Polycyclic Aromatic Hydrocarbons: 15 Listings

Reasonably anticipated to be human carcinogens

Also known as PAHs or polynuclear aromatic hydrocarbons

The term "polycyclic aromatic hydrocarbon" (PAH) commonly refers to a large class of organic compounds that contain carbon and hydrogen and consist of two or more fused aromatic rings. Fifteen individual PAHs (not the entire class) are listed separately in the Report on Carcinogens as *reasonably anticipated to be a human carcinogen:*

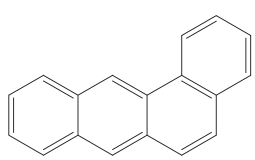
- Benz[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*j*]-fluoranthene, benzo[*a*]pyrene, dibenz[*a,h*]acridine, dibenz[*a,j*]acridine, dibenz[*a,h*]anthracene, 7*H*-dibenzo[*c,g*]-carbazole, dibenzo[*a,h*]pyrene, dibenzo[*a,i*]pyrene, and indeno[1,2,3-*cd*]pyrene were first listed in the *Second Annual Report on Carcinogens* (1981).
- Benzo[*k*]fluoranthene, dibenzo[*a,e*]pyrene, dibenzo[*a,l*]pyrene, and 5-methylchrysene were first listed in the *Fifth Annual Report on Carcinogens* (1989).

The chemical structures of the 15 listed PAHs are shown below. Evidence for their carcinogenicity from studies in experimental animals is then discussed separately for each PAH. However, most of the information on mechanisms of carcinogenesis, cancer studies in humans, use, production, exposure, and regulations is common to all 15 listed PAHs and therefore is discussed for the overall class of PAHs, following the discussions of cancer studies in experimental animals.

Benz[*a*]anthracene

CAS No. 56-55-3

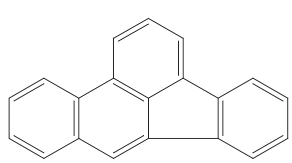
Also known as BA



Benzo[*b*]fluoranthene

CAS No. 205-99-2

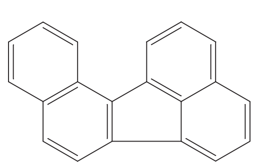
Also known as B[*b*]F



Benzo[*j*]fluoranthene

CAS No. 205-82-3

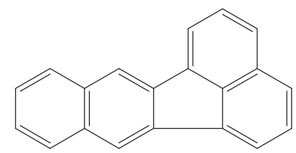
Also known as B[*j*]F



Benzo[*k*]fluoranthene

CAS No. 207-08-9

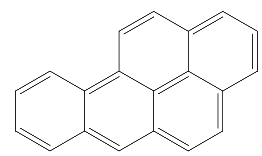
Also known as B[*k*]F



Benzo[*a*]pyrene

CAS No. 50-32-8

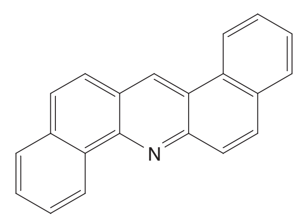
Also known as B[*a*]P



Dibenz[*a,h*]acridine

CAS No. 226-36-8

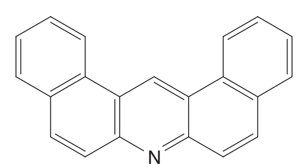
Also known as DB[*a,h*]AC



Dibenz[*a,j*]acridine

CAS No. 224-42-0

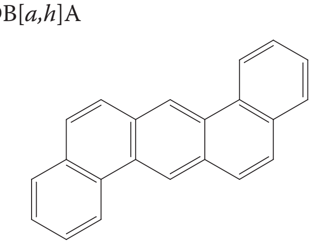
Also known as DB[*a,j*]AC



Dibenz[*a,h*]anthracene

CAS No. 53-70-3

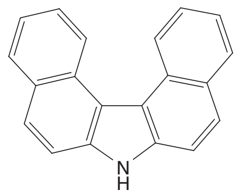
Also known as DB[*a,h*]A



7H-Dibenzo[*c,g*]carbazole

CAS No. 194-59-2

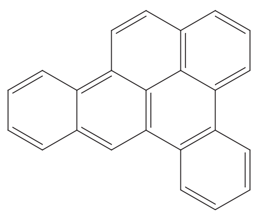
Also known as 7H-DB[*c,g*]C



Dibenzo[*a,e*]pyrene

CAS No. 192-65-4

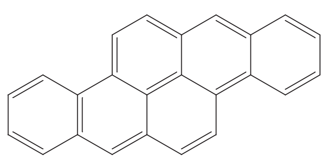
Also known as DB[*a,e*]P



Dibenzo[*a,h*]pyrene

CAS No. 189-64-0

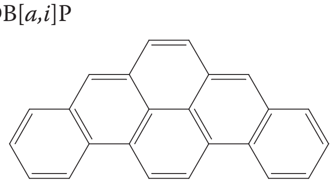
Also known as DB[*a,h*]P



Dibenzo[*a,i*]pyrene

CAS No. 189-55-9

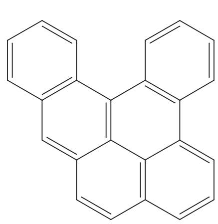
Also known as DB[*a,i*]P



Dibenzo[*a,l*]pyrene

CAS No. 191-30-0

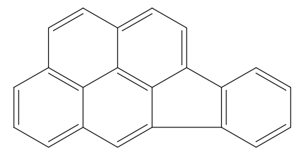
Also known as DB[*a,l*]P or dibenzo[*def,p*]chrysene



Indeno[1,2,3-*cd*]pyrene

CAS No. 193-39-5

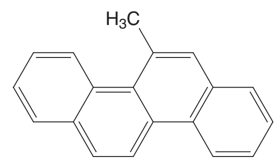
Also known as IP



5-Methylchrysene

CAS No. 3697-24-3

Also known as 5-MC



Carcinogenicity

The 15 individual PAHs are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

*Benz[*a*]anthracene*

Benz[*a*]anthracene caused tumors in mice at several different tissue sites and by several different routes of exposure. Benz[*a*]anthracene administered by stomach tube to adult mice or by subcutaneous injection to newborn mice caused benign or malignant lung tumors (adenoma or adenocarcinoma). Administration by stomach tube also caused liver cancer (hepatocelluar carcinoma) in adult mice. Benz[*a*]anthracene caused tumors in mice at the site of administration: skin tumors were observed after application to the skin, cancer at the injection site (sarcoma) after subcutaneous injection, and urinary-bladder cancer (carcinoma) after implantation in the bladder (IARC 1973).

Since benz[*a*]anthracene was listed in the *Second Annual Report on Carcinogens*, additional studies in mice have been identified. In newborn mice, intraperitoneal injection of benz[*a*]anthracene caused benign lung tumors (adenoma) in both sexes and benign or malignant liver tumors (adenoma or carcinoma) in males (Levin *et al.* 1984, Wislocki *et al.* 1986, Von Tungeln *et al.* 1999).

*Benzo[*b*]fluoranthene*

Benzo[*b*]fluoranthene caused tumors in mice by two different routes of exposure. Dermal application of benzo[*b*]fluoranthene caused skin tumors, and subcutaneous injection of benzo[*b*]fluoranthene caused cancer at the injection site (sarcoma) (IARC 1973). Since benzo[*b*]fluoranthene was listed in the *Second Annual Report on Carcinogens*, additional studies in rodents have been identified. Benzo[*b*]fluoranthene caused lung cancer (carcinoma) in female rats exposed by intrapulmonary implantation (Deutsch-Wenzel *et al.* 1983). Intraperitoneal injection of benzo[*b*]fluoranthene caused benign lung tumors (adenoma) in male strain A/J mice (a strain with a high spontaneous incidence of lung cancer) (Ross *et al.* 1995, Nesnow *et al.* 1998) and benign or malignant liver tumors (hepatocellular adenoma or carcinoma) in newborn male mice (Lavoie *et al.* 1987).

*Benzo[*j*]fluoranthene*

Dermal exposure to benzo[*j*]fluoranthene caused benign or malignant skin tumors (papilloma or carcinoma) in female mice (IARC 1973). Since benzo[*j*]fluoranthene was listed in the *Second Annual Report on Carcinogens,* additional studies in rodents have been identified. Intrapulmonary injection of benzo[*j*]fluoranthene caused lung cancer (squamous-cell carcinoma) in female rats (IARC 1983). In newborn mice, intraperitoneal injection of benzo[*j*]fluoranthene caused benign and malignant lung tumors (alveolar/bronchiolar adenoma and carcinoma) in both sexes and benign or malignant liver tumors (hepatocellular adenoma or carcinoma) in males (Lavoie *et al.* 1987, 1994).

*Benzo[*k*]fluoranthene*

Benzo[*k*]fluoranthene caused tumors in two rodent species, at two different tissue sites, and by two different routes of exposure. Intrapulmonary injection of benzo[*k*]fluoranthene caused lung cancer (squamous-cell carcinoma) in female rats, and subcutaneous injection of benzo[*k*]fluoranthene caused cancer at the injection site (sarcoma) in mice of both sexes (IARC 1983).

*Benzo[*a*]pyrene*

Benzo[*a*]pyrene caused tumors in eight species, including nonhuman primates, at several different tissue sites, and by several different routes of exposure. Benzo[*a*]pyrene had both local and systemic carcinogenic effects and caused tumors after a single dose, after prenatal exposure, and in newborn mice. Benzo[*a*]pyrene caused lung tumors (1) in mice after dietary exposure, prenatal exposure, or subcutaneous or intravenous injection, (2) in rats after administration in the trachea or the bronchus, and (3) in hamsters and nonhuman primates after intratracheal instillation (Andervont and Shimkin 1940, IARC 1973). Oral administration (in the diet or drinking water or by stomach tube) also caused forestomach and esophageal tumors in mice and hamsters, intestinal tumors in hamsters, and mammary-gland tumors in female rats (Horie *et al.* 1965, IARC 1973). Mammary-gland tumors in rats were also observed after intravenous injection. Benzo[*a*]pyrene caused skin tumors in prenatally exposed mice and in dermally exposed mice, rats, and rabbits. Cancer at the injection site (sarcoma or fibrosarcoma) was observed in mice, rats, hamsters, guinea pigs, newts, monkeys, and nonhuman primates exposed by subcutaneous injection and in mice exposed by intraperitoneal injection (IARC 1973).

Since benzo[*a*]pyrene was listed in the *Second Annual Report on Carcinogens,* numerous additional studies in experimental animals have been identified. These studies reported that benzo[*a*]pyrene caused tumors (1) by additional routes of exposure (including inhalation and other types of injections), (2) in additional species of experimental animals (including fish), and (3) at several additional tissue sites. In studies published since the early 1980s, benzo[*a*]pyrene caused tumors at the following tissue sites:

- The upper respiratory system (mainly the nose and larynx) and upper digestive system (mainly the pharynx, but also the forestomach and esophagus) in male hamsters exposed by inhalation (Thyssen *et al.* 1981).
- Lymphoma in mice exposed by intraperitoneal injection (IARC 2010) or intracolonic injection (Toth 1980, Anderson *et al.* 1983) and in transgenic male and female mice following oral exposure (de Vries *et al.* 1997, Kroese *et al*. 1997).
- The liver in male mice exposed prenatally (Anderson *et al.* 1995) or by intraperitoneal injection (Wislocki *et al.* 1986, Lavoie *et al.* 1987, Rodriguez *et al.* 1997, Von Tungeln *et al.* 1999) and in fish following dietary exposure (Hendricks *et al.* 1985, Hawkins *et al.* 1988), intraperitoneal injection (Hendricks *et al.* 1985), or injection into the fish embryo (transchorionic injection) (Black *et al.* 1988).
- The tongue and larynx (papilloma or carcinoma) in female mice following dietary exposure (Culp *et al.* 1998, Goldstein *et al.* 1998).
- The anus in mice of both sexes exposed by intracolonic injection (Toth 1980).
- The cervix in female mice exposed by intravaginal injection (Näslund *et al.* 1987).

Other studies (not described here) confirmed the earlier findings or found that benzo[*a*]pyrene caused tumors at similar tissue sites in additional species or by additional routes of exposure. Lung tumors were observed following exposure by (1) intratracheal or intrabronchial instillation in female mice (Kim and Lee 1996) and in rabbits of both sexes (Hirao *et al.* 1980), (2) intracolonic injection in female mice (Anderson *et al.* 1983), (3) intrafetal administration in mice of both sexes (Rossi *et al.* 1983), and (4) intrapulmonary injection in rats (Deutsch-Wenzel 1983, Wenzel-Hartung 1990). Intracolonic injection of benzo[*a*]pyrene in mice also caused tumors at tissue sites where it had previously been shown to cause tumors by other routes of exposure: the forestomach, esophagus, mammary gland, and skin (Toth 1980, Anderson *et al.* 1983). Benzo[*a*]pyrene caused forestomach tumors in mice exposed by intraperitoneal injection (Weyand *et al.* 1995), mammary-gland tumors in rats exposed by intramammary injection (Cavalieri *et al.* 1988, 1991), and sarcoma in mice exposed by intraperitoneal injection. Benzo[*a*]pyrene implanted in the buccal cavity caused intestinal tumors in rats (Solt *et al.* 1987), and a single intraperitoneal injection of benzo[*a*]pyrene caused abdominal tumors (mesothelioma and sarcoma) in rats (Roller *et al.* 1992).

*Dibenz[*a*,*h*]acridine*

Dibenz[*a,h*]acridine caused tumors in mice at several different tissue sites and by several different routes of exposure. Subcutaneous or intravenous injection of dibenz[*a,h*]acridine caused lung tumors; subcutaneous injection also caused cancer at the injection site (sarcoma), and dermal exposure caused skin tumors (IARC 1973). Since dibenz[*a,h*]acridine was listed in the *Second Annual Report on Carcinogens,* one study in rats has been identified. Intrapulmonary implantation of pellets containing dibenz[*a,h*]acridine caused lung cancer (carcinoma) in female rats (Deutsch-Wenzel 1983).

*Dibenz[*a*,*j*]acridine*

Dibenz[*a,j*]acridine caused tumors in mice at several different tissue sites and by two different routes of exposure. Dermal exposure to dibenz[*a,j*]acridine in mice caused benign or malignant skin tumors (papilloma, carcinoma, or epithelioma). Subcutaneous injection of dibenz[*a,j*]acridine caused cancer at the injection site (sarcoma) in all mouse strains tested and lung tumors in strain A mice (a strain with a high spontaneous incidence of lung cancer) (IARC 1973).

*Dibenz[*a*,*h*]anthracene*

Dibenz[*a,h*]anthracene caused tumors in several species of experimental animals, at several different tissue sites, and by several different routes of administration. Dibenz[*a,h*]anthracene caused lung tumors in mice after a single intravenous or subcutaneous injection (IARC 1973), in newborn mice after intraperitoneal injection (Buening *et al.* 1979), and in hamsters after intratracheal instillation (Pott *et al.* 1978). In mice, oral exposure to dibenz[*a,h*]anthracene caused cancer of the lung (adenomatosis or alveologenic carcinoma) and mammary gland (carcinoma), benign or malignant tumors of the forestomach (squamous-cell papilloma or carcinoma), and tumors of the blood vessels (hemangioendothelioma) (IARC 1973). Exposure to dibenz[*a,h*]anthracene by injection or dermal application also caused local tumors: (1) cancer at the injection site (sarcoma) in rats, guinea pigs, and adult and newborn mice exposed by subcutaneous injection and in pigeons and fowl exposed by intramuscular injection, (2) kidney cancer (adenocarcinoma) in frogs exposed by injection into the kidneys, and (3) benign or malignant skin tumors (papilloma or carcinoma) in mice exposed dermally (IARC 1973).

Since dibenz[*a,h*]anthracene was listed in the *Second Annual Report on Carcinogens,* additional studies in rodents have been identified. Lung tumors were observed following administration of dibenz[*a,h*]-anthracene by intraperitoneal injection in male strain A/J mice (increased tumor incidence and number of tumors per animal) (Ross *et al.* 1995, Nesnow *et al.* 1996, 1998) and by intrapulmonary implantation in female rats (Wenzel-Hartung *et al.* 1990). Intraperitoneal injection of dibenz[*a,h*]anthracene also caused benign and malignant liver tumors (adenoma and carcinoma) in newborn male mice (Fu *et al.* 1998).

*7H-Dibenzo[*c,g*]carbazole*

7*H*-Dibenzo[*c,g*]carbazole caused tumors in several species of experimental animals, at several different tissue sites, and by several different routes of exposure. Administration of 7*H*-dibenzo[*c,g*]-carbazole by stomach tube caused benign and malignant tumors of the liver (hepatocellular adenoma and carcinoma) and forestomach (papilloma and carcinoma) in mice. Administration by intravenous injection or subcutaneous injection caused lung tumors in mice, and administration by intratracheal instillation caused respiratory-system cancer (squamous-cell adenocarcinoma and carcinoma of the bronchus, trachea, and larynx) in hamsters. In mice and rats, administration by subcutaneous injection also caused cancer at the injection site (sarcoma), and dermal application caused benign and malignant skin tumors (papilloma and carcinoma). In a dog, injection of 7*H*-dibenzo[*c,g*]carbazole into the urinary bladder (intravesicular injection) caused benign and malignant urinary-bladder tumors (transitional-cell papilloma and carcinoma) (IARC 1973).

Since 7*H*-dibenzo[*c,g*]carbazole was listed in the *Second Annual Report on Carcinogens,* additional studies in mice have been identified, in which additional routes of exposure to 7*H*-dibenzo[*c,g*]-carbazole were reported to cause liver, skin, and lung tumors. Dermal exposure or subcutaneous injection caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma) (Warshawsky *et al.* 1994, Mitchell and Warshawsky 1999, Taras-Valero *et al.* 2000), and subcutaneous injection also caused skin tumors (Taras-Valero *et al.* 2000). In male strain A/J mice, a single intraperitoneal injection of 7*H*-dibenzo[*c,g*]carbazole caused benign lung tumors (adenoma) (Warshawsky *et al.* 1996, Gray *et al.* 2001).

*Dibenzo[*a,e*]pyrene*

Dibenzo[*a,e*]pyrene caused tumors in mice at two different tissue sites and by two different routes of exposure. Dermal exposure to dibenzo[*a,e*]pyrene caused benign and malignant skin tumors (carcinoma, epithelioma, and papilloma) in females, and subcutaneous injection of dibenzo[*a,e*]pyrene caused cancer at the injection site (sarcoma) in both sexes (IARC 1973).

*Dibenzo[*a,h*]pyrene*

Dibenzo[*a,h*]pyrene caused tumors in two rodent species, at two different tissue sites, and by several different routes of administration. Dermal exposure to dibenzo[*a,h*]pyrene caused benign and malignant skin tumors (papilloma, sebaceous-gland adenoma, epithelioma, and carcinoma) in mice of both sexes (IARC 1973). Cancer at the site of administration (sarcoma) was observed in mice of both sexes following subcutaneous injection of dibenzo[*a,h*]pyrene and in female rats following subcutaneous implantation of paraffin disks containing dibenzo[*a,h*]pyrene (IARC 1973, Bahna *et al.* 1979).

Since dibenzo[*a,h*]pyrene was listed in the *Second Annual Report on Carcinogens,* additional studies in rodents have been identified. Intraperitoneal injection of newborn mice with dibenzo[*a,h*]pyrene caused lung tumors in both sexes and liver tumors in males (Chang *et al.* 1982). In female rats, intramammary injection of dibenzo[*a,h*]-pyrene caused cancer of the mammary gland (fibrosarcoma or adenocarcinoma) (Cavalieri *et al.* 1989), and subcutaneous injection caused cancer at the injection site (sarcoma) (Bahna *et al.* 1979).

*Dibenzo[*a,i*]pyrene*

Dibenzo[*a,i*]pyrene caused tumors in two rodent species, at two different tissue sites, and by several different routes of administration. Dermal exposure to dibenzo[*a,h*]pyrene caused benign or malignant skin tumors (papilloma or epithelioma) in mice, and subcutaneous injection caused cancer at the injection site (sarcoma) in mice and hamsters (IARC 1973).

Since dibenzo[*a,i*]pyrene was listed in the *Second Annual Report on Carcinogens,* additional studies in rodents have been identified. Intraperitoneal injection of newborn mice with dibenzo[*a,i*]pyrene caused lung tumors in both sexes and liver tumors in males (Chang *et al.* 1982), and intratracheal instillation caused respiratory-system cancer (mostly squamous-cell carcinoma, but also adenocarcinoma and anaplastic carcinoma) in hamsters of both sexes (Sellakumar and Shubik 1974, Stenbäck and Sellakumar 1974). Dibenzo[*a,i*]-pyrene administered by intramammary injection caused cancer of the mammary gland (fibrosarcoma and adenocarcinoma) in female rats (Cavalieri *et al.* 1989).

*Dibenzo[*a,l*]pyrene*

Dibenzo[*a,l*]pyrene caused tumors in mice at two different tissue sites and by two different routes of exposure. Subcutaneous injection of dibenzo[*a,l*]pyrene caused cancer at the injection site (sarcoma) in mice of both sexes (IARC 1973), and dermal exposure caused skin tumors in female mice (IARC 1983).

Since dibenzo[*a,l*]pyrene was listed in the *Fifth Annual Report on Carcinogens,* additional studies in experimental animals have been identified, which reported that dibenzo[*a,l*]pyrene caused tumors (1) by additional routes of exposure (oral, prenatal, and intraperitoneal injection), (2) in additional species of experimental animals (rats, hamsters, and fish), and (3) at additional tissue sites, including sites distant from the route of administration. Administration of dibenzo[*a,l*]pyrene by stomach tube to female mice caused ovarian tumors (predominantly granulosa-cell tumors) (Buters *et al.* 2002). Dietary administration of dibenzo[*a,l*]pyrene to fish caused benign or malignant liver tumors (hepatocellular adenoma or carcinoma or cholangiocellular adenoma) and benign tumors of the stomach (papillary adenoma) and swim bladder (papillary adenoma) (Reddy *et al.* 1999a,b). Intraperitoneal injection of dibenzo[*a,l*]pyrene caused lung tumors in strain A/J mice (Prahalad *et al.* 1997). Lung and liver tumors were observed in prenatally exposed mice (Yu *et al.* 2006) and in newborn mice exposed by intraperitoneal injection (Platt *et al.* 2004); lung tumors occurred in both sexes, and liver tumors in males. In addition, prenatal exposure to dibenzo[*a,l*]pyrene caused T-cell lymphoblastic lymphoma in mice of both sexes (Yu *et al.* 2006). Local tumors also were observed in rats and hamsters: intramammary injection of dibenzo[*a,l*]pyrene caused mammary-gland cancer (adenocarcinoma or fibrosarcoma) in female rats (Cavalieri *et al.* 1989, 1991), and application of dibenzo[*a,l*]pyrene directly to the tongue caused cancer of the oral cavity (squamous-cell carcinoma) in female hamsters (Schwartz *et al.* 2004).

*Indeno[*1,2,3-cd*]pyrene*

Indeno[1,2,3-*cd*]pyrene caused tumors in mice at two different tissue sites and by two different routes of exposure. Dermal exposure to indeno[1,2,3-cd]pyrene caused benign and malignant skin tumors (papilloma and carcinoma) in females, and subcutaneous injection caused cancer at the injection site (sarcoma) in males (IARC 1973). Since indeno[1,2,3-*cd*]pyrene was listed in the *Second Annual Report on Carcinogens,* an additional study in rodents has been identified. Intrapulmonary administration of indeno[1,2,3-*cd*]pyrene caused lung cancer (carcinoma) in female rats (Deutsch-Wenzel 1983).

5-Methylchrysene

5-Methylchrysene caused tumors in mice at two different tissue sites and by two different routes of exposure. Dermal exposure to 5-methylchrysene caused skin cancer (carcinoma) in females, and subcutaneous injection caused cancer at the injection site (sarcoma) in males (IARC 1983). Since 5-methylchrysene was listed in the *Fifth Annual Report on Carcinogens,* additional studies in mice have been identified. Intraperitoneal injection of 5-methylchrysene caused lung tumors in male strain A mice (Ross *et al.* 1995, Nesnow *et al.* 1998) and lung and liver tumors in newborn mice of both sexes (Hecht *et al.* 1985, el-Bayoumy *et al.* 1989).

Studies on Mechanisms of Carcinogenesis

Most PAHs with potential biological activity range in size from two to six fused aromatic rings (IARC 2010). Because of the vast range in molecular weight of PAHs, several of the physicochemical properties that are critical to their biological activity also vary greatly. Five properties in particular have a decisive influence on the biological activity of PAHs: their vapor pressure, their adsorption on surfaces of solid carrier particles, their absorption into liquid carriers, their lipid-aqueous partition coefficient in tissues, and their limits of solubility in the lipid and aqueous phases of tissues. These properties are intimately linked with the metabolic activation of the most toxic PAHs, and an understanding of the nature of this interaction helps in the understanding of their deposition and disposition. It has been proposed that PAHs share a similar mechanism of carcinogenic action. In general, PAHs are converted to oxides and dihydrodiols, which in turn are oxidized to diol epoxides. Both oxides and diol epoxides are ultimate DNA-reactive metabolites. PAH oxides can form stable DNA adducts, and diol epoxides can form stable and depurinating adducts with DNA through formation of electrophilic carbonium ions. Most of the 15 listed PAHs have been shown to be initiators of skin cancer (IARC 1983, 2010). The International Agency for Research on Cancer concluded that benzo[*a*]pyrene was carcinogenic to humans based on data on the mechanism of carcinogenicity (IARC 2010).

Cancer Studies in Humans

No epidemiological studies on exposure to the individual PAHs were identified. Individual PAHs are found in the environment not in isolation but as components of highly complex mixtures of chemicals. PAHs are very widespread environmental contaminants, because they are formed during incomplete combustion of materials such as coal, oil, gas, wood, or garbage or during pyrolysis of other organic material, such as tobacco or charbroiled meat. Data on the carcinogenicity of PAHs in humans are available only for mixtures containing PAHs. It is difficult to ascertain the carcinogenicity of the component PAHs in these mixtures because of potential chemical interactions and the presence of other carcinogenic substances in the mixtures. In 2005, IARC reevaluated PAHs. Although certain occupations with high PAH exposure (e.g., coal gasification and coke production) were classified as carcinogenic in humans, the roles of individual PAHs could not be defined (IARC 2010).

Properties

Three of the listed PAHs (dibenz[*a,h*]acridine, dibenz[*a,j*]acridine, and 7*H*-dibenzo[*c,g*]carbazole) contain a nitrogen atom as part of a ring and therefore are classified as heterocyclic PAHs. The PAHs can exist as leaflets, plates, needles, or at room temperature and range in color from colorless to yellow, green or blue. All PAHs are soluble in water and slightly soluble in ethanol, acetone or acid; most are soluble in benzene. Physical and chemical properties of the 15 PAHs are listed in the table below. In addition to the properties listed in the table, benzo[*a*]pyrene has a specific gravity of 1.351 and a vapor density relative to air of 8.7, and dibenzo[*a,h*]anthracene has a specific gravity of 1.282 (HSDB 2009).

Use

IARC (1983) reported that no commercial uses or applications were known for dibenzo[*a,h*]pyrene, dibenzo[*a,i*]pyrene, and 5-methyl-

PAH	Physical form	MW[a]	MP (°C)[a]	BP (°C)[a]	Log K_{ow}[b]	Sol. at 25°C (g/L)[b]	VP at 25°C (mm/Hg)[b]
BA	colorless leaflets or plates with greenish-yellow fluorescence	228.3	160	437.6	5.79	9.4×10^{-6}	2.1×10^{-7}
B[*b*]F	colorless needles	252.3	168	NR	5.78	1.2×10^{-6}[a,c]	5.0×10^{-7}
B[*j*]F	orange needles or yellow plates	252.3	166	NR	6.11	2.5×10^{-6}[c]	2.62×10^{-8}
B[*k*]F	pale-yellow needles	252.3	217	480	6.84[a]	8.0×10^{-7}	9.7×10^{-10}
B[*a*]P	pale-yellow needles	252.3	179 to 179.3	310 to 312 at 10 mm Hg	5.97	1.62×10^{-6}	5.49×10^{-9}[a]
DB[*a,h*]AC	yellow crystals	279.4	226[b]	NR	5.73	1.59×10^{-3}	1.85×10^{-9}
DB[*a,j*]AC	yellow needles or prisms	279.4	216	NR	5.63	1.8×10^{-5}	1.85×10^{-9}
DB[*a,h*]A	colorless leaflets, plates, or crystals	278.3	266	524	6.5[a]	2.49×10^{-6}	1.0×10^{-10}
7H-DB[*c,g*]C	needles	267.3	158	NR	5.58	6.3×10^{-5}[c]	3.4×10^{-9}
DB[*a,e*]P	pale-yellow to yellow-red needles	302.4	233.5	NR	7.28	8.02×10^{-8}	7.03×10^{-11}
DB[*a,h*]P	yellow plates	302.4	317	NR	7.28	3.5×10^{-8}	6.41×10^{-12}
DB[*a,i*]P	greenish-yellow needles, prisms, or lamellae	302.4	280	275 at 0.05 mm Hg	7.28	5.54×10^{-7}	1.78×10^{-11}
DB[*a,l*]P	yellow plates	302.4	162.4	NR	7.71[a]	3.6×10^{-7}	4.8×10^{-10}
IP	yellow plates	276.3	163.6	536	6.7	1.9×10^{-7}	1.25×10^{-10}
5-MC	needles with brilliant bluish-violet fluorescence in UV light.	242.3	117.5	NR	6.07	6.2×10^{-5}[a]	2.53×10^{-7}

Sources: [a]HSDB 2009 except as indicated. [b]ChemIDplus 2009 except as indicated. [c]Temperature not specified. MW = molecular weight. MP = melting point. BP = boiling point. Sol = water solubility. VP = vapor pressure. NR = not reported.

chrysene. The remaining twelve listed PAHs are used only in biochemical, biomedical, laboratory, or cancer research (HSDB 2009). At least five of the listed PAHs are present in coal tar, which is used as a fuel in the steel industry in open-hearth and blast furnaces (HSDB 2009). Coal tar is also used in the clinical treatment of skin disorders such as eczema, dermatitis, and psoriasis. Coal tar is distilled to produce a variety of products, including coal-tar pitch and creosote. At least two of the listed PAHs are present in coal-tar pitch, which is used primarily as a binder for aluminum smelting electrodes in the aluminum reduction process. Coal-tar pitch is also used in roofing, in surface coatings, for pitch-coke production, and for a variety of other applications (IARC 1985). At least two of the listed PAHs are found in creosote, which is used to preserve railroad ties, marine pilings, and telephone poles. Some creosote is used for fuel by steel producers (NIOSH 1977). At least three of the listed PAHs are present in bitumens and asphalt, which are used for paving roads, sound- and water-proofing, and coating pipes.

Production

PAHs are not produced for commercial use in the United States (IARC 1983, HSDB 2009). In 2015, combined U.S production and imports of benzo[*a*]pyrene were in the range of 10 million to 50 million pounds, and combined production and imports of indeno[1,2,3-*cd*]pyrene were less than 25,000 lb (EPA 2016); no data were found for the other 13 PAHs. Production data for tar, tar pitch, creosote, mineral oils, and coke, which contain various PAHs, are included in their respective profiles in the Report on Carcinogens (see Coal Tars and Coal-Tar Pitches, Coke-Oven Emissions, and Mineral Oils: Untreated and Mildly Treated).

Exposure

PAHs are ubiquitous in the environment, and the general population is exposed to measurable background levels (IPCS 1998). Sources of PAHs in ambient air (both outdoors and indoors) include forest fires, volcanoes, industrial emissions, residential and commercial heating with wood, coal, or other biomass fuels (oil and gas heating produce much lower quantities of PAHs), motor-vehicle exhaust (especially diesel), and other indoor sources such as cooking and tobacco smoke (IARC 1983, IPCS 1998). Food is a major source of exposure to PAHs for the general population (IPCS 1998). Skin contact with PAH-contaminated soils and the use of dermally applied pharmaceutical products based on coal tar also have been identified as sources of exposure for the general population (Jongeneelen *et al.* 1985, Viau and Vyskocil 1995, IPCS 1998, Jongeneelen 2001).

According to the U.S. Environmental Protection Agency's Toxics Release Inventory, industrial releases of PAHs to the environment peaked in 2000, when over 4.9 million pounds was released, mostly to on-site and off-site landfills and to air. Releases have been relatively stable at a lower level since 2002. In 2008, 1,192 facilities released over 1.2 million pounds of PAHs to air, water, or on- or off-site landfills (mostly to air or landfills) (TRI 2010).

In the past, benzo[*a*]pyrene often was used as a marker for measuring exposure to PAHs. However, it is now possible or even common to measure many PAHs individually. Mean concentrations of individual PAHs in ambient urban air usually range from 1 to 30 ng/m^3 (IPCS 1998). The concentrations of PAHs in the air during winter, when residential heating is a major source, generally are at least an order of magnitude higher than those in summer (IPCS 1998). Areas near sources such as motor-vehicle traffic also have higher air concentrations of PAHs. For individuals who smoke, mainstream tobacco smoke is a major source of exposure to PAHs. Concentrations of total PAHs in mainstream smoke ranged from 1 to 1.6 μg/cigarette. Sidestream smoke is a major source of PAHs in indoor air. Concentrations of benzo[*a*]pyrene in sidestream smoke ranged from 52 to 95 ng/cigarette — more than three times the concentration in mainstream smoke.

PAHs in water may originate from surface runoff (e.g., from the erosion of asphalt pavement or from air deposition of smaller particles) (IPCS 1998). Industrial effluents also can contribute to PAH concentrations in surface waters. However, concentrations of PAHs in water usually are very low, because of their low solubility. Surface-water concentrations typically do not exceed 50 ng/L; higher concentrations are found in more contaminated areas. PAH concentrations are higher in rainwater than in surface waters (100 to 200 ng/L, with some samples exceeding 1,000 ng/L). Because PAHs have very high octanol-water partition coefficients (log K_{ow}), they bind tightly to soil particles and are relatively immobile in soil; therefore, concentrations in groundwater and drinking water typically are very low (0.02 to 1.8 ng/L), and concentrations of PAHs in sediment may be very high, ranging up to several thousand micrograms per kilogram.

Estimates of daily PAH intake from food vary widely, ranging from a few nanograms to a few micrograms per person. Sources of PAHs in the diet include barbecued, grilled, broiled, and smoke-cured meats; roasted, baked, and fried foods (prepared by high-temperature processing); breads, cereals, and grains (at least in part from gas or flame drying of grains); and vegetables grown in contaminated soil or with surface contamination from atmospheric deposition of PAHs (IARC 1983, IPCS 1998, JECFA 2005). The Joint United Nations Food and Agriculture Organization–World Health Organization Expert Committee on Food Additives and Contaminants determined a representative mean daily human intake of benzo[*a*]pyrene to be 4 ng/kg of body weight and a high-end daily human intake of total PAHs to be 10 ng/kg (JECFA 2005). Among common foods, the highest PAH levels were found in grilled or barbecued steak, chicken with skin and bones, and hamburgers, especially when "well done" or "very well done" (Larsson *et al.* 1983, Lijinsky 1991, Lodovici *et al.* 1995, Kazerouni *et al.* 2001). Because PAHs form on or near the surface of meat, rather than in the interior, foods that are cooked to the same degree without being exposed to flames do not show significant levels of PAHs. However, a study of PAHs in the Italian diet indicated a total PAH concentration of about 4 ng/g in fried beef (Lodovici *et al.* 1995) and benzo[*a*]pyrene concentrations of up to about 4 ng/g in well-done grilled meat. PAHs are also introduced by certain methods of preserving meat and other food products (Lijinsky 1991). In foods smoked in traditional smoking kilns, the average concentration was 1.2 μg/kg for benzo[*a*]pyrene and 9 μg/kg for total PAHs, compared with 0.1 μg/kg for benzo[*a*]pyrene and 4.5 μg/kg for total PAHs in foods treated in a modern kiln (Guillen 1994).

Accumulation of PAHs in foods of animal origin, especially livestock, is due mainly to the consumption of contaminated feed (Ramesh *et al.* 2004). Unprocessed foods such as vegetables, fruits, vegetable oils, dairy products, and seafood can be contaminated with PAHs by deposition of particles and vapors from the atmosphere and uptake from soil, water, and sediment (Roth *et al.* 1998, Ramesh *et al.* 2004). PAH levels are low in cereals and beans, but drying techniques used for preservation, such as combustion gas heating and smoking, increase concentrations of PAHs in these foods. Eggs and dairy products such as cheese, milk, and butter contain low levels of PAHs. Consumption of seafood, especially bottom-feeding shellfish and finfish, may contribute considerably to the amount of PAHs in the diet. Species near the top of the food chain, such as humans, do not bioaccumulate PAHs, because of their higher capacity to metabolize PAHs (Ramesh *et al.* 2004).

A specific urinary metabolite of pyrene, 1-hydroxypyrene, has been suggested as a biomarker of human exposure to PAHs (Jongeneelen *et al.* 1985, Jongeneelen 2001). In representative samples from the general population, 1-hydroxypyrene has been detected in the urine of nearly all individuals, at median concentrations typically less than 0.1 µmol/mol of creatinine (Huang *et al.* 2004). The National Health and Nutrition Examination Survey analysis of 2,312 urine samples collected from the U.S. general population in 1999 to 2000 found a geometric mean concentration of 1-hydroxypyrene of 0.039 µmol/mol of creatinine (95% CI = 0.034 to 0.046 µmol/mol). The level for adult smokers was three times that for nonsmokers (geometric mean = 0.080 vs. 0.025 µmol/mol). These data are comparable with other data on non-occupationally exposed populations in Europe and Canada.

Occupational exposure to PAHs is primarily through inhalation and dermal contact. Industrial processes that involve the pyrolysis or combustion of coal and the production and use of coal-derived products, including coal tar and coal-tar-derived products, are major sources of occupational exposure to PAHs. Workers in coal-tar production plants, coking plants, bitumen and asphalt production plants, coal-gasification sites, smoke houses, aluminum-production plants, coal-tarring facilities, and municipal trash incinerators are exposed to PAHs. Exposure may also result from inhaling engine exhaust and using products that contain PAHs in a variety of other industries, such as mining, oil refining, metalworking, chemical production, transportation, and the electrical industry (Vanrooij *et al.* 1992). Studies in Germany measured concentrations of PAHs in the breathing zone of chimney sweeps during so-called "black work"; the PAHs in the air samples varied depending on the type of fuel burned (oil, oil/solid, or solid) (Knecht *et al.* 1989). Specific occupational exposure to coal tar, coal-tar pitch, creosote, mineral oils, and coke that contain various PAHs is described in the profiles for these substances (see Coal Tars and Coal-Tar Pitches, Coke Oven Emissions, and Mineral Oils). Concentrations of PAHs in coal-tar products may range from less than 1% to 70% or more (ATSDR 2002). Occupational exposure can lead to PAH body burdens among exposed workers that are considerably higher than those in the general population. There is growing awareness that uptake of PAHs through the skin is substantial (Jongeneelen 2001). Dermal uptake has been shown to contribute to the internal exposure of workers to PAHs; a study in the creosote industry found that the total internal dose of PAHs did not necessarily correlate with inhalation-exposure levels alone, and that dermal exposure contributed significantly (Vanrooij *et al.* 1992).

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

Mobile Source Air Toxics: Polycyclic organic matter is listed as a mobile source air toxic for which regulations are to be developed.

Registration of Fuels and Fuel Additives: Registration requirements for manufacturers of designated fuels or fuel additives include a characterization of emission products, including benzo[*a*]anthracene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*a*]pyrene, dibenzo[*a,h*]anthracene, and indeno[1,2,3-*c,d*]pyrene, generated by evaporation and by combustion of the fuel or additive/base fuel mixture in a motor vehicle.

National Emission Standards for Hazardous Air Pollutants: Polycyclic organic matter is listed as a hazardous air pollutant.

Urban Air Toxics Strategy: Polycyclic organic matter is identified as one of 33 hazardous air pollutants that present the greatest threat to public health in urban areas.

Clean Water Act

Effluent Guidelines: Polynuclear aromatic hydrocarbons are listed as toxic pollutants.

Water Quality Criteria: Based on fish or shellfish and water consumption = 0.012 µg/L for benzo[*k*]fluoranthene, 0.0012 µg/L for benz[*a*]anthracene, benzo[*b*]fluoranthene, and indeno[1,2,3,-*cd*]pyrene, and 0.00012 µg/L for benzo[*a*]pyrene and dibenzo[*a,h*]anthracene; based on fish or shellfish consumption only = 0.013 µg/L for benzo[*k*]fluoranthene, 0.0013 µg/L for benz[*a*]anthracene, benzo[*b*]fluoranthene, and indeno[1,2,3-*cd*]pyrene, and 0.00013 µg/L for benzo[*a*]pyrene and dibenzo[*a,h*]anthracene.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = ranges from 1 lb to 5,000 lb for the various PAHs.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: All 15 PAHs are listed substances subject to reporting requirements.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of specific PAHs = U018, U022, U063, U064, U137.

Numerous specific PAHs are listed as hazardous constituents of waste.

Safe Drinking Water Act

Maximum contaminant level = 0.0002 mg/L for benzo[*a*]pyrene.

Food and Drug Administration (FDA, an HHS agency)

Maximum permissible level in bottled water = 0.0002 mg/L for benzo[*a*]pyrene.

Limits on PAH levels in various color additives are prescribed in 21 CFR 74 and 178.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = exposure by all routes should be as low as possible for benz[*a*]anthracene, benzo[*b*]fluoranthene, and benzo[*a*]pyrene.

References

Anderson LM, Priest LJ, Deschner EE, Budinger JM. 1983. Carcinogenic effects of intracolonic benzo[*a*]pyrene in beta-naphthoflavone-induced mice. *Cancer Lett* 20(2): 117-123.

Anderson LM, Ruskie S, Carter J, Pittinger S, Kovatch RM, Riggs CW. 1995. Fetal mouse susceptibility to transplacental carcinogenesis: differential influence of Ah receptor phenotype on effects of 3-methylcholanthrene, 12-dimethylbenz[*a*]anthracene, and benzo[*a*]pyrene. *Pharmacogenetics* 5(6): 364-372.

Andervont HB, Shimkin MB. 1940. Biological testing of carcinogens. II. Pulmonary-tumor-induction technique. *J Natl Cancer Inst* 1: 225-239.

ATSDR. 2002. *Toxicological Profile for Wood Creosote, Coal Tar Creosote, Coal Tar, Coal Tar Pitch, and Coal Tar Pitch Volatiles*. Agency for Toxic Substances and Disease Registry. http://www.atsdr.cdc.gov/toxprofiles/tp85.pdf.

Bahna L, Podany V, Benesova M, Godal A, Dufour M, Jacquignon P, Vachalkova A. 1979. Carcinogenicity and polarographic-behavior of dibenzo[*a,h*]-pyrene,4,11-diazadibenzo[*a,h*]pyrene and 7,14-diazadibenzo[*a,h*]-pyrene. *Neoplasma* 26(1): 23-28.

Black JJ, Maccubbin AE, Johnston CJ. 1988. Carcinogenicity of benzo[*a*]pyrene in rainbow-trout resulting from embryo microinjection. *Aquat Toxicol* 13(4): 297-308.

Buening MK, Levin W, Wood AW, Chang RL, Yagi H, Karle JM, Jerina DM, Conney AH. 1979. Tumorigenicity of the dihydrodiols of dibenzo[*a,h*]anthracene on mouse skin and in newborn mice. *Cancer Res* 39(4): 1310-1314.

Buters JTM, Mahadevan B, Quintanilla-Martinez L, Gonzalez FJ, Greim H, Baird WM, Luch A. 2002. Cytochrome p450 1B1 determines susceptibility to dibenzo[*a,l*]pyrene-induced tumor formation. *Chem Res Toxicol* 15(9): 1127-1135.

Cavalieri E, Rogan E, Sinha D. 1988. Carcinogenicity of aromatic hydrocarbons directly applied to rat mammary gland. *J Cancer Res Clin Oncol* 114(1): 3-9.

Cavalieri EL, Rogan EG, Higginbotham S, Cremonesi P, Salmasi S. 1989. Tumor-initiating activity in mouse skin and carcinogenicity in rat mammary-gland of dibenzo[*a*]pyrenes—the very potent environmental carcinogen dibenzo[*a,l*]pyrene. *J Cancer Res Clin Oncol* 115(1): 67-72.

Cavalieri EL, Higginbotham S, Ramakrishna NVS, Devanesan PD, Todorovic R, Rogan EG, Salmasi S. 1991. Comparative dose-response tumorigenicity studies of dibenzo[*a,l*]pyrene versus 7,12-dimethylbenz[*a*]-anthracene, benzo[*a*]pyrene and 2 dibenzo[*a,l*]pyrene dihydrodiols in mouse skin and rat mammary-gland. *Carcinogenesis* 12(10): 1939-1944.

Chang RL, Levin W, Wood AW, Lehr RE, Kumar S, Yagi H, Jerina DM, Conney AH. 1982. Tumorigenicity of bay-region diol-epoxides and other benzo-ring derivatives of dibenzo[*a,h*]pyrene and dibenzo[*a,i*]pyrene on mouse skin and in newborn mice. *Cancer Res* 42(1): 25-29.

ChemIDplus. 2009. *ChemIDplus Advanced*. National Library of Medicine. http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp and select Registry Number and search on CAS number. Last accessed: 10/7/09.

Culp SJ, Gaylor DW, Sheldon WG, Goldstein LS, Beland FA. 1998. A comparison of the tumors induced by coal tar and benzo[*a*]pyrene in a 2-year bioassay. *Carcinogenesis* 19(1): 117-124.

De Vries A, van Oostrom CT, Dortant PM, Beems RB, van Kreijl CF, Capel PJ, van Steeg H. 1997. Spontaneous liver tumors and benzo[*a*]pyrene-induced lymphomas in *XPA*-deficient mice. *Mol Carcinog* 19(1): 46-53.

Deutsch-Wenzel RP, Brune H, Grimmer G, Dettbarn G, Misfeld J. 1983. Experimental studies in rat lungs on the carcinogenicity and dose-response relationships of eight frequently occurring environmental polycyclic aromatic hydrocarbons. *J Natl Cancer Inst* 71(3): 539-544.

El-Bayoumy K, Shiue GH, Amin S, Hecht SS. 1989. The effects of bay-region methyl substitution on 6-nitrochrysene mutagenicity in *Salmonella typhimurium* and tumorigenicity in newborn mice. *Carcinogenesis* 10(9): 1685-1689.

EPA. 2016. *Chemical Data Reporting Summary: Benzo*[a]*pyrene, Indeno[1,2,3-*cd*]pyrene, Benzo*[a]*anthracene, Benzo*[b]*fluoranthene, Benzo*[j]*fluoranthene, Benzo*[k]*fluoranthene, Dibenz*[a,h]*acridine, Dibenz*[a,j]*acridine, Dibenz*[a,h]*anthracene, 7H-Dibenzo*[c,g]*carbazole, Dibenzo*[a,e]*pyrene, Dibenzo*[a,h]*pyrene, Dibenzo*[a,i]*pyrene, Dibenzo*[a,l]*pyrene, 5-Methylchrysene.* U.S. Environmental Protection Agency. https://chemview.epa.gov/chemview and search on CAS number or substance name and select Manufacturing, Processing, Use, and Release Data Maintained by EPA and select Chemical Data Reporting Details.

Fu PP, Von Tungeln LS, Chiu LH, Zhan DJ, Deck J, Bucci T, Wang JC. 1998. Structure, tumorigenicity, microsomal metabolism, and DNA binding of 7-nitrodibenz[*a,h*]anthracene. *Chem Res Toxicol* 11(8): 937-945.

Goldstein LS, Weyand EH, Safe S, Steinberg M, Culp SJ, Gaylor DW, Beland FA, Rodriguez LV. 1998. Tumors and DNA adducts in mice exposed to benzo[*a*]pyrene and coal tars: implications for risk assessment. *Environ Health Perspect* 106: 1325-1330.

Gray DL, Warshawsky D, Xue WL, Nines R, Wang Y, Yao RS, Stoner GD. 2001. The effects of a binary mixture of benzo[*a*]pyrene and 7*H*-dibenzo[*c,g*]carbazole on lung tumors and K-*ras* oncogene mutations in strain A/J mice. *Exp Lung Res* 27(3): 245-253.

Guillen MD. 1994. Polycyclic aromatic compounds: extraction and determination in food. *Food Addit Contam* 11(6): 669-684.

Hawkins WE, Walker WW, Overstreet RM, Lytle TF, Lytle JS. 1988. Dose-related carcinogenic effects of water-borne benzo[*a*]pyrene on livers of 2 small fish species. *Ecotoxicol Environ Saf* 16(3): 219-231.

Hecht SS, Radok L, Amin S, Huie K, Melikian AA, Hoffmann D, Pataki J, Harvey RG. 1985. Tumorigenicity of 5-methylchrysene dihydrodiols and dihydrodiol epoxides in newborn mice and on mouse skin. *Cancer Res* 45(4): 1449-1452.

Hendricks JD, Meyers TR, Shelton DW, Casteel JL, Bailey GS. 1985. Hepatocarcinogenicity of benzo[*a*]pyrene to rainbow-trout by dietary exposure and intraperitoneal injection. *J Natl Cancer Inst* 74(4): 839-851.

Hirao F, Nishikawa H, Yoshimoto T, Sakatani M, Namba M, Ogura T, Yamamura Y. 1980. Production of lung-cancer and amyloidosis in rabbits by intrabronchial instillation of benzo[*a*]pyrene. *Gann* 71(2): 197-205.

Horie A, Hohchi S, Kuratsune M. 1965. Carcinogenesis in the esophagus. II. Experimental production of esophageal cancer by administration of ethanolic solution of carcinogens. *Gann* 56(5): 429-441.

HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB and search on CAS number. Last accessed: 10/7/09.

Huang WL, Grainger J, Patterson DG, Turner WE, Caudill SP, Needham LL, Pirkle JL, Sampson EJ. 2004. Comparison of 1-hydroxypyrene exposure in the US population with that in occupational exposure studies. *Int Arch Occup Environ Health* 77(7): 491-498.

IARC. 1973. *Some Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds.* IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 3. Lyon, France: International Agency for Research on Cancer. 271 pp.

IARC. 1983. *Polynuclear Aromatic Compounds, Part 1. Chemical, Environmental and Experimental Data*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 32. Lyon, France: International Agency for Research on Cancer. 477 pp.

IARC. 1985. *Polynuclear Aromatic Compounds, Part 4: Bitumens, Coal-tars and Derived Products, Shale-oils and Soots.* IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 35. Lyon, France: International Agency for Research on Cancer. 271 pp.

IARC. 2010. *Some Non-heterocyclic Polycyclic Aromatic Hydrocarbons and Some Related Exposures.* IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 92. Lyon, France: International Agency for Research on Cancer. 853 pp.

IPCS. 1998. *Environmental Health Criteria No. 202. Selected Non-Heterocyclic Polycyclic Aromatic Hydrocarbons*. International Programme on Chemical Safety. http://www.inchem.org/documents/ehc/ehc/ehc202.htm.

JECFA. 2005. Polycyclic aromatic hydrocarbons. In *Evaluation of Certain Food Contaminants.* 64th Report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization. http://whqlibdoc.who.int/trs/WHO_TRS_930_eng.pdf. pp. 61-79.

Jongeneelen FJ, Leijdekkers CM, Bos RP, Theuws JLG, Henderson PT. 1985. Excretion of 3-hydroxy-benzo[*a*]pyrene and mutagenicity in rat urine after exposure to benzo[*a*]pyrene. *J Appl Toxicol* 5(5): 277-282.

Jongeneelen FJ. 2001. Benchmark guideline for urinary 1-hydroxypyrene as biomarker of occupational exposure to polycyclic aromatic hydrocarbons. *Ann Occup Hyg* 45(1): 3-13.

Kazerouni N, Sinha R, Hsu CH, Greenberg A, Rothman N. 2001. Analysis of 200 food items for benzo[*a*]pyrene and estimation of its intake in an epidemiologic study. *Food Chem Toxicol* 39(5): 423-436.

Kim SH, Lee CS. 1996. Induction of benign and malignant pulmonary tumours in mice with benzo[*a*]pyrene. *Anticancer Res* 16(1): 465-470.

Knecht U, Bolm-Audorff U, Woitowitz HJ. 1989. Atmospheric concentrations of polycyclic aromatic hydrocarbons during chimney sweeping. *Br J Ind Med* 46(7): 479-482.

Kroese ED, Dortant PM, van Steeg H, van Oostrom CTM, van der Houven, van Oordt CW, *et al.* 1997. Use of Eμ-*PIM*-1 transgenic mice for short-term *in vivo* carcinogenicity testing: lymphoma induction by benz[*a*]pyrene, but not by TPA. *Carcinogenesis* 18: 975-980.

Larsson BK, Sahlberg GP, Eriksson AT, Busk LA. 1983. Polycyclic aromatic hydrocarbons in grilled food. *J Agric Food Chem* 31(4): 867-873.

Lavoie EJ, Braley J, Rice JE, Rivenson A. 1987. Tumorigenic activity of non-alternant polynuclear aromatic hydrocarbons in newborn mice. *Cancer Lett* 34(1): 15-20.

Lavoie EJ, He ZM, Wu Y, Meschter CL, Weyand EH. 1994. Tumorigenic activity of the 4,5- and 9,10-dihydrodiols of benzo[*j*]fluoranthene and their *syn*- and *anti*-diol epoxides in newborn mice. *Cancer Res* 54(4): 962-968.

Levin W, Chang RL, Wood AW, Yagi H, Thakker DR, Jerina DM, Conney AH. 1984. High stereoselectivity among the optical isomers of the diastereomeric bay-region diol-epoxides of benz[*a*]anthracene in the expression of tumorigenic activity in murine tumor models. *Cancer Res* 44(3): 929-933.

Lijinsky W. 1991. The formation and occurrence of polynuclear aromatic-hydrocarbons associated with food. *Mutat Res* 259(3-4): 251-261.

Lodovici M, Dolara P, Casalini C, Ciappellano S, Testolin G. 1995. Polycyclic aromatic hydrocarbon contamination in the Italian diet. *Food Addit Contam* 12(5): 703-713.

Mitchell KR, Warshawsky D. 1999. Frequent Ha-*ras* mutations in murine skin and liver tumors induced by 7*H*-dibenzo[*c,g*]carbazole. *Mol Carcinog* 25(2): 107-112.

Naslund I, Rubio CA, Auer GU. 1987. Nuclear DNA changes during pathogenesis of squamous carcinoma of the cervix in 3,4-benzopyrene-treated mice. *Anal Quant Cytol Histol* 9(5): 411-418.

Nesnow S, Ross JA, Stoner GD, Mass MJ. 1996. Tumorigenesis of carcinogenic environmental polycyclic aromatic hydrocarbons in strain A/J mice: linkage to DNA adducts and mutations in oncogenes. *Polycycl Aromat Compd* 10(1-4): 259-266.

Nesnow S, Mass MJ, Ross JA, Galati AJ, Lambert GR, Gennings C, Carter WH, Stoner GD. 1998. Lung tumorigenic interactions in strain A/J mice of five environmental polycyclic aromatic hydrocarbons. *Environ Health Perspect* 106: 1337-1346.

NIOSH. 1977. *Criteria for a Recommended Standard: Occupational Exposure to Coal Tar Products*. National Institute for Occupational Safety and Health. http://www.cdc.gov/niosh/78-107.html.

Platt KL, Dienes HP, Tommasone M, Luch A. 2004. Tumor formation in the neonatal mouse bioassay indicates that the potent carcinogen dibenzo[*def,p*]chrysene (dibenzo[*a,l*]pyrene) is activated *in vivo* via its *trans*-11,12-dihydrodiol. *Chem Biol Interact* 148(1-2): 27-36.

Pott F, Mohr U, Brockhaus A. 1978. [Studies on the combined effects of benzopyrene and dibenz[*a*]-anthracene with SO_2 and NO_2 inhalation on the golden hamster.] [In German]. In *[Air Hygiene and Silicosis Research],* Rothe H, ed. Essen, Germany: Girardet. pp. 225–226 (as cited in IARC 2010).

Prahalad AK, Ross JA, Nelson GB, Roop BC, King LC, Nesnow S, Mass MJ. 1997. Dibenzo[*a,l*]pyrene-induced DNA adduction, tumorigenicity, and Ki-*ras* oncogene mutations in strain A/J mouse lung. *Carcinogenesis* 18(10): 1955-1963.

Ramesh A, Walker SA, Hood DB, Guillen MD, Schneider K, Weyand EH. 2004. Bioavailability and risk assessment of orally ingested polycyclic aromatic hydrocarbons. *Int J Toxicol* 23(5): 301-333.

Reddy AP, Harttig U, Barth MC, Baird WM, Schimerlik M, Hendricks JD, Bailey GS. 1999a. Inhibition of dibenzo[*a,l*]pyrene-induced multi-organ carcinogenesis by dietary chlorophyllin in rainbow trout. *Carcinogenesis* 20(10): 1919-1926.

Reddy AP, Spitsbergen JM, Mathews C, Hendricks JD, Bailey GS. 1999b. Experimental hepatic tumorigenicity by environmental hydrocarbon dibenzo[*a,l*]pyrene. *J Environ Pathol Toxicol Oncol* 18(4): 261-269.

Rodriguez LV, Dunsford HA, Steinberg M, Chaloupka KK, Zhu LJ, Safe S, Womack JE, Goldstein LS. 1997. Carcinogenicity of benzo[*a*]pyrene and manufactured gas plant residues in infant mice. *Carcinogenesis* 18(1): 127-135.

Roller M, Kamino K, Rosenbruch M. 1992. Carcinogenicity testing of bladder carcinogens and other organic compounds by the intraperitoneal and intravesical route. In *Environmental Hygiene III*. Seemayer N, Hadnagy W, eds. Berlin: Springer-Verlag. pp. 95-98.

Ross JA, Nelson GB, Wilson KH, Rabinowitz JR, Galati A, Stoner GD, Nesnow S, Mass MJ. 1995. Adenomas induced by polycyclic aromatic-hydrocarbons in strain A/J mouse lung correlate with time-integrated DNA adduct levels. *Cancer Res* 55(5): 1039-1044.

Rossi L, Barbieri O, Sanguineti M, Staccione A, Santi LF, Santi L. 1983. Carcinogenic activity of benzo[*a*]-pyrene and some of its synthetic derivatives by direct injection into the mouse fetus. *Carcinogenesis* 4(2): 153-156.

Roth MJ, Strickland KL, Wang GQ, Rothman N, Greenberg A, Dawsey SM. 1998. High levels of carcinogenic polycyclic aromatic hydrocarbons present within food from Linxian, China may contribute to that region's high incidence of oesophageal cancer. *Eur J Cancer* 34(5): 757-758.

Schwartz J, Baker V, Larios E, Desai D, Amin S. 2004. Inhibition of experimental tobacco carcinogen induced head and neck carcinogenesis. *Oral Oncol* 40(6): 611-623.

Sellakumar A, Shubik P. 1974. Carcinogenicity of different polycyclic hydrocarbons in the respiratory tract of hamsters. *J Natl Cancer Inst* 53(6): 1713-1719.

Solt DB, Polverini PJ, Calderon L. 1987. Carcinogenic response of hamster buccal pouch epithelium to 4 polycyclic aromatic hydrocarbons. *J Oral Pathol* 16(6): 294-302.

Stenbäck F, Sellakumar. 1974. Lung tumor induction by dibenz[*a,i*]pyrene in Syrian golden-hamster. *Zeitschrift für Krebsforschung und Klinische Onkologie* 82(3): 175-182.

Taras-Valero D, Perin-Roussel O, Plessis MJ, Zajdela F, Perin F. 2000. Tissue-specific activities of methylated dibenzo[*c,g*]carbazoles in mice: carcinogenicity, DNA adduct formation, and CYP1A induction in liver and skin. *Environ Mol Mutagen* 35(2): 139-149.

Thyssen J, Althoff J, Kimmerle G, Mohr U. 1981. Inhalation studies with benzo[*a*]pyrene in Syrian golden-hamsters. *J Natl Cancer Inst* 66(3): 575-577.

Toth B. 1980. Tumorigenesis by benzo[*a*]pyrene administered intracolonically. *Oncology* 37(2): 77-82.

TRI. 2010. *TRI Explorer Chemical Report.* U.S. Environmental Protection Agency. http://www.epa.gov/triexplorer and select Polycyclic Aromatic Compounds. Last accessed: 3/25/10.

Vanrooij JG, Bodelier-Bade MM, De Looff AJ, Dijkmans AP, Jongeneelen FJ. 1992. Dermal exposure to polycyclic aromatic hydrocarbons among primary aluminium workers. *Med Lav* 83(5): 519-529.

Viau C, Vyskocil A. 1995. Patterns of 1-hydroxypyrene excretion in volunteers exposed to pyrene by the dermal route. *Sci Total Environ* 163: 187-190.

Von Tungeln LS, Xia QS, Fu PP. 1999. Benz[*a*]anthracene is a potent liver tumorigen in the neonatal B6C3F$_1$ mouse. *Polycycl Aromat Compd* 16(1-4): 245-254.

Warshawsky D, Barkley W, Miller ML, Ladow K, Andringa A. 1994. Carcinogenicity of 7*H*-dibenzo[*c,g*]-carbazole, dibenz[*a,j*]acridine and benzo[*a*]pyrene in mouse skin and liver following topical application. *Toxicology* 93(2-3): 135-149.

Warshawsky D, Talaska G, Jaeger M, Collins T, Galati A, You L, Stoner G. 1996. Carcinogenicity, DNA adduct formation and K-*ras* activation by 7*H*-dibenzo[*c,g*]carbazole in strain A/J mouse lung. *Carcinogenesis* 17(4): 865-871.

Wenzel-Hartung R, Brune H, Grimmer G, Germann P, Timm J, Wosniok W. 1990. Evaluation of the carcinogenic potency of 4 environmental polycyclic aromatic-compounds following intrapulmonary application in rats. *Exp Pathol* 40(4): 221-227.

Weyand EH, Chen YC, Wu Y, Koganti A, Dunsford HA, Rodriguez LV. 1995. Differences in the tumorigenic activity of a pure hydrocarbon and a complex mixture following ingestion: benzo[*a*]pyrene vs manufactured-gas plant residue. *Chem Res Toxicol* 8(7): 949-954.

Wislocki PG, Bagan ES, Lu AYH, Dooley KL, Fu PP, Hanhsu H, Beland FA, Kadlubar FF. 1986. Tumorigenicity of nitrated derivatives of pyrene, benz[*a*]anthracene, chrysene and benzo[*a*]pyrene in the newborn mouse assay. *Carcinogenesis* 7(8): 1317-1322.

Yu Z, Loehr CV, Fischer KA, Louderback MA, Krueger SK, Dashwood RH, *et al.* 2006. *In utero* exposure of mice to dibenzo[*a,l*]pyrene produces lymphoma in the offspring: role of the aryl hydrocarbon receptor. *Cancer Res* 66(2): 755-762.