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Polynuclear aromatic hydrocarbons in Drinking-water

Background document for development of
WHO *Guidelines for Drinking-water Quality*

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Preface

One of the primary goals of WHO and its member states is that "all people, whatever their stage of development and their social and economic conditions, have the right to have access to an adequate supply of safe drinking water." A major WHO function to achieve such goals is the responsibility "to propose ... regulations, and to make recommendations with respect to international health matters ...."

The first WHO document dealing specifically with public drinking-water quality was published in 1958 as International Standards for Drinking-Water. It was subsequently revised in 1963 and in 1971 under the same title. In 1984–1985, the first edition of the WHO Guidelines for drinking-water quality (GDWQ) was published in three volumes: Volume 1, Recommendations; Volume 2, Health criteria and other supporting information; and Volume 3, Surveillance and control of community supplies. Second editions of these volumes were published in 1993, 1996 and 1997, respectively. Addenda to Volumes 1 and 2 of the second edition were published in 1998, addressing selected chemicals. An addendum on microbiological aspects reviewing selected microorganisms was published in 2002.

The GDWQ are subject to a rolling revision process. Through this process, microbial, chemical and radiological aspects of drinking-water are subject to periodic review, and documentation related to aspects of protection and control of public drinking-water quality is accordingly prepared/updated.

Since the first edition of the GDWQ, WHO has published information on health criteria and other supporting information to the GDWQ, describing the approaches used in deriving guideline values and presenting critical reviews and evaluations of the effects on human health of the substances or contaminants examined in drinking-water.

For each chemical contaminant or substance considered, a lead institution prepared a health criteria document evaluating the risks for human health from exposure to the particular chemical in drinking-water. Institutions from Canada, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Norway, Poland, Sweden, United Kingdom and United States of America prepared the requested health criteria documents.

Under the responsibility of the coordinators for a group of chemicals considered in the guidelines, the draft health criteria documents were submitted to a number of scientific institutions and selected experts for peer review. Comments were taken into consideration by the coordinators and authors before the documents were submitted for final evaluation by the experts meetings. A "final task force" meeting reviewed the health risk assessments and public and peer review comments and, where appropriate, decided upon guideline values. During preparation of the third edition of the GDWQ, it was decided to include a public review via the world wide web in the process of development of the health criteria documents.

During the preparation of health criteria documents and at experts meetings, careful consideration was given to information available in previous risk assessments carried out by the International Programme on Chemical Safety, in its Environmental Health

Criteria monographs and Concise International Chemical Assessment Documents, the International Agency for Research on Cancer, the joint FAO/WHO Meetings on Pesticide Residues, and the joint FAO/WHO Expert Committee on Food Additives (which evaluates contaminants such as lead, cadmium, nitrate and nitrite in addition to food additives).

Further up-to-date information on the GDWQ and the process of their development is available on the WHO internet site and in the current edition of the GDWQ.

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The work of the following coordinators was crucial in the development of this document and others in the Addendum:

P. Chambon, Health Environment Hygiene Laboratory of Lyon, Lyon, France (inorganic constituents)
U. Lund, Water Quality Institute, Horsholm, Denmark, (organicconstituents)
H. Galal-Gorchev, Urban Environmental Health, World Health Organization, Geneva, Switzerland (pesticides)
E. Ohanian, Environmental Protection Agency, Washington, D.C, USA (disinfectants and disinfection by-products)

The coordinators for the overall administrative and technical aspects of this document were, respectively, J. Kenny and H. Galal-Gorchev, Urban Environmental Health, WHO, Geneva, Switzerland.

Ms Marla Sheffer of Ottawa, Canada, was responsible for the scientific editing of the document.

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GENERAL DESCRIPTION

PAHs are a class of diverse organic compounds containing two or more fused aromatic rings of carbon and hydrogen atoms. They are ubiquitous pollutants formed from the combustion of fossil fuels and are always found as a mixture of individual compounds. Owing to their low solubility and high affinity for particulate matter, PAHs are not usually found in water in notable concentrations. Their presence in surface water or groundwater is an indication of a source of pollution. PAHs are only slowly biodegradable under aerobic conditions and are stable to hydrolysis. The relative concentrations of PAHs in air, water, and food are usually the same, although this can change depending on certain sources of pollution. In drinking-water, the PAHs detected in the highest concentrations are fluoranthene (FA), phenanthrene, pyrene (PY), and anthracene. Of the six PAHs usually measured in water for regulatory purposes, FA is the only PAH that is detected to any significant extent. Some PAHs are known carcinogens, but many of these have not been measured in drinking-water, have not been detected in drinking-water (e.g. dibenzo[*a*,*e*]pyrene, dibenzo[*a*,*h*]pyrene, chrysene), or have been found in relatively low concentrations in drinking-water. BaP, a carcinogen, is the most extensively studied PAH (WHO, 1996).

Chlorinated PAHs may be formed where residual chlorine is present in drinking-water (Shiraishi et al., 1985). Little is known about the toxicity of these compounds compared with that of their parent compounds (Bhatia et al., 1987).

The PAHs discussed in this document were chosen on consideration of their solubility, their presence in surface water and drinking-water from water survey data, and their classification as known or suspected carcinogens.

Identity

Compound	*CAS no.*	*Molecular formula*	*No. of aromatic rings*	*Abbreviation used*
Fluoranthene	206-44-0	$C_{16}H_{10}$	4	FA
Pyrene	129-00-0	$C_{16}H_{10}$	4	PY
Benz[*a*]anthracene	56-55-3	$C_{18}H_{12}$	4	BaA
Benzo[*b*]fluoranthene	205-99-2	$C_{20}H_{12}$	5	BbFA
Benzo[*j*]fluoranthene	205-82-3	$C_{20}H_{12}$	5	BjFA
Benzo[*k*]fluoranthene	207-08-9	$C_{20}H_{12}$	5	BkFA
Benzo[*a*]pyrene	50-32-8	$C_{20}H_{12}$	5	BaP
Dibenz[*a*,*h*]anthracene	53-70-3	$C_{22}H_{14}$	5	DBahA
Benzo[*ghi*]perylene	191-24-2	$C_{22}H_{12}$	6	BghiP
Indeno[1,2,3-*cd*]pyrene	193-39-5	$C_{22}H_{12}$	6	IP

Physicochemical properties *(WHO, 1997)*

At ambient temperatures, PAHs are colourless to yellow solids. The general characteristics common to the class are high melting and boiling points, low vapour pressures, and low water solubilities; the latter tend to decrease with increasing molecular mass. PAHs are highly lipophilic.

PAH	Melting point (°C)	Boiling point (°C)	Vapour pressure at 25°C (kPa)	Water solubility at 25°C (µg/litre)	Henry's law constant at 25°C ($kPa \cdot m^3$/ mol)	n-Octanol–water partition coefficient (log K_{ow})	Organic carbon normalized sorption coefficient (log K_{oc})[c]
FA	108.8	375	1.2×10^{-6}	260	6.5×10^{-4}	5.22	4.0–6.4
PY	150.4	393	6.0×10^{-7}	135	1.1×10^{-3}	5.18	4.0–6.5
BaA	160.7	400	2.8×10^{-8}	14	n.g.[d]	5.61	4.5–7.3
BbFA	168.3	481	6.7×10^{-8}	1.2[b]	5.1×10^{-5}	6.12	n.g.
BjFA	165.4	480	2.0×10^{-9}[a]	2.5[b]	$4.4\times10^{!5}$	6.12[a]	n.g.
BkFA	215.7	480	1.3×10^{-11}	0.76	n.g.	6.84[a]	4.0–7.0
BaP	178.1	496	7.3×10^{-10}	3.8	3.4×10^{-5}	6.50	4.0–8.3
DBahA	266.6	524	1.3×10^{-11}	0.5 (27°C)	7×10^{-6}[a]	6.50	n.g.
BghiP	278.3[a]	545	1.4×10^{-11}	0.26	2.7×10^{-5}	7.10	5.6–6.1
IP	163.6	536	1.3×10^{-11}	62[b]	2.9×10^{-5}	6.58	n.g.

[a] Calculated.
[b] Temperature not given.
[c] Range of measured data for sediments and soils.
[d] Not given.

Major uses

Only a small number of PAHs are produced commercially, including FA and PY, which are used mainly as intermediates in the production of fluorescent dyes (FA) and perinon pigments (PY) (Franck & Stadelhofer, 1987; Griesbaum et al., 1989). In 1993, one of the greatest producers worldwide manufactured <50 t of FA and <500 t of PY (WHO, 1997).

Coal and crude oils contain PAHs in considerable concentrations owing to diagenetic formation in fossil fuels (IARC, 1985, 1989). As a consequence, the compounds are also found in coal and mineral oil products such as coke, bitumen, coal tar (and creosote), heating oils, vehicle fuels, lubricating and cutting oils, and printing colour oils (Grimmer et al., 1981; IARC, 1984; Tetzen, 1989; Menichini et al., 1990).

PAHs in the environment are almost always derived from anthropogenic activities. The largest amount of PAHs enters the environment via the atmosphere from incomplete combustion processes, such as processing of coal and crude oil (e.g. refining, coal gasification, coking), industrial use of coal and mineral oil products (aluminium production, iron and steel production, foundries), heating (power plants and residential heating using wood, coal, and mineral oil), fires (e.g. forest, straw, agriculture, cooking), incineration of refuse, vehicle traffic, tobacco smoking, and volcanic activities (for quantitative data on the release of PAHs in the environment, see WHO, 1997).

Environmental fate

PAHs are emitted mainly into the atmosphere and have been detected long distances from their source (Bjørseth & Sortland, 1983; McVeety & Hites, 1988). Because of their low vapour pressures, compounds with five or more aromatic rings will exist mainly adsorbed to airborne particulate matter, such as fly ash and soot. Those with four or fewer rings will occur both in the vapour phase and adsorbed to particles (Hoff & Chan, 1987; Baker & Eisenreich, 1990).

PAHs reach the hydrosphere mainly by dry and wet deposition and road runoff but additionally from industrial wastes containing PAHs and leaching from creosote-impregnated wood. PAHs are adsorbed strongly to the organic fraction of sediments and soils. Leaching of

PAHs from the soil surface layer to groundwater is assumed to be negligible owing to the adsorption and to biodegradation in the aerobic soil surface layer, although their presence in groundwater has been reported, mainly at contaminated sites. The volatility of the compounds from water phases is low, with half-lives of 500 and 1550 hours for BaA and BaP, respectively (Southworth, 1979).

The compounds are very slowly biodegradable under aerobic conditions in the aqueous compartment. The biodegradation rates decrease drastically with increasing number of aromatic rings. In laboratory experiments with soil samples, the calculated half-lives for the selected compounds vary widely, from about 100 days to a couple of years (Bossert & Bartha, 1986; Coover & Sims, 1987; Park et al., 1990; Wild et al., 1991). PAHs are stable towards hydrolysis.

The most important degradation process for PAHs in air and water is indirect photolysis under the influence of hydroxyl radicals. Under laboratory conditions, the reaction of the compounds with airborne hydroxyl radicals shows maximum half-lives between about 3 and 11 hours (Atkinson, 1987). For pure water, the photodegradation half-lives appear to be in the range of hours (Mill et al., 1981; Mill & Mabey, 1985), whereas the half-lives increase drastically when sediment/water partitioning is taken into account (Zepp & Schlotzhauer, 1979).

Measured bioconcentration factors (BCFs) for the compounds in the aquatic environment vary widely owing to different measurement techniques and are especially high for some algae (BCF = 2398–55 800), crustaceans (BCF = 180–63 000), and molluscs (BCF = 58–8297). Bioconcentration factors in fish appear to be much lower than in these organisms because of rapid biotransformation processes (BCF = 10–4700) (WHO, 1997).

In summary, it can be concluded that sediments and soils are the main sinks for PAHs in the environment and that PAHs with four or more aromatic rings are persistent in the environment (Mackay et al., 1992).

ANALYTICAL METHODS

A preconcentration step for sample enrichment may be necessary for the analysis of PAH levels in uncontaminated aqueous samples. Further, considerable adsorption losses during collection and storage of samples have to be taken into account. Apart from liquid/liquid extraction procedures (e.g. with dichloromethane), various solids have been successfully used for the preconcentration: Tenax-GC, XAD resins, open-pore polyurethane foam (PUF), and bonded-phase silica gel (van Noort & Wondergem, 1985; Basu et al., 1987). Detection is carried out by gas chromatography with a flame ionization or a mass selective detector and by high-performance liquid chromatography with an ultraviolet or a fluorescence detector. The detection limits are between 0.01 and 200 ng/litre (Basu & Saxena, 1978a; Desideri et al., 1984).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

Numerous studies refer to the occurrence of PAHs in the environment. The compounds were detected in all environmental compartments. The concentrations differ widely owing to the widely differing sampling locations and conditions.

In the matrices air, water, and food, the relative concentrations of the selected PAHs appear to be in the order of FA ˜ PY > BghiP ˜ IP > BbFA ˜ BkFA > BaA ˜ BaP > DBahA. Very few data were available for BjFA; its concentration is probably in about the same range as those of BbFA and BkFA.

Air

In the absence of industrial or other point sources of pollution, PAHs in the atmosphere are mainly from residential heating and vehicle traffic. The levels of individual substances vary over several orders of magnitude and are generally in the range between <0.1 and 100 ng/m^3 (WHO, 1997). PAHs are mainly adsorbed to airborne particulate matter.

Water

Apart from highly industrially polluted rivers, the concentrations of individual PAHs in surface and coastal waters are generally =50 ng/litre (WHO, 1997). Concentrations above this level (sometimes into the 10 µg/litre range) indicate contamination by PAHs mainly through industrial point sources and shipyards, atmospheric deposition, and urban runoff. Ships for inland navigation are periodically treated with coal tar to prevent corrosive damage. The leaching/abrasion of this coating is a source of PAHs (Berbee, 1992). In addition, wood preserved with creosote can leach PAHs into the environment, especially into waters where wood is used for bank protection or harbours and in the disposal of creosote-impregnated railway ties (Berbee, 1992; Sandell & Tuominen, 1996).

PAH levels in uncontaminated groundwater are usually in the range of 0–5 ng/litre. Leaching of PAHs from soils into groundwater is negligible, as the compounds tend to adsorb strongly to the soil organic matter (Woidich et al., 1976; Stuermer et al., 1982). Only at heavily contaminated sites do the PAHs reach the groundwater, giving concentrations above 10 µg/litre (Environment Canada, 1994).

Elevated concentrations of PAHs (predominantly FA, BbFA, PY, IP, phenanthrene) were observed in rainwater and especially in snow and fog (WHO, 1997). This is probably a result of the adsorption of the compounds to air particulate matter, which is finely dispersed into the water during wet deposition.

The typical concentration range for the sum of the selected PAHs in drinking-water is from about 1 ng/litre to worst cases of 11 µg/litre (see Table 1 [after the references]). Many individual PAHs are at concentrations below the detection limit. As an example, in 1988–1989, the sum of the six Borneff PAHs was below the detection limit of 5 ng/litre in 88% (5287 of 5975) of drinking-water samples from waterworks in Germany; the concentrations were below 40 ng/litre in 10% (588 samples); and concentrations above 200 ng/litre were detected in 0.08% (5 samples) (Dieter, 1994).

The main source of PAH contamination in drinking-water is usually not the raw water sources but the coating of the drinking-water distribution pipes. At least in the past, coal tar was a common coating material for water pipes, used to give effective protection against corrosion. After the passage of drinking-water through those pipes or after repair work, significantly increased PAH levels have been detected in the water (Vu Duc & Huynh, 1981; Basu et al., 1987; Davi et al., 1994); for example, a concentration of 2.7 µg of Borneff PAHs per litre was detected in one sample of such water (State Chemical Analysis Institute, 1995). Although WHO has called for a cessation of this practice (WHO, 1996), many countries still have a large amount of pipes lined with coal tar coating. If BaP is present at elevated concentrations in drinking-water, this is indicative of the presence of particulate matter (e.g. from the deterioration of the coal tar coating).

Table 1. Concentrations of the selected PAHs in drinking-water (ng/litre)

Location, year [reference]	Source of water	FA[b]	PY	BaA	BbFA[b]	BjFA	BkFA[b]	BaP[b]	DBahA	BghiP[b]	IP[b]
Austria, 1976 [1]	Spring water and well-water	3.5–6.5	1.6–3.5	n.d.–1.9	0.2–0.8		0.2–0.8	0.1–0.7		0.3–0.9	tr–0.7
USA, 1976–1977 [2,3]	Treated water from polluted source	2.4–24				0.2–1.2	0.1–0.7	0.2–1.6		0.4–4.0	0.7–2.2
Norway, 1978–1981 [4,5]	Tap-water	0.58–24	<0.3–15	0.1–5.5	0.05–4.0	0.03–0.14	0.02–0.10	<0.04–2.0	1.2	0.4–1.1	0.4–1.2
Canada, 1987–1990 [6]	Treat-ment plant water	<5–623	40		<5–40		<5–40	<5		<5	<5
Poland, 1984 [7]	Spa water	4–21			4–29		3–48	4–21		9–51	9–57
Switzerland, 1981 [8]	Reser-voir[a]	150–3400			9–14		1–5	tr–2		n.d.	tr
	Tap-water	3.3			0.4–0.6		0.1–0.9	0.1–1		n.d.	tr
Italy, 1991–1993 [9]	Treat-ment plant	<20	<10 max. 30	<10 max. 20	<20		<10	<10	<20	<20	<20
	<20			<20		<10	<10	<20	<20	<20	
	Fountain; new coal tar lining										
England & Wales, 1996 [10]	Tap-water (hard water)	585			20		6	14		12	8
	Tap -water (soft water)	6520			1600		490	914		432	953

n.d. = not detected; tr = traces.
[a] The authors attribute these high levels to the use of coal tar distribution pipes.
[b] PAHs measured for regulation purposes in the EEC (Borneff PAHs).
References:
[1] Woidich et al. (1976) [6] Environment Canada (1994)
[2] Thruston (1978) [7] Babelek & Ciezkowski (1989)
[3] Basu & Saxena (1978b) [8] Vu Duc & Huynh (1981)
[4] Kveseth et al. (1982) [9] Davi et al. (1994)
[5] Berglind (1982) [10] Drinking Water Inspectorate, personal communication (1997)

In Canada, significantly increased levels of PAHs in drinking-water were reported for which the reason is not known (Environment Canada, 1994). Also, the PAH concentrations in spa waters from 10 different spas in the Sudetes region (Poland) are surprisingly high (Babelek & Ciezkowski, 1989). In most of the PAH-contaminated spas, groundwater, presumably polluted, also contributes to the spa water.

In the majority of drinking-water samples taken in England and Wales, PAHs are not detected above the standard (EEC, 1980; CEC, 1995) for PAHs of 0.2 µg/litre. Only 5% of the reported samples fail to meet the standard. In practically every case where the PAH standard has been exceeded, the only PAH detected to any significant extent is FA. This is indicative of a coal tar pitch lining in good condition where the hard groundwater very slowly dissolves the lining. There are very few cases where other PAHs have been detected in significant

concentrations, and these occur mainly where soft corrosive water is derived from surface water sources. This is probably indicative of physical deterioration of the lining, releasing particulate containing PAHs into the water supply (Drinking Water Inspectorate, personal communication, 1997).

Food

PAHs have been detected in fresh vegetables, fruits, and cereals as a result of the deposition of airborne PAHs, particularly near industrial sources or in areas with high traffic (Tuominen et al., 1988; de Vos et al., 1990; Dennis et al., 1991). PAHs have also been found in mussels, snails, and fish from contaminated waters (Sirota & Uthe, 1981; Rostad & Pereira, 1987; Speer et al., 1990). PAHs are also present at elevated levels in some vegetable oils and margarine (Dennis et al., 1991; Thomson et al., 1996), probably formed during processing. PAHs are also formed during some methods of food preparation, such as char-broiling, grilling, roasting, frying, or baking. The highest levels were detected in smoked and grilled meat and fish samples (up to about 200 µg/kg) (WHO, 1997).

Estimated total exposure and relative contribution of drinking-water

For the general population, the major routes of exposure to PAHs are from inhalation via ambient and indoor air and ingestion via food.

For ambient air, residential heating and vehicle traffic appear to be the main sources of exposure. In the direct vicinity of an emission source, a maximum intake of 1 µg of BaP per day may be reached (WHO, 1987; LAI, 1992). For the other selected compounds, maximum intakes of between 0.004 (DBahA) and 0.06 (BbFA) µg/day were estimated (Chen et al., 1980; Guicherit & Schulting, 1985). For indoor air, an important contribution is from smoking. In this case, the BaP intake may almost reach that for polluted ambient air. Especially in developing countries, the use of open fires for heating and cooking may further increase PAH exposure (Mumford et al., 1987; Raiyani et al., 1993).

The main contributors of PAHs to the total dietary intake appear to be cereals, oils, and fats. The oil and fat group has high individual PAH levels, whereas the cereal group, although never containing high individual PAH concentrations, is a main contributor by weight to total intake in the diet. Smoked meat and fish products, although containing the highest PAH levels, appear to be low to modest contributors, as they are minor components of the usual diet (Larsson, 1982, 1986; Dennis et al., 1983, 1991; Maga, 1986). However, it should be noted that various countries and cultures have very different diets and methods of cooking, which may result in exposure to very different amounts of PAHs.

There are a few studies on daily intake of individual PAHs from food from western Europe (Dennis et al., 1983; Vaessen et al., 1984; de Vos et al., 1990; Pfannhauser, 1991; Turrio-Baldassarri et al., 1996) and Canada (WHO, 1996). The results for the individual PAHs were in the same range. BaP, BghiP, PY, and FA can each reach a maximum daily intake of =10 µg per person; for each of DBahA, IP, BkFA, and BaA, the maximum daily intake is =0.5 µg per person. The maximum/median intake levels for the PAHs selected in this guideline, in µg/day per person, have been estimated to be as follows: FA (4.3/0.6); PY (4.0/0.6); BaA (0.14/0.02); BbFA (1.0/0.005); BjFA (0.9/0.03); BkFA (0.3/0.04); BaP (0.36/0.05); DBahA (0.10/0.015); BghiP (7.6/0.12); and IP (0.31/0.025) (Pfannhauser, 1991).

From the intake data for food and the drinking-water levels (see Table 1 [after the references]), it can be estimated that about 1% of the total dietary intake of PAHs is from drinking-water, assuming a consumption of 2 litres/day. Where there are elevated PAH levels from contamination by coal tar coatings, which would occur mainly during and after repair work, PAH intake from drinking-water could be equal to or even exceed other dietary intakes.

Exposure via the oral and inhalation pathways varies considerably depending on diet and lifestyle, with inhalation exposure being of greater importance where indoor levels of PAHs are high because of smoking (Greenberg, 1996; Ihme & Wichmann, 1996; Jansen et al., 1996).

KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Absorption

PAHs are absorbed in experimental animals and humans through the pulmonary tract, the gastrointestinal tract, and the skin. Absorption of BaP, DBahA, and PY was high (30–90%) following low and high oral doses in rats (Chang, 1943; Foth et al., 1988; Withey et al., 1991). Absorption from the gastrointestinal tract occurs rapidly. Oral administration of FA, PY, and BaA to rats caused peak concentrations of these compounds in the blood after 1–2 hours (Lipniak & Brandys, 1993). The intestinal absorption of the individual PAHs is highly dependent on their solubility, their lipidity, the presence of bile (Rahman et al., 1986), and the lipidity of the various PAH-containing foods ingested. Whereas oils enhanced the absorption of BaP, water and solid food suppressed the absorption (Kawamura et al., 1988).

Distribution

In laboratory animals, PAHs become widely distributed in the body following administration by any one of a variety of routes and are found in almost all internal organs, particularly those rich in lipid (WHO, 1997). Maximum concentrations of BaA in perfused tissues (e.g. liver, blood, brain) were achieved within 1–2 hours after administration of high oral doses (76 and 152 mg/kg of body weight). In lesser perfused tissues (e.g. adipose and mammary tissue), maximum levels of this compound were reached in 3–4 hours (Bartosek et al., 1984). In male Wistar rats receiving a gavage dose of 2–15 mg of [^{14}C]-pyrene per kg of body weight, the fat had the highest levels of radioactivity, followed by the kidney, liver, and lungs (Withey et al., 1991). Orally absorbed DBahA in rats was also widely distributed to several tissues. After continuous oral administration of 0.5 µg of [^{3}H]BaP daily to male rats for up to 7 days, the radioactivity persisted in liver, kidney, lung, and testis (Yamazaki & Kakiuchi, 1989). Orally administered BaP (200 mg/kg of body weight) has been shown to cross the placental barrier and has been detected in fetal tissues (2.77 µg/g) (Shendrikova & Aleksandrov, 1974). Using ^{14}C-tagged BaP, a BaP concentration 1–2 orders of magnitude lower in embryonic than in maternal tissues was determined after oral administration in mice (Neubert & Tapken, 1988). Differences in concentrations in the fetus among the various PAHs appeared to be highly dependent on the gastrointestinal absorption of the compound.

Metabolism

The metabolism of PAHs is complex. Generally, the process involves epoxidation of double bonds, a reaction catalysed by the cytochrome P-450-dependent monooxygenase, the rearrangement or hydration of such epoxides to yield phenols or diols, respectively, and the conjugation of the hydroxylated derivatives. Reaction rates vary widely, and interindividual variations of up to 75-fold have been observed, for example, with human macrophages, mammary epithelial cells, and bronchial explants from different donors. Most metabolism results in detoxification, but some PAHs in some situations become activated to DNA-binding species, principally diol-epoxides, that can initiate tumours (WHO, 1997).

Although the PAHs are similar, they have structural differences that are the basis for differences in metabolism and relative carcinogenicity. The metabolism of the more carcinogenic, alternant (equally distributed electron density) PAHs, such as BaP, BaA, and DBahA, seems to differ in some ways from that of non-alternant (uneven electron density

distribution) PAHs, such as FA, BbFA, BkFA, BjFA, IP, BghiP, and PY (Phillips & Grover, 1994; ATSDR, 1995).

In general, little is known about the metabolism of most PAHs, particularly in non-rodent species. It should be noted that there appear to be species differences in the enzymes that activate PAHs (Michel et al., 1995) and in the formation of DNA adducts (Kulkarni et al., 1986).

Excretion

PAH metabolites and their conjugates are excreted predominantly via the faeces and to a lesser extent in the urine. Conjugates excreted in the bile can be hydrolysed by enzymes of the gut flora and reabsorbed. It can be inferred from available data on total body burdens in humans that PAHs do not persist for long periods in the body and that turnover is rapid. This excludes those PAH moieties that become covalently bound to tissue constituents, in particular to nucleic acids, and are not removed by repair (WHO, 1997). The excretion of urinary metabolites is a method used to assess internal human exposure of PAHs.

EFFECTS ON LABORATORY ANIMALS AND IN VITRO TEST SYSTEMS

The toxicological effects of the PAHs are summarized individually in order of molecular weight, with emphasis on oral studies where available. The toxicology of FA is described in the most detail because this is the PAH found in notable quantities in tap-water where there is contamination by coal tar coatings and because of the uncertain classification of this PAH.

Research on the toxicological effects of PAHs has been focused on the carcinogenicity of some selected compounds, but usually employing dermal, inhalation, or subcutaneous rather than oral exposure. The carcinogenic classification of the various PAHs is given in Table 2. There are only limited studies on non-carcinogenic end-points.

Table 2. Evaluation of individual PAHs for carcinogenicity in animals and humans

PAH	WHO, 1997[a]	IARC, 1987[b]
BaA	positive	2A
BbFA	positive	2B
BjFA	positive	2B
BkFA	positive	2B
BghiP	negative	3
BaP	positive	2A
DBahA	positive	
FA	(positive)[c]	3
IP	positive	
PY	(questionable)	

[a] Based on animal carcinogenicity studies only.
[b] 2A — probably carcinogenic to humans; 2B — possibly carcinogenic to humans; 3 — not classifiable as to human carcinogenicity.
[c] Recent data on FA since this meeting could change the FA rating to questionable.

Fluoranthene (FA)

The oral LD_{50} for FA in the rat is about 2000 mg/kg of body weight (range 1270–3130 mg/kg of body weight) (Smyth et al., 1962).

Male and female CD-1 mice (20 per sex per group; 30 per sex for controls) were given FA by gavage for 13 weeks at 0, 125, 250, or 500 mg/kg of body weight per day and then sacrificed and autopsied (US EPA, 1988). All treated mice exhibited nephropathy, increased salivation, and increased liver enzyme levels in a dose-dependent manner. Mice given 500 mg/kg of body weight per day had increased food consumption and increased body weight. At doses of 250 and 500 mg/kg of body weight per day, statistically increased serum glutamate–pyruvate transaminase (SGPT) levels and increased absolute and relative liver weights were noted, as well as compound-related microscopic liver lesions (indicated by pigmentation) in 65 and 87.5% of the mice, respectively. Based on these increased SGPT levels, kidney and liver pathology, and clinical and haematological changes, the NOAEL is 125 mg/kg of body weight per day [Source: Integrated Risk Information System (IRIS). Online. Cincinnati, OH, US Environmental Protection Agency, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment].

Mutagenicity and related end-points

In vitro genotoxicity studies for FA are mostly positive, but *in vivo* genotoxicity studies are mostly negative (IARC, 1983; US EPA, 1992; ATSDR, 1995; WHO, 1997).

FA tested positive with metabolic activation for gene mutation in *Salmonella typhimurium*, in the *Escherichia coli* SOS chromotest for DNA damage, and in *in vitro* tests in mammalian cells for DNA damage, mutation, and chromosomal effects.

After oral administration of FA at 750 mg/kg of body weight, *in vivo* tests for sister chromatid exchange in mouse bone marrow were negative (Palitti et al., 1986). FA did not show any evidence of genotoxicity in the mouse bone marrow micronucleus or rat liver unscheduled DNA synthesis test systems following acute oral administration at levels of up to 2000 mg/kg of body weight (Stocker et al., 1996).

A major FA–DNA adduct has been identified in most of the tissues examined (including liver, lung, heart, kidney, spleen, and thymus) in Sprague-Dawley rats chronically fed FA in the diet (Gorelick et al., 1989). In BLU:Ha and CD-1 mice treated intraperitoneally with tumorigenic doses of FA (total of 3.5 mg over 2 weeks), highest levels of FA–DNA adduct were found in the lung (Wang et al., 1995a,b).

Dermal carcinogenicity studies

Dermal application of 1% FA 3 times a week for 1 year to the backs of 20 female Swiss-Albino Ha/ICD/Mill mice did not induce skin tumours (Hoffmann et al., 1972), nor did 250 µg of FA applied to 15 male C3H mice for 82 weeks (Horton & Christian, 1974).

Application of 40 µg of FA alone caused no tumours in 50 female Swiss mice treated for 440 days, but FA was a co-carcinogen in a study in which the same dose of FA in combination with BaP induced a 2-fold increase in mouse skin tumours compared with BaP alone (van Duuren & Goldschmidt, 1976).

FA did not exhibit tumour-initiating activity after 24 weeks in 30 female Swiss mice topically administered 10 doses (0.1 mg per animal) followed by promotion with croton oil for 20 weeks (Hoffmann et al., 1972).

Pyrene (PY)

Male and female CD-1 mice (20 per sex per group) given PY by gavage at doses of 0, 75, 125, or 250 mg/kg of body weight per day in corn oil for 13 weeks exhibited kidney effects (renal tubular pathology, decreased kidney weights) (US EPA, 1989). The low dose (75

mg/kg of body weight per day) was considered the NOAEL for nephropathy and decreased kidney weights [Source: Integrated Risk Information System (IRIS). Online. Cincinnati, OH, US Environmental Protection Agency, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment].

Mutagenicity and related studies gave negative or equivocal results. There were no oral carcinogenicity studies. Skin painting assays in mice for complete carcinogenesis or initiating capacity have been negative or inconclusive. Mice injected intraperitoneally did not show significant elevated tumour rates. A ^{32}P-postlabelling test for covalent DNA binding of PY to mouse skin *in vivo* gave negative results. PY was co-carcinogenic with BaP in a mouse skin assay (WHO, 1997).

Benz[a]anthracene (BaA)

Male B6AF1/J newborn mice (40 per group) were administered 1.5 mg of BaA per day by oral gavage twice over 3 days (Klein, 1963). After 568 days of observation, increased incidences of hepatomas and pulmonary adenomas (80% and 85%, respectively) were noted, compared with the controls with solvent only (10% and 30%). No malignant tumours were observed. In a parallel study with the same dose 3 times weekly over 5 weeks with sacrifice at 547–600 days, 100% hepatomas and 95% pulmonary adenomas were noted (controls: 10% and 35%).

C57BL mice receiving a total dose of 0.5, 4, or 8 mg of BaA by gavage showed forestomach papillomas (0/13, 1/10, and 1/8, respectively) after 16 months (Bock & King, 1959).

BaA is genotoxic. It produces tumours in most assays in mice treated dermally, intraperitoneally, and subcutaneously. There are indications of immunotoxicity and fetotoxicity in subcutaneous studies. DNA adducts were detected in mouse skin after dermal application of BaA (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Benzo[b]fluoranthene (BbFA)

BbFA is genotoxic. Exposure of rats to BbFA by lung implantation resulted in tumour formation, as did intraperitoneal exposure of newborn mice. Skin painting and initiation/promotion studies in mice were positive. DNA adducts were detected *in vitro* and *in vivo* (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Benzo[j]fluoranthene (BjFA)

From limited studies, there is evidence that BjFA is genotoxic and carcinogenic. BjFA showed tumorigenic activity in one skin painting assay, in initiation/promotion studies, and in the newborn mouse intraperitoneal bioassay. Exposure of rats by lung implantation did not result in tumour formation. DNA adducts were detected *in vitro* and in mouse skin *in vivo* after topical application of BjFA (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Benzo[k]fluoranthene (BkFA)

From the available evidence, BkFA is genotoxic and carcinogenic. Skin painting assays were not positive, but initiation/promotion studies resulted in increased tumour incidence. No significant tumorigenic activity was found in a lung adenoma bioassay in newborn mice. Lung implantation of BkFA produced tumours in rats. DNA adducts have been detected *in vitro* and *in vivo* (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Benzo[a]pyrene (BaP)

BaP is genotoxic in a variety of *in vitro* tests with metabolic activation and in *in vivo* studies. In mice, oral administration of BaP induces tumours of the forestomach. It induces mammary gland tumours after oral administration in rats. BaP has produced skin tumours after dermal application in mice, rats, rabbits, and guinea-pigs. It produced lung and respiratory tumours when administered intratracheally to rats and hamsters. Lung implantation of BaP in rats caused pulmonary tumours. BaP administered intraperitoneally induced lung and hepatic tumours in mice. It was carcinogenic after subcutaneous administration to mice, rats, hamsters, guinea-pigs, and some primates. BaP binds to DNA and forms DNA adducts in target organs.

BaP was discussed in the 1993 WHO *Guidelines for drinking-water quality* (WHO, 1996). Only the oral studies on BaP and coal tar published since then are given here. It should be noted that further long-term oral studies are in progress.

The tumorigenic activity of BaP (and coal tar; see section 5.3) after ingestion was investigated (Weyand et al., 1995). BaP (16 or 98 mg/kg of feed, equal to 41 and 257 µg/day, respectively) in a basal gel diet was fed to female A/J mice (30 per group) for 260 days. After sacrifice, forestomach tumours and pulmonary adenomas were diagnosed and counted. The incidence of forestomach tumours after oral administration was 20% and 100%, respectively; tumour multiplicity was 0.24 and 4.22. The incidence of forestomach carcinomas in mice with forestomach tumours was 8% and 52%, respectively. Controls ingesting basal gel diet only showed no forestomach tumours. Whereas 16 mg/kg of feed did not induce a significant level of lung tumours (36%; 25 mice; 0.48 tumours per mouse), ingestion of 98 mg/kg of feed induced lung tumours in 52% of the mice (27 mice; 0.59 tumours per mouse). Nineteen per cent of the controls on basal diet showed pulmonary adenomas (21 mice; 0.19 tumours per mouse). It should be noted that A/J mice are susceptible to pulmonary tumours.

In a 2-year carcinogenicity bioassay, female $B6C3F_1$ mice were fed BaP at 0, 5, 25, or 100 mg/kg of feed (see also study with coal tar, section 5.3) (Culp et al., 1996). Forestomach tumours were induced in all groups of mice fed BaP. A 6% incidence was observed at the 5 mg/kg of feed dose (18.5 µg/day), with the incidence increasing sharply to 78% at the 25 mg/kg of feed dose (90 µg/day) and then to 98% at 100 mg/kg of feed (350 µg/day). All of the mice fed BaP at 100 mg/kg of feed were removed by 80 weeks because of morbidity or death. A linear dose–response was observed between BaP dose and adduct levels in the forestomach of mice fed the same doses in a 4-week study.

Dibenz[a,h]anthracene (DBahA)

There are only limited studies on oral exposure to DBahA, but they do provide some evidence for carcinogenicity through this route.

In a lifetime study, mammary carcinomas were observed in 1/20 female and 13/24 pseudo-pregnant BALB/c mice dosed with 0.5% DBahA after 15 weeks of dosing (Biancifiori & Caschera, 1962). No control group was included.

DBA/2 mice (21 per sex) were given DBahA in an aqueous olive oil emulsion (0.8 mg of DBahA per day) for 200 days (Snell & Stewart, 1962). In general, the animals did not tolerate the vehicle well, and extensive dehydration and emaciation led to early death. At the end of the exposure, almost all surviving treated mice (14 males and 13 females), but only one of the control mice, showed pulmonary adenomatosis, alveologenic carcinoma, mammary carcinoma, and haemangioendotheliomas.

DBahA is genotoxic *in vitro* and *in vivo*. It causes tumours in various organs in mice after oral administration and is a potent carcinogen in several species after various routes of administration. It forms DNA adducts in mouse skin *in vitro* and *in vivo* (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Benzo[ghi]perylene (BghiP)

There are insufficient data on the genotoxic potential of BghiP, although the existing evidence is positive. BghiP tested negative for carcinogenicity activity and tumour-initiating activity in mouse skin. It was negative in the rat lung implantation assay. It has shown some co-carcinogenicity with BaP in mouse skin. BghiP binds to DNA *in vitro* and *in vivo* (US EPA, 1992; ATSDR, 1995; WHO, 1996, 1997).

Indeno[1,2,3-cd]pyrene (IP)

The limited data on the genotoxicity of IP are generally positive. IP has tumour-initiating activity in mouse skin and is carcinogenic in rat lungs. It bound to mouse skin with the formation of DNA adducts (US EPA, 1992; ATSDR, 1995; WHO, 1997).

Comparative studies

The following is a summary of the comparative studies on tumorigenic activity of individual PAHs, which have been used as the basis for comparative potency factors (see section 7). Full details and discussion of the adequacy of the databases are given in the original references and elsewhere (Clement Associates, 1988; US EPA, 1992). In general, it can be said that data from the skin painting and lung implantation studies have been used preferentially to those of initiation/promotion experiments and intraperitoneal studies for estimating comparative potencies. There are no comparative studies on oral administration.

Exact comparative data are given only where this is possible (e.g. where single PAHs were tested in the same experiment at the same dose).

Carcinogenicity studies

Dermal

Skin-painting studies

Solutions of 0.5% BaP, BbFA, BjFA, or BkFA were applied dermally 3 times weekly to female Swiss Millerton mice (20 per group) through their lifetime, and the number of skin tumours was determined (Wynder & Hoffmann, 1959b). The percentages of papillomas/carcinomas for these compounds after 4 months were 70/20, 95/10, 40/5, and 0/0, respectively. Minimal activity (10 papillomas) was found with BkFA after 11 months. **BaP > BbFA > BjFA > BkFA**.

In a similar study regime, 0.01% solutions of BaP or DBahA applied dermally to mice (20 per group) showed 10%/10% and 15%/5% papillomas/carcinomas after 6 months. A 0.1% solution of FA and 10% solution of PY showed no activity (Wynder & Hoffmann, 1959a). **BaP = DBahA >> FA; PY.**

A further study compared the carcinogenicity of BaP, BghiP, and IP applied dermally to mice 3 times weekly as above (Hoffmann & Wynder, 1966). A dose of 0.05% of BaP, BghiP, or IP produced 17/20, 0/20, and 0/20 tumour-bearing mice, showing that BaP is more potent than either of the other PAHs. There were no controls. **BaP >> BghiP; IP.**

In a lifetime skin painting assay with female NMRI mice, BaP and BbFA were carcinogenic, BjFA was weakly carcinogenic, and BkFA and IP had no cancer-inducing effects (Habs et al., 1980). **BaP >> BbFA > BjFA > BkFA; IP**.

Initiation/promotion assay

Ten doses of BaP, BghiP, or IP at a total dose of 0.25 mg per mouse were applied every second day to the backs of Swiss Millerton mice followed by promotion with 2.5% croton oil in acetone. Tumour-bearing animals were reported as 24/30, 2/27, and 5/30, respectively (Hoffmann & Wynder, 1966). **BaP >> IP > BghiP.**

In an initiation/promotion assay in CD-1 mice, four PAHs (BaP, BbFA, BjFA, and BkFA) were each applied at a total dose of 30 µg in 10 subdoses over 20 days to the shaved backs of 20 mice per group (LaVoie et al., 1982). Ten days after completion of the initiation, promotion was begun by thrice-weekly application of 12-*O*-tetradecanoylphorbol-13-acetate in 0.1 ml of acetone. The skin tumours were predominantly squamous cell papillomas. After 20 weeks (10 weeks for BaP), the percentage of skin tumour-bearing animals was 85, 45, 30, and 5, respectively. The vehicle controls had no tumours. **BaP > BbFA > BjFA > BkFA.**

Other routes

Intraperitoneal injection in newborn mice

Other routes

Intraperitoneal injection in newborn mice

The tumorigenic activity of the non-alternant PAHs (BbFA, BjFA, BkFA, and IP) as well as BaP was evaluated by injecting intraperitoneally a total of 0.5, 1.1, 2.1, 2.1, or 0.5 µmol of each compound, respectively, in dimethyl sulfoxide in aliquots of 5, 10, or 20 µl on days 1, 8, and 15 of life, respectively, to CD-1 mice (LaVoie et al., 1987). A direct comparison was not possible owing to differences in the total amount injected; however, both BbFA and BjFA exhibited significant tumorigenic activity, whereas neither BkFA nor IP was tumorigenic under these conditions. There were problems with the solubility of IP. **BaP > BbFA = BjFA > BkFA; IP**.

Lung implantation

Deutsch-Wenzel et al. (1983) and Wenzel-Hartung (1990) investigated the carcinogenic effects of PAHs after intrapulmonary injection and assessed the relative potencies with respect to epidermoid carcinomas and pleomorphic sarcomas. A rank order was based on BaP as reference substance: **DBahA (1.91) – BaP (1.00) – BbFA (0.11) – IP (0.08) – BkFA (0.03) – BjFA (0.03)**. BghiP showed no tumour-producing effects.

Subcutaneous injection

Dose–response curves for BaP and DBahA were established following a single subcutaneous injection of the PAHs in tricaprylin into the right axilla of male C3H mice (Bryan & Shimkin, 1943). Ninety-nine per cent of the tumours detected were spindle-cell sarcomas. Vehicle control response levels were not included. Under the conditions in this experiment, the potency of DBahA was estimated to be 4.5 times that of BaP. **DBahA >> BaP.**

In a study with C57 black mice, 8/10 males and 6/10 females had injection-site tumours 60–80 weeks after 10 weekly subcutaneous injections of 1 mg of BaA (Boyland & Sims, 1967). After a dose of 1 mg of DBahA, 20/20 males and 17/20 females had tumours. **DBahA > BaA.**

Further evidence

Sebaceous gland assay

Application of carcinogenic PAHs to mouse skin leads to the destruction of sebaceous glands, hyperplasia, hyperkeratosis, and even ulceration (Bock, 1964). A sebaceous gland assay has been used as a screening method for the tumorigenic potential of PAHs. Acute topical application of BaP, BaA, or DBahA was reported to suppress sebaceous glands (Bock & Mund, 1958). ***BaP = DBahA > BaA.*** *In a further sebaceous gland assay using other PAHs, it was found that, compared with BaP, the activity was* ***BaP > BbFA = BjFA = BkFA = IP*** *(Habs et al., 1980).*

DNA adduct formation

In a ^{32}P-postlabelling test for covalent DNA binding of PAHs to mouse skin in vivo following a single topical application, relative DNA adduct levels were ***BaP > BaA = DBahA = BghiP*** *(Reddy et al., 1984). DNA adducts were not detected with PY. In a similar study, the relative covalent binding of PAHs to DNA was* ***BbFA > BjFA > BkFA > IP*** *(Weyand et al., 1987). In an in vitro study, the relative covalent binding of PAHs to DNA was reported as* ***BaP > DBahA > BaA > PY*** *(Grover & Sims, 1968).*

Summary

The results of these carcinogenicity and other studies, although not always giving the identical order, can be summarized as follows: ***BaP = DBahP > BaA > BbFA > BjFA > BkFA > IP > FA > BghiP > PY.***

FA has been included in very few comparative studies, but the above placing is probably correct (see recent studies in section 5.1.1).

A quantitative evaluation of comparative studies in this section has been attempted by several authors, leading to near agreement on values of relative potencies using BaP as 1 (see Table 3).

Table 3. Relative potencies of PAHs considered in this evaluation

Compound	**Ref. 1**	**Ref. 2**	**Ref. 3**	**Ref. 4**	**Ref. 5**	***Ref. 6***	***Summary*[a]**
Benz[a]anthracene	0.145	0.1	0.1	0.1	0.1	*0.1*	***0.1***
Benzo[a]pyrene	1.0	1.0	1.0	1.0	1.0	*1.0*	***1.0***
Benzo[b]fluoranthene	0.141	0.1	0.1	0.1	0.1	*0.1*	***0.1***
Benzo[ghi]perylene	0.022	0.01	0.01	0.01			
Benzo[j]fluoranthene			0.1			*0.1*	***0.1***
Benzo[k]fluoranthene	0.061	0.1	0.1	0.1	0.01	*0.1*	***0.1***
Dibenz[a,h]anthracene	1.11	5	1.0	1.0	1.0	1.0	**1.0**
Fluoranthene		0.001	0.001	0.001			
Indeno[1,2,3-cd]pyrene	0.232	0.1	0.1	0.1	0.1	0.1	**0.1**
Pyrene	0.81	0.001	0.001	0.001			

[a] *BghiP, FA, and PY are not included owing to their negative or uncertain rating as carcinogens.*

References:

1. Krewski et al. (1989)
2. Nisbet & LaGoy (1992)
3. Malcolm & Dobson (1994)
4. Kalberlah et al. (1995)
5. US EPA (1993)
6. McClure & Schoeny (1995)

Studies with coal tar

Contamination of drinking-water with PAHs occurs mostly from the leaching of these compounds from coal tar coated distribution pipes. Some studies relevant to toxicity resulting from the presence of coal tar in drinking-water are therefore mentioned here, although they are not directly applicable. It should be remembered that the relative amounts of PAHs (and other compounds) in drinking-water depend on their solubility in water (e.g. FA is very soluble), and the chemical profile and concentrations will be different from that of coal tar itself.

Coal tars, also known as manufactured gas plant residue (MGP), are complex mixtures containing over 1000 compounds, of which at least 30 are PAHs. The chemical composition varies with changes in feedstocks and processing temperatures. Coal tars are known skin carcinogens when applied topically to experimental animals, and this carcinogenicity correlates with their high PAH content (Wallcave et al., 1971). There are comparatively few studies on the carcinogenic potential of coal tars after chronic ingestion. Only those studies relevant to oral toxicity are mentioned here.

Mutagenicity and related end-points

Coal tar paints (CTP) used in potable supply systems have been found to be mutagenic in the Ames test with metabolic activation (Robinson et al., 1984; Silvano & Meier, 1984). In a mutagenicity study on water from water distribution pipes before and after the water

treatment process, the mutagenic activity did not correlate with the levels of PAHs in the water (Basu et al., 1987).

Carcinogenicity

CTP was positive in a dermal initiation/promotion assay with SENCAR mice, and one coal tar product was positive when tested as a complete carcinogen in the mouse at 2 µl per dermal application once weekly for 30 weeks (Robinson et al., 1984). The biological responses to the products were greater than expected from their PAH content.

In a further study, a suspension of CTP particulate was administered to groups of 40 female A/J mice by gavage over 8 weeks (Robinson et al., 1987). Total doses of 24, 240, or 1320 mg of CTP particulate resulted in 35%, 97%, and 72% of the mice developing lung tumours (tumour multiplicity: 0.46, 4.27, 4.33). Twenty-nine per cent of the control mice had lung tumours (tumour multiplicity: 0.32). Forestomach tumours were induced only at the highest dose of 1320 mg of CTP particulate. Controls had no forestomach tumours.

Female A/J mice (30 per group) were fed a basal gel diet for 260 days with 0.1% or 0.25% coal tar (MGP; 7 and 16.3 µg of BaP per day, as MGP contained 2.76 mg of BaP per g) (Weyand et al., 1995). Seventy per cent and 100% of the mice developed lung tumours, with a multiplicity of 1.19 and 12.17 tumours per mouse, respectively. Nineteen per cent of the controls had tumours, with a tumour multiplicity of 0.19 tumours per mouse. No forestomach tumours were found. Comparing these results with those reported in the same study with pure BaP (41 and 257 µg/day; see section 5.1.7), MGP produced a considerably higher lung tumour rate than would be expected from its BaP content. In contrast, pure BaP produced forestomach tumours, which was not the case with MGP at the given concentrations.

In a follow-up study using the same dose and administration regimen (i.e. basal gel diet) in female A/J mice for 2 weeks, DNA adducts induced by MGP and BaP in mouse lung and forestomach were characterized (Weyand & Wu, 1995). The major adduct in forestomach was attributable to BaP. Three adducts were detected in mouse lung, two of which could be contributed by BbFA and BaP, respectively, but the major DNA adduct could not be attributed to any of the PAHs identified as constituents of MGP.

In a 2-year carcinogenicity bioassay, female B6C3F$_1$ mice were fed 0, 0.01, 0.03, 0.1, 0.3, 0.6, or 1.0% coal tar containing 2.24 mg of BaP per g (Culp & Beland, 1994; Culp et al., 1996). Forestomach tumours were found in each dose group, with the incidence increasing sharply from 6% in mice fed 0.1% coal tar to 30% at the 0.3% coal tar dose (equivalent to 8.4 µg and 19.1 µg of BaP per day, respectively). The incidence of forestomach tumours was approximately the same at 0.3% and 0.6% coal tar but declined at the 1.0% dose, apparently as a result of mortality from a high incidence of small intestinal adenocarcinomas in mice fed 0.6% or 1.0% coal tar. Lung tumour incidence was not reported. A parallel study with 18.5, 90, or 350 µg of BaP per day resulted in a tumour incidence of 6%, 78%, and 98%, respectively. In BaP-treated mice, one major DNA adduct was observed; this adduct accounted for 7–15% of the forestomach adducts in mice fed coal tar. A dose-related increase was observed in adduct levels in the forestomachs of BaP- and coal tar-fed mice.

From the above study, it can be seen for comparison that the same (6%) forestomach tumour incidence was noted at an oral dose of 18.5 µg of BaP per day and a 0.1% dose of coal tar containing 8.4 µg of BaP per day (i.e. coal tar has more than twice the tumorigenic potency as BaP).

Therefore, it seems that the effects of complex mixtures may be different from those of the PAHs alone. Interaction of PAHs and other compounds in coal tar may cause higher or lower tumour rates than can be expected from their content of known carcinogenic PAHs.

EFFECTS ON HUMANS

Human exposure to PAHs is not to individual compounds but to a mixture of these compounds in either occupational or environmental situations. There are no reports on the effects of oral ingestion by humans of the PAHs selected for evaluation, although people who consume grilled or smoked food do ingest these compounds.

A high lung cancer mortality in Xuan Wei, China, has been linked to PAH exposure from unvented coal combustion (Mumford et al., 1987; Lewtas et al., 1993). PAHs present in tobacco smoke (mainstream and sidestream) are implicated as contributing to lung and other cancers (IARC, 1986; Grimmer et al., 1987, 1988).

Most available human data are from inhalation and percutaneous absorption of PAHs from a large range of occupational exposures. In earlier times, following high dermal exposure, chimney sweeps developed skin cancers, especially scrotal cancer. Epidemiological studies are available for workers exposed at coke ovens in coal coking and coal gasification, in asphalt works, in foundries, in aluminium production plants, and from diesel exhaust (Verma et al., 1992; Armstrong et al., 1994; Partanen & Boffetta, 1994; Costantino et al., 1995). In all these occupations, there is also exposure to other chemicals, making a direct correlation of cause to increased levels in lung cancer more problematic. There is additionally the confounding factor of smoking. Evaluation of these studies shows, however, that it is plausible that the increased risk of lung cancer occurring in several of these occupations can be attributed at least in part to PAHs (WHO, 1997).

Biomarkers have been developed to assess internal PAH exposure (WHO, 1997). Most studies focus on measurement of PAH metabolites in urine, of which 1-hydroxypyrene is the most widely used (Levin, 1995). Pyrene is normally abundant in environmental PAH mixtures. Increased urinary levels of 1-hydroxypyrene have been found, for example, in patients cutaneously treated with coal tar, in workers exposed to creosote oil, in coal tar distillery workers, in road paving workers, in coke oven workers, and in workers exposed to bitumen fumes (Jongeneelen et al., 1986, 1988a,b; Clonfero et al., 1989; Burgaz et al., 1992; Jongeneelen, 1992; Ny et al., 1993; Levin et al., 1995). Significant correlations were obtained between urinary 1-hydroxypyrene of coke oven workers or city residents and levels of PY or BaP in the ambient air (Zhao et al., 1990, 1992; Sherson et al., 1992). A controlled human exposure study showed that a 100- to 250-fold increase in a dietary dose paralleled a 4- to 12-fold increase in urinary 1-hydroxypyrene elimination (Buckley & Lioy, 1992). Trial studies suggest that urinary 1-hydroxypyrene may be a useful marker of PAH pollution in the environment (Kanoh et al., 1993). Background levels amount to 0.06–0.23 μmol/mol of creatine in non-smokers. Smokers have about double that level (WHO, 1997).

GUIDELINE VALUES

Evidence that mixtures of PAHs are carcinogenic in humans comes primarily from occupational studies of workers. Cancer associated with exposure to PAH-containing mixtures in humans occurs predominantly in the lung and skin following inhalation and dermal exposure, respectively. There are no data available for humans for the oral route.

There are only a few animal carcinogenicity studies on oral administration of PAHs. BaA, BaP, DBahA, and mixtures of PAHs (coal tar) were tested orally and were carcinogenic. Most studies found forestomach tumours in rodents. The best data are from the BaP study by Neal & Rigdon (1967), described in WHO (1996), although this study is inadequate in many respects (Rugen et al., 1989; Collins et al., 1991). Results from recent studies with BaP by Weyand et al. (1995) and Culp et al. (1996), although limited, are in agreement with risk calculations based on this older study.

Further information is available on the carcinogenicity of single PAHs from experiments with dermal application. Following dermal exposure, BaA, BaP, BbFA, BjFA, BkFA, DBahA, and IP are tumorigenic in mice. FA was not positive in the mouse skin assay but was found to be tumorigenic in the intraperitoneal lung adenoma assay in newborn mice. The relevance of these types of short-term cancer bioassays is under discussion. From the limited data available, BghiP and PY are not carcinogenic. With the exception of PY (equivocal results), all PAHs discussed here are genotoxic at least in vitro (ATSDR, 1995; WHO, 1997). Table 2 compares evaluations of individual PAHs for carcinogenicity in animals and humans.

It is not possible to assess directly the risk of PAHs to humans for the oral route owing to a lack of human data. One must rely on animal data to estimate the risk of exposure to individual PAHs, not forgetting that humans are exposed to mixtures of PAHs and not to pure individual PAHs. The extrapolation of risk to humans from animal data is complicated: the relevance of forestomach tumours in rodents when considering extrapolation to humans is not clear. There is some indication that there are interspecies differences in the enzymes that activate PAHs (Michel et al., 1995); further, intraspecies differences in susceptibility in humans may be due to differences in cytochrome P-450 enzymes (Guengerich & Shimada, 1991).

Guideline value for BaP

The guideline value for BaP, one of the most carcinogenic PAHs, in drinking-water corresponding to an excess lifetime cancer risk of 10^{-5} was estimated as 0.7 µg/litre (WHO, 1996). This is based on the oral carcinogenicity study of Neal & Rigdon (1967) and calculated using a two-stage birth–death mutation model, which incorporates variable dosing patterns and time of sacrifice (Thorslund & Farrar, 1990). The data of Weyand et al. (1995) and Culp et al. (1996) on forestomach tumour incidence in mice give nearly identical results, giving support for the validity of the Neal & Rigdon (1967) study.

If BaP is present in drinking-water at significant concentrations, this indicates the presence of coal tar particles, which may arise from seriously deteriorating coal tar linings.

Guideline value for FA

FA is the PAH most commonly detected in drinking-water, primarily in association with coal tar linings of cast or ductile iron distribution pipes. A guideline value for this PAH was estimated from a 13-week oral gavage study in mice with a NOAEL of 125 mg/kg of body weight per day, based on increased SGPT levels, kidney and liver pathology, and clinical and haematological changes. An uncertainty factor of 10 000 (100 for inter- and intraspecies variation, 10 for the use of a subchronic study and inadequate database, and 10 because of clear evidence of co-carcinogenicity with BaP in mouse skin painting studies) gives a TDI of 0.0125 mg/kg of body weight per day. Assuming a 60-kg adult drinking 2 litres of water per day with an allocation of 1% of the TDI to water, because there is significant exposure from food, a health-based value of 4 µg/litre (rounded figure) can be calculated.

This health-based value is significantly above the concentrations normally found in drinking-water. Under usual conditions, therefore, the presence of FA in drinking-water does not represent a hazard to human health. For this reason, the establishment of a numerical guideline value for FA is not deemed necessary.

Relative potency of other PAHs compared with BaP

Attempts have been made to compare the carcinogenicity of individual PAHs using BaP as a standard. Although there are no comparative studies on the oral toxicity of PAHs, there are

several comparative studies based on mouse skin carcinogenesis, initiation/promotion on mouse skin, intrapulmonary administration to rats, subcutaneous injection in mice, and intraperitoneal injection in newborn mice. There have been various attempts to rank selected PAHs in order of potential potencies based on these studies (see Table 3). Owing to the fact that the relative potencies of the individual PAHs were comparable in these studies, although the route of application was different, it is assumed that the relative carcinogenicity of these compounds is also similar for the oral and other routes of application.

Complex mixtures

It cannot be assumed that the carcinogenic effects of individual PAHs are additive or that PAHs present in a mixture (e.g. coal tar) act in the same way as each PAH individually. There is ample evidence for enhancement or inhibition of carcinogenicity by other PAHs (see Warshawsky et al., 1993; ATSDR, 1995).

Recommendations

Although WHO (1996) called for the use of coal-tar-based pipe linings to be discontinued, it is apparent from reports in the recent literature that coal tar linings are still being used in new as well as in existing pipes. Furthermore, monitoring studies in areas where these coal tar linings are still in existence show that, depending on the conditions (particularly where soft corrosive water is being carried), the linings seem to be deteriorating, releasing particulate matter containing PAHs into the water supply. Such particulate matter is also released during repair work on water pipes with coal-tar-based linings. This particulate matter is likely to contain the more carcinogenic PAHs (e.g. BaP).
It is recommended, as before, that:

the use of coal-tar-based and similar materials for pipe linings and coatings on storage tanks be discontinued; and

the monitoring of levels of individual indicator PAHs (including FA and BaP) and not just total PAHs in drinking-water continue, with the objective of detecting where coal-tar-based linings are deteriorating, so that they can be replaced in a timely manner by new pipes.

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