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Research Paper

Extensive use of organochlorine pesticides in agriculture: Environmental and health concerns: A review

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ABSTRACT

Pesticides are widely used in agriculture mainly to increase crop yields to cater huge supply of food products for increasing world population, as well as to protect crops from pests and control insect-borne diseases. Increased use of pesticides (especially Organochlorine pestides) results in contamination of the environment and the excess accumulation of pesticide residues in food products and severe health impact, which has always been a matter of serious concern. Pesticide residues in food and crops are directly related to the irrational application of pesticides to the growing crops. Accumulated oganochlorine pesticide residues in food products have been associated with a broad variety of human health hazards, ranging from short-term effects to long-term toxic effects. The preventive measures for pesticide residues in the developing countries are limited due to a shortage of funds and lack of defined government regulations. The impact of pesticide residues can be minimized by taking certain measures such as the rational use of pesticides, promoting organic farming, exploit natural and bio pesticides, and proper implementation and amendment of pesticide-related laws. The present article has been planned to review various aspects of organochlorine pesticide residues including their accumulation in air, soil, water and food products, impact on human health, and the preventive measures to counter their toxic effects.

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Key words: Agriculture, OC pesticides residues, hazards, human health, pesticides, environment.

INTRODUCTION

Agricultural sector is the largest consumer of pesticides (about 85% of the world's production). The use of pesticides has offered significant economic benefits by enhancing the production and yield of food and fibres and control various pests. In addition, pesticides are also used in public health activities to control the spread of vectors borne diseases (such as malaria and dengue) and unwanted plants (for example, grass And weeds), in the landscaping, parks and gardens. They are also helpful to inhibit or prevent the spread of insect's pests, bacteria, fungi, and algae in refrigerators electronic devices, Paints, carpets, paper, cardboard and food packaging materials (Gilden et al., 2010). Pesticides are one of the few and most important toxic substances released deliberately into the environment to kill unwanted organism. Though the term pesticide is often misunderstood to refer only to insecticides, it is also applicable to herbicides, fungicides, and various other substances used to control unwanted pests' (Matthews, 2006). Organochlorine pesticides (OCPs) belongs to the class of hydrocarbons characterize by its cyclic structure; most of the organochlorine pesticides (e.g., aldrin, chlordane, dichlorodiphenyltrichloroethane (DDT), dieldrin, endrin, heptachlor, and hexachlorobenzene) contain persistent organic pollutants (POPs) that resist degradation and thus remain in the environment for many years (Sharma et al., 2015; Yadav et al., 2015). In addition, these compounds have the potential to accumulate potentially and biomagnify, they can be bio-concentrated 7 million times relative to its initial concentration (Hernández et al., 2013). Repeated application of pesticides leads to the loss of biodiversity and increased resistance of pests, and its effect on other species contributes to the resurgence of pests (Damalas and Eleftherohorinos, 2011). It is estimated that > 95% application of pesticides may affect non-target organisms and become widely dispersed in the environment (Simeonov et al., 2013), such as soil (Kumar et al., 2014), air (Devi et al., 2011), water(Lari et al., 2014) and food (Yu et al., 2012). Similar to other chronic organic contaminants such as polychlorinated biphenyls and polychlorinated dibenzo-p-dioxins/furans (PCDDs/Fs), when these chlorinated compounds are introduced into the environment, they are distributed very slowly and gradually and become part of air, soil, water and persist in living organisms. OCPs are capable of spreading over long distances through atmospheric movement along with human and animal activities. Even large flocks of migratory birds can be a considerable contribution to the spread of these environmental pollutants (Alcock et al., 2008).

However, unintended exposure to pesticides can be extremely dangerous to humans and other organisms because they are designed to be poisonous (Sarwar, 2015). Organochlorine pesticides were extensively used in agriculture throughout the world between 1950 and 1970 (Li and Macdonald, 2005). In recent years, OCPs have gained worldwide concern for decades because of their long half-lives and potential adverse effects on human health (Androutsopoulos et al., 2013). Most of OCPs were banned for use in 1970s in many countries, but many developing countries continue using them in agricultural industry and for malaria control due to their low-cost and effectiveness; as a result of their extensive application, they have been detected in maternal blood (Qu et al., 2010), and even umbilical cord blood (Yanxin Yu et al., 2013), placenta (Ren et al., 2011), and human breast milk(Parsehian, 2008). OCPs can be absorbed into an organism's body through the skin, respiration or if ingested, can be absorbed through the gut wall. Susceptibility to absorption is not consistent across all OCPs with Cyclodienes, hexachlorocyclohexane, endosulfan and lindane passing more freely across the skin barrier than compounds such as dicofol, toxaphene, DDT, mirex and methoxychlor (Amdur et al.,1992). OCPs are quickly consumed in the small intestinal tract and utilise the circulatory system to spread across the body and accumulate in human cells with high fat contents, with a constant exchange occurring between veins and cells. As such, these chemicals are detectable in vein cells (whole veins, cord veins, serum and plasma), adipose cells (identified throughautopsies and living subjects), muscles, hair and breast milk (Tsatsakis et al., 2008; Jakszyn et al., 2009; Tsang et al., 2011; Appenzeller and Tsatsakis, 2012; Mrema et al., 2013). Epidemiological documentation shows increases in occurrence and incidence of diseases related to endocrine-disrupting chemicals, such as breast and prostate cancer, obesity, diabetes, and a decline in fertility in the last 50 years (Coster and van Larebeke, 2012). The present study has been planned to review various aspects of organochlorine pesticide residues including accumulation of pesticide residues in food grains, environmental and various hazards to human health due to pesticide residues as well as preventive measures for the minimization of the impact of organochlorine pesticide residues on human health.

Organochlorine pesticide use in agro-system

The basic advantages of OCPs usage is to get the higher outcome from produce. Improving food production efficiency is one of the greatest concerns the world currently faces. With the human population predicted to grow to nearly 10 billion by 2050, we will need to develop effective and sustainable approaches to feeding the next generation of inhabitants. Current evidence suggests an increase of approximately 97 million per year (Margni et al., 2002). The UN's Food and Agriculture Organization (FAO) has released a startling prediction that global food production needs to increase by 70%, in order to keep speed with the demand of growing population. However, creating a tremendous increase in food manufacturing is replete with difficulties especially given the limited land area available for expansion of agriculture (Saeedi et al., 2016). The importance of pesticides for the most developing nations around the world is proven. Efforts to increase food production capacity are stimulated by the great number of challenges we currently face, such as world population expected to exceed 10 billion by 2050 creating a drastically decreased ratio of arable land to population (Shokrzadeh and Saravi, 2009; Saeedi Saravi and Dehpour, 2016). The use of chemical pesticides has provided a valuable aid to agricultural production, and increasing crop protection and yield. However, the discovery of pesticide residues in various sections of the environment has raised serious concerns regarding their use; concerns which will outweigh the overall benefits derived from them (Ali et al., 2014; Sharma et al., 2014). Organochlorine pesticides (OCPs) have been in wide usage across the world to control agricultural pests and vector borne diseases (Abhilash and Singh, 2009; Zhang et al., 2011). Amongst the OCPs in regular usage, dichlorodiphenyltrichloroethane (DDT), hexachlorocyclohexane (HCH), endosulfan, aldrin, chlordane, dieldrin, endrin, heptachlor, mirex, hexachlorobenzene (HCB) and toxaphene, metoxychlor, and metolachlor are persistent organic pesticides. OCPs are very stable compounds and their half-lives can range from a few months to several years; in some cases decades (Cremlyn, 1991). It has been estimated that the degradation of DDT in soil ranges from 4 to 30 years, while other

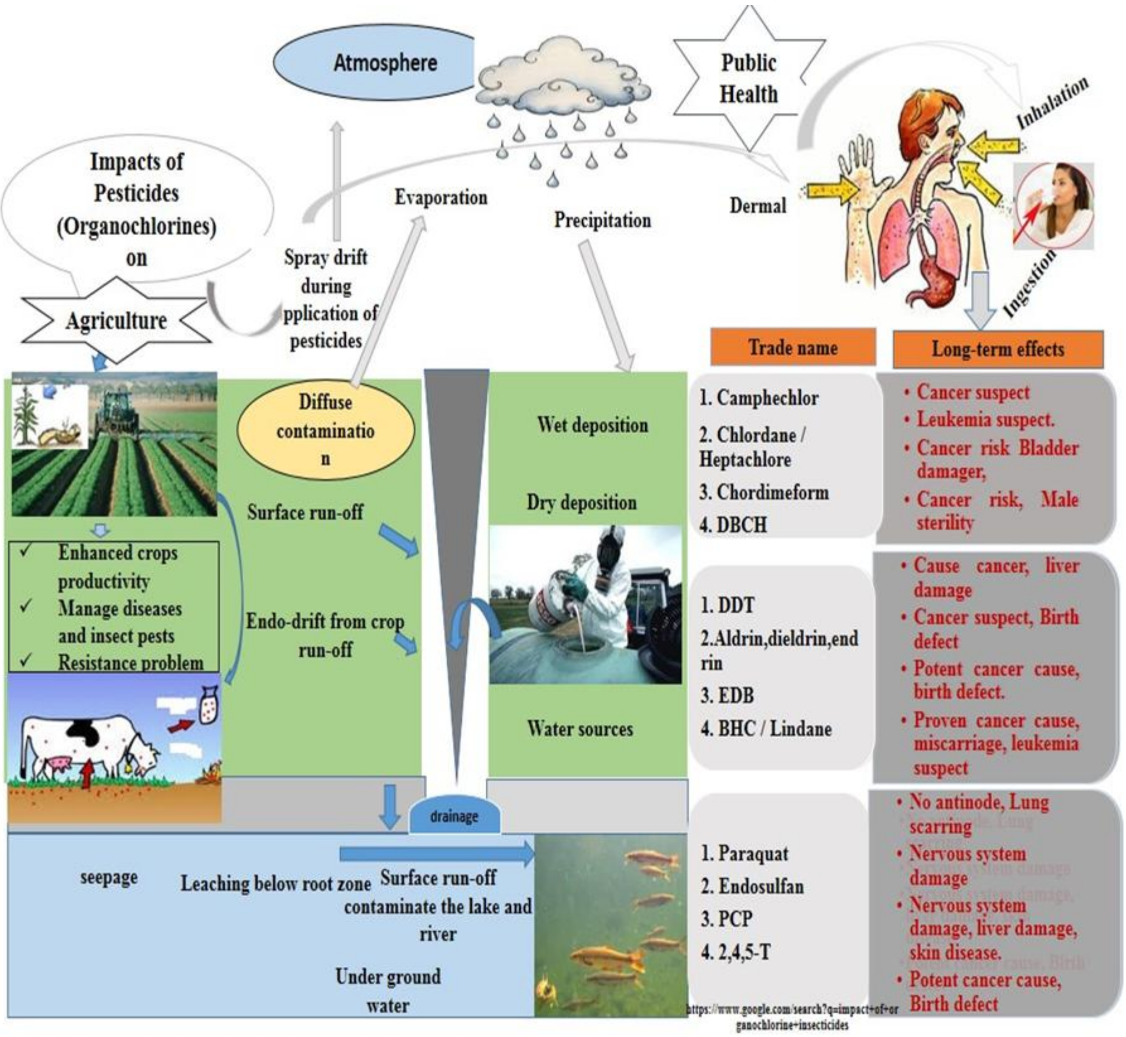


Figure 1: Overview of organochlorine pesticides use and impact on agriculture and public health.

chlorinated OCPs may remain stable for many years after their use (Afful and Anim, 2010). Because of their inability to break down in the environment, their degradation is restricted by chemical, physical, biological and microbiological means (Swackhamer and Hites, 1988; Darko and Acquaah, 2007; Afful and Anim, 2010; Centers for Disease Control and Prevention (CDC) 2017) (Figure 1). They are liposoluble compounds and are capable of bioaccumulating in the fatty parts of biota such as breast milk, blood and fatty tissues (Ntow et al., 2008) in the food chain. As a result, human beings are exposed to the effects of these micropollutants by eating foods in contact with contaminated soil or water (Belta et al., 2006; Júnior and Ré-Poppi, 2007). The over use of these pesticides does not only causes contamination the environmental but also causes serious diseases in humans and high toxicity in most aquatic life (Aiyesanmi et al.,2012) and soil microflora (Megharaj, 2002). The side effects due the exposure to OCPs is dependent on the type used and mode of inducing pest mortality, level of exposure and length of exposure is also critical. Exposure in the environment then allows the pesticides to enter the body through the four major tracks, such as breathing, skin, dental, and ocular (Shokrzadeh and Saravi, 2009).

Organochlorine pesticides OCPs, chemistry, toxicity and persistence in environment

The basic physical characteristics of organochlorine pesticides are high persistence, low polarity, low aqueous solubility and high lipid solubility. Organochlorine pesticides can come into the environment after pesticide applications, polluted wastes discarded into landfills, and discharges from industrial units that synthesize these chemicals. They are volatile and stable; some can adhere to the soil and air, thus increasing the chances of high persistence in the environment, and are identified as agents of chronic exposure to animals and humans. Table 1 shows a comprehensive summary of major organochlorine

Table 1: Overview of some major health problem related to organachlorine pesticides (OCPs).

Disease	Pesticides class	Reference
Breast cancer	β-HCH and p,p′-DDE HCB DDT,DDE, PCB,DDT	(Arrebola et al., 2015; Parada et al., 2016; Randhawa et al., 2015; Jun Li et al., 2013)
Liver cancer	DDT adjusted for DDE level	(McGlynn et al., 2006)
Epithelial ovarian cancer	β-HCH, endosulfan I, p'p'-DDT, p'p'-DDE,heptachlor	(Sharma et al., 2015)
Uterine cervix cancer	Aldrin, DDE. g-HCH, endosulfan, heptachlor	(Polanco Rodríguez et al., 2017)
Bladder Cancer	p,p'-DDD, p,p'-DDT, p,p'-DDE	(Boada et al., 2016)
Malignant breast cancer	p,p0-DDT, PCBs	(Wassermann et al., 1976)
Invasive ductal cancer (IDC)	HCH, PCTA and pp-DDE	(Yang et al., 2015)
Induce breast cancer cell proliferation	p,p0-DDE	(Aubé and Ayotte, 2011)
K-ras mutations in pancreatic cancer	p,p0-DDT	(López et al., 2014)
colorectal cancer growth	p,p'- DDT	(Song et al., 2014)
pancreatic cancer	DDE, DDT and PCBs	(Jane et al., 2000)
Metastatic Prostate Cancer	[β-HCH, γ-HCH, DDT, DDE	(Koutros et al., 2015)
Depression	Aldrin,	(Beard et al., 2013)
Cardiovascular disease	PCB	(Kim and Lee, 2015)
Alzheimer's disease (AD)	Aroclor	(Medehouenou et al., 2014)
Autism spectrum disorders (ASD)	p,p′-DDE DDT	(Ornoy and Ergaz, 2015) (Roberts et al., 2007)
Parkinson's disease (PD)	Endosulfan Heptachlor	(Caudle and Miller, 2005; Wilson and Caudle, 2014; Chen et al., 2017)
Decreased sperm concentration	Higher p,p-DDE concentrations	(Aneck-Hahn et al., 2007)
Decreased sperm concentration	DT–DDE	(Messaroset al., 2009)
Chronic bronchitis asthma	DDT exposures	(Jane et al., 2008; Kolani and Sanda, 2016)
Metabolic syndrome (hypertension, central obesity, dyslipidemia and dysglycemia)	PCBs.	(Rosenbaum and Pavuk, 2017)
Insulin resistance and diabetes	PCBs	(Lee et al., 2011)
Decrease sperm quality	DDT, HCH	(Perry, 2008)

pesticides with their chemical name, structure, toxicity, Chemical type and persistence in the environment. They have a related chemical structure, showing chlorine substituted aliphatic or aromatic rings. Due to their structural resemblances, these compounds share certain physicochemical characteristics such as persistence, bioaccumulation and toxicity. One basic character that they share across the spectrum is persistence, where persistence is defined as half-life greater than two months in water or six months in soil sediment. The persistence of OC compounds varies from moderate persistence with half-life of approximately 60 days to high persistence with half-life up to 10 15 years. The most commonly used pesticide in agricultural practice is dichlorodiphe nyltrichloroethane (DDT), which is moderately hazardous, with high persistence and a half-life of 2–15 years (Augustijn-Beckers et al., 1994). The use of DDT is now banned in many countries but it is still illegally used in most of the developing countries. This applies also to endosulphan, an insecticide which is highly hazardous and has moderate persistence with a half-life of fifty days and is used in the production of cashew.

Toxicity mechanism of organochlorine insecticides

The CYP450 family of enzymes is important for both the activation and detoxification of OPs. The relative rates at which organophosphorothioates (OPTs) insecticides are activated and detoxified may be an important determinant of toxicity. Independently of the chemical structure, bioactivation of OPTs such as malathion, chlorpyrifos, diazinon, azynphos-methyl and parathion to the very highly toxic oxon forms is carried out by the same CYP4 0 systems (Buratti et al., 2005). These insecticides feature a thiophosphate moiety that is subjected to oxidative desulfuration in which the CYP450s remove the sulfur atom attached to the phosphorus and insert atomic oxygen (Figure 2). This results in covalent binding of sulfur to CYP, a reaction that occurs preferentially at cysteine residues leading to an irreversible inactivation of the enzymes that catalyze the reactions. This mechanism based inhibition of CYP450 is a suicide reaction for the P450 carrying out the reaction (Hodgson and Rose, 2007; Kyle et al., 2013).

Organochlorine pesticides residues in environment

As pesticides are designed to be toxic to particular groups of organisms, they can have considerable adverse environmental effects on other living creatures as well as diverse media including air, soil, or water (Aktar et al., 2009). Organochlorine pesticide pollution in various environmental media (such as air, water, and soil) is thus explained bellow.

Organochlorine pesticide residues in air

Pesticides from non-target agricultural crops or volatilization from the treated area may contaminate air, soil, and water. Various instances of pesticide drift occur during every application, even from ground equipment (Yates et al., 2002). Pesticide drift accounts for approximately 2 to 25% chemical loss during application; this can spread over a wide area, from a few yards to several hundred miles. There are many cases of pesticides drifting, in the world, every year (Que et al., 1975). More than 80–90% of pesticides are volatilized within a few days of application on crops or in the health sector (Majewski and Capel, 1995). Atmospheric sources of OCPs include direct emissions and Volatilizes from the surface of water and soil. Many pesticides volatilize (that is, evaporate from the soil and foliage, and move away from the initial application area) and reach into every area of the environment, thereby contaminating them adversely (U.S. Geological Surve, 1995; Rodríguez et al., 2018). Higher levels of HCHs and DDTs were reported in the tropical coastal atmosphere from India and were measured in higher amounts tween 1.45–35.6 and 0.16–5.93 ng/m^{-3}, respectively (Babu et al., 2003). Highly populated and agricultural areas along Indian coastal length and industrial and agricultural areas of Punjab Province, Pakistan were also found contaminated with higher levels of OCPs (Zhang et al., 2008; Syed et al., 2013).

Organochlorine pesticide residues in soil

Sediment is an environmental matrix which is considered as the ultimate sink for POPs (Bhattacharya et al., 2003) and as the best media for temporary and long term monitoring of contaminants (Guzzella et al., 2005). Sediments mainly comprised organic, inorganic particles and detritus which are relatively heterogeneous in terms of biological, physical and chemical characteristics (Bhattacharya et al., 2003). POPs make their way to sediments through surface runoff, leaching, vapour phase, ultimately accumulation and settling in sediments (Sarkar et al., 2008) for a very long time due to their long half- life times (El Nemr et al., 2013). Glaciers are one of the major sources of POPs as they transport huge amounts of rock debris and sediments in their load (Encyclopedia of Earth, 2015). During the water runoff from glaciers, higher amounts of sediments moves in the plains and rivers. These sediments contain some POPs in higher concentrations as compared with the water samples based on hydrophobic properties of POPs, that is, the levels of HCH concentrations were fairly low in water samples when compared with the sediments (Sarkar et al., 2008). The authors highlighted that weathered and aged agricultural soils were the main sources of contamination of DDT in the sediments. Furthermore, another important source was suggested to be the recent illegal use of DDT in the river catchments even after its ban in the country (Malik et al., 2009). Bhattacharya et al. (2003) reported increasing levels of HCHs, DDTs and endosulfan sulfate during pre monsoon months. The order of OCPs was in the following pattern: HCHs N endosulfan sulfate N DDTs N α-endosulfan. Among the DDT metabolites, p-p′-DDT and p′-p′-DDE were found at higher levels with almost 70 to 90% of the total DDTs in the sediments. This distribution of metabolites indicated that DDT was actively degraded in the sediments via dehydrochlorination produced either by biotic or by the abiotic decomposition reaction. Domestic and industrial discharges, extensive agricultural chemicals application and soil erosion were considered as the main sources of OCPs in the study area. At the same location, Malik et al. (2009) conducted another study to analyze DDT in soil depths and results showed that up to 91% of soil samples were found contaminated with DDT along with 67% of those samples that showed the residual DDT levels higher than the value of DDT minimum risk level in the soils (N0.05 μgg^{-1}). Yadav et al. (1981) also reported upward and increasing trend of DDT near the surrounding area of DDT

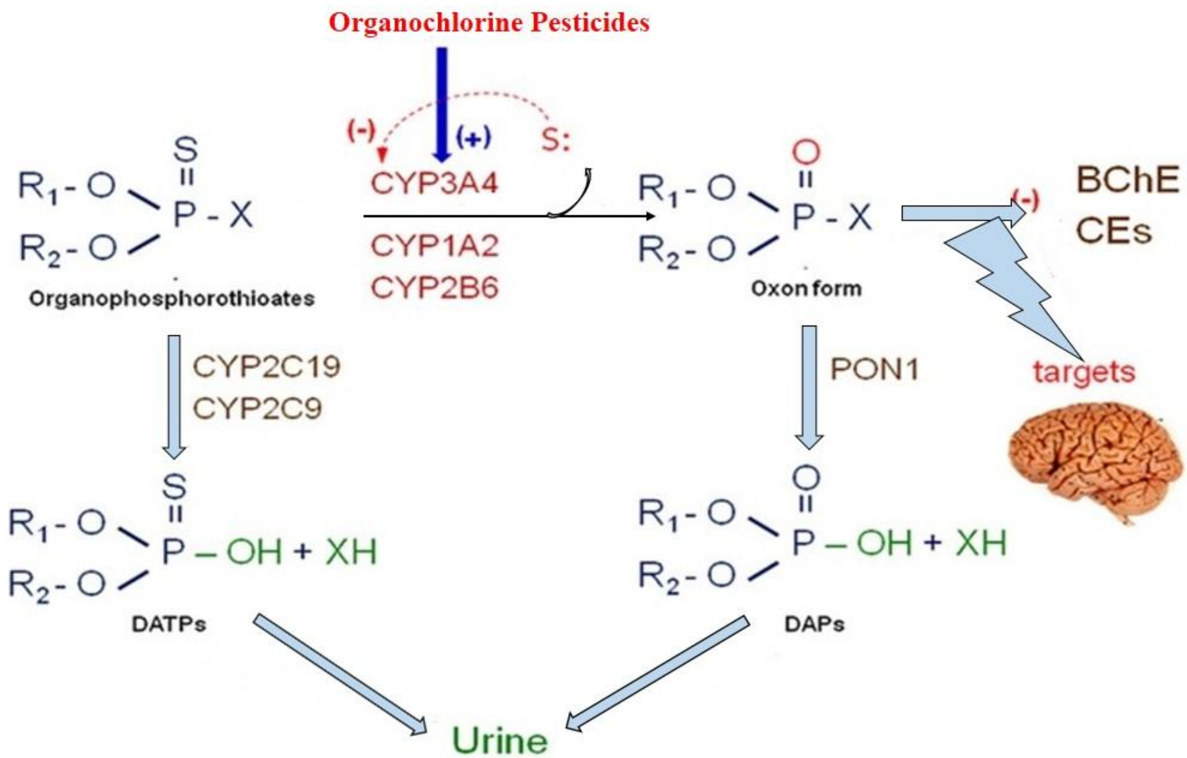


Figure 2: Specific CYP450s may both bioactivate the parent organophosphorothioates (OPTs) to highly toxic oxon forms and concurrently detoxify them by dearylation to form dialkylthiophosphates (DATPs), inactive metabolites. CYP2C9 or CYP2C19 are the isoforms responsible for the dearylation reaction. Bioactivation of OPTs is also carried out byCYP450 systems. At low concentrations, oxon derivatives formation is catalyzed by CYP1A2 and CYP2B6, whereas CYP3A4 is relevant only at high concentrations. The oxon form is a strong esterase inhibitor that can be effectively scavenged by pseudocholinesterase (BChE) and carboxylesterases (CEs), and the remaining free (non-detoxified) amount may reach target organs where inhibit acetylcholinesterase. The oxon can be alternatively hydrolyzed by paraoxonase-1 (PON1) yielding dialkylphosphates (DAPs), inactive metabolites that are excreted through the urine. OPT insecticides feature a thio-phosphate moiety that is subjected to oxidative desulfuration in which the CYP450s remove the sulfur atom attached to the phosphorus and insert atomic oxygen. This is a suicide reaction for the P450 carrying out the reaction. Given that organochlorine pesticides, such as endosulfan- and DDT, are CYP3A4 inducers, prior exposure to these compounds can potentiate OPs toxicity, particularly when these compounds occur at high concentrations (Hernández et al., 2013) with slight modification.

manufacturing plant. According to the authors, the mean value of DDT was 0.34 ppm in 1974, which became upward in 1978 to 1.43 ppm and in 1983 to 1.67 ppm. The authors also suggested the decrease in levels of residual DDT as the distance from the DDT manufacturing plant increases.

Persistent organochlorine pesticide residues in water

OCPs can enter into the aquatic environment through several routes and processes. Major sources and routes into the water included deposition and air–water exchange processes (Guzzella et al., 2011), used as pesticides for crops and malarial control (Ahad et al., 2010; 2001; Ali, 1991; Tariq et al., 2006), ponding irrigation, leaching (Flury et al., 1994), careless disposal of pesticide containers, agricultural runoff and washing of equipment's (Ahad et al., 2010, 2001; Tariq et al., 2006, 2004). In Pakistan, it has been reported that ground water contamination with persistent chemicals is greatly attributed to many factors including shallow water, characteristics of soil and rigorous spraying of the pesticides (Jabbar et al., 1993; Tariq et al., 2004a; 2007b). Among all the components of DDT and HCH, p,p-DDT & γ- HCH were present in major amount in the contaminated water samples collected from India. The contribution of o,p-DDT, p,p-DDT, p,p-DDE, α- HCH, β- HCH, γ- HCH, heptachlor epoxide and Dieldrin were 66.67 % (2008), 66.67% (2009) and 33.33%.

Persistent organochlorine pesticide residues in food

Some classes of pesticides manifest their harm to human health as both exterior discomfort and internal, less visible damage to the body. Pesticide residues are present in all agro-ecosystems, but the real risk to human health is through exposure to residues in primary and derived agricultural products (Jeyaratnam, 1990). Though the application of OCPs has been prohibited in many of the countries, they are still marketed and present in the environment and in human body tissues (Needham et al., 2005; Freire et al., 2014). The persistence of OCPs in the food chain and environment is linked to their slow breakdown and lipophilicity, disposal from animal bodies is a slow process. These pesticides are deposited in the individual adipose cells by making use of infected food, particularly fish and animal fat, consequently building-up and causing harm to the organism (Davis et al., 1993; Barnhoorn et al., 2009).P ersistence pollutant in the food chain may also be responsible for acute effects such as simple skin and eyes discomfort to the general malaise and to serious, chronic problems related to neurological system as well as light intellectual malfunction (e.g. neurobehavioral modifications feelings changes,), psychomotor malfunction, depressive mood and loss of life due to mental illness, neurodegenerative diseases (e.g. Parkinson's and Alzheimer's diseases) and serious neurodevelopment problems and cancers (Migliore and Coppedè, 2009; Kanthasamy et al., 2012; Mustafa et al., 2013). In Nigeria, organochlorines are the most common pesticides applied to food crops on field and during storage (State, 2011). The pesticides detected in the in cereal grains in present study were in the following range; Aldrin (0.03 to 0.13 mg/kg), Dichloran (0.01 mg/kg), Dieldrin (0.018 to 0.02 mk/kg), Endrin (0.0003 to 0.03 mk/kg), Endosulfan (0.005 to 0.02 mg/kg), Heptachlor epoxide (0.02 mg/kg), Lindane (0.25 to 1.25 mg/kg), Methoxychlor (0.03 to 1.17), Mirex (0.008 to 0.02 mg/kg), and DDT (0.04 mg/kg), respectively (Anzene et al., 2014). Beef samples from Buoho had DDE concentration of 31.89 μg/kg in the fat and 5.86 μg/ kg in the lean beef. 1, 1, 1-trichloro-2, 2-bis-(4'-chlorophenyl) ethane (DDT) recorded an average concentration of 545.22 μg/kg in beef fat and 18.85 μg/kg in lean beef samples from Kumasi abattoir (Darko and Acquaah, 2007). The concentration level of the studied organochlorines followed the order: p, p' dichloro-diphenyl-trichloroethane (DDT) > endosulfan>=,p'-DDT >lindane>dieldrin>endrin>aldrin>chlorothanolin, while the order of contamination in the analyzed organs was liver > kidney > meat. Heat treatment of the meat, kidney and liver samples (boiling for 90 min) produced an overall reduction of 62.2, 44.5, 37.7, 29, 31, 34.3 and 30.8% in lindane, o, p'-DDT, endosulfan, p, p'-DDT, chlorothanolin, aldrin, dieldrin, and endrin, respectively (Letta and Attah, 2013). One of the methods used to reduce the effect of pesticide residue in food is to eat organic foods than non-organic ones. According to standard meta-analyses, the frequency of occurrence of detectable pesticide residues was four times higher in non-organic crops than organic crops (Baranski et al., 2014). There is evidence that indicated that organic food consumption can reduce exposure to pesticide residues in food (Smith-Spangler et al., 2012).

Human exposure to organochlorine pesticides

Human exposure to insecticides begins during the period of early prenatal stage and lasts through to the (breast-feeding) neonatal periods, and these stages are very critical for the normal development and differentiation of various sensitive body organs and systems. In fact, after exposure, these toxic chemicals cross the placenta to the foetus and are secreted into the breast milk (Perera et al., 2005). The dietary exposure route in adults accounts for more than 90% of total exposure, while workers may also be exposed through inhalation and skin contact of the organochlorine compound. Organochlorine compounds are rapidly absorbed by the small intestine and enter into the circulatory system where they are distributed throughout the different body parts and stored in body tissues with high lipid contents. As a result of the constant exchange between blood and tissues, these toxic chemicals are able to pass into the bloodstream (cord blood, whole blood, serum and plasma tissues), adipose tissue (in autopsies and living subjects), muscles, and hair and breast milk (Tsatsakis et al., 2008; Adu-Kumi et al., 2010; Covaci et al., 2002; Dewailly et al., 1999; Jakszyn et al., 2009; Kawakami et al., 2017; Król et al., 2013; Li et al., 2008). Exposure to persistent organochlorine chemicals have been found to be associated with health effects including cancer (Aronson et al., 2000; Arrebola et al., 2015; Cohn et al., 2015; Mathur et al., 2002), reproductive defects (Nicolopoulou-Stamati and Pitsos, 2001) and behavioural changes (Zala and Penn, 2004). Further studies have shown that these effect are believe to be associated to their capability to disrupt the function of specific enzymes, hormones, growth factors, neurotransmitters, as well as to inducing key genes involved with metabolism of steroids and xenobiotic (Kleanthi et al., 2008).

Pesticides are formulated to control or eliminate harmful unwanted pests, but it is not surprising that a formulation designed to interfere with an animal's biological functioning can also lead to human health and fitness issues through the stimulation of diverse human physiological processes. Previous work shows that pesticide sprays can indeed be harmful to workers, consumers and any person involved in their handling, production and transport (Luminita, 2017; Saeedi and Shokrzadeh, 2014; Shokrzadeh and Saeedi, 2009). Moreover, there is evidence that the risk of contracting cancer may be raised not just for those handling pesticides, but also for the general population living in an area with higher exposure of pesticides in the environment (Parro´n et al., 2014).

Some classes of pesticides manifest their harm to human health both as exterior discomfort and internal, less visible damage to the body. Though the application of OCPs has been prohibited in many of the countries, they are still marketed and present in the environment and in human body tissues (Needham et al., 2005; Freire et al., 2014). The persistence of OCPs in the food chain and environment is linked to their slow breakdown and lipophilicity; disposal from animal bodies is a slow process. These pesticides are deposited in the individual adipose cells by making use of infected food, particularly fish and animal fat, consequently building-up and causing harm to the organism (Davis et al., 1993; Barnhoorn et al., 2009). The side effects due the exposure to OCPs is dependent on the type used and mode of inducing pest mortality, level of exposure and length of exposure which is also critical. Exposure in the environment then allows the pesticides to enter the body through the four major tracks, such as breathing, skin, dental, and ocular (Saeedi and Shokrzadeh, 2014).

Adverse effects of organochlorine pesticides exposure on human health

Organochlorine pesticides (OCPs) such as dichlorodiphenyltrichloroethane (DDT), hexachlorocyclohexanes (HCHs), chlordanes, hexa-chlorobenzene (HCB) and Mirex are persistent, lipophilic chemicals that are known to accumulate in human tissues (Lange et al., 2014). They also degrade slowly in humans, animals, air, water and soil and are subject to long-range transport (Yu et al., 2013; Sharma et al., 2014). Thus, exposure to OCPs has been associated with human health risk of arthritis, skin disease, bone disorder, endocrine disruption, developmental abnormalities, reproduction failure, and cancer and nerve disorder. For humans, food is the major pathway for exposure to OCPs (Sudaryanto et al., 2006; Hedley et al., 2010). The risk of health hazards due to organochlorine pesticides exposure depends not only on how toxic the ingredients are but also on the level of exposure. In addition, certain people such as children, pregnant women, or aging populations may be more sensitive to the effects of pesticides than others chemicals.

Cancers

Pesticides constitute a diverse class of chemicals extensively used for prevention of harmful effects caused by pests. Among the large number of different pesticides is the organochlorines (OCs). Thus exposure to an environment comprised of widely used chemicals designed to treat pests (e.g., insects), have been associated with adverse human health outcomes such as cancers (Alavanja et al., 2004; Blair et al., 2015), reproductive defects(Nicolopoulou-Stamati and Pitsos, 2001) and behavioural changes (Zala and Penn, 2004). Numerous experiments have confirmed the harmful effects of DDT on humans (Cárdenas-González et al., 2013; Wong et al., 2015) (Table 2). There are four broad categories of risk factors for cancer including lifestyle, genetic/familial, reproductive/ hormonal and environmental. However, these known risk aspects describe only a small fraction of cases. Further studies have shown that the hormones effects and environmental factors are becoming increasingly important as breast cancer risk factors (Fredslund and Jørgensen, 2012; Olsen et al., 1997; Salehi et al., 2008; Zhang et al., 2015). Research focussing on agricultural workers indicates that a greater risk of prostate cancer may be associated with the use of pesticides, primary amongst them being OCPs (Band et al., 2011). Moreover, some of the OCPs, e.g. DDT, HCH, chlordane, HCB, and heptachlor, have been found to be 'most likely carcinogenic' to human (Group 2B) by the International Agency for Research on Cancer (Stewart and Wild, 2014). Organochlorine pesticides were reported to increase the risk of hormone-related cancers including breast, prostate, stomach and lung cancer (Wolf et al., 1993). Recently, dioxins have been found in human ovarian follicular fluid, which may lead to the development of endometriosis. Exposure to dioxins can cause several autoimmune diseases, including multiple sclerosis and eczema (Sinaii et al., 2002). Organochlorines can function as xenoestrogens and compounds such as TCDD, methoxychlor and alachlor were reported to exert effects on human and experimental animals due to inhibited synthesis and increased degradation of thyroid hormones. Moreover, it has been reported that the negative effects of organochlorine pesticide may not be universally applicable and may be dependent on their particular distribution and use. Securing the environmental safety, reliability of quality of pesticides and safety in its application are widely seen as important challenges for pesticide governance. As a result, small-hold farmers have suffered problems due to the lack of proper information available regarding the safety and correct use of pesticides (Belay et al., 2015).

Respiratory and skin diseases

According to the World Health Organization, chronic respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), were the leading cause of total world morbidity (6.2%) and the third leading cause of all global deaths (7.1%) in 2008 (Physician, 2014). Asthma is the most common chronic disease, affecting ~14% of children in the world, and its prevalence has been increasing for several decades (Pearce et al., 2007). In addition, respiratory diseases are the most common causes of death among children under 5 years of age (Phuong et al., 2017). It is now accepted that, besides viruses and bacteria, environmental agents can induce or exacerbate airway inflammation, which can be a predictor of chronic respiratory diseases (Dalphin, 1998; Michielsen et al., 2002) (Table 2). Some environmental risk factors are now well known, such as allergens, tobacco smoke, gaseous or particulate air pollutants, and exposure to certain chemicals, such as pesticides (Bessot et al., 1996; Hoppin et al., 2003). However, the overuse of these agro-chemical

Table 2: Some important organochlorine pesticides (OCPs), their chemical structures, toxicity, chemical type and persistence in environment. Copy from (Jayaraj and Sreedev, 2016) with slight modification.

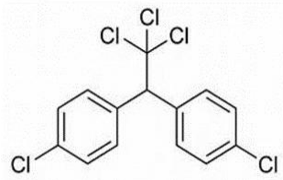
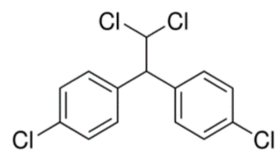
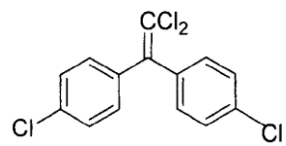
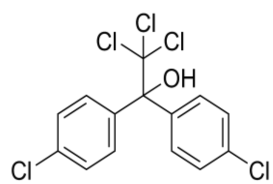
Chemical name	Structural formula	Chemical Type	Toxicity LD_{50}	WHO classification based on rat oral LD_{50}	Persistence in environment
(1) Dichlorodiphenyltri-chloroethane (DDT) $C_{14}H_9Cl_5$	 	Acaricide Insecticide	**Rat:** Oral: 113–130 mg/kg Dermal: 2510 mg/kg **Mice:** Oral: 150–300 mg/kg **Gunia Pigs:** Oral: 300 mg/kg **Rabbit:** Oral: 400 mg/kg	Moderately hazardous	High Persistence Half-life: 2–15 years
(2) 1,1-dichloro-2,2bis (p-chlorophenyl)ethane (DDD)	 	Insecticide	**Rat:** Oral: 4000 mg/kg	Acute hazard is unlikely	High Persistence Half-life: 5–10 years
(3) Dichloro diphenyl dichloroethane (DDE)	 	Insecticide	**Rat:** Oral: 800–1240 mg/kg	Slightly hazardous	High Persistence Half-life: 10 years
(4) Dicofol $C_{14}H_9Cl_5O$	 	Acaricide	**Rat:** Oral:684–1495 mg/kg **Rabbit:** Oral: 1810 mg/kg Dermal: 2.1 g/kg	Moderately hazardous	Moderate persistence Half-life: 60 days

Table 2: Continued.

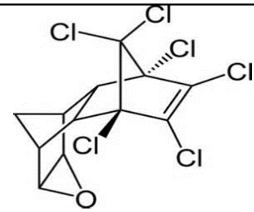
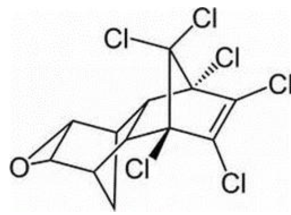
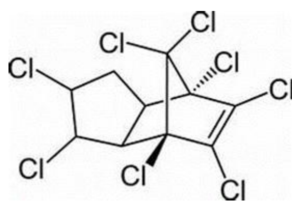
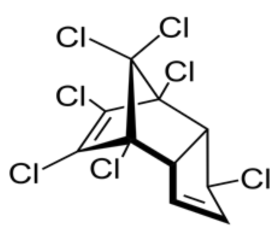
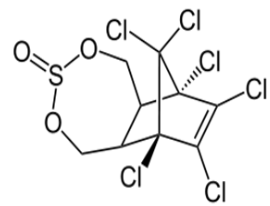
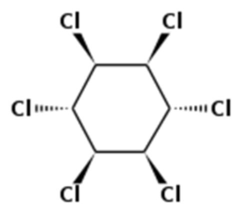
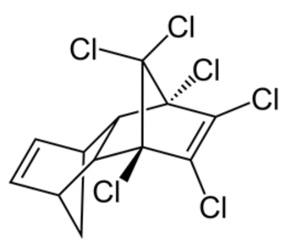
(5) Endrin $C_{12}H_8Cl_6O$		Avicide insecticide	**Rat:** Oral: 3 mg/kg Dermal: 15 mg/kg **Mouse:** Oral: 1.37g/kg Intravenous: 2300 g/kg	Highly hazardous	Moderate Persistence Half-life: 1Day to 12 Years
(6) Dieldrin $C_{12}H_8Cl_6O$		Insecticide	**Rat:** Oral: 46 mg/kg Dermal: 50–120 mg/kg **Mouse:** Oral: 38–77 mg/kg **Dog:** Oral: 56–120 mg/kg **Rabbit:** Oral: 45–50 mg/kg	Highly hazardous	High Persistence Half-life: 9 months
(7) Chlordane $C_{10}H_6Cl_8$		Insecticide	**Rat:** Oral: 200 to 700 mg/kg Dermal: 530–690 mg/kg **Mice:** Oral: 145–430 mg/kg Dermal: 153 mg/kg **Rabbit:** Dermal: 780 mg/kg	Moderately hazardous	High Persistence Half-life: 10 years
(8) Heptachlor $C_{10}H_5Cl_7$		Insecticide	**Rat:** Oral: 40– 220 mg/kg Dermal:119–320 mg/kg **Mouse:** Oral: 30–68 mg/kg **Rabbit:** Dermal: 2000 mg/kg	Highly – Moderately hazardous	High Persistence Half-life: 2 years

Table 2: Continued.

(9) Endosulfan $C_9H_6Cl_6O_3S$		Insecticide	**Rat:** Oral: 18 to 220 mg/kg Dermal:74 mg/kg **Rabbits:** Dermal:200–359 mg/kg	Highly hazardous	Moderate Persistence Half life Alpha Isomer:35daysBeta Isomer:150days
(10) Lindane $C_6H_6Cl_6$		Acaricide Insecticide Rodenticide	**Rat:** Oral: 88 – 270 mg/kg **Mouse:** Oral: 59–246 mg/kg	Moderately hazardous	High Persistence Half-life: 15 months
(11) Aldrin $C_{12}H_8Cl_6$		Insecticide	Oral: 39 to 60 mg/kg Dermal: 100 mg/kg **Mouse:** Oral: 44 mg/kg **Dog:** Oral: 65–95 mg/kg	Highly hazardous	Moderate Persistence Half-life: 4–7 years

substances may have effects on community health, mainly in vulnerable populations, for example, children and pregnant women living in agriculture areas. It has been demonstrated through bio monitoring, that in agricultural areas, inhabitants have elevated urinary levels of pesticide metabolites. Persistence pollutant in the food chain may also be responsible for acute effects such as simple skin and eyes discomfort to the general malaise and to serious, chronic problems related to neurological system as well as light intellectual malfunction (e.g. neurobehavioral modifications feelings changes), psychomotor malfunction, depressive mood and loss of life due to mental illness, neurodegenerative diseases (e.g. Parkinson's and Alzheimer's diseases) and serious neurodevelopment problems and cancers (Migliore and Coppedè, 2009; Kanthasamy et al., 2012; Mustafa et al., 2013). Moreover, some of the OCPs, e.g. DDT, HCH, chlordane, HCB, and heptachlor, have been found to be 'most likely carcinogenic' to human (Group 2B) by the International Agency for Research on Cancer (Stewart and Wild, 2014). Pesticide classification is currently set according to WHO categories, which is based on the threat posed by use of the pesticide, and these have been divided into categories as shown in Table 3.

Other related diseases caused by the exposure of OCP

Some classes of pesticides manifest their harm to

Table 3: Classification of pesticides based on toxicity criteria (World Health Organization, 2010).

Type	Toxicity level	LD_{50} for the rate (mg/Kg body weight)	
		Oral	Dermal
la	Extremely hazardous	<5	<5
lb	Highly hazardous	5-50	5-50
l1	Moderately hazardous	50-2000	50-2000
U	Unlikely to present acute hazard	2000 or higher	-------

human health as both exterior discomfort and internal, less visible damage to the body. Though the application of OCPs has been prohibited in many of the countries, they are still marketed and present in the environment and in human body tissues (Needham et al., 2005; Freire et al., 2014). In children, exposure to dioxins showed significant positive associations with learning disability (LD) (Lee et al., 2007). Risk of attention deficit hyperactivity disorder (ADHD) at higher levels of p,p'-DDE and PCBs exposure was reported (Sagiv et al., 2010). Prenatal exposure to p,p'-DDE and its presence in cord serum was found to lead to disappearance of neuronal development after 12 months of infant age (Torres-Sánchez et al., 2009). Epidemiological studies have shown that exposure to persistent organic pollutants, mainly organochlorine pesticides, is strongly associated with type 2 diabetes. Some persistent organic pollutants, such as highly chlorinated PCBs and transnonachlor, were associated with the incidence of type 2 diabetes in obese people (Lee et al., 2006). Detection of organochlorine pesticides in human breast milk was reported from many places in the world. In Croatia, p,p'-DDE was found to be the dominant organochlorine pesticide in human breast milk (Klinčić et al., 2014). Exposure of infants to chlordanes via breast milk was reported as a potential health risk in Korea (Lee et al., 2013). Another study from Korea also revealed the presence of organochlorine pesticides (OCPs) chlordanes, aldrin, dichlorodiphenyltrichloroethane (DDTs), dieldrin, heptachlors, endrins, hexachlorocyclohexanes (HCHs), hexachlorobenzene (HCB), toxaphenes and mirex, in milk (Kim et al., 2013). Organochlorine pesticides HCB, β-HCH, pp'DDE, pp'DDT, pp'DDT and Σ-DDT were present in breast milk of the population in Guerrero, Mexico, proportionally to exposure (Chávez-Almazán et al., 2014). Several of the most prevalent forms include leukaemia, non-Hodgkin's lymphoma, and brain, bone, breast, ovarian, prostate, testicular and liver cancers (Cantor et al., 1992). A study reported that children who live in homes where their parents use pesticides are twice as likely to develop brain cancer as those who live in residences in which no pesticides are used (Bradman et al., 2007; CDC, 2011). There is also mounting evidence that exposure to organochlorine pesticides disrupts the endocrine system (Mnif et al., 2011), the reproductive system, and embryonic development. Endocrine disruption can cause infertility and a variety of birth defects and developmental defects in offspring, including hormonal imbalances and incomplete sexual development, impaired brain development, behavioural disorders, and many others (Alavanja et al., 2004).

FUTURE PROSPECTS AND CONCLUSIONS

Although pesticides are developed to prevent or control insect pests in agricultural system. Current review reveals that higher levels of OCPs are widely distributed in different environmental compartments and food, which causes serious harmful effects on human health. There are indeed many inherent problems in conducting large-scale trials to directly assess the causality of human health issues related to the use of pesticides. The excess consumption of pesticides contributes in the accumulation of pesticide residues in food grains and vegetables associated with variety of human health hazards, including damage to central and peripheral nervous systems, cancer, allergies and hypersensitivities, reproductive disorders, and disruption of the immune system. The impact of pesticide residues can be minimized by preventive measures such as rational use of pesticides, washing and proper processing of food products, practicing organic farming, use of natural pesticides, bio-pesticides, and strict implementation and amendment of pesticide-related laws.

To reduce the risk posed by exposure to OCPs, we need to drastically reduce the presence of harmful chemicals in our ecosphere (our air, water, ground and food). There should be further application of non-toxic and cultural methods of agriculture to achieve sustainable control of our insect and weed problems rather than maintaining a reliance of pesticide synthetic compounds. Plant-derived chemical components and sustainable methods of biological control are key to our community's health and health of the ecosphere. Stricter regulations regarding aerial spraying and establishment of buffer areas could be implemented to reduce the effects of drift. A reduction in the application of OCPs to crops, soil and water systems may be achieved through using non-chemical control methods to kill pests.

The public should be informed of the threat of diseases cause by the exposure of OCPs and the link to exposure to those facing frequent exposure should be carefully monitored for development of diseases. Laboratory testing should be available for assessing OCPs such as DDE and, PCBs and the major metabolite of DDT, in blood vessels or in adipose cells. The sharing of data acquired through monitoring should be anonymised and be made available as widely as possible to allow interpretation by the wider scientific community. Women should be made aware of the potential risks associated with breast-feeding if they have been subjected to OCPs. Otherwise, the overall health benefits of breast-feeding may be outweighed by any threat of exposure of the baby to OCPs. Lastly, ongoing study is needed on these pollutants, their body burden, prospective health effects and methods to diminish their bioavailability in food and environment. Additionally, effective strategies are needed to control their manufacturing and release into the atmosphere.

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