene-soluble coal tar pitch fraction	ACGIH (2005)
2	National Institute for Occupational Safety and Health	Air	0.1 mg m^{-3}	Recommended exposure limit (REL) for coal tar pitch volatile agents	NIOSH (2010)
3	National Institute for Occupational Safety and Health Administration	Air	0.2 mg m^{-3} for benzene-soluble coal tar pitch fraction	Permissible exposure limit (PEL) for benzene soluble fraction of coal tar volatiles	NIOSH (2010)
4	Canadian Council of Ministers of the Environment	Soil	0.6 mg m^{-3}	Total potency equivalents for soil contaminated with coal tar or creosote mixtures	CCME (2010)
5	U.S. Environmental Protection Agency	Water	0.0001 mg L^{-3}	Maximum contaminant level (MCL) for benz(a) anthracene	US EPA (2000)
			0.0002 mg L^{-3}	MCL for benzo(a)pyrene, benzo(b)fluoranthene, benzo(k) fluoranthene, chrysene	
			0.0003 mg L^{-3}	MCL for dibenz(a,h)anthracene	
			0.0004 mg L^{-3}	MCL for indenol(1,2,3-c,d)pyrene	
			0.0002 mg L^{-3}	MCL for benzo(a)pyrene, benzo(b)fluoranthene, benzo(k) fluoranthene, chrysene	

chromotest (Mersch-Sundermann et al., 1992; Nylund et al., 1992). PAHs such as benzo[*ghi*]fluoranthene, benzo[*j*]fluoranthene, benzo[*a*]pyrene, chrysene, dibenzo[*a,l*]pyrene, fluoranthene, and triphenylene exhibited high genotoxicity when incubated in the presence of an exogenous metabolic activation mixture (White, 2002). Concerning the induction of germ cell effects, benzo[*a*]pyrene, benzo[*a*]anthracene, and chrysene gave positive results in chromosome aberrations and/or dominant lethals in rodents (Jung et al., 2013). Nonetheless, no quantitative estimation of the genetic risk associated with PAH exposure was made on the basis of such data, with little evaluation of transmissible effects. For other PAH compounds (anthranthene, benzo[*ghi*]fluoranthene, benzo[*c*]phenanthrene, 1-methylphenanthrene, perylene, and triphenylene), the evidence of genotoxicity is limited and mainly based on results obtained in in vitro systems. Further studies, especially in vivo, are hence needed to clarify the genotoxic potential of these PAHs.

8. Biomarkers of exposure to PAH

Several methods have been developed to assess internal levels of PAHs after exposure from the environment and workplaces. In many studies, 1-Hydroxypyrene, a metabolite of pyrene, has been widely used as urinary biomarker of PAH exposure (Jongeneelen, 2001; Mcclean et al., 2004, 2012; Sobus et al., 2009; Stroomberg et al., 2003). Most importantly, pyrene is present in all PAH mixtures at relatively high concentrations (2–10% of the total PAH load). In certain environments, the pyrene content of the total PAH is fairly constant (McClean et al., 2012; Stroomberg et al., 2003).

From a study comparing the dietary effect on five male volunteers of low- and high-PAH content meals, a 100 to 250-fold increase in a dietary benzo(a)pyrene (BaP) dose was seen to induce a four- to 12-fold increase in urinary 1-OHPy elimination (Buckley and Lioy, 1992). Likewise, ten volunteers eating charbroiled beef for five days had a 10–80 fold increase in 1-OH-pyrene glucuronide excretion in urine which returned to background level within 24–72 h (Kang et al., 1995). The intake of pyrene from cigarette smoking (12 nmol day^{-1}) was comparable to that of a diet of normal foods (9.4 nmol day^{-1}) (Duarte-Salles et al., 2010). Tobacco smokers who are not exposed to PAHs have about twice the level of 1-hydroxypyrene in their urine relative to non-smokers (Hecht, 2002; Srogi, 2007; Van Rooij et al., 1994). However, 1-Hydroxypyrene cannot always be used to predict the extent of exposure to benzo[*a*]pyrene or other carcinogenic PAHs as the relative content of pyrene and benzo[a]pyrene may vary considerably (Srogi, 2007).

It should be noted that the concentration or excretion of parent PAH compounds or metabolites in body fluids or urine is not only dependent on external exposure but also on absorption, biotransformation, and excretion, which can vary considerably between individuals. Adducts of benzo[*a*]pyrene with DNA in peripheral lymphocytes and other tissues with proteins (such as albumin) have also been used as an indicator of the dose of reactive metabolites. As binding of electrophilic PAH metabolites to DNA is thought to be a key step in the initiation of cancer, measurement of DNA adducts could be an indicator of PAH exposure and also of the dose of the ultimate reactive metabolite (Perera et al., 2011). DNA adducts with reactive metabolites (mainly diol epoxides) of benzo[*a*]pyrene and other PAHs have been identified in humans exposed to smoking or living in polluted areas in numerous previous studies (e.g., Perera et al., 2005). PAH-DNA adducts have also been detected in peripheral white blood cells following human exposure to charbroiled meat (Kang et al., 1995). In a study of forest fire-fighters in the USA, levels of PAH-DNA adducts in blood cells were not found to correlate with recent fire-fighting activity but instead with recent consumption of charbroiled meat (Rothman et al., 1993). Furthermore, it is surprising to find that the PAH DNA-adduct levels were relatively low in US army personnel fighting oil field fires in Kuwait, possibly because of a lower intake of charbroiled meat (Poirier, 1991).

9. Regulation

PAH compounds are typically constituents of complex mixtures. Some PAHs are potent carcinogens, which may interact with a number of other compounds. U.S. government agencies have established standards that are relevant to PAH exposures in the workplace and the environment. There is a standard relating to PAH in the workplace as well as in drinking water. The National Institute for Occupational Safety and Health (NIOSH) has recommended that the workplace exposure limit for PAHs should be set at the lowest detectable concentration such as recommended exposure limit (REL) of 0.1 mg m^{-3} for coal tar pitch volatile agents for a 10-hour workday or 40-hour workweek (NIOSH, 2010). Water quality criteria for PAH exposure such as a maximum contaminant level (MCL) was also set for benzo(a)pyrene, the most carcinogenic PAH, at 0.2 ppb (US EPA, 2000). According to the WHO guidance (2003), the unit risk of lung cancer of BaP is 87×10^{-6} ng m^{-3} for lifetime exposure. Many member states of WHO have set the guideline values for BaP between 0.1 and 1.3 ng m^{-3}. Table 4 summarizes the standards and regulations for PAHs set by different agencies. In Europe, BaP is the target of regulation in ambient air because of its highest toxic equivalent factor (a function of concentration multiplied by toxicity), and it is also taken as a marker compound which is proportional to the total PAH load. In European air, the target annual average concentration is not to be exceeded in the PM_{10} fraction in 1 ng m^{-3} (European Commission, 2005). Recent data suggest that this target is being exceeded in many locations around Europe — particularly in the east of the continent (European Environment Agency, 2012).

10. Conclusion

To learn more about the significance of PAHs in the environment, enormous efforts have been devoted to quantifying the level of emissions, assessing ambient concentrations, characterizing speciation, and determining temporal/spatial trends. Currently, there is broad agreement on the main emission sources but harmonization of emission estimation and reporting is still at an early stage of development.

Data from a number of occupational health studies suggest that there is an association between lung cancer and exposure to PAH compounds. The most important exposure route for lung cancer would appear to be via inhalation. Several PAHs have been acknowledged as probable or possible human carcinogens, most of which are known to be associated with airborne particles. BaP, a probable human carcinogen found in appreciable concentrations in the atmosphere, can be used as a marker of the carcinogenic risk of airborne PAH. Indeed, the WHO considers BaP in their air quality guidelines when deriving a unit risk factor. However, currently there are insufficient exposure data to assess their harmful effects and consequently insufficient information to assess the need for or, indeed, define additional objectives for ambient air quality. Due to the widely varying physical and chemical properties of PAHs, their measurement is often difficult and costly. Methodology for sampling, analysis, and emission estimation will need to be harmonized in order to properly assess current ambient concentrations, the effect of future control measures, and to refine any further action which may be required to adequately assess their human health impacts.

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