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Review

Endocrine disrupting chemicals in the atmosphere: Their effects on humans and wildlife

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ABSTRACT

Endocrine disrupting chemicals (EDCs) are exogenous agents that interfere or disrupt the normal synthesis, secretion, transportation, binding and metabolism of natural hormones; eventually dysregulating homeostatic mechanisms, reproduction and development. They are emitted into the atmosphere during anthropogenic activities and physicochemical reactions in nature. Inhalation of these EDCs as particulate and gaseous vapors triggers their interaction with endocrine glands and exerts agonist or antagonists actions at hormone receptors. The endocrine disruption at nanogram levels of EDC's has gained concern in the last decade, due to infertility among men and women, early puberty, obesity, diabetes and cancer. Thus, the review explores the literature that addresses the major occurring EDCs in the atmosphere including phthalates, polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), brominated flame retardants (BFRs), dioxins, alkylphenols (APs) and perfluorinated chemicals (PFCs). Sources, fate, half-life, mechanism, measured concentrations in air, bioaccumulation in tissues, laboratory exposures correlating to toxicological effects of these EDCs in humans and wildlife are discussed.

Contents

Abbreviations: EDCs, endocrine disrupting chemicals; PCBs, polychlorinated biphenyls; PAHs, polyaromatic hydrocarbons; BFRs, brominated flame retardants; Aps, alkylphenols; PFCs, perfluorinated chemicals; POPs, persistent organic pollutants; ER, estrogen receptor; NOAEL, no observed adverse effect level; LOAEL, lowest observed adverse effect level; MRL, minimal risk level; AhR, aryl hydrocarbon receptor; TEF, toxic equivalency factor; TEQ, toxicity equivalence; TDI, tolerable daily intake; OSHA, occupational safety and health administration; PEL, permissible exposure limit; TCDDs, tetrachlorinated dibenzo-p-dioxins; APEs, alkylphenol polyethoxylates; NP, nonylphenol; PFAAs, perfluoroalkylated acids; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; FASAs, perfluorinated sulfonamides; FASEs, perfluorinated sulfonamide ethanols; N-Et-FOSA, N-ethyl perfluorooctane sulfonamide.

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1. Introduction

During the 20th century, a number of synthetic chemicals were developed to meet a wide variety of medical, scientific, agricultural and industrial needs. Though these chemicals provided economic and social benefits, their disposal led to the release of many chemicals into the environment (UNEP, 2004). Inhalation of such chemicals present in the atmosphere as pollutants is recognized as the major cause of environmental health problems (Al-Hamad et al., 2008). Combustion of municipal solid wastes, automobile exhausts, spraying of pesticides and herbicides, flaring activities, volatilization of synthetic chemicals, application of air fresheners, hair sprays, cosmetics and other activities release EDCs into the atmosphere as aerosols, dusts and particulates (Lintelmann et al., 2003) (Fig. 1).

The public concern about the impacts of EDCs on both human health and environment grew particularly during the last few decades. This was mainly focused on the endocrine system which is liable for disruption at many potential points by diverse group of chemicals (EFSA, 2013). The mechanism in disruption involves agonist or antagonist action for the receptors, interference of metabolic pathways and other bodily actions. Eventually turning on, shutting off or modified hormonal signals occur leading to decreased fertility, increased birth defects, altered sexual expression, and certain types of cancers (UNEP/WHO, 2013).

Aimed at highlighting the consequences of continued global industrialization stretches, the article offers a review about sources, fate, half-life, mechanism, molecular response, impending consequences, bioaccumulation and negative impacts on humans and wildlife due to EDCs present in the atmosphere. We have reviewed eight major endocrine disruptors of different classes affecting the atmosphere including phthalates, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, dioxins, brominated flame retardants, pesticide, alkylphenols and perfluorinated chemicals.

2. Fate and half-life of EDCs

The fate and half-life of EDCs depend on their physicochemical properties and the nature of environment they reside in (Wiberg et al., 2009). Persistent organic pollutants (POPs), EDCs are truly multimedia contaminants occurring in all parts of the environment: atmosphere, inland waters, sea waters, sediments, soils and vegetation (Wang et al., 2012). Global transport of EDCs occurs mainly through long range atmospheric and ocean water routes making their presence ubiquitous even in remote regions like the Arctic (Lohmann et al., 2007). In the environmental compartments, the EDC distribution is governed by three equilibrium partitioning coefficients: air–water, water–octanol and octanol–air. Most of the EDCs in the atmosphere are present in gaseous phase, while a few sorb onto suspended and few sorb to particles due to their semi-volatile nature. They are transported by dry and wet gaseous vapor deposition, volatilization, sorption, dissolution, sedimentation, re-suspension and erosion in the environment (Martina et al., 2013).

Natural removal of EDCs from the atmosphere is induced by both biotic and abiotic processes (Fig. 2). Biotic process involves microbial degradation in surface waters, soil and sediments; abiotic process includes: hydrolysis, direct and indirect photolysis, and oxidation/reduction reactions. EDCs that accumulated in soil and sediment are potentially volatilized back to the atmosphere when levels in the air are reduced (Lohmann et al., 2007). EDCs in water partition into particles and dissolved phases that deposit to bottom sediments or taken up by aquatic biota. From the sediment, EDCs are transported back to the water column via diffusion or resuspension (Lohmann et al., 2007). During these environmental cycling, certain EDCs enter the food chain and bioaccumulate in tissues through inhalation and ingestion causing endocrine disruption of the system.

3. Mechanism involved in endocrine disruption by EDCs

Human and wildlife exposure to atmospheric EDCs occur via inhalation and dermal contact. In vivo studies predict numerous mechanisms to be involved in the disruption of the endocrine system by the activation of receptors at nanomolar (nM) levels and non-genomic pathways at micromolar (mM) levels resulting in the genomic instability and alteration in hormone feedback regulation (Iguchi and Katsu, 2008). In a biological system, the gene networks and target cell activities are controlled by hormones through the activation of nuclear receptors and by binding to the responsive elements in the promoter of target genes. Such activation of receptors is disrupted by EDCs that mimic endogenous hormones and bind to ligands resulting in conformational changes

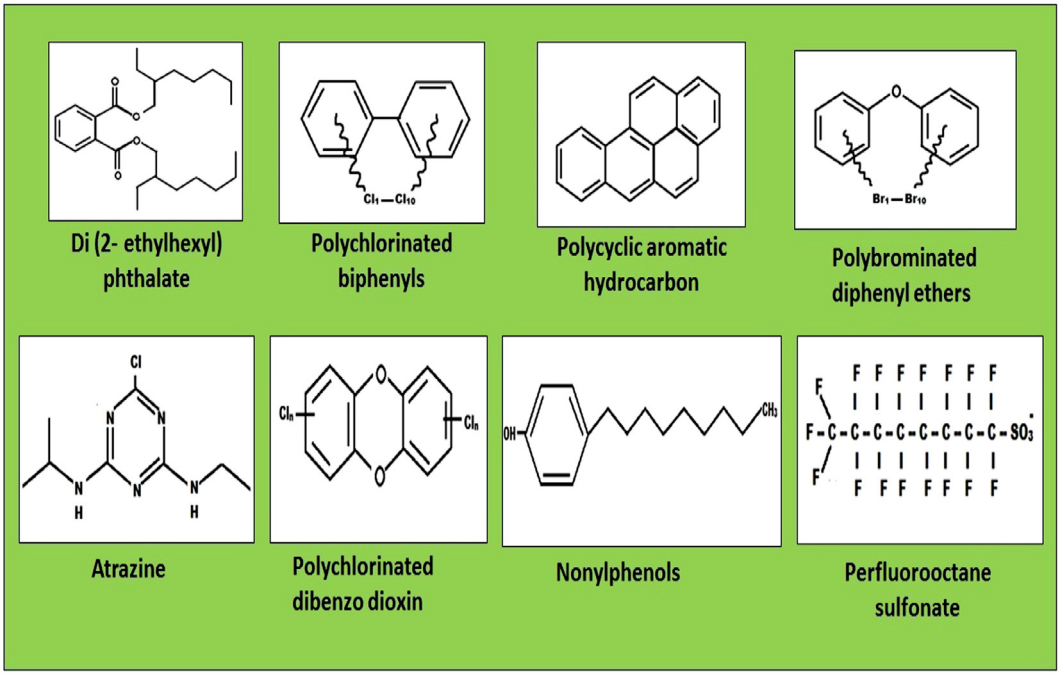

Fig. 1. Major EDCs present in the atmosphere.

and difference in functional and regulatory activities of gene expression (Vijayanathan et al., 2007) (Fig. 3). Xenoestrogens such as endosulfan and nonylphenols showed similar structure dependent induction of luciferase activity in MCF-7 and MDA-MB-231 breast cancer cells transfected with a construct linked to ER α and luciferase (Wu et al., 2008).

Apart from exhibiting genomic response, EDCs also modify transcriptional signals by inhibiting or synthesizing new proteins. EDCs mimicking endogenous steroid hormones can induce rapid non-genomic response by binding plasma membrane receptors and acting through second messenger-triggered signal cascades resulting in the changes in cellular motility, signaling processes and rapid hormonal synthesis (Watson et al., 2007). Membrane estrogen receptor (mER) activation causes release of Ca^{++} ions, altered prolactin secretion, cell proliferation, cellular immune response and maternal/paternal behavior (Wozniak et al., 2005). Interaction with cytosolic receptor activates the signal transducing molecules: cAMP, adenylate cyclase, calcium, phosphatidylinositol 3-kinase (PI3K), protein kinase B (PKB) and G-proteins (Silva et al., 2010).

4. Molecular response at cellular and organismal level

Response variation occurs at species level, hence endocrine disruption from invertebrates to mammals remains unclear even after numerous studies on exposure, gene response and adverse effects. E.g. six species of fish: zebra fish (*Danio rerio*), medaka (*Oryzias latipes*), fathead minnow (*Pimephales promelas*), stickleback (*Gasterosteus aculeatus*), roach (*Rutilus rutilus*), and carp (*Cyprinus carpio*) showed similar ERα sensitivity to 17β-estradiol and differences in response to p,p′-dichorodiphenyltrichloroethane (DDT) (Iguchi and Katsu, 2008). The chemicals affecting hormonal activities in vertebrates also affects several invertebrate species, nevertheless response variation occurs (Fox, 2005). ER homolog genes identified in sea slugs (*Aplysia* sp.), octopus (*Octopus vulgaris*) and rock shells (*Thais clavigera*) showed no ligand binding but displayed ligand-independent gene activation (Iguchi et al., 2007). This evidences the absence of functional nuclear-type ER in invertebrates rather the presence of membrane ERs similar to vertebrates.

5. Impending consequences of endocrine disruption at various trophic levels

Exposure to the emerging EDCs in the environment by wildlife and humans has set several hypotheses suggesting interference in sex determination, sex reversal, mortality, neurodisorders, hormonal activation and cell proliferation. The freshwater ostracod, *Eucypris virens* showed increased mortality on exposure to pyriproxyfen at a concentration ranging 3–30 nM (Vandekerkhove et al., 2007). Medaka (*O. latipes*) inhabiting water contaminated with 11.6–23.5 μg L^{-1} alkylphenol concentrations showed abnormal sex determination, lower fertilization rates among parental male fishes due to feminization, ovotestis and vitellogenesis (Kayama et al., 2003). Among African clawed frogs, *Xenopus laevis*, atrazine at 100 ng L^{-1} levels induced hermaphroditism, testicular oogenesis and reduced testicular volume, testosterone, germ cell and sertoli cell numbers (Hayes et al., 2010a, 2010b).

In higher vertebrates though the exact concentration of EDCs potential in inducing endocrine disruption is difficult to predict, animal models and cell studies reveal possible concentrations. As low as 60 μg L^{-1} of DDE (dichlorodiphenyldichloroethylene) is potential to induce androgenic effects in male test animals (Raloof, 1995). After the spill of DDT into Lake Apopka, inhabiting male alligators met the consequences of demasculinization and feminization which included failure of testis to descend, infertility, partially unfused phallus and development of vaginal pouch (Raloof, 1995). In bald eagles (*Haliaeetus leucocephalus*) that fed on fish of the Great Lakes reported the presence of 100 mg L^{-1} PCB concentration in the eggs (Colborn, 1991) and

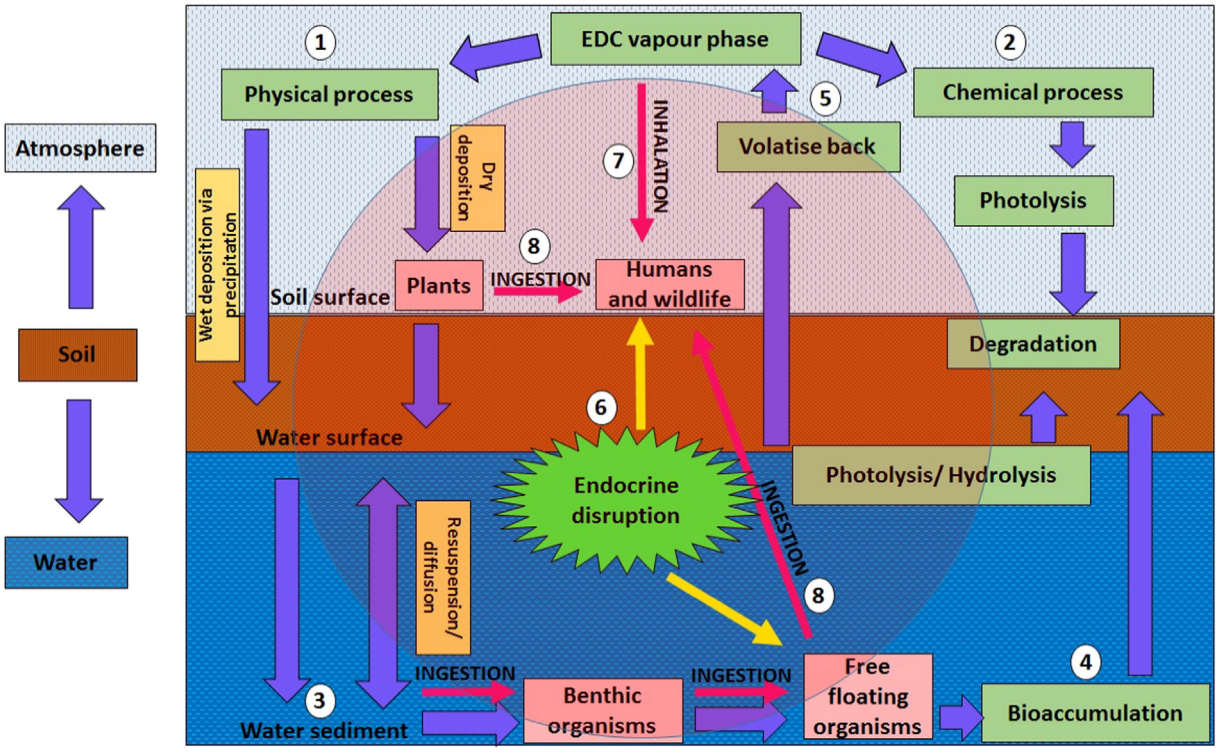

Fig. 2. Fate of EDCs in the environment and interaction with biota: From the atmosphere, EDCs in the vapor phase are transferred to soil surface either by physical process (1) or by chemical process (2). Physical process involves wet deposition and dry deposition while chemical process involves photolysis. Both of the process may ultimately lead to degradation or further transfer of EDC to water bodies (3) where resuspension or diffusion occurs; certain EDCs are adsorbed to the sediments. Bioaccumulation of persistent EDC among aquatic organisms occurs (4) and certain EDCs are volatilized back to the atmosphere (5). In this cycle, human and wildlife exposure are threatened to endocrine disruption (6) via inhalation of EDC from the atmosphere (7) and consumption of EDC deposited primary producers and bioaccumulated tissues of secondary consumers (8).

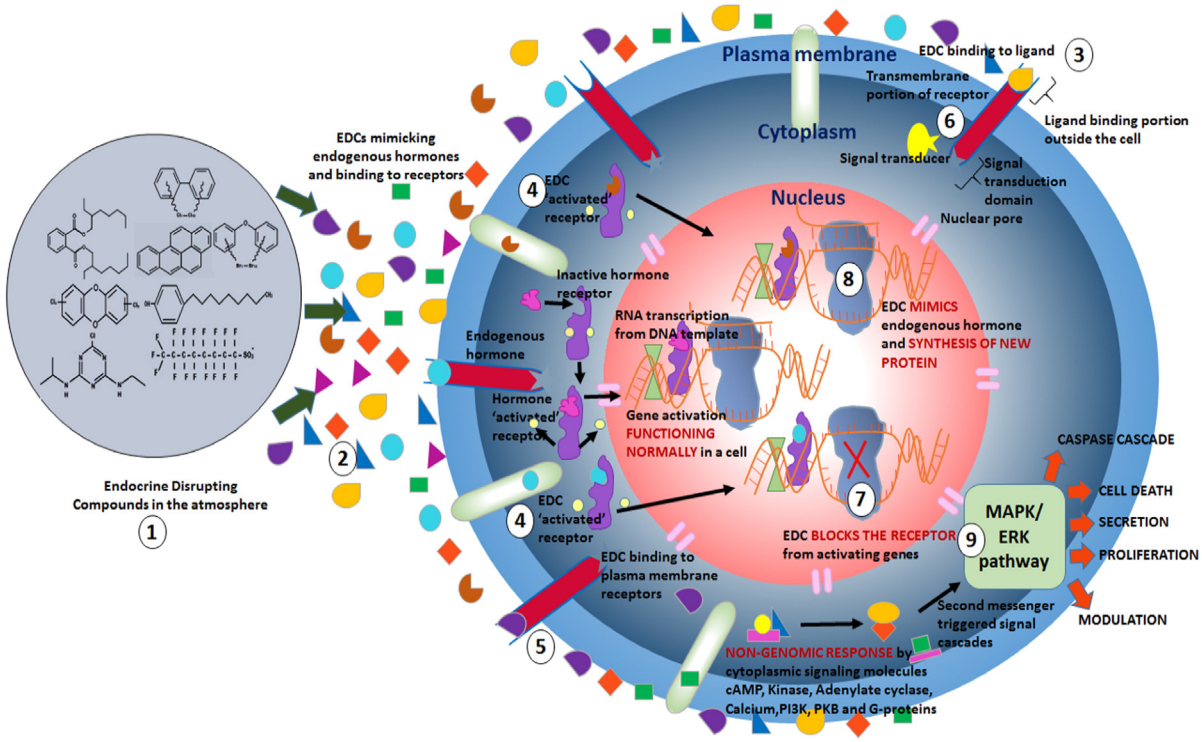

Fig. 3. Mechanisms involved by cell in response to EDCs: EDCs in the atmosphere (1) are present as aerosols or particulate phase. On inhalation, they are capable of exhibiting endocrine disruption either by genomic or non-genomic pathway in a cell. EDC (2) has certain specificity and potency in binding either to ligands (3), nuclear receptors (4) or membrane bound receptors (5). After binding to ligand, alteration in signal transduction occurs (6); in the case of EDC activated nuclear receptors either mRNA transcription is terminated (7) or new protein is synthesized (8). Certain EDCs bind to cytoplasmic signaling molecules and exhibit non-genomic pathway (9).

42 ppm in the brains of nestling eagles (Kozie and Anderson, 1991). As a result increased deformities, high mortality and reduced hatching rates prevailed among bald eagles.

In mammals, studies on dietary intake and body burden of dioxin like compounds have shown several endocrinal disorders (EPA, 1994). Dietary intake of 4 ng kg^{-1} induced chloracne in rabbits (*Lepus curpaeums*) and 1–25 μg kg^{-1} in monkeys (*Macaca mulatta*) induced chloracne, endometriosis, decreased learning object ability, offspring viability, and altered lymphocyte subsets. In terms of body burden, human (*Homo sapiens*) exposure and accumulation of dioxins and dioxin like compounds in lipophilic tissues of mother (1.46 μg kg^{-1}) induced birth defects, low birth weights, developmental delays and down regulation of EGFR (epidermal growth factor receptor) in the placenta. Other effects include: decreased testosterone (83 ng kg^{-1}), decreased testis size (14 ng kg^{-1}), cancer (0.11–7.0 μg kg^{-1}), chloracne (0.045–3.0 μg kg^{-1}), hepatic sequestration (0.15 μg kg^{-1}) and altered glucose tolerance (14–110 ng kg^{-1}).

6. Major EDCs: sources, measured concentration in air, exposure, bioaccumulation and health impacts

6.1. Phthalates

Phthalates are the dialkyl or alkyl aryl esters of phthalic acid added to plastics as modulators of the properties of materials. They are used in the manufacture of polyvinylchloride (PVC) products, building materials, toys, clothing, cosmetics, perfumes, food packaging and medical appliances (Wormuth et al., 2006). Usually phthalates are not physically bound to the polymers making their diffusion easier out of the plastics into the environment. Release of household and industrial wastewater from production and processing units and disposal of materials are sources of phthalates occurring in the environment (Cifci and Arikan, 2013).

Airborne phthalates are a significant source for its ubiquitous presence in the environment (Xie et al., 2005). Phthalates are degraded by photolysis and by the microorganisms under both aerobic and anaerobic conditions (Liang et al., 2008). Though they are not highly persistent in most of the environmental compartments, longer half-lives are expected under anaerobic and nutrient-poor environments (Peterson and Staples, 2003). This makes phthalates to display long range atmospheric transport potentials (Cousins et al., 2003). The average total daily ambient exposure of phthalates in U.S. was estimated to be 0.27 mg d^{-1}, through food (0.25 mg d^{-1}), water (0.02 mg d^{-1}) and air (0.4 μg d^{-1}) excluding workplace and indoor air (Tickner et al., 1999).

Phthalates were detected in gaseous phase and as particulates, both in indoor and outdoor air (Fig. 4). Indoor air had 12.0 mg m^{-3} of phthalates of which diethyl phthalate, DEP (2.29 mg m^{-3}), butylbenzyl phthalate, BBP (3.97 mg m^{-3}) and diethyl hexyl phthalate, DEHP (2.43 mg m^{-3}) were the most abundant phthalates accounting 72% of $\sum_6$ phthalates (Pie et al., 2013). Outdoor air along North Sea to Arctic had phthalates ranging 0.03–5.03 ng m^{-3} as particulates and 1.11–3.09 ng m^{-3} in gaseous phase (Xie et al., 2007).

In laboratory study exposure to DEHP via inhalation, rats (*Rattus norvegicus*) showed increased lung and liver weight, foam cell proliferation and thickened alveolar septa with 50 mg m^{-3} as NOAEL (no observed adverse effect level) and 1000 mg m^{-3} as less serious LOAEL (lowest observed adverse effect level) (Klimisch et al., 1991). No inhalation minimal risk limit (MRL) was derived for DEHP due to inadequate data on inhalation exposure. The MRLs for intermediate and chronic-duration oral exposure of 15–364 days were derived to be 0.1 and 0.06 mg kg^{-1} d^{-1}. These MRLs were derived based on NOAEL of 5.8 and 14 mg kg^{-1} d^{-1} for testicular pathology in male rats and decreased fertility in mouse (ATSDR, 2002). In human (*H. sapiens*) neonates, exposure to 0.001–4.2 mg h^{-1} for 12–30 days through artificial ventilation caused respiratory distress and pathological changes resembling hyaline membrane disease (ATSDR, 2002). Oral exposure in rat at the

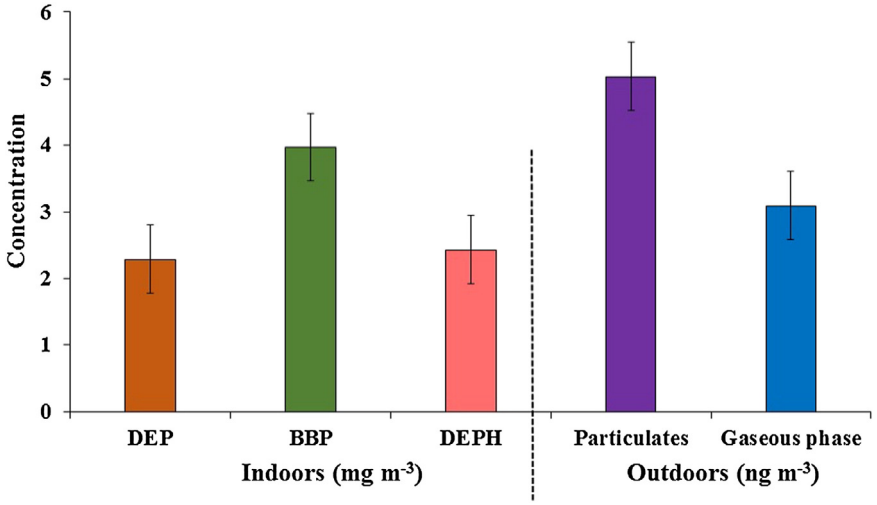

Fig. 4. Graphic illustration of indoor phthalates measured in the apartments of Hangzhou, China (Pie et al., 2013) and outdoor phthalates along North Sea to Arctic (Xie et al., 2007).

dose of 750 mg kg^{-1} d^{-1} in diet from the 14th day of gestation to the 3rd day of nursing resulted in testicular and epididymal atrophy, agenesis, hemorrhagic testes and hypospadias (ATSDR, 2002). Fetal death, exencephaly, open neural tubes and reduced pup size were observed in mouse (*Mus musculus*) exposed to 1000 mg kg^{-1} d^{-1} in diet for 2 days.

Correlating to the laboratory exposures, phthalates are found to be associated with reproductive disorders in both men and women. Phthalates in semen (0.08–1.32 mg/L) among men are related to declined semen quality and infertility (Zhang et al., 2006). Phthalate monoesters (monoethyl hexyl phthalate, MEHP and monobutyl phthalate, MBP) in maternal urine excretion (24.9 and 78.4 ng L^{-1}) and exposure of fetus to phthalates in amniotic fluid (22.8 and 85.2 ng mL^{-1}) significantly induced anti-androgenic in male infants characterized by short anogenital distances (Huang et al., 2009). Exposure to phthalates in women was associated with pre-mature thelarche (96.5 ± 134.0 ng L^{-1}), pregnancy loss (MEHP, 377.6 ng mL^{-1}; MBP, 255.1 ng mL^{-1}) and other disorders such as smaller pre-ovulatory follicles, anovulation or delayed ovulation, longer estrous cycle, decreased synthesis of estradiol, decreased serum progesterone and increased serum follicle-stimulating hormone (FSH) (Chou et al., 2009; Toft et al., 2012). On the other hand, the studies about the effects of phthalates on the wildlife remain scarce; some in utero investigations found phthalates to hinder the male rat (*R. norvegicus*) reproductive tract development in a dose-additive manner via reducing the fetal testis hormone synthesis (Gray et al., 2006; Howdeshell et al., 2007).

6.2. Polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) are aromatic, synthetic chemicals formed by two linked benzene rings with some or all of the hydrogen substituted by chlorine atoms. PCBs vary in appearance from oily liquids to white crystalline solids or hard non-crystalline resins. They are thermally stable, resistant to oxidation, acids, bases, and other chemical agents, and have excellent dielectric properties (D'Mello, 2003). PCBs have been used commercially since 1929 as insulating fluid in transformers, capacitors and as plasticizers in open systems comprising numerous building materials including adhesives, caulk, ceiling tiles, paints and sealants (Thomas et al., 2012). PCBs in caulk and other sealants often exceed 1% by weight and migrate from their source products creating the potential for exposure (MacIntosh et al., 2012).

PCBs have high environmental persistence, resistance to metabolize in organism and tendency to accumulate in lipids which favor their ubiquitous presence in the environment. Low water solubility and low vapor pressure of PCBs coupled with air, water and sediment transport processes move them from regional contaminated sites to remote areas (Beyer and Biziuk, 2009). Resistance of PCB increases with chlorine percentage; less chlorinated PCBs are water soluble, volatile and biodegrade while highly chlorinated PCBs sorb strongly to particulate matter (Beyer and Biziuk, 2009).

Based on the toxicity, persistence, accumulation and mechanism in binding aryl hydrocarbon receptor (AhR) similar to dioxins, 12 PCB congeners (4 non-ortho and 8 mono-ortho substituents) are classified into 'dioxin like-PCBs' (van den Berg et al., 2006). These PCBs have chlorines in a minimum of four at lateral positions (3, 3′, 4, 4′, 5, 5′) and none (non-) or only one (mono-) at ortho positions (2, 2′, 6, or 6′) of the biphenyl. The non-ortho dioxin-like PCBs bind to the AhR and causes dioxin-like toxicity in fish, birds and mammals while mono-ortho chlorinated dioxin-like PCBs cause dioxin-like toxicity in birds and mammals, not generally in fish. To facilitate risk assessment and regulatory control exposure of these compounds, toxic equivalency factors (TEFs) (Table 1) and toxicity equivalence (TEQ) are calculated relative to the reference compound, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). TEF refers to relative toxicity of a compound and TEQ to the concentration in environmental and biological media.

Atmospheric concentration of PCB in indoor and outdoor varies greatly depending on the source and meteorology (Fig. 5). Thomas et al. (2012) investigated PCB's inside six New York City schools. The median concentrations in the schools ranged from <50 to 807 ng m^{-3}, while the variability among the individual classrooms ranged between 236 and 2920 ng m^{-3}. Ambient air concentration of $\sum_{41}$ PCBs measured at industrial regions of Aliaga, Turkey ranged 0.13–231 ng m^{-3} (Elife et al., 2012). In another study at electronic waste dismantling facility, the measured concentration of $\sum_{27}$ PCBs was relatively higher ranging between 4.23 and 11.35 ng m^{-3} (Li et al., 2008). The urban and sub-urban areas of Izmir, Turkey had gaseous phase concentration of PCBs as high as 23.5 ng m^{-3} and 109.7 ng m^{-3}, respectively (Demircioglu et al., 2011).

The detected levels of PCBs in human tissues varied with samples and population of the country. Among Japanese, Chinese, Poles and Indians, the PCB levels in breast milk were 140, 292.7, 153.0 and 32.5 ng g^{-1} lw (lipid weight) and non-ortho PCB levels were 19.0 and 30.89 ng g^{-1} lw among Japanese and Americans (Antonio et al., 2008). PCB levels in serum were 4.11 and 12.85 ng g^{-1} lw among Italians and Chinese. No inhalation MRL was derived for inhalation exposure due to inadequate data. Intermediate-duration and chronic-duration oral exposure of 15–364 days were derived to be 0.03 and 0.02 μg kg^{-1} d^{-1}. These MRLS were derived based on LOAELs of 0.0075 and 0.005 mg kg^{-1} d^{-1} for neurobehavioral alterations in infant monkeys and immunological effects in adult monkeys (ATSDR, 2000).

Provisional tolerable daily intake (TDI) of PCB for the Great Lake residents was estimated to be 1000 ng kg bw^{-1} d^{-1} and the average lifetime daily intake was 27.58 ng kg bw^{-1} d^{-1}, calculated on the basis of 70-year lifespan (Haines et al., 1998).

Laboratory exposure via inhalation in rats with less serious LOAEL of 0.009–1.5 mg m^{-3} increased thyroid hormones, T_3 (3,3,5-triiodo-L-thyronine) and T_4 (tetraiodo-L-thyronine) in serum and slightly degenerated renal tubules (ATSDR, 2000). In guinea pigs, *Cavia porcellus* 16% decreased body weight and slight vacuolation was observed with less serious LOAEL of 1.5–5.4 mg m^{-3} (ATSDR, 2000). Oral exposure in rat with less serious LOAEL of 0.5–2500 mg kg^{-1} d^{-1} resulted in increased serum cholesterol, serum corticosterone, liver weight, adrenal weight, decreased T_4 hormone, vacuolar degeneration and uterine weight.

Correlating to the laboratory exposures, in humans PCB-153, 138, 180 and ∑PCB were in the concentration of 409.92, 177.63, 123.91 and 455. 61 ng g^{-1} lw. Its exposure at early pregnancy elevated thyroid stimulating hormone (TSH) (9.4 mL U L^{-1}; normal value: 0.35–3.5 mL U L^{-1}), total thyroxine (9.0 μg dL^{-1}; normal value: 4.5–12.5 μg dL^{-1}) and reduced T_4 level (38.1 ng dL^{-1}; normal value: 86–187 ng dL^{-1}) (Abdelouahab et al., 2013). Prenatally exposed infants to PCBs showed lower birth weight, smaller head circumference and alterations in the thyroid hormone homeostasis (Sadau et al., 2002) while exposed children showed altered neural development, cognitive, motor and learning abilities (Park et al., 2009; Roze et al., 2009). Among wildlife, polar bears (*Ursus maritimus*) showed reduced ability of the immune system to combat common infections (such as influenza, Reo virus and Herpes virus), waned testosterone production in males, elevated progesterone in females, altered behavior and thyroid hormone levels (Lie et al., 2004; Sonne, 2010).

6.3. Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are a large group of organic compounds with two or more fused aromatic rings. Based on origin: pyrogenic PAHs are formed by the incomplete combustion of fossil fuels, forest fires and tobacco smoke; petrogenic PAHs are present in crude oil, its product, and coal (Vasudevan and Aruazhagan, 2007). PAHs enter the environment primarily through sewage, road runoffs, smelter industries and oil spills (Durand et al., 2004; Vasudevan et al., 2007; Mascarelli, 2010). The offshore PAHs enter water through oil seeps, spills and discharges from offshore oil installations (Kemsley, 2012; Mascarelli, 2010; Lavrova and Kostianoy, 2011).

PAHs display relatively low water solubility and high solubility in lipids. When emitted into the atmosphere, most low vapor pressure PAHs are adsorb on particles (Johnsen et al., 2005) and are transported over long distances before to be deposited onto soil, vegetation or surface waters (Crimmins et al., 2004). PAH particulates and aerosols undergo photodecomposition by solar radiation (Hafez et al., 2008) and biodegradation by microorganisms such as *Ochrobactrum* sp., *Enterobacter cloacae* and *Stenotrophomonas maltophilia* (Arulazhagan and Vasudevan, 2009, 2011). In the atmosphere, PAHs can also react with free radicals, ozone, nitrogen oxides and sulfur dioxide to yield diones, nitro and dinitro PAHs and sulfonic acids. In soil, PAHs are degraded by microorganisms producing biosurfactant, rhamnolipid e.g. *Pseudomonas fluorescens* NSI (Vasudevan and Aruazhagan, 2007).

The increased concern about PAH carcinogenicity has promoted extensive measurement of their concentration worldwide (Fig. 6). Recently Morville et al. (2011) investigated PAHs in three different sites (urban, suburban and rural) of France. The mean concentrations were 92 ng m^{-3} for the rural site (Erstein), 127 ng m^{-3} for the urban site (Strasbourg) and 149 ng m^{-3} for the suburban one (Schiltigheim). At all of the three sites, low molecular weight PAHs (MW < 200 g mol^{-1}) were present at highest concentrations and the more abundant compounds were naphthalene (53.7 ng m^{-3}), phenanthrene (26.2 ng m^{-3}), acenapthalene (25.9 ng m^{-3}) and fluorene (11.8 ng m^{-3}) (Morville et al., 2011). PAH concentration in the industrial regions, Aliaga and Izmir of Turkey, was 1.6–838 ng m^{-3} with wide variability (Elife et al., 2012).

Table 1
Toxic equivalency factors for dioxin like PCBs.

Type of PCB	Congeners	TEF
Non-ortho	3,3′,4,4′-Tetrachlorobiphenyls (77)	0.0001
	3,3′,4′,5-Tetrachlorobiphenyls (81)	0.0003
	3,3′,4,4′,5-Pentachlorobiphenyls (126)	0.01
	3,3′,4,4′,5,5′-Hexachlorobiphenyls (169)	0.03
Mono-ortho	2,3,3′,4,4′-Pentachlorobiphenyls (105)	0.00003
	2,3,4,4′,5-Pentachlorobiphenyls (114)	0.00003
	2,3′,4,4′,5-Pentachlorobiphenyls (118)	0.00003
	2′,3,4,4′,5-Pentachlorobiphenyls (123)	0.00003
	2,3,3′,4,4′,5-Hexachlorobiphenyls (156)	0.00003
	2,3,3′,4,4′,5′-Hexachlorobiphenyls (157)	0.00003
	2,3′,4,4′,5,5′-Hexachlorobiphenyls (167)	0.00003
	2,3,3′,4,4′,5,5′-Heptachlorobiphenyls (189)	0.00003

Source: van den Berg et al. (2006).

PAH exposure to humans occurs through consumption of contaminated food, drinking water, inhalation of cigarette smoke, automobile exhausts and contaminated air from occupational settings (Diggs et al., 2011). Smoking a cigarette causes an intake of 20–40 ng of benz [a]pyrene (Phillips, 1996). In urban areas, exposure to airborne PAHs is very high in densely populated regions; food also appears a major source by the intake of grilled or charred meats, smoked food, contaminated cereals and vegetables (Srogi, 2007). In rural areas and most of the developing countries, the coal and biomass burning for cooking and heating lead to high indoor concentrations of PAHs. Since they are rapidly metabolized in humans and other organisms, biomonitoring of both parental PAHs and metabolites (1-hydroxypyrene) in the urine of individuals ensures the exposure (Tairova et al., 2009).

Occupational exposure to PAHs is of significant concern because they promote cancer hitting colon, rectus, digestive, respiratory and urinary tracts and, breast (Brody and Rudel, 2003; Bosetti et al., 2007; Diggs et al., 2011; Hofmann et al., 2013). The level of occupational exposures is considerably from aluminum production plants (6 ng m^{-3}), coke ovens (135–200,000 ng m^{-3}) and iron foundries (6400 ng m^{-3}). Occupational Safety and Health Administration's (OSHA) permissible exposure limit (PEL) for coal tar products and mineral oil mists is 0.2 and 5 mg m^{-3} averaged over an 8-hour exposure period. No inhalation and oral (acute or chronic) MRLs were derived because of inadequate human or animal dose–response data. The MRLs for intermediate-duration oral exposure (15–364 days) to acenaphthene and fluoranthene were 0.6 and 0.4 mg kg^{-1} d^{-1}. These MRLs were derived based on minimal LOAEL of 175 and 125 mg kg^{-1} d^{-1} for increased relative liver weight in mice (ATSDR, 1995).

In laboratory studies, mice were induced with different concentrations of 7, 12-dimethyl benz[a]anthracene; targeted organs showed susceptibility to the bone marrow, skin, lung cancer, ovarian and uterus cancer at the dosage of 20–200 μg $mouse^{-1}$ d^{-1} (Buters et al., 2003). Chronic exposure via inhalation in humans with serious LOAEL of 0.0001 mg m^{-3} reduced lung function, abnormal chest X-ray, cough and bloody vomit, throat and chest irritation (ATSDR, 1995). In golden hamsters (*Mesocricetus auratus*), serious LOAEL of 9.5 mg m^{-3} was found to be of cancer effect level (CEL), causing increased respiratory tract tumors and neoplasms of the upper respiratory tract (ATSDR, 1995).

Correlating to the laboratory exposures, epidemiologic studies have reported an increase in lung cancer in humans exposed to coke oven emission, roofing tar emissions, and cigarette smoke (ATSDR, 1995). Among wildlife, PAHs induce hemolytic anemia in oiled seabirds via oxidative attack of erythrocytes by PAH metabolites resulting in hemoglobin leakage and formation of Heinz bodies. In such case, haptoglobin and ferritin are up-regulated to sequester free Hb and iron in the circulation (Gera et al., 2007). PAHs are also associated with endocrine

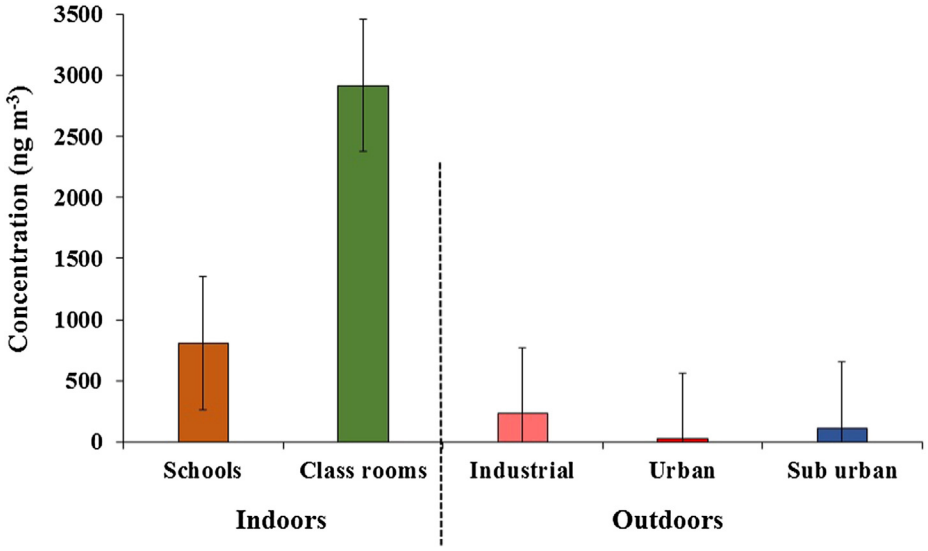

Fig. 5. Graphic illustration of indoor PCBs measured in the Schools of New York City (Thomas et al., 2012); outdoor PCBs at industrial region of Aliaga, Turkey (Elife et al., 2012); and urban and sub-urban areas of Izmir, Turkey (Demircioglu et al., 2011).

cancers including leiomyomas of the vagina, cervix and uterus, adrenal and thyroid tumors and mammary adenocarcinomas as found among Beluga whales (*Delphinapterus leucas*) of the St Lawrence estuary in Canada (McAloose and Newton, 2009).

6.4. Brominated flame retardants

In ancient Egypt about 450 BC, alum was used to reduce the flammability of wood, and ever since that time flame retardants have been used in various materials. The halogen containing compounds are used today as flame retardants in electronic equipment, textiles, plastics, paints and printed circuit boards (Chen et al., 2012) preventing fire eruptions by capturing free radicals (Birnbaum and Staskal, 2004). The most commonly used brominated flame retardants (BFRs) are polybrominated diphenyl ethers (PBDEs) and biphenyls (PBBs), 1, 2-bis (2, 4, 6-tribromophenoxy) ethane (BTBPE), hexabromocyclododecane (HBCD) and bisphenol-A ethers (Chen et al., 2012). BFRs are highly lipophilic with low water solubility, low vapor pressure and high bioconcentration factors (BCF) (Darnerud, 2003). In the atmosphere, PBDE partitions between the vapor and particulate phase significantly influencing the deposition, degradation, transport and subsequent fate in the environment (Chen et al., 2006a, 2006b) (Table 2).

The BTBPE in air (vapor and particles) and precipitation was studied by Salamova and Hites (2011) from 2005 to 2009 at five stations (two urban, one rural and two remote) belonging to the US Integrated Atmospheric Deposition Network around the Great Lakes (Fig. 7). The highest mean concentrations in vapor, particulate and precipitation (rain and melted snow) from the urban sites (Chicago and Cleveland) were 0.8 pg m^{-3}, 1.0 pg m^{-3} and 0.1 ng L^{-1}, from the rural site (Sturgeon Point) were 0.2 pg m^{-3}, 0.5 pg m^{-3} and 0.05 ng L^{-1} and at the remote sites (Sleeping Bear Dunes and Eagle Harbor) were 0.3 pg m^{-3}, 0.9 pg m^{-3} and 0.04 ng L^{-1}, respectively. In another study, the mean (and maximum) concentrations of BTBPE in dust sampled in schools, homes and offices in Belgium and the United Kingdom were 78 (1741), 33 (1019) and 80 (384) ng g^{-1}. The mean exposure via high dust ingestion was estimated to be 0.05 and 0.01 ng kg bw^{-1} d^{-1} for toddlers and adults (Ali et al., 2011). The highly BTBPE contaminated e-waste sites had the concentration of 20 ng m^{-3} in the dismantling hall (Sjodin et al., 2004) and 4.49–398 pg m^{-3} in the outdoors (Tian et al., 2012).

The 2, 4-dibromophenol (DBP) concentration in fish, mussels and seabirds from Norway and Faroe Island was found at the concentration of 21 and 86 ng g^{-1} ww in the liver of Atlantic cod (*Gadus morhua*) and 7 and 13 ng g^{-1} ww in Blue mussels (*Mytilus edulis*) from Norway and Faroe Islands; 1–2 ng g^{-1} ww in the eggs of Black Guillemot (*Cepphus grylle*) from the Faroe Islands (Schlabach et al., 2011). Tribromophenol-allyl ethers (TBP-AE) were detected in the blubber (5.4–9.1 ng g^{-1} ww) and brain (3.1–10 ng g^{-1} ww) of harp seals from the Barents and Greenland Seas (von der Recke and Vetter, 2007). In human milk from primiparae and multiparae Japanese women, the concentration of 2, 4, 6 and 2, 4, 5-TBPs was 1.8–110 and 0.81–3.90 ng g^{-1} lw respectively (Ohta et al., 2004). Other biomonitoring data on PBDE concentration in humans emphasize: 75 ng g^{-1} lw in adipose tissues (Johnson-Restrepo et al., 2005), 37 ng g^{-1} lw in maternal serum (Mazdai et al., 2003), 39 ng g^{-1} lw in fetal serum (Mazdai et al., 2003) and 61 ng g^{-1} lw in serum pools (Sjodin et al., 2004). The tentative exposure estimate for high seafood consumers is 40 ng kg bw^{-1} d^{-1} and for 3 month old breastfeeding infants with an average human milk consumption (800–1200 mL d^{-1}) would be of 3–4 ng kg bw^{-1} d^{-1} (EFSA, 2012).

In the laboratory studies, exposure to lower brominated diphenyl ethers with less serious LOAELs of 3.7–202 mg m^{-3} in rats significantly induced reversible rapid breathing, hepatocytomegaly, alveolar histiocytosis, chronic lung inflammation and the absence of corpora lutea in ovaries (ATSRD, 2004). The MRL of 0.006 mg m^{-3} was derived for intermediate-duration inhalation exposure to lower brominated BDEs based on NOEL of 1.1 mg m^{-3} which exhibited changes in thyroid hormones in rats when exposed intermittently to commercial octaBDE mixture for 13 weeks (Great Lakes Chemical Corporation, 2001). The MRL of 10 mg kg^{-1} d^{-1} for intermediate-duration oral exposure to decaBDE was derived based on NOAEL of 1000 mg kg^{-1} d^{-1} for developmental toxicity in rats exposed to decaBDE for 19 days during gestation (Hardy et al., 2002). The PBBs and PBDEs with LOAELs of 3–3000 and 1200–7780 mg kg^{-1} d^{-1} in rats decreased thyroid plasma T_4 hormone, increased hepatic phospholipids, darkened kidney and adrenal glands, induced hepatocytic swelling, necrosis, porphyrin accumulation, ulcers, splenic fibrosis, hematopoiesis, lymphoid hyperplasia, liver neoplastic nodules, hepatocellular adenomas and carcinomas, follicular cell hyperplasia and granulomas (ATSRD, 2004).

Correlating to the responses of laboratory studies, PBDE exposure in humans has also lead to liver toxicity, disruption of thyroid hormone levels, developmental neurotoxicity, and reproductive toxicity. In

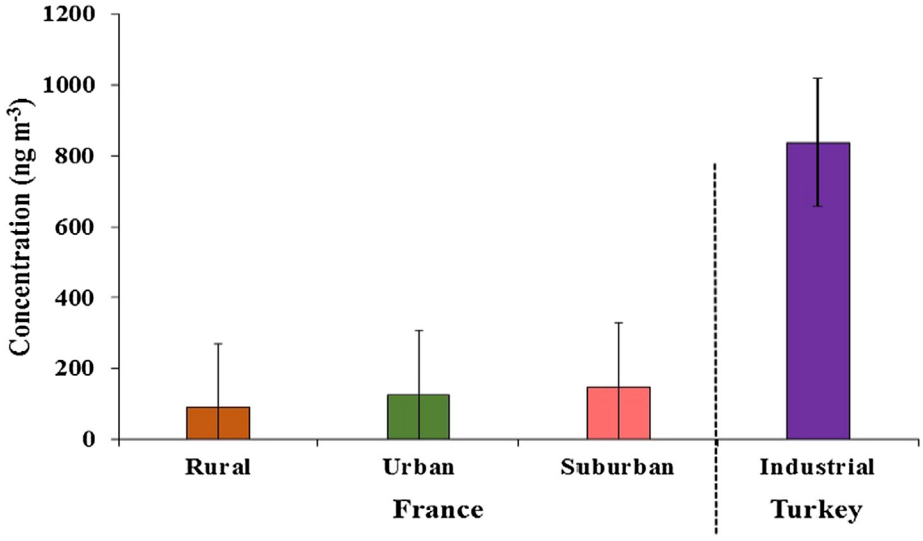

Fig. 6. Graphic illustration of PAHs measured at rural (Erstein), urban (Strasbourg) and sub-urban (Schiltigheim) areas of France (Morville et al., 2011) and at industrial areas of Aliaga and Izmir of Turkey (Elife et al., 2012).

animals, only few species of large mammals have been studied; of which most are predators, expected to have highest body burdens of contaminants, as a consequence of biomagnification. The high body burdens of hydrophobic contaminant PBDE were found in animals such as seals (*Phoca vitulina*), porpoises (*Phocoena phocoena*), dolphins (*Stenella coeruleoalba*), whales (*D. leucas*) and polar bears (*U. maritimus*) (Noel et al., 2009). Moreover, a study of little brown bats (*Myotis lucifugus*) in USA revealed the highest concentrations of PBDEs ever found in any wild animal (13,000 ng g^{-1} lw); these were thought to be caused by the fact that the bats consumed POP-contaminated insects of between 50 and 100% of their bw d^{-1} (Kannan et al., 2010).

6.5. Pesticides

Pesticides are substances or chemical mixture intended for preventing, destroying, repelling or lessening the damage of any pest. In India, pesticides are frequently used for agriculture and control of diseases such as malaria, filariasis, dengue, Japanese encephalitis, cholera, and so forth (Neelam et al., 2013). The fate of pesticides in soils with a different cropping land use has been extensively studied worldwide including India (Senthil Kumar et al., 2009). Pesticides enter the soil by direct treatment or being washed off from the plant surface during rainfall. They are relatively hydrophobic, resistant to degradation, and able to accumulate in soils and sediments (Hu et al., 2010).

Recently, the widespread contamination and toxicity of synthetic organic pesticides have become a serious environmental problem (Fig. 8). In a study by Devi et al. (2011), three locations at Manipur, India: Imphal (urban), Thoubal (rural) and Waithou (alpine) were selected to assess the seasonal release of selected organochlorine pesticides (OCPs) into the atmosphere. At alpine, hexachlorohexane (HCH) 403 and 349 pg m^{-3} during the hot (Mar to May) and rainy seasons (Jun to Sep) seasons, respectively. The DDTs were high in concentration with 384 pg m^{-3} at rural and 379 pg m^{-3} at urban during hot seasons. The endosulfans and chlordane concentrations were high during hot seasons (260 pg m^{-3}) and low during monsoon (44 pg m^{-3}) at rural site. In another study by Duyzer (2003) on atmospheric deposition for Dutch coastal and inland waters, up to 50 different pesticides were observed in precipitation and air. The concentration of 17 of these pesticides in precipitation exceeded the maximum permissible level for surface water and 22 exceeded the standard for drinking water of 100 ng L^{-1}.

The use of pesticides has led to increased agricultural production but in the meantime induced adverse effects on the human health and environment (Ejaz et al., 2004). More than 120 endocrine disruptive pesticides are known, covering numerous chemical classes (McKinlay et al., 2008; Faniband et al., 2014) (Table 3).

The bioaccumulation of pesticides has been widely studied in wildlife and humans which mainly depends on the inhalation and consumption of meat, fat, vegetables, green leaves and pesticide contaminated water. In a study, hexacholorobenzene (HCB) was detected in nestling bald eagle (*H. leucocephalus*) plasma from four areas in southwestern British Columbia and one site in California. The detected mean concentrations were 0.20, 0.26, 0.35, 0.31, and 0.08 μg kg^{-1} ww, for Central Fraser Valley, Lower Fraser Valley, Nanaimo/Crofton area, Barkley Sound, and Santa Catalina Island, respectively (Cesh et al., 2008). In the blubber of 7 pilot whales, 5 harbor porpoises, 12 Beluga whales, 2 northern fur seals, and 2 ringed seals the concentration of HCB ranges was 43–465, 223–1,070, 81.9–952, 138–74 and 125–156 ng g^{-1} ww (Becker et al., 1997). In cow tissues the mean concentration of HCB was 1.394, 1.061 and 0.550 μg kg^{-1} ww in the ovaries, mammary glands and liver (Sitarska et al., 1995). HCB in the follicular fluid of cattle, sheep, goats, and pigs from local farms in Greece was at the mean concentrations of 1.77, 1.25, 1.63, and 0.78 ng mL^{-1}, respectively (Kamarianos et al., 2003).

Human exposure to HCB was analyzed among farmers and their spouse. The mean concentration in serum ranged between 0.12–0.26 and 0.05–0.24 ng mL^{-1} for those from Iowa and <0.05–0.15 and 0.16–0.17 ng mL^{-1} for those from North Carolina (Brock et al., 1998). Workers at a new hazardous waste incinerator in Constanti, Spain had mean plasma levels of HCB ranging 19.4–854.0 μg kg^{-1} lipid with mean as 152 μg kg^{-1} lipid (Domingo et al., 2001). In human milk samples from women residing in the agricultural region (Salinas) and urban (San Francisco Bay) of California, the mean concentrations of HCB were 191 and 223 pg g^{-1}, respectively (Weldon et al., 2011).

Due to inadequate data on inhalation exposure of HCB in humans and animals, MRL was not derived. MRLs for oral acute, intermediate or chronic exposure were 0.008, 0.0001 and 0.00007 mg kg^{-1} d^{-1} based on the LOAEL of 2.5, 0.01 and 0.022 mg kg^{-1} d^{-1} for hyperactivity in rat offspring, minimal ovarian effects in monkeys and hepatic effects in rats (ATSDR, 2013). In rats, the inhalation exposure to HCB at less serious LOAEL of 33–35 mg m^{-3} led to slight impairment of pulmonary immune defenses. In pigs (*Sus domesticus*), 90 day exposure to less serious LOAEL of 50 mg kg^{-1} d^{-1} of HCB retarded the development of the testis. In monkeys (*Macaca fascicularis*), less serious LOAEL of 1–

Table 2
Solubility, partition coefficients and half-lives of the principle EDCs occurring in the atmosphere.

Endocrine disrupting chemicals	Water solubility at (mg/L) 25 °C	Log K_{OW}	Log K_{OC}	Log K_{OA}	Mean half-life in air (h)	References
Phthalates						
Di (2-ethylhexyl) phthalate	0.27	7.6	5.83	12.55	6	HSDB (2010); ATSDR (2002)
Di butyl phthalate	13	4.9	3.80	8.63	7.4	HSDB (2001); EPA (2006a, 2006b)
Di ethyl phthalate	1080	2.6	2.18	7.02	22.2	Medellin-Castillo et al. (2013); WHO (2003)
Polychlorinated biphenyls						
2,2′,3,4,5′-Pentachlorobiphenyl	0.0463	6.24	n.a.	9.16	3330	Safdari and Golmohammadi (2010); Yuyin et al. (2008)
2,3′,4′-Trichlorobiphenyl	0.353	5.7	n.a.	8.92	2720	Safdari and Golmohammadi (2010); Yuyin et al. (2008)
Polycyclic aromatic hydrocarbons						
Anthracene	0.045	4.540	4.47	7.34	60	Mackay et al. (1997); Kidd and James (1992); Yuyin et al. (2008)
Benzo[a]anthracene	0.011	5.91	5.30	10.80	300	Mackay et al. (1997); Earl et al. (2004); Yuyin et al. (2008)
Benzo[a]pyrene	0.0038	6.04	6.01	10.71	40	Mackay et al. (1997); Earl et al. (2004); Yuyin et al. (2008)
Phenanthrene	1.1	4.57	4.36	7.45	1040	Mackay et al. (1997); Earl et al. (2004); Yuyin et al. (2008)
Naphthalene	31.7	3.37	3.11	5.13	1210	HSDB (2004, 1995); ATSDR (1995); Earl et al. (2004); Yuyin et al. (2008)
Brominated flame retardants						
2,2′,4,4′-Tetrabromodiphenyl ether	0.011	6.0	n.a.	9.8	22416	ATSDR (2004); Chen and Bunce (2003); Kelly et al. (2007)
2,2′,4,4′,5-Pentabromodiphenyl ether	0.0024	6.8	n.a.	11.2	40.8	Kelly et al. (2007)
Decabromodiphenyl ether	0.02–0.03	9.9	n.a.	13.1	318	WHO IPCS (1994); Kelly et al. (2007), Arnot et al. (2005)
Pesticides						
Hexachlorobenzene	0.0062	5.73	3.59	4.47	4310	Farmer et al. (1976); Lewis (1981); Hansch et al. (1995); Yuyin et al. (2008)
γ-Hexachlorocyclohexane	17	3.72	3.04	n.a.	3330	Hollifield (1979); Hansch et al. (1995); Ripping (1972); Yuyin et al. (2008)
Dioxins and furans						
2,3,7,8-Tetrachloro-dibenzofuran	0.085	6.31	n.a.	n.a.	2190	Yuyin et al. (2008)
2,3,7,8-Tetrachloro-dibenzo-p-dioxin	19.3 ng/L	6.8	7.15	9.70	1860	Mackay et al. (2006); HSDB (1995, 1999); Yuyin et al. (2008)
Alkylphenols						
4-Nonylphenol	7.0	5.8	4.63	n.a.	5.0	SRC (2003); Groshart et al. (2001)
4-Tert-octylphenol	5.0	5.3	3.42	n.a.	6.1	SRC (2003); Groshart et al. (2001)
4-Tert-butylphenol	700	3.3	n.a.	n.a.	6.3	SRC (2003)
Perfluorintaed chemicals						
Perfluorooctane sulfonate	570	n.a.	2.57	6.63	2736	EPA factsheet (2012); Arnot and Gobas (2006)
Perfluorooctanoic acid	9.5×10^3	n.a.	2.06	5.73	2160	EPA factsheet (2012); Arnot and Gobas (2006)

Note: n.a. — not available.

10 mg kg^{-1} d^{-1} for 90 days led to increased length of menstrual cycle, decreased serum progesterone level and ovulatory levels of estradiol and degenerative lesions in oocytes (Foster et al., 1995).

Correlating to laboratory exposures, in humans OCPs are associated with a variety of adverse pregnancy outcomes, including miscarriage, preeclampsia (characterized by hypertension during pregnancy), intrauterine growth retardation (IUGR), poor weight gain during fetal development, and preterm delivery (Stillerman et al., 2008; Slama and Cordier, 2010). Other effects include cancer, neurological damage, immune suppression, birth defects and endocrine disruption (Wang et al., 2008). In wildlife, signs of endocrine disruption such as gonadal abnormalities and the feminization of males, interference with

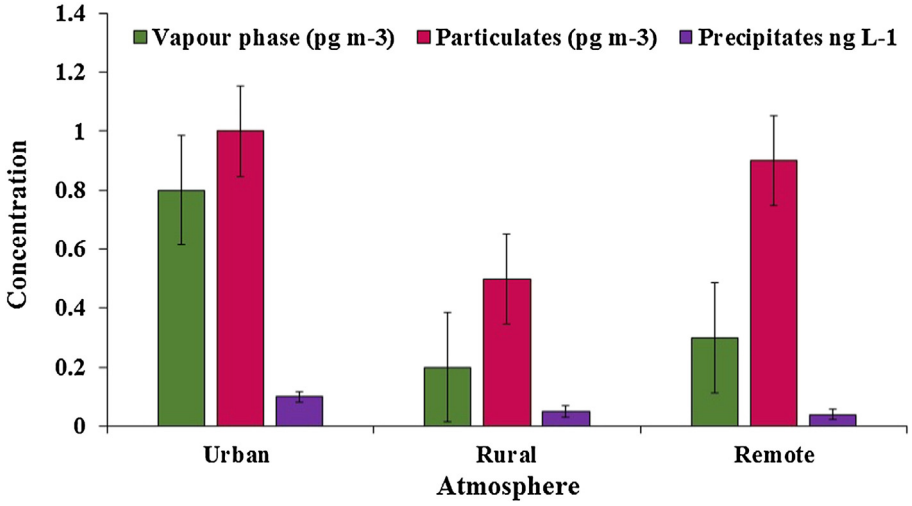

Fig. 7. Graphic illustration of BFRs measured at urban (Chicago, Illinois and Cleveland, Ohio), rural (Sturgeon Point, New York) and remote (Sleeping Bear Dunes, Michigan, and Eagle Harbor, Michigan) areas of USA (Salamova and Hites, 2011).

metamorphosis, changing behavior and retarded development are frequently found among frogs and toads (Hayes et al., 2010a, 2010b).

6.6. Dioxins

The lemma dioxins are commonly adopted to mean 210 organic chemicals, among which 75 congeners are polychlorinated dibenzo-p-dioxins (PCDDs), and 135 are polychlorinated dibenzo-furans (PCDFs). Prior to industrialization, low concentrations of dioxins existed in nature due to natural combustion and geological processes; e.g. wood rotting fungi and some mushrooms which break down lignin with chlorinating and oxidizing compounds, forming dioxins (CPCB, 2007). In industries though dioxins are not produced commercially, they are formed as by-products when reaction temperature is not well controlled in chemical manufacturing processes (CPCB, 2004). Dioxins are also produced in small concentrations when organic materials are burned in the presence of chlorine ions or atoms in the fuel formulae (EPA, 2006a, 2006b).

The transport of dioxins across the environment depends on particulate size (CPCB, 2011), while the partitioning features change with the number and position of chlorines in the molecules. Chlorines also improve the resistance to decomposition and solubility in lipids (Webster and Mackay, 2007), which allow them to persist in the environment and bioaccumulate (Letcher et al., 2010). Depending upon the capability to bind Ah receptors, elicit toxic response, persist and accumulate in the food chain; dioxins are affirmed to TEF for risk assessment in humans and mammals (EPA, 2010) (Table 4).

The baseline contamination and contributory role of incinerators in PCDD and PCDF into pollution were determined at three different sites in proximity to three solid waste plants (SWPs) in Italy (Caserini et al., 2004) (Fig. 9). The first site was an agricultural, cattle-breeding, flattish area of the Po Valley, the second site was an industrial district of the Veneto Region where the SWP incinerators were not equipped with best available technology (BAT) and the third site was Adige Valley, SWPs were equipped with BAT for flue gas cleaning. The concentration of PCDD/Fs concentrations was 22–125, 144–337 and 10–67 fg m^{-3} TEQ, respectively. In another study in Germany, PCDD/Fs concentrations were measured at rural, suburban and urban areas. The ambient concentrations ranged from 5 to 50, 10 to 100 and 20 to 220 fg m^{-3}, respectively (WYGE, 2008). In both studies, the industrialized urban areas experienced the maximum concentration of PCDD/Fs.

Dioxins biomagnify in trophic levels within food webs due to the persistency and accumulation in tissues. Few e.g. for exposure and occurrence in biological samples are as follows: Among the fish sampled from estuarine site of bleached kraft paper mill, TCDD concentration was higher in the fish (15.6 pg g^{-1} ww) that were sampled 2 km downstream than the fish (1.47 pg g^{-1} ww) sampled in upstream areas (Hodson et al., 1992). The TCDD concentration in pooled blubber samples of ringed seals (*Phoca hispida*), Beluga whales (*D. leucas*) and polar bears (*U. maritimus*) from several areas of Canadian north ranged between 2 and 37 pg g^{-1} ww (Norstrom et al., 1990). In contrast to marine mammals, concentration of TCDD in caribou (*Rangifer tarandus*) was extremely low. In the adipose tissues of herds in the east Canadian Arctic, TCDDs were in the range of 0.14–0.73 ng kg^{-1} lw (Hebert et al., 1996).

In comparison to the human exposure, Schecter et al. (1996) reported that the mean daily exposure to CDDs/CDFs TEQ for an adult (65 kg body weight) ranges from 34 to 167 pg TEQ with daily adult intake of CDDs/CDFs ranging from 0.52 to 2.57 pg TEQ kg bw^{-1} while WHO (2000) has set up a tolerable daily intake (TDI) range of 1–4 pg TEQ. In humans, out of 15 breast milk samples collected from primiparous women of Taranto, Southern Italy, 4 breast milk samples had far above the legal limit of human consumption, 3 pg g^{-1} (Bianco et al., 2013). Similar to this study, human milk samples analyzed from Faroe Island had 4.3–13.0 pg g^{-1} dioxins (Fangstrom et al., 2005). Occupational exposure being a significant source, workers involved in trichlorophenol production had elevated TCDD blood levels, with the mean concentration of 332 μg L^{-1} (Papke et al., 1992). Workers with chloracne and other illness were accidently exposed 32 years earlier and had 49 pg g^{-1} lw of TCDDs (Schecter and Ryan, 1988).

Laboratory studies suggest TCDD MRLs of acute, intermediate and chronic oral exposure to be 0.005, 0.0007, 0.000001 μg kg^{-1} d^{-1}. The corresponding MRLs were derived based on NOAEL of 0.005, 0.0007 and LOAEL 1.2×10^{-4} of μg kg^{-1} d^{-1} (Burleson et al., 1996; DeCaprio et al., 1986; Schantz et al., 1992). MRL for inhalation exposure was not derived due to insufficient data in humans and mammals. In female rhesus monkeys (*M. mulatta*), oral exposure of less serious LOAEL of 70 μg kg^{-1} d^{-1} induced blepharitis, acne, facial alopecia, carcinoma, epithelial hyperplasia in renal pelvis, mild anemia, endometriosis, increased liver weight and reduced heart weight (ATSDR, 1998). In female rats (*R. norvegicus*), serious LOAEL of 1 μg kg^{-1} d^{-1} malformed external genitalia, decreased fertility, thyroxine level, reproductive lifespan and estrogen level in female offsprings (ATSDR, 1998). In male rats, decreased testis descent, sperm production, testosterone and masculine sexual behavior in male offsprings were observed.

In correlation to the laboratory exposures, dioxins cause choking of the lungs, increases susceptibility to breast cancer (CPCB, 2004; Dai and Oyana, 2008), mood alterations, reduced cognitive performance, diabetes, changes in white blood cells, dental defects, endometriosis, decreased male/female ratio of births and decreased testosterone and (in neonates) elevated thyroxin levels (CPCB, 2007). Short term exposure to high levels of dioxin is suspected to cause chloracne, other related

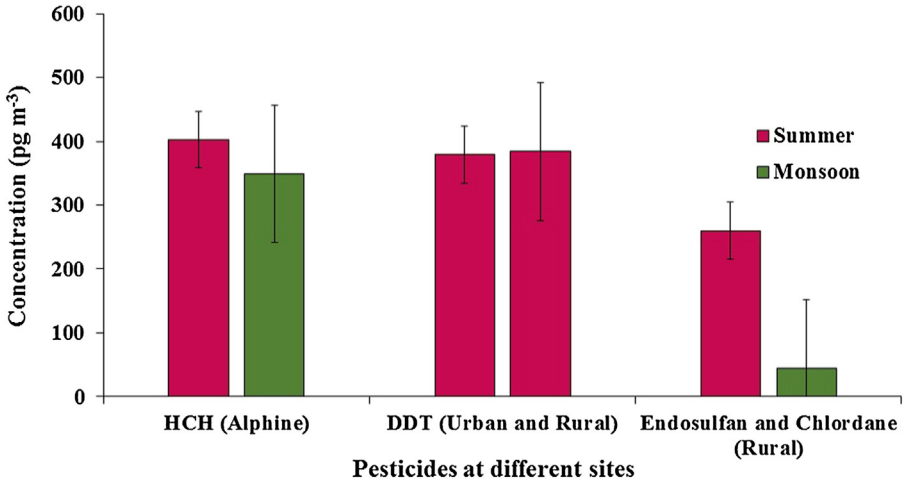

Fig. 8. Graphic illustration of seasonal variation in pesticide concentration measured at alpine (Waithou), urban (Imphal) and rural (Thoubal) areas of Manipur, India (Devi et al., 2011).

skin disorders, immune system toxicity, gastrointestinal ulcers, and neurotoxic effects. Long term exposures even at low concentrations may alter reproductive functions including congenital and neonatal development abnormalities (CPCB, 2004). Among wildlife, dioxins are EDCs with crucial impact on reproduction in a wide range of species (Mocarelli et al., 2011).

6.7. Alkylphenol

Alkylphenol polyethoxylate compounds (APEs) are widely used as non-ionic surfactants in detergents, pesticides, herbicides, emulsifiers, paints, cosmetics, plastic wares and even in jet fuel (Cevdet et al., 2009). They are commonly found in wastewater discharges and effluents from sewage treatment plants (Chen et al., 2006a, 2006b). In sewage treatment plants, APEs are degraded aerobically with sequential cleavage of ethyl moieties to alkylphenols (APs) (Kayama et al., 2003). APs bind strongly to soil followed by the application of sewage sludge to agricultural land and the aerobic degradation by microorganisms such as *Bacillus cereus*, *Arthrobacter* sp., *Bacillus licheniformis*, *Halomonas salina*, *Bacillus pumiolus* and *Pseudomonas aeruginosa* (Gayathri and Vasudevan, 2010) takes place. Nonylphenol (NP) is the most abundant derivatives of APEs demonstrated to stay biologically active for a longer period of time in the body than an endogenous estrogen (Brown and Reinhard, 2003).

Several studies have detected APs in indoor and outdoor air (Saito et al., 2004; Ying, 2006). Volatilization from soil, sorption to air particulates and air/soil exchange are outdoor source of 4-nonylphenol (4-NP) and 4-t-octyphenol (4-t-OP) in the atmosphere while polymer resins in wall and floor coverings are indoor source (Saito et al., 2004) (Fig. 10).

Table 3
Class of pesticides exhibiting endocrine disruption.

Endocrine disrupting pesticides	Class	M.W. (g/mol)	pKa	Log K_{OW}
Alachlor (H)	Chloroacetanilide	269.8	0.62	3.09
Aldicarb (I)	Carbamate	190.3	n.a	1.15
Aldrin (I)	Organochlorine	364.9	n.a	6.5
Atrazine (H)	Benzidines/Aromatic amines	215.7	4.14, 10.7	−0.97
Bendiocarb (I)	Carbamate	223.2	8.8	1.7
Carbaryl (I)	Carbamate	201.2	10.4	2.36
Carbofuran (I)	Carbamate	221.2	n.a	1.8
Chlordane (I)	Organochlorine	409.8	n.a	2.78
Chlorpyrifos methyl (I)	Organothiophosphate	322.5	n.a	4
DDT and metabolites (I)	Organochlorine	354.5	n.a	6.91
Deltamethrin (I)	Pyrethroid	505.2	n.a	4.6
Diazinon (I)	Organothiophosphate	304.4	2.6	3.69
Dieldrin (I)	Chlorinated hydrocarbon	380.9	n.a	3.7
Diflubenzuron (I)	Benzamide	310.7	n.a	3.89
Endosulfan (I)	Organochlorine	406.9	n.a	4.75
Endrin (I)	Organochlorine	380.9	n.a	3.2
Fenbuconazole (F)	Triazole	336.8	n.a	3.79
Fenitrothion (I)	Organothiophosphate	277.2	n.a	3.32
Flusilazole (F)	Organosilicon	315.4	2.5	3.87
Glyphosate (H)	Phosphanoglycine	168.1	0.78	−3.2
HCB (F)	Organochlorine	284.8	n.a	3.93
HCH (lindane) (I)	Organochlorine	290.8	n.a	3.61
Hexaconazole (F)	Triazole	314.2	2.3	3.9
Iprodione (F)	Imidazole	330.2	n.a	3.1
Malathion (I)	Organophosphate	330.4	n.a	2.75
Methoxychlor (I)	Organochlorine	345.7	n.a	5.83
Oxamyl (I)	Carbamate	219.3	n.a	−0.44
Parathion (I)	Organophosphate	291.3	n.a	3.83
Prochloraz (F)	Imidazole	376.7	3.8	3.53
Pyripyroxifen (I)	Pyridine-based	321.4	6.87	5.37
Resmethrin (I)	Synthetic pyrethroid	338.4	n.a	5.43
Simazine (H)	Triazine	201.7	1.62	2.3
Toxaphene (I)	Organochlorine	411.8	n.a	3.3
Tebuconazole (F)	Triazole	307.8	n.a	3.7
Vinclozolin (F)	Dicarboximide	286.1	n.a	3.02

Note: n.a. — not available; source: Wissem et al. (2011).

In a USA study, levels of NP in air ranged between 0.01 and 81 ng m^{-3}, with seasonal trends (Ying, 2006). In another investigation, APs that were detected in Tokyo, Japan were 4-tert-butylphenol (4-t-BP), 4-t-OP, and 4-NP affected both indoor and outdoor air. In indoors, the frequency of detection and concentrations was higher than outdoors. The maximum levels of 4-t-BP, 4-t-OP, and 4-NP in indoor were 387, 45.7 and 680 ng m^{-3}, respectively (Saito et al., 2004).

NP competes with estrogen and bind to estrogen receptor affecting reproduction and development (Colborn et al., 1993). Medaka (*O. latipes*) exposed to NP concentrations >11.6 μg L^{-1} had increased hepatic vitellogenin levels, altered sex ratios in offsprings, formed testis–ova, decreased fecundity, fertility and ratio of motile spermatozoa (Hara et al., 2007). NP exposures were also associated with increased intersex frogs, altered sex ratios, and increased gonadal development (Mackenzie et al., 2003). In tubifex worms (*Tubifex tubifex*), concentration of 600 μg g^{-1} sediment was lethal to few, in the case of survivor worms empty spermatheca or spermatheca with no spermatozons and ovaries with undeveloped ovocytes were observed (Bettinetti and Provini, 2002). Snails (*Lymnaea* sp.) exhibited decreased fecundity at 100 μg L^{-1} along with decreased egg masses, increased embryo mortality, and delayed development (Lalah et al., 2007).

In laboratory studies, oral exposure to NPs in rats (*R. norvegicus*) induced decreased epididymal sperm density, increased estrous cycle length, decreased ovarian weights and accelerated vaginal opening in pups with NOAELs and LOAELs of 13–19 and 43–64 mg kg bw^{-1} d^{-1} (Cal/EPA, 2009). In Japanese quail (*Coturnix japonica*) embryos, 10 μg g^{-1} egg increased the disappearance of the lymphoid cells from the lymphoid of the bursa. In the female embryos, 100 μg g^{-1} egg decreased the height of simple cuboidal epithelial cells surrounding the thyroid follicle and in the male embryo, its follicle-like structure in the thymus increased (Razia et al., 2006). Correlating to the human exposure, NPs tend to affect estrogen responsive tissues such as the testis in males, and mammary glands and placentas in females. In a longitudinal study of fetal exposures to EDCs in Japan, NP was detected in the umbilical cords, and evidence showed puberty in prenatally exposed boys and girls occurred at an earlier age (Mori, 2000).

6.8. Perfluorinated chemicals

Perfluorinated chemicals (PFCs) are synthetic compounds characterized by long, fully fluorinated carbon chains with different functional head groups which enable them to strongly resist to degradation (Fromme et al., 2009). PFCs are used in a variety of products to resist to grease, oil, stains, and water, and are also used in fire-fighting foam (Bjorklund et al., 2009). PFC contamination in the environment originates from direct or indirect anthropogenic sources. Direct sources include manufacture and use of perfluoroalkylated acids (PFAAs), whereas indirect sources include product impurities and production of chemicals that may degrade to PFAA (Prevedouros et al., 2006). In the atmosphere, the volatile and neutral PFC precursors are transported by air masses over long distances before or while they are degraded to more persistent PFAA such as perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) (Ellis et al., 2004). When PFAA enter aquatic phases in the environment, they are likely to travel long distances by transport with oceanic currents to remote areas like the Arctic (Armitage et al., 2006) and tend to accumulate in Arctic mammals (Lau et al., 2007; Yamashita et al., 2005).

In the past few years PFCs were determined in air of different regions across the earth and PFC detection in the Arctic atmosphere drew a lot of scientific interest (Shoeib et al., 2006). Detected concentration of PFCs in the Northern hemisphere, Canadian Arctic and Atlantic Ocean was 2, 11 and 40 pg m^{-3} (Shoeib et al., 2006; Dreyer et al., 2009a; Jahnke et al., 2007). PFC concentration from populated parts of the Northern hemisphere, Central Europe, Asia and Northern America was 972, 243, 2466 and 403 pg m^{-3} (Dreyer et al., 2009b; Barber et al., 2007; Oono et al., 2008; Stock et al., 2004). Although only few measurements of

Table 4
Toxic equivalency factors for dioxins and furans.

Dioxins and furans	Congeners	TEF
Polychlorinated dibenzo-*p*-dioxins (*PCDDs*)	2,3,7,8-Tetra CDD	1
	1,2,3,7,8-PentaCDD	1
	1,2,3,4,7,8-HexaCDD	0.1
	1,2,3,6,7,8-HexaCDD	0.1
	1,2,3,7,8,9-HexaCDD	0.1
	1,2,3,4,6,7,8-HeptaCDD	0.01
	OctaCDD	0.0003
Polychlorinated dibenzofurans (*PCDFs*)	2,3,7,8-TetraCDF	0.1
	1,2,3,7,8-PentaCDF	0.03
	2,3,4,7,8-PentaCDF	0.3
	1,2,3,4,7,8-HexaCDF	0.1
	1,2,3,6,7,8-HexaCDF	0.1
	1,2,3,7,8,9-HexaCDF	0.1
	2,3,4,6,7,8-HexaCDF	0.1
	1,2,3,4,6,7,8-HeptaCDF	0.01
	1,2,3,4,7,8,9-HeptaCDF	0.01
	OctaCDF	0.0003

Source: van den Berg et al. (2006).

volatile PFC in indoor air have been carried out so far, the PFC concentrations were higher than in outdoor air (Fig. 11). Jahnke et al. (2007) observed concentrations of fluorotelomer alcohol (FTOHs) and perfluorinated sulfonamides/perfluorinated sulfonamide ethanols (FASAs/FASEs) as high as 20–300 and 20–200 pg m^{-3}, respectively in the office air.

The PFCs are well studied in marine ecosystem from zooplanktons to mammals; the most frequently analyzed tissues are the liver and blood due to proteophilic nature of PFC's and accumulation in the enterohepatic system: liver, gall bladder and blood proteins (Conder et al., 2008). Tomy et al. (2004) studied the whole body samples of zooplankton (*Calanus hyperboreus*), shrimp (*Pandalus borealis*, *Hymenodora glacialis*) and Arctic cod (*Boreogadus saida*) from the eastern Canadian Arctic. The mean PFOS, PFOA and N-ethyl perfluorooctane sulfonamide (N-EtFOSA) concentrations were 1.8, 2.6 and 0.39 ng g^{-1} ww in zooplanktons; 0.35, 0.17 and 10.4 ng g^{-1} ww in shrimps 1.3, 0.16 and 92.9 ng g^{-1} ww in Arctic cod.

Among birds, liver samples of black-legged kittiwake (*Rissa tridactyla*) and glaucous gull (*Larus hyperboreus*) from the eastern Canadian Arctic had the mean PFOS of 10.0 and 20.2 ng g^{-1}, respectively (Tomy et al., 2004). The narwhal (*Monodon monoceros*) and Beluga (*D. leucas*) liver samples from the eastern Canadian Arctic had the mean PFSOA of 10.9 and 12.6 ng g^{-1} ww and PFOS of 6.2 and 20.9 ng g^{-1} ww, respectively (Tomy et al., 2004). In the pooled liver samples of 5 East Greenland polar bears, PFOS level was 1285 ng g^{-1} ww (Bossi et al., 2005); in mink (*Mustela vison*) from Watson Lake, Canada the mean PFOS and PFOSA levels were 8.7 and 1.4 ng g^{-1} ww (Martin et al., 2004); in arctic fox (*Alopex lagopus*) from Arviat, Canada the mean PFOS and PFOSA levels were 250 and 19 ng g^{-1} ww, respectively (Martin et al., 2004).

The MRLs for both inhalation and oral exposure are not derived for PFCs due to lack of sufficient data in human and animal models (ATSDR, 2009). In laboratory studies, female rats exposed to PFOA via inhalation to less serious LOAELs of 10–25 mg m^{-3} showed 18% increased liver weight and 12% decreased weight gain on gestational days 6–10. In male rats, 7.6 mg m^{-3} increased liver weight, induced hepatocellular hypertrophy and necrosis; 84 mg m^{-3} resulted 7% body weight loss by the 5th day of exposure, 380–18,600 mg m^{-3} induced red nasal discharge, dry rales, lacrimation, reddening of eyes, corneal opacity and corrosion, stomach irritation, liver enlargement, pulmonary edema and excessive salivation (ATSDR, 2009). Oral exposure of Rhesus monkeys with less LOAEL of 10–30 mg kg^{-1} d^{-1} induced hypoactivity, prostration, emesis, increased liver weight and decreased serum total T_4 (TT_4) and free T_4 (FT_4) (ATSDR, 2009).

Correlating to the laboratory exposures, PFC exposure in humans was associated with abnormal enlargement of Leydig cells and adenomas raising the concern of infertility in men (Vested et al., 2014). Due occupational exposure, workers in PFOS manufacturing facility with 1–2 μg mL^{-1} PFOS in serum experienced higher T_3 levels and increased risk of bladder and prostate cancer (Alexander et al., 2003; Olsen et al., 2003). Increased risk of infertility and irregular menstrual cycle was also observed among women with higher levels of PFOA and PFOS in serum (Fei et al., 2009).

7. Initiative steps to control the exposure to EDCs

EDCs in relation to interaction and disruption of endocrine system, both humans and wildlife are most vulnerable to non-communicable diseases at all stages of life (Table 5). Despite numerous studies on exposure, bioaccumulation and adverse effects, the confounding factors remain obscure due to large number of potential target species, varied life history strategies, differences in physiological mechanisms and lack of basic understanding of endocrine regulation for many species. The advances in understanding of EDCs have been based mainly on information derived from studies in developed regions. There is still a major lack of data from large parts of the world, particularly from Africa, Asia and Central and South America (UNEP/WHO, 2013). The rising needs and lifestyle indicates the increasing burden of the endocrine diseases across the globe most likely affecting the future generation.

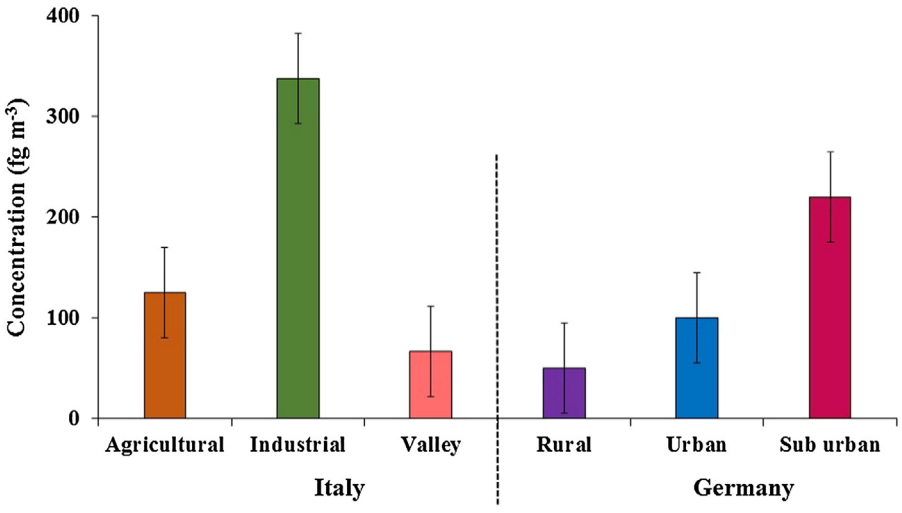

Fig. 9. Graphic illustration of dioxin and furan concentrations measured at agricultural, urban and valley (Po valley, Veneto region and Adige valley) near solid waste plants of Italy (Caserini et al., 2004); rural, sub-urban and urban areas of Germany (WYGE, 2008).

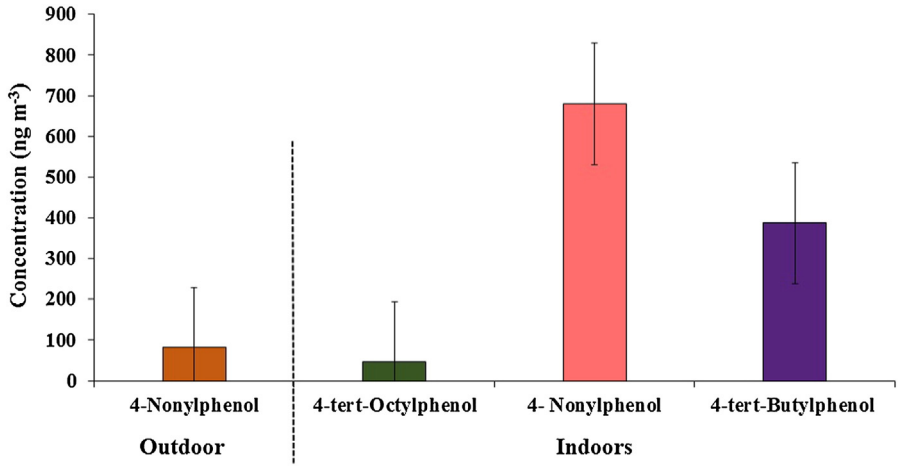

Fig. 10. Graphic illustration of outdoor 4-nonylphenol concentration measured in USA (Ying, 2006) and indoor alkylphenols in houses and offices of Tokyo, Japan (Saito et al., 2004).

Based on the future needs to prevent and control the body burdens and diseases, and improve the health of wildlife and humans, UNEP/WHO (2013) has identified the following initiative steps:

(1) *Strengthening the knowledge of EDCs:* It is a critical time to understand the effects of the mixtures of chemicals to which humans and wildlife are exposed at once. There is a need for assessment of EDC actions and account the characteristics of the endocrine system, their sensitivity and key variations at different stages of lifecycle. The efficiency of existing testing protocols to identify the effects of exposure to mixture or single EDC inducing combined risks needs to be improved. EDCs are no longer limited to estrogenic, androgenic and thyroid pathways; they also interfere with metabolism, fat storage, bone development and the immune system. New approaches are needed to examine the effects of mixtures of EDCs on disease susceptibility, the etiology and effects that may pass on to upcoming generations.

(2) *Improved testing for EDCs:* Validated screening and testing systems have been developed by a number of governments, and it requires considerable time and effort to ensure that these systems function properly. These systems include both in vitro and in vivo end-points and various species, including fish, amphibians and mammals to predict toxicity and assess the risk. EDC research over the past decade has revealed the complex interactions of some chemicals with endocrine systems which may escape detection in current validated test systems. Thus, there is a need to uncover the number of chemicals for which there is no information and allow effective consideration of research from all levels — from in vitro mechanistic data to human epidemiological data.

(3) *Reducing exposures and thereby vulnerability to disease:* It is imperative to know the nature of EDCs to which humans and wildlife are exposed, together with information about their concentrations in the blood, placenta, amniotic fluid and other tissues, across lifespan, sexes, ethnicities (or species of wildlife) and regions. Many information gaps currently exist with regard to what is found in human and wildlife tissues, more so for developing countries, countries with economies in transition and for chemicals that are less bioaccumulative in the body. Biomonitoring of exposures at all critical stages of lifetime such as fetal development, early childhood and the reproductive years is also needed to meet the demand. Since, EDCs are generally present in trace levels and complex matrices, highly selective and sensitive analytical methods are to be developed.

(4) *Identifying endocrine active chemicals:* Identifying chemicals with endocrine disrupting potential among all of the chemicals used and released worldwide is a major challenge. Though high production volume chemicals could be traced, the complexity increases with the chemicals used as additives and the production of unknown or unintended by-products during chemical manufacturing, combustion processes and via environmental transformations. To know the source of exposure, the active ingredients in pharmaceuticals, pesticides, personal hygiene products and cosmetics where thousands of chemicals are applied, there is a need to declare the chemical constituents in products, materials and goods.

(5) *Creating enabling environments for scientific advances, innovation and disease prevention:* Exposure to EDCs and their effects on human and wildlife health are a global problem requiring global solutions. More programs are needed that will foster collaboration and data sharing among scientists and between governmental agencies and countries. To protect human health from the combined effects of exposures to EDCs, poor nutrition and poor living conditions, there is a need to develop programs and collaborations among developed and developing countries and those in economic transition. There is also a need to stimulate new adaptive approaches that break down institutional and traditional scientific barriers and stimulate interdisciplinary and multidisciplinary team science.

(6) *Methods for evaluating evidence:* There is currently no widely agreed system for evaluating the strength of evidence of associations between exposures to chemicals (including EDCs) and adverse health outcomes. A transparent methodology is missing. The need for developing better approaches for evaluating the strength of evidence, together with improved methods of risk assessment, is widely recognized. Methods for synthesizing the science into evidence-based decisions have been developed and validated in clinical arenas. However, due to differences between environmental and clinical health sciences, the evidence base and decision context of these methods are not applicable to exposures to environmental contaminants, including EDCs. To meet this challenge, it is necessary to exploit new methodological approaches.

8. Conclusion

Chemical contamination in the environment coupled with widespread human and wildlife exposure underscores the urgency of implementing international policies against chemicals floating in the global market. In India, the chemical industry produces several

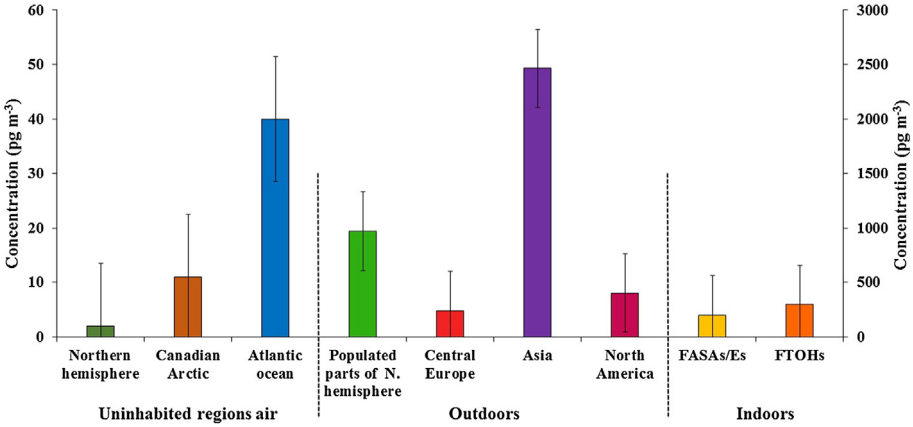

Fig. 11. Graphic illustration of perfluorinated chemical concentrations measured at uninhabited regions of Northern hemisphere, Canadian Arctic and Atlantic ocean (Shoeib et al., 2006; Dreyer et al., 2009a; Jahnke et al., 2007); outdoors of populated parts of Northern hemisphere, Central Europe, Asia, North America (Dreyer et al., 2009b; Barber et al., 2007; Oono et al., 2008; Stock et al., 2004); and indoors of office (Jahnke et al., 2007).

thousands of products and byproducts, ranging from plastics and petrochemicals to cosmetics and toiletries (Indian chemical industry: A sector study, 2007) but inadequate information and awareness prevail on safety data and toxic exposure to these chemicals. European Commission estimates over 30,000 chemicals in the European market produced or imported at over 101.97 hyl (MKU units) annum^{-1}. Existing European Union rules allow continued use of chemicals that were put in the market prior to 1981, without submission of safety data. Such chemicals still make up over 90% of the market, where the majority of chemicals now in use have inadequate publicly available scientific data to assess their safety (Brown, 2003). Regulations should require manufacturers and importers: to provide safety information on industrial chemicals annually marketed, to include safety data information on toxicity and environmental fate, usage and the amount of chemical produced, to ensure that chemicals they produce, import or use do not adversely affect human health or the environment and to obtain prior authorization before using chemicals of very high concern (GAO, 2005).

Studies over the atmosphere of North Atlantic, the Great Lakes, and the North Sea reveal atmospheric deposition to be a significant source for open water contamination with persistent EDCs (Xie et al., 2005). Immense exploration on wildlife and human health predicts body tissues to be the repository for EDCs and as a source in transferring chemicals to progenies and predator. WHO (2012) that plausible exposure to EDCs could damage certain reproductive and developing systems in humans. However, wide uncertainties remain about the exposure, mechanism, binding sites and toxicity exerted by endocrine disruptors. The observed concentrations of persistent EDCs in both indoor and outdoor air pose severe threat to all people experiencing prolonged exposure to them. Improvement in reliability and sensitivity to measure the quality of air inhaled by cost effective bioassays, biosensors and other analytical techniques are needed to assess the severity of exposure. Both monitoring and legislative activities will improve the information concerning EDCs and abate their impact on health. Air quality monitoring programs by government bodies and better reach of information on green chemistry, EDCs and health effects perceive to minimize the consequences of exposure.

9. Summary

The persistent organic pollutants capable of interfering hormonal feedback regulations and metabolic pathways by mimicking endogenous hormones are termed as endocrine disrupting chemicals (EDCs). Inhalation is one of the significant source of exposure, due to atmospheric transport of EDCs in gaseous phase and as particulates even to the remote regions of the Arctic and Antarctic. The fate of the EDCs depends on the environmental media where they exist, their liability to physicochemical reactions and tendency to bioaccumulate. The mechanism of EDC in a cell involves both genomic and non-genomic pathways. The ultimate effects of exposure are decreased fertility, increased birth defects, altered sexual expression, and increased cancer prevalence. The eight predominant EDCs in the atmosphere are as follows:

(1) Phthalates are dialkyl aryl esters of phthalic acid used as plasticizers in most of the PVC products. They are not bound physically to the polymers making diffusion easier into the environment. The atmospheric concentration ranges between 0.03 and 12.0 mg m^{-3}. Exposure to phthalates is associated with declined sperm quality and infertility in men; longer estrous cycles, decreased synthesis of estradiol, progesterone and increased serum FSH in women; shorter anogenital distances in the newborn boys; and premature thelarche among girls. Though in wildlife, phthalate exposure studies are less, in laboratory animals, phthalates tend to induce reproductive disorders.

(2) PCBs are two benzene ringed chemicals with some or all of the hydrogen substituted by chlorine atoms. They have high environmental persistence, and tendency to accumulate in lipids favoring their ubiquitous presence in the environment. The atmospheric concentration ranges between 4.23 and 2920 ng m^{-3}. In human effects include elevated thyroid hormone concentration during early pregnancy in women; lower birth weight, smaller head circumference and alterations in the thyroid hormone homeostasis in infants; and altered neural development, cognitive, motor and learning abilities in children. Polar bears showed susceptibility to common infections, altered behavior and thyroid hormone levels, waned testosterone production in males and elevated progesterone in females.

(3) PAHs are organic compounds with two or more fused aromatic rings, with low water solubility and high solubility in lipids. The atmospheric concentration ranges between 11.8 and 92 ng m^{-3}; and in humans and wildlife, PAHs are reported to be carcinogenic.

(4) BFRs are halogenated compounds that prevent fire eruptions by capturing free radicals. They are highly lipophilic with low water solubility, low vapor pressure and high bioconcentration factors. The atmospheric concentration ranges between 0.2 and 398 pg m^{-3}. In humans, BFRs tend to evoke the liver, developmental, and reproductive toxicity along with disruption of thyroid hormone levels. Though in animals high body burdens are studied, effects are not well reported. Laboratory animal studies show similar effects as in humans.

(5) Pesticides include broad range of compounds mainly:

Table 5
Most persistent EDCs in the atmosphere and their health effects.

Endocrine disrupting compounds	Taxa	Target system/gland	Mechanism of action	Clinical symptom	References
Phthalate di-2-ethylhexyl phthalate (DEPH), di-n-butyl phthalate (DnBP),	Human (*Homo sapiens*): children	Thyroid gland	Induction of IGF-I (insulin like growth factor-I) mRNA in reproductive tissues and lowering of IGF-I levels	Reduced serum level of T_3, hypothyroidism, growth retardation	Bowman et al. (2005); Lin et al. (2008)
di-methyl phthalate (DMP), diethyl phthalate (DEP), di-butyl-benzyl phthalate (DBBP)	Rat (*Rattus norvegicus*)	Thyroid gland	Binding of T_3 to transport proteins; interaction with active T_3 uptake at plasma membrane; antagonistic activity at thyroid receptors	Reduced thyroid weight, hyperactivity (smaller follicles, increased number, size and iodine content of lysosomes)	Shimada and Yamauchi (2004); Shen et al. (2009)
	Rat: male	Reproductive system	Estrogenic and anti-androgenic activity	Reduced anogenital distance, areola, nipple malformation, cryptorchidism and permanently incomplete preputial separation	Moore et al. (2001)
	Rodent: female	Reproductive system	Anti-estrogenic activity	Decreased serum estradiol level, prolonged estrous cycle and no ovulation	Lovekamp and Davis (2001)
Polychlorinated biphenyls aroclor 1254, PCB 118, PCB 77	Human: male	Prostate gland	Inhibition of estrogen sulfotransferase activity in the liver and increased bioavailability of estrogen in the body	Prostate cancer	Kester et al. (2002); Charles et al. (2003);
	Rat	Thyroid gland	Alteration of the thyroid gland structure and its metabolism, binding to the thyroid hormone binding protein in the blood	Reduced T_4 level in serum, reduced serum half-life of T_4, reduced ability of the thyroid gland to respond to TSH	Gauger et al. (2004); Martin and Klaassan (2010)
	Human: children, adolescent	Thyroid gland and the immune system	Antagonistic activity	Increased prevalence of ear infection and chicken pox; lowered immune system function and greater susceptibility to diseases; retard growth and affected intellectual and behavioral development	Weisglas-Kuperus et al. (2000)
Polycyclic aromatic hydrocarbon Benzo[a]pyrene (BaP), benz[a]	Immature rat	Uterus	Estrogenic activity	Increased uterine weight, hypertrophy of luminal epithelium	Kummer et al. (2008)
anthracene (BaA), fluoranthene (Fla), benzo[k]fluoranthene (BkF)	Human: female	Breast	Estrogenic activity: association with AhR and initiation of series of cell changes leading to altered cell signaling and increased DNA mutation	Disruption of normal cell functioning, increased levels of DNA-PAH adducts (hallmarks of tumor development) — breast cancer	Gammon et al. (2002); Kemp et al. (2006); Hung et al. (2012)
Brominated flame retardants tetrabromobisphenol A (TBBPA), polybrominated diphenyl ethers (PBDEs), polybrominated biphenyls (PBBs)	African clawed frog (*Xenopus laevis*)	Thyroid gland	Antagonistic activity: Binding with TR (thyroid hormone receptor) binding protein, down-regulating the transport protein transthyretin (TTR) and transmembranal thyroid hormone transport	Decreased level of circulating thyroid hormone, impairs TH-dependent metamorphosis	Jagnytsch et al. (2006); Fini et al. (2007); Richardson et al. (2008);
Pesticides atrazine, chlordane, chlorpyrifos methyl, endosulfan, dichlorodiphenyltrichloroethane (DDT), hexachlorobenzene (HCB)	American leopard frog (*Rana pipiens*)	Reproductive system	Estrogenic and anti-androgenic activity. Induction of aromatase activity in turn increased endogenous estrogen production	Demasculinization (failure to induce spermatogenesis), feminization (induction and growth of oocytes): hermaphrodites (testicular oogenesis) and gonadal dysgenesis	Hayes et al. (2002a,b)
	Human: male	Reproductive system	Competition with estradiol and binding with estrogen receptor	Delayed sexual maturity and interference with sex hormone synthesis (decreased semen quality, sperm count, spermatogonial cells and defects in sperm morphology occurs)	Saiyed et al. (2003); Cerrillo et al. (2005); Vested et al. (2014)
Dioxins and furans 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD)	Rat	Thyroid gland and nervous system	Interference with thyroid hormone's critical role in myelination and signaling the development of brain	Demyelination (loss of myelin sheath insulating nerve); alteration of oligodendroglial lineage, platelet derived growth factor alpha receptor, myelin basic protein (MBP) mRNAs and expression	Fernandez et al. (2010)
	Human: male, female	Reproductive system	Estrogenic/antiandrogenic/antiestrogenic activity	Reduced sperm concentration and motility; reduced estradiol, increased FSH	Mocarelli et al. (2008)
Alkylphenols 4-nonylphenol, 4-tert-octylphenol, 4-tert-butylphenol	Human	Breast	Alteration of mRNA expression for ER α isoforms in the brain; estrogenic/antiandrogenic activity	Breast cancer, reduced sperm count.	Brody et al. (2007)
	Rainbow trout (*Oncorhynchus mykiss*)	Reproductive system	Alteration of mRNA expression level for gonadotropin releasing hormone (GnRH); estrogenic activity	Increased vitellogenesis in the liver, inhibition of spermatogenesis, cytological changes in germ and sertoli cells, increased ovosomatic index	Vetillard and Bailhache (2006)
Perfluorinated chemicals perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), fluorotelomer alcohols (FTOHs)	Human, monkey, rat	Thyroid gland	Up regulation of hepatic glucuronidation enzymes and deiodinases in the thyroid gland, binding to TTR	Increased FT_4 and decreased TSH, T_3 and T_4 in serum	Olsen and Zobel (2007); Weiss et al. (2009); Yu et al. (2009)

organochlorines, organophosphates, carbamates, pyrethroids, thio-carbamates, triazines and triazoles. They are hydrophobic, resistant to degradation and accumulate in soils and sediments. The atmospheric concentration ranges between 44 and 403 pg m^{-3}. In humans, OCPs are associated with adverse pregnancy outcomes, cancer, neurological damage, immune suppression and birth defects. Gonadal abnormalities and feminization of males, interference with metamorphosis, changing behavior and retarded development are reported among frogs and toads.

(6) Dioxins are polychlorinated compounds with significant resistance to decomposition and solubility in lipids making them persist in the environment and bioaccumulate. The atmospheric concentration ranges between 5 and 337 fg m^{-3}. In humans dioxins tend to cause choking of the lungs, increased susceptibility to breast cancer, mood alterations, reduced cognitive performance, diabetes, changes in white blood cells, dental defects, endometriosis, decreased male/female ratio of births, decreased testosterone, elevated thyroxin levels, chloracne, immune system toxicity, gastrointestinal ulcers and neurotoxic effects. In wildlife, reduced sperm production, reproductive failure, reproductive impairment and decreased fecundity are reported.

(7) Alkylphenols are used as non-ionic surfactants or antioxidants commonly found in wastewater discharges and effluents from sewage treatment plants. NPs are biologically active for a longer period of time in the body than an endogenous estrogen. The atmospheric concentration ranges between 0.01 and 680 ng m^{-3}. In humans, estrogen responsive tissues such as the testes in males, mammary glands and placentas in females are affected and also early puberty in prenatally exposed boys and girls is reported. In wildlife, effects of NPs are widely studied in which feminization, decreased fecundity, infertility, altered sex ratio and other reproductive toxicity are reported.

(8) PFCs are characterized by long, fully fluorinated carbon chains with different functional head groups which enable them to strongly resist to degradation. The atmospheric concentration ranges between 2 and 2466 pg m^{-3}. In humans, PFCs are associated with infertility, cancer and adverse pregnancy outcomes. In laboratory exposed animals hepatic toxicity, lacrimation, reddening of eyes, excessive salivation, decreased thyroid hormone levels and reproductive disorders are reported.

The review concludes, predicting the urging demands in the development of analytical techniques, sensing systems and testing protocols which would satisfy the needs in understanding EDCs. Improvement of scientific technology in the developing countries, enforcement of green chemistry, promotion of collaborative projects, workshops and biomonitoring worldwide by the present generation will be the initiative steps to lessen the consequences of EDCs on the next generation.

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