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ORIGINAL PAPER

Global footprints of organochlorine pesticides: a pan-global survey

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Abstract Organochlorine pesticides (OCPs) are ubiquitous environmental contaminants widely used all over the world. These chlorinated hydrocarbons are toxic and often cause detrimental health effects because of their long shelf life and bioaccumulation in the adipose tissues of primates. OCP exposure to humans occurs through skin, inhalation and contaminated foods including milk and dairy products, whereas developing fetus and neonates are exposed through placental transfer and lactation, respectively. In 1960s, OCPs were banned in most developed countries, but because they are cheap and easily available, they are still widely used in most third world countries. The overuse or misuse of OCPs has been rising continuously which pose threats to environmental and human health. This review reports the comparative occurrence of OCPs in human and bovine milk samples around the globe and portrays the negative impacts encountered through the long history of OCP use.

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Introduction

Organochlorines (OCs) are the group chlorinated compound with high environmental persistence and are widely used all around the world as a potent pesticides. They are highly to moderately soluble in most organic solvents and the solubility usually increases with the temperature. They are lipophilic in nature and have a very low biodegradation rate (Rani et al., 2017).

The organochlorine pesticides (OCPs) were extensively used worldwide in the 1950s and 1960s to increase the supremacy in a variety of crops, to compensatethe demand of ever-growing world population. OCPs, first synthesized in 1884, became noticeable during the WWII for its use as an insecticide to control vectors for diseases such as malaria and typhus (Al Antary et al., 2015). The postwar era saw OCPs being used extensively in the agricultural sector as a potent pesticide in addition to its use in IRS (indoor residual sprays) for vector control (Al Antary et al., 2015). The OCPs provided cheap and remarkably effective option for disease management, thereby leading to an increase in agricultural production (Keswani, 2019, 2021).

Basic properties of most of the OC compounds include retaining stability in normal physical or biochemical processes by virtue of their strong carbon–chloride covalent bond, no polarity causing low solubility in water and high solubility in hydrocarbon-like environment (lipophilicity), such as in adipose tissue (Angulo et al., 1999; Borgå et al., 2002; Falandysz et al., 2004; Solomon & Weiss, 2002). These properties make OCs beneficial in industrial field, resulting in production of approximately 15,000 OC classes that found vast range of uses in manufacture of industrial products, viz. plasticizers, solvents, lubricants, dielectric fluids and pesticides (Keswani et al., 2019). The natural level of OC substances is very low and thus harmless, including the 2000 compounds that are known to be produced by living organisms (Tian, 2011). OCPs are divided into four groups:

- Dichlorodiphenylethane or diphenyl aliphatics [DDT (dichlorodiphenyltrichloroethane), DDD (dichlorodiphenyldichloroethane), dicofol, ethylan, chlorobenzilate and methoxychlor]
- Cyclodienes [CHL (chlordane), aldrin, dieldrin, heptachlor, endrin, dodecachloropentacyclodecane (mirex) and endosulfan (cyclic ester of sulfuric acid)]
- Cylohexanes [α-HCH, β-HCH and lindane (ϒ isomer of HCH)]
- Chlorinated camphenes [toxaphene and chlordecone]

The most ample of all man-made OC compounds are the PCBs (polychlorinated biphenyls) and the pesticide DDT, which were used widely in the USA since 1945 (Gebremichael et al., 2013). The Stockholm Convention was implemented in May 2001 to eliminate the POPs (persistent organic pollutants) from the environment by banning the production and restricting their agriculture and industrial uses. The OCs that were included in the convention as POPs were aldrin, CHL, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene (HCB), mirex and toxaphene (http://www.pops.int/) (Table 1).

Every year, approximately 3 million new cases of pesticide poisoning are reported worldwide with more than 10% resulting in death, as estimated by WHO (Tian, 2011). DDT is the most frequently used OC compound in developing countries. OCPs are stable, with low solubility in water, with high affinity to lipids and long shelf life, making it prolonged and tenacious threat to the ecosystem (Al Antary et al., 2015). Even when the ban of OC compounds in China was implemented in 1983, considerable amounts of this hazardous pesticide are still found in environment (Ezequiel, Miguel, Gustavo, and Nora, 2015). OCP has capability to constantly accumulate without disintegration in the human fatty and adipose tissues over a period of time; therefore, even minimal exposure over time may result in potential health risks (Klinčić et al., 2014). The exposure to OCP can be through various sources. Direct exposure in farmers and workers involved in OCP production, supply and indoor residual sprays (IRS) or indirect exposure through drinking groundwater, food and air or contact are some of the routes through which OCP can enter human system (Tian, 2011). According to reports, approximately 25 million agricultural workers are exposed to pesticide poisoning globally (Aslam, Rais, and Alam, 2013). The toxicity of OCP depends upon the human doses and period of exposure. Exposure to doses around 280 mg/kg shows symptoms such as nausea, vomiting, convulsions, fatigue, flu-like symptoms, whereas chronic exposures affect various organ systems such as hepatic, renal, nervous and immune system, resulting in cancers, neurologic symptoms, infertility and other disorders (Al Antary et al., 2015).

The adverse effects of OCP on human health and environment led to an international call for its ban in late 1960s (Hernik et al., 2014). The ban was successful in developed countries, but in developing countries, its low cost, easy availability and effectiveness as pesticides and vector control caused hindrance in complete ban of OCPs (Hernik et al., 2014). India alone uses over 88,000 metric tons of pesticides annually out of which 70% are OCPs (Tian, 2011).

Table 1 Major OCs, their structure, chemical formula and physical properties. Source: https://pubchem.ncbi.nlm.nih.gov (accessed on March 15, 2021)

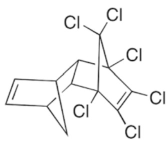
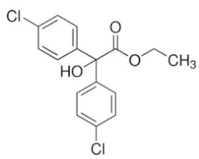
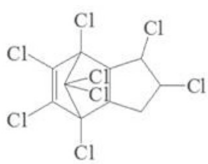
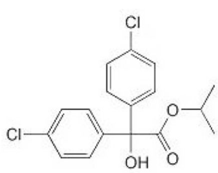
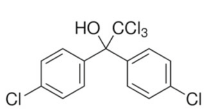
Name	Structure	Formula	MW (g/mol)	Solubility	Appearance	MP (°C)	BP (°C)	PubChem CID
Aldrin		$C_{12}H_8Cl_6$	364.9	ethanol, ether, and acetone.	colorless to dark-brown crystalline solid	104	145	12310947
Chlorobenzilate		$C_{16}H_{14}Cl_2O_3$	325.2	most organic solvents, including petroleum oils, benzene, and methyl alcohol	light brown crystalline solid	37 °C	146-148	10522
CHL		$C_{10}H_6Cl_8$	409.8	miscible with aliphatic and aromatic hydrocarbon solvents, including deodorized kerosene	colorless, viscous liquid	106	175	5993
Chloropropylate		$C_{17}H_{16}Cl_2O_3$	339.2		white powder	73	148-150	22094
Dicofol		$C_{14}H_9Cl_5O$	370.5	white crystalline, wettable powder	colorless solid	77.5	180	8268

Table 1 continued

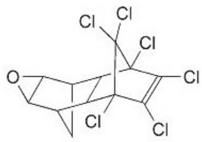
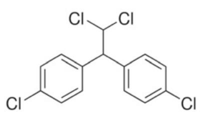
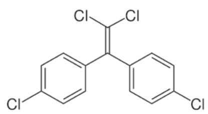
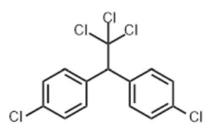
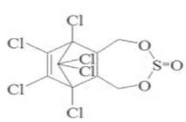
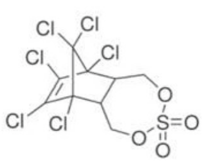
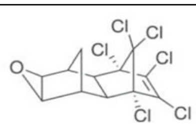
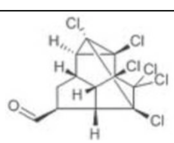
Dieldrin		$C_{12}H_8Cl_6O$	380.9	aromatic solvents; moderately soluble in acetone	light-tan flaked solid	176-177	385	969491
DDD		$C_{14}H_{10}Cl_4$	320	organic solvents and slightly in chloroform	colorless crystalline solid	109.5	350	6294
DDE		$C_{14}H_8Cl_4$	318	fat and most organic solvents	white crystalline solid	89	336	3035
DDT		$C_{14}H_9Cl_5$	354.5	acetone, ether, benzene, carbon tetrachloride, kerosene, dioxa ne, and pyridine	colorless crystalline	108.5	260	3036
Endosulfan		$C_9H_6Cl_6O_3S$	406.9	xylene, kerosene, chlor oform, acetone, and alcohol	Brown crystals	70- 100	106	3224
Endosulfan sulfate		$C_9H_6Cl_6O_4S$	422.9	water		181.5		13940
Endrin		$C_{12}H_8Cl_6O$	380.9	acetone, benzen e, carbon tetrachloride, h exane, and xylene	white crystalline , odorless solid	200	245	12358480
Endrin-aldehyde		$C_{12}H_8Cl_6O$	380.9		White solid	235	435	12147604

Table 1 continued

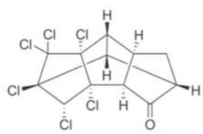
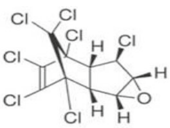
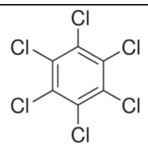
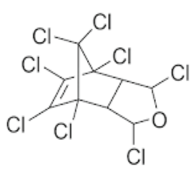
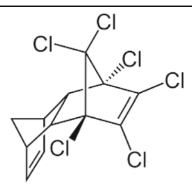
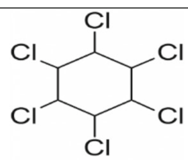
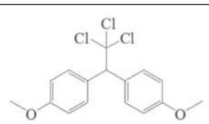
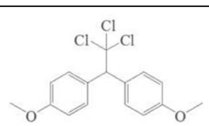
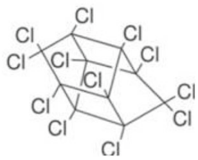
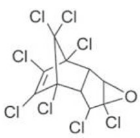
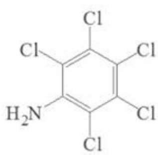
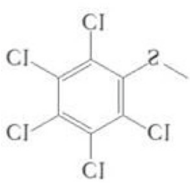
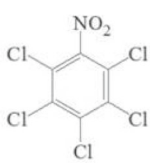
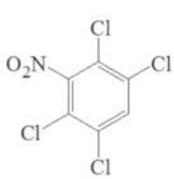
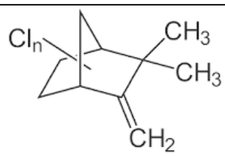
Endrin-ketone		$C_{12}H_8Cl_6O$	380.9		White solid	280	457.7	97299269
Heptachlorepoxide		$C_{10}H_5Cl_7O$	389.3			160-161.5	425.5	13930
HCB		C_6Cl_6	284.8	benzene, chloroform, and ether	white crystalline	231	323-326	8370
isobenzan		$C_9H_4Cl_8O$	411.7	ether, acetone, benzene, xylene, heavy aromatic naphtha	whitish to light-brown crystalline powder		120-122	9271
Isodrin		$C_{12}H_8Cl_6$	364.9			104-105	145	2087
Lindane		$C_6H_6Cl_6$	290.8	acetone and benzene	white crystalline powder	112.5	323.4	727
Methoxychlor		$C_{16}H_{15}Cl_3O_2$	345.6	ethyl ether, benzene, and alcohol	Colorless to light-yellow crystals with a slight, fruity odor	87	346	4115
Methoxychlor		$C_{16}H_{15}Cl_3O_2$	345.6	alcohol	Colorless to light-yellow crystals	87	346	4115

Table 1 continued

Mirex		$C_{10}Cl_{12}$	545.5		Solid	485		16945
Oxychlordane		$C_{10}H_4Cl_8O$	423.7		solid	144	353	13785700
Pentachloroaniline		$C_6H_2Cl_5N$	265.3	alcohol, ether, and petroleum ether		235		10693
Pentachlorothioanisole		$C_7H_3Cl_5S$	296.4					15766
Quintozene		$C_6Cl_5NO_2$	295.3	CO_2, benzene, and chloroform	Off-white or yellow crystals	144	328	6720
Tecnazene		$C_6HCl_4NO_2$	260.9	ethanol, benzene, and chloroform	pale yellow crystals	99.5	304	8330
Toxaphene		$C_{10}H_9Cl_9$	448.2			65- 90	155	40544

Impact on ecosystem

The OCPs are long-term persistent molecules in the environment, commonly called POPs, because of their slow degradation rate and high lipophilicity, that also accounts for the bioaccumulation of OCP and PCB molecules in the ecosystem (Kumar et al., 2008; Nakata et al., 2005).

Humans, being at the top of food chain, have high threat of exposure to these pesticides. OCPs from the fields and industry contaminate the soil, water bodies and the aquatic ecosystem. Being volatile, they also possess a huge threat as air contaminant. The ill effects of OCPs can also be defined in terms of its toxic and harmful impact on many non-target organisms (Al Antary et al., 2015).

The Stockholm Convention, regulates the worldwide production, use and monitoring of POPs. The initial "dirty dozen" agents included in Stockholm Convention were aldrin, CHL, DDT, dieldrin, endrin, heptachlor, HCB, mirex and toxaphene. HCH isomers such as α-α, β-β and ϒ-ϒ were also included in the list of POPs of the Stockholm Convention in 2009 because of the potential adverse effect of HCH on environment and humans (ATSDR, 2002b; Organization, 2007, 2010). Endosulfan α-α and β-β and its metabolite endosulfan sulfate were included in the list of POPs by Stockholm Convention.

India, China and Russia were among the nations who opted out on total ban of OCPs, in Stockholm Convention, (Dash et al., 2007). The decision of incomplete ban on the production and use of DDT was because no other option was available for malarial vector control (Studies by Eriksson 1989).

In India, DDT was banned for agricultural use in 1989 (Corsolini et al., 1995; Voldner & Li, 1995), but is still in use as pest control agent for vectors in malaria, kala-azar, dengue, etc. HCH ban on production and sale came into effect only from April, 1997 onwards (Mukherjee & Gopal, 2003). Lindane is also under restricted production and can only be used for termite control in agriculture and infrastructures (The Gazette of India, 2007). Lindane affects the nervous system, hepatic and renal functioning, and a potential carcinogen, like all other OCPs (ATSDR 2005; Humphreys et al., 2008).

DDT and DDE are the most abundant OC compounds found in any ecosystem. The biological half-life of DDT metabolites-p,p'-DDT and p,p'-DDE was found to be 6 and 10 years, respectively (ATSDR, 2002a; Gao et al., 2000).

Human exposure

The OCP contamination on the human body is mainly through two routes: inhalation of contaminated air and consumption of animal-based foods such as fishes and other seafood from the contaminated water bodies, milk and dairy products (Wang et al., 2013).

The characteristic properties of OCPs such as biomagnification and lipophilicity make them a greater risk factor for humans (Li et al., 2008; Misumi et al., 2005). As humans are on the top of food chain, they consume the maximum OC pesticide burden than other living organisms of the same chain.

Routes of exposure

The OCPs easily enter the human body through nasal and oral route, i.e., inhalation of contaminated air or through animal-based food. The exposure to OC substances may also occur through skin absorption (Ezequiel, Miguel, Gustavo, and Nora, 2015). It is estimated that approx. 95% of OC pesticide intake in human body is through contaminated food (Darnerud et al., 2006; Fierens et al., 2003) in which milk and dairy products constitute 30% of the total (Focant, Pirard, Thielen, and De Pauw 2002; Bordajandi et al., 2004).

Bioaccumulation of OCs in fishes and other animals and their products (meat and dairy products) due to its high fat solubility contributes in major exposure of OCP in human via ingestion (Pandit et al., 2002). Approx. 90% of PCB and dioxin intake is via food and not from drinking water (Croes et al., 2012). Another way is through regular and long-term skin absorption of OCs and other endocrine disrupters (mainly parabens, bisphenols, phthalates and benzophenones) present in cosmetic products (Ishaq & Nawaz, 2018; Rêgo et al., 2019). Many cosmetics of underarm and upper breast area are with estrogenic activity and their regular use may lead to continuous dermal exposure and consequently to the absorption and accumulation in underlying tissues (Tomovska, Hristova, Trajkovska, and Gjorgievski, 2013). OC compounds bioaccumulate in human body, precisely in human adipose tissue, breast milk and blood due to its lipophilicity. However, adipose tissue reflects steady concentration of lipophilic chemicals, while whole blood, serum and plasma's OC compound concentration is influenced by blood lipids, and may be biased (Aslam, Rais, and Alam, 2013). Human hair can represent a person's total exposure to POPs from both endogenous and exogenous sources, making it a possible biomonitor for evaluating OCs and other POP exposure for public health (Raab et al., 2011). Measuring body burdens of OC substances and their metabolites indicates almost correct exposure value and is helpful in making coalition between exposure and health outcome (Aslam, Rais, and Alam, 2013). As even small amount of exposure over prolonged period of time can cause magnified accumulation, levels of OCs in human tissues are positively associated with increasing age and with the rate of consumption of polluted products (Berruga, Molina, Althaus, and Molina, 2016; Tian, 2011). It has been observed that vegetarians (i.e. people consuming vegetables, fruits and grain with no animal products) have much lower levels of OCs compared to individuals who consume animal-based products (Tian, 2011). Additionally, inhabitants of developed countries (North America and Western Europe) have lower levels of OCs than inhabitants of developing countries, probably reflecting differences in exposure (Klinčić et al., 2014).

Prenatal and antenatal exposure

The OCPs accumulate approximately twenty times more in infants than the adult. The high rate of OCP transfer in early life results in accumulation of 6% of total OC pesticide burden acquired during the life span to happen in the first six months itself (Chen et al., 2015). The prenatal exposure to some OCPs such as DDT increases the risk of premature birth and low birth weight and can harm the mother's ability to breast feed (Rogan & Ragan, 2003). The other OCPs such as β-HCH on prenatal exposure results in altered thyroid hormone levels and can affect the child's brain and neural development (Alvarez-Pedrerol et al., 2008). The reports show the decline in maternal OC pesticide burden during the lactation period (Croes et al., 2012; Hooper et al., 2007; Skaare & Polder, 1990). But other studies contradict this finding by stating that the level of OC pesticide in breast milk increases or remains same (Ennaceur & Driss, 2010; LaKind et al., 2009; Lee et al., 2013). Human breast milk provides the noninvasive specimen to access maternal OCP burden and infant exposure to the same for accessing the risk factor associated with it. The WHO (1984) established ADI (Acceptable daily intake) for DDT at20 µg/Kg body wt./day for adults (Smith, 1999).

Fetal exposure of OC substances and other POPs is mainly through placental transfusion (Zhou et al., 2011). The exposure to OCPs (PCBs, DDT, DDE and dioxins) is determined by blood analysis of infants' umbilical cord (Tian, 2011). However, a recent study suggests that placenta may cause hindrance in transfer of OCs from maternal to fetal circulation (Witczak et al., 2016). The study shows that OCs accumulate in the placenta and the concentration was always higher in maternal blood than cord blood (Kang, Park, Chang, and Choi 2008). OC compounds exposure continues postnatal via lactation. Many studies have suggested that the OC levels decline significantly during pregnancy and lactation due to high alcohol consumption (Rojas-Squella et al., 2013; Shaker & Elsharkawy, 2015). Lactation is the major cause of lowering OC burden in women (Mishra & Sharma, 2011). Thus, it can be concluded that infant has already accumulated burden of OC substances from the very first months of its existence (Yalçın et al., 2015).

Since OCs are lipophilic, they are accumulated in mammary glands and secreted along with breast milk. Therefore, human breast milk is the major source of exposure to newborn infants (Schiavone et al., 2010). Mother's breast milk analysis gives a measure of postnatal exposure, and by the age of four year, child's blood can also be used for analysis purpose (Tian, 2011). It is an established fact that OCs are mobilized from fat deposits only during starvation or lactation (Song, Ma, Tian, Tong, & Guo, 2013a, b). As the fetal and the neonatal periods are important periods regarding the development and differentiation of human body, the possibility of exposure to OCs during these times are of particular concern. The secretion of OCPs through breast milk can reduce the maternal OC pesticide burden, but exposes the infant at an early stage.

There are evidences that suggest that mammals are more susceptible to ill effects of OCs and other POPs during fetal and neonatal period than adulthood (Rojas-Squella et al., 2013). The reason behind this is many. Firstly, the fetus may be exposed during the extremely sensitive and crucial period of organogenesis and development. Secondly, because many of the normal detoxification mechanisms and the immune system of the fetus and infants are not fully developed, exposure to even low doses of OCs may lead to adverse effects (Luzardo et al., 2012). Thirdly, fetuses and infants are exposed to unusually high levels of OCs compared to their total body mass and it cannot be metabolize or excreted at the same rate as the OC intake (Song, Ma, Tian, Tong, & Guo, 2013a, b).

OC toxicity

OCs are transformed in human body by hepatic cytochrome P^{450} enzymes (Johri et al., 2008), and because of its high lipophilicity, the OCPs show high affinity to the central nervous system (CNS), liver and adipose tissues. The pesticides are metabolized by the formation of glucuronide conjugates (dieldrin), sulfur (endosulfan) and phenolic (lindane) derivatives, and then, they are eliminated from the body by the passage of urine, bile, feces and breast milk (Sullivan & Krieger, 2001).

The difference in biodistribution of different OCP compounds also dictates its toxicity, such as in HCH isomers, where β-HCH always shows more concentration, while ϒ-HCH rarely reaches high concentration in the samples. The reason behind this observation is that the α-HCH and ϒ-HCH is rapidly metabolized into β-HCH inside liver (Willett et al., 1998).

In the same manner, the presence of p-p' DDE in the sample indicates the previous exposure of DDT in the area, as p-p' DDE is the intermediate DDT metabolite. The ratio DDE/DDT is one of the main tools to reflect whether the DDT exposure was recent or long term. The more the concentration of DDE (in comparison with DDT), the older the exposure to DDT in the area from where the analyzed sample was collected. The ratio DDE/DDT when greater than one reflects the lack of any recent exposure (Terrones et al., 2000). Being the POP, the DDE/DDT ratio is particularly useful to estimate the risk factor for DDT.

The OCPs are highly toxic, even lethal for the human being. They can disturb the endocrine system even at low level (Colborn, Vom Saal, and Soto, 1993; Kalpana, 1999). They mainly have neurobehavioral effects (Handal et al., 2007), interfere with the reproductive system (Tiemann, 2008), affect the immunological system (Reed et al., 2004) and have carcinogenic effects (Snedeker, 2001).

The acute poisoning symptom includes nausea, vomiting, oropharyngeal burning, anxiety, gastrointestinal disturbances, etc. Lindane, dieldrin, endrin, CHL, heptachlor, toxaphene and strobane have higher chances of causing seizures.

Hepatic

The hepatic function and disruption of OCPs are carried out mainly by inducing the enzymes that perform drug transformation of anticoagulants, barbiturates, analgesics, anti-inflammatory drugs, etc. and endogenous substances such as steroid hormones. This also explains the anti-estrogenic effect of OCPs. The DDT and its metabolites such as DDD, DDE and DDA [2,2-Bis(4-chlorophernyl)-acetic acid] are potent enzyme (CYP450) inducers (Stehr-Green, 1989).

The presence of β-HCH and p, p' DDE levels in fatty tissue is positively related to the gall stone disease (Ji et al., 2016). The studies also shows that the expression of cholesterol transporters ABCG5/G8 in liver can be induced by the presence of β-HCH and p, p' DDE levels (Yu et al., 2002).

Central nervous system

The binding capacity of diphenyl aliphatic group such as DDT, DDD, DDE, dicofol, ethylan, chlorobenzilate and methoxychlor, to sodium ion reduces transport of potassium ion across the cell and increases the sodium ion transport inside the cell. The voltage channels across axonal membrane play an active role in Na^{+} binding and delay of inactivation gates. These events finally result in muscle twitching, convulsions and eventually death (Crinnion, 2009; Nomura & Casida, 2011). These effects are also the characteristics symptoms of acute poisoning of OCPs.

Other group of OCPs such as cyclodienes interacts with GABA neurotransmitter receptor and inhibits the chloride ion cell entry. The blockage of inhibitory stimulus across the cell membrane causes hyperabnormal CNS excitability (Ezequiel, Miguel, Gustavo, and Nora, 2015). This function of cyclodienes is opposite to the working of diphenyl aliphatic groups.

The OC exposure is also linked with other nervous system disruptions such as neuro-endocrine dysfunctions (Briz Herrezuelo, 2011; Tiemann, 2008), deficits in learning and memory, as well as locomotives and behavioral disorders (Mariussen & Fonnum, 2006).

Endocrine system

A vast number of the OCPs such as DDT and its derivatives, methoxychlor, dieldrin, endosulfan and lindane have xeno-estrogenic effects (Johnson et al., 1992; Lemaire et al., 2006). The OC compounds act on ER-α and ER-β. OCPs can also affect the retinoic acid receptor (RAR) and the pregnenolon X receptor (PXR) (Lemaire et al., 2006). They also have the ability to repress the activation of androgen receptor, particularly progesterone (Guo et al., 2008). DDT in particular inhibits the testosterone synthesis (Kelce et al., 1995).

Immunological toxicity

The OCPs on long-term exposure affect various vital enzymes and proteins, viz. antioxidant enzymes, neurotransmitter receptors and transporters (Slotkin & Seidler, 2009), metabolic enzymes such as acetyl cholinesterase, ion channels or pumps–Mg^{2+} Na^{+}/K^{+} and Ca^{2+} ATPase in the plasma and mitochondrial membrane (Jia & Misra, 2007) and are affected by the chronic exposure of OCPs.

Carcinogenic effects

The bioaccumulation of various OCPs plays an important role in increasing risk factor for cancers of breast, lung, cervix, prostate, endometriosis, hypospadias and cryptorchidias being the most common (Ritchie et al., 2003; Rodríguez et al., 2017; Soroush et al., 2016).

The direct association between the amount of exposure to OCPs and cancers is still a matter of ongoing debate. Indeed, in addition to their known estrogenic characteristics, OCs have been especially implicated as risk factors for breast cancers because of their high affinity to breast tissues. However, OCs such as lindane and DDT have been shown to increase cell proliferation of MCF-7 human breast cancer cells (Zou & Matsumura, 2003).

The interaction of OCs with endocrinological processes resulting in toxic effects in human and animals is supported by many studies, but the studies linking the effect of pesticides on MAPK cascades are scarce. Heptachlor is known to cause hepatocyte proliferation in rats either by induction of ERK phosphorylation or by the inhibition of apoptosis (Okoumassoun et al., 2003). Many studies suggest heptachlor as potent human mitogen by suggesting that it increases the amount of phosphorylated ERK1/2 in human lymphocytes (Ledirac et al., 2005). However, if we consider the more recent studies, heptachlor, like endosulfan, is shown to induce apoptosis in lymphocytes of human (Rought et al., 2000; Villeneuve et al., 2000).

Global impact of ocps

Asian countries

In Taiwan, China, the limited use of OCPs and the use of substitutes in agricultural practice instead have resulted in the use of DDT from 3595 ng/g to 333 ng/g of breast milk. The minimum amount of DDT was 19 ng/g and HCH was 0.8 ng/g (Chao et al., 2006). The levels in China were found lowest among the Asian countries. It was lower than Thailand, Indonesia and Vietnam. The mean concentration of α-HCH was 0.133 ng/g lipids, and DDT concentration was found to be 0.161 ng/g lipid (Wang et al., 2018).

In other study conducted on breast milk samples from the 12 provinces of China, twenty-three OC pesticide compounds were tested positive in the samples. The most abundant OCPs were DDTs, HCHs and HCB with the average concentration of 527.2, 231.8 and 32.8 ng/g lipid, respectively. CHLs, aldrins and mirex were also present in the samples but at relatively low concentration. The low DDE/DDT ratio suggested recent use of DDT in the Fujian region of China. The infant EDI (Estimated Daily Intakes) values for DDTs, HCHs and HCB were close or higher than the suggested TDIs by the Canada's guidelines in five regions (JinZhu et al., 2010).

In Shanghai region of China, breast milk collected over five years demonstrates a decreasing trend of DDT, HCH and HCB level. All the samples had high level of p,p'-DDE (average 655.4 ng/g lipid wt.) and β-HCH (average 172.5 ng/g lipid wt.). The estimated daily intakes (EDIs) of HCH in 56% sample exceeded the TDIs given by Canada guidelines (0.3 µg/Kg body wt.), but for HCB (0.10 µg/Kg body wt.) and DDT, the EDIs was found below the suggested TDIs (Grasso et al., 2012).

Dicofol or Kelthane (trade name) is manufactured from DDT and can be a source of DDT contamination (Qiu et al., 2005; Turhan & Turgut, 2009). In China, the breast milk level of dicofol was very low, thus suggesting that it does not play any role in total DDT contamination (Fujii et al., 2011).

In Beijing, China, HCB was detected in 100% analyzed breast milk samples. The average concentration of HCB in the breast milk was 55 µg/Kg fat (range 10.9 -0.160.5 µg/Kg fat). The EDIs value for the infant (0.20 µg/Kg body wt./day) was found to be higher than TDIs value (0.17 µg/Kg body wt./day) as suggested by WHO guidelines (Song et al., 2013a, 2013b). Comparing the observed value to the survey of 2002 (Sun et al., 2005), there is a decrease of 92% in the concentration of HCB in human breast milk. This sharp decrease is attributed to the ban of HCB production since 2004 in China (Wang et al., 2010). On comparison, the mean value of HCB in breast milk in China was either higher than the other developing Asian countries or in the same range (Devanathan et al., 2009; Sudaryanto et al., 2005).

In India, continuous analysis of breast milk samples as well as bovine milk samples is carried out to estimate the hazardous effect of OCP residue in the ecosystem (Abhilash & Singh, 2009). The studies have shown a declining trend in the mean concentration of OCPs and increase in DDT metabolites in comparison with the non-metabolized DDT, but the rate is slow in comparison with the developed nations and some other developing countries. The presence of various OCPs in samples at alarming level is mainly because of the delayed and partial ban in India, comparing to developed nations and its continuous use, i.e., DDT is still in use for vector control as no better option is available, while HCH is used in paint industry (Abhilash & Singh, 2009; Corbel & N'Guessan, 2013).

In Haryana (India), following the ban of HCH and DDT for agricultural use in 1988, the comparison of bovine milk samples collected in 1992 and 1998 shows a decline of 67.5% in ΣHCH concentration and 92.8% in ΣDDT concentration. The study also shows that the main contaminant during 1992 was p,p'-DDT, but during the analysis of 1998 sample, p,p' -DDE was found to be the main contaminant, suggesting very limited recent exposure of DDT (Kaushik, Sharma, Gulati, and Kaushik 2011).

The main source of dairy contamination was attributed to the presence of HCH and DDT in dry and green fodder (Kang et al., 2002), use of insecticide for malaria control, presence of HCH and DDT in air, groundwater (Asi et al., 2008), dry aerial fallout and seed cakes (the feed supplement for cattle during winter) which is made from cotton and soyabean seeds mainly (Kumar & Nath, 1996; Nag & Raikwar, 2008).

The mean DDT concentration was found to be 14.32 ng/g lipid wt. in the breast milk samples collected from Chennai. In the two decades after global OC pesticide ban, the DDTs and HCH level in human breast milk showed escalation (Devanathan et al., 2009). The reason behind this could be the illegal use of DDT for agriculture practice even after the ban.

In Assam (India), the mean level of ΣDDT and ΣHCH concentration was found to be 3040 and 2525 ng/g lipid wt., respectively, in the breast milk samples (Sharma et al., 2014). The EDIs for infants exceeded the TDI for DDT (20 µg/Kg body wt./day) and HCH (0.3 µg/Kg body wt./day) given by FAO/WHO, in all the obtained samples (Henson & Humphrey, 2009).

Milk samples from the local dairy farms of Maharashtra (India) showed abundance of HCH isomers and DDT. The mean concentration of ΣDDT and ΣHCH was 0.026 and 0.052 mg/Kg, respectively. The residue value of ΣDDT and β-HCH did not cross the tolerance limit of 1.0 mg/Kg and 0.075 mg/Kg, respectively, set by the FAO/WHO (Pandit et al., 2001).

Among the milk products, butter and cheese showed the higher accumulation of OCPs. This is supported by other studies conducted in Slovakia (Čonka et al., 2014), India (Gill et al., 2009) and Mexico (Akhtar & Ahad, 2017). The bovine milk samples from the urban Delhi showed the presence of lindane in all the analyzed samples (range 0.0001–1.082 µg/g) with 50% of sample exceeding the MRLs value. The presence of p,p'-DDT in 70% of sample (mean concentration 0.01565 µg/g) and p,p'-DDE with the mean concentration of 0.0996 µg/g in 80% of sample is attributed to the fact that DDT is still in use in India (Aslam, Rais, and Alam, 2013).

The region of Punjab (India) also showed the same trend. 312 bovine milk samples were taken directly from the farm for the study and were found contaminated with mainly DDT (1.6 µg/Kg milk), ϒ-HCH (0.9 µg/Kg milk), β-endosulfan (1.2 µg/Kg milk) and endosulfan sulfate (0.6 µ/Kg milk). Out of the total samples, the MRLs for lindane exceeded in only 12 samples, while for DDT the MRL crossed in 18 samples. In addition, 1 sample had endosulfan significantly above MRL value (Bedi et al., 2015). This could be because of the continuous use of DDT in India.

According to the USEPA, at the lower bound limit of these pesticides, the population is safe from its hazardous health effect. But at the 95th percentile of upper bound limit, these values possess a risk factor for the infants and children (Rajan et al., 2015).

Pakistan also showed the slow decreasing rate of OC pesticide residues in the samples. Some samples showed worrying results, but other samples showed the success of OC pesticide ban and measure taken to control its hazardous effects (Eqani et al., 2012). The milk samples from the local market in Sahiwal were analyzed and found that the mean value for DDT (4.2 µg/Kg), DDE (3.13 µg/Kg) and endosulfan sulfate (91.3 µg/Kg) was lower than the MRLs value of 40, 40 and 100 µg/Kg, respectively. On the other hand, dieldrin, ϒ-HCH (11.82 µg/Kg), α-endosulfan (112.69 µg/Kg) and β-endosulfan (107.16 µg/Kg) crosses the MRLs of 6, 100 and 100 µg/Kg, respectively (Ishaq & Nawaz, 2018).

The pesticide residue analysis in the dairy sample obtained from the cotton growing belt of Punjab, Pakistan, showed the contamination of aldrin, DDT, DDE and endosulfan in 35%, 10%, 9% and 7% of the samples, respectively. The concentration of aldrin in the samples was found to be highest with the mean value of 0.68 µg/mL of milk. The mean concentration of DDE and DDT was 0.04 and 0.01 µg/mL of milk, respectively. The low level of DDT residue in all the samples is indicator of successful ban of DDT use (ul Hassan, Tabinda, Abbas, and Khan, 2014).

South Korea showed successful results of OC pesticide ban. The total concentration of OCPs ranged from < LOD to 559 ng/g lipid wt. It is found to be lower than European, African and Asian population. The total concentration of OCPs was found to be related to the consumption of more seafood (Bokyung et al., 2013). The estimated daily intakes (EDI) of OCPs were calculated to be 625–1259 ng/Kg body wt./day. It was lower than the threshold value provided by the USEPA and Health Canada (Epa, 2008; Lee et al., 2013).

In the Asiatic regions of Turkey, DDT, β-HCH, aldrin and heptachlor were the most abundant OCPs found in the milk sample. The median values of DDTs, β-HCH and aldrin in breast milk were found to be 126.5, 48.5 and 22.1 ng/g lipid wt., respectively. 4% of milk samples were OCP-free and other OCPs such as endosulfan, endrin and other isomers of HCH were detected in less than 25% of samples (Yalçın et al., 2015).

In Mersin, Turkey, p,p'-DDE 325.047 ng/g lipid, β-HCH 36.297 ng/g lipid, p,p'-DDT 10.536 ng/g lipid, dieldrin 8.559 ng/g lipid, HCB 5.447 ng/g lipid, oxychlordane 1.586 ng/g lipid and cis-heptachlorepoxide 0.001 ng/g lipid were the main OCPs found in the human breast milk samples (Çok et al., 2012). The proposed TDI by the Health Canada Guideline did not exceed for any of the OC compounds. Compared to the previous data (Cok et al., 2011), a decreasing trend of OCP concentration in breast milk was observed. The current β-HCH levels (36.297 ng/g lipid) showed a lower value on comparison from the previous studies performed in Turkey (490 ng/g lipid: 285 ng/g lipid: 149 ng/g lipid, respectively) (Cok et al., 2004, 2005; Erdogˇrul & Şener, 2005). The presence of OCPs in the milk samples was not affected by the maternal age, education, gestational age, parity, infant gender, sleep pattern of infant, etc. The presence of α-HCH was more frequent in milk sample from anemic mothers in comparison with the milk sample from non-anemic mothers (Yalçın et al., 2015).

In Turkey, cow, buffalo and sheep's milk was found to be contaminated with twenty-one different pesticides, namely α, β, ϒ and δ HCH, HCB, heptachlor, aldrin, trans-CHL, α and β endosulfan, cis-CHL, dieldrin, p,p'-DDE, endrin, p,p'-DDT, methoxychlor, etc. The maximum concentration was of β-HCH (63.36 ng/mL), followed by the mean concentration of methoxychlor (27.17 ng/mL). The EDI levels did not cross the ADI values recommended by the Codex Alimentarius Commission (Bulut et al., 2011).

In Iran, the mean concentration of α-HCH, β-HCH and ϒ-HCH was 1123, 1520 and 419 ng/g lipid, respectively. The total DDT concentration was found to be 15 ng/g lipid. The mean concentration of HCB was found to be 570 ng/g lipid, which exceeded the MRL threshold (Shahmoradi et al., 2019).

European countries

In Norway, the mean concentration of α-HCH, β-HCH and ϒ-HCH was found to be 2, 0.12 and 0.0914 ng/g lipid, respectively, in human breast milk samples (Li & Macdonald, 2005).

In Spain, HCB was found in all the conventional and organic brand samples of milk under study with the median value of 2.22 ng/g fat, but it was always below the MRLs by the European Legislation (Molina et al., 2005). The ΣHCH level in conventional samples was 2.69 ng/g fat, which was higher than the 1.38 ng/g lipid value of the organic milk samples. The p,p'-DDE concentration in conventional and organic sample was found to be 4.85 and 4.74 ng/g fat, respectively. The EDIs for all the OC pesticide compounds were found to be lower than the TDI established by the European Food Safety Authority (EFSA) (Luzardo et al., 2012).

According to the First Regional Monitoring Report of Western Europe and Other State Group Region (UNEP 2009), the mean DDT concentration was found to be 156.3, 126.5, 81.9, 69.6 and 33.1 ng/g lipid wt. in the breast milk samples obtained from Belgium, Turkey, Sweden, Norway and Finland, respectively (Yalçın et al., 2015).

In Greece, the supplementary feed given to sheep and goats during winter was found to be contaminated with OCPs; the milk samples from the farms were not identified as any health hazard and were safe for the human consumption (Tsiplakou et al., 2010). The main OC pesticide contamination found in the animal feed was the α and β isomers of endosulfan with the mean concentration of 2.82 and 2.39 mg/kg, respectively. The average value of total endosulfan (5.36 mg/Kg) was much higher than the MRLs given by the European Union Pesticide Residue Legislation.

In 2013, the highest concentration of contaminants was found in the raw milk sample obtained from the region of Lysinin. Average values of p,p'-DDE, p,p'-DDT and aldrin in Lysinin were 4.574, 1.88 and 4.76 ng/g (w/w), respectively. 20% of sample exceeded the permissible limit for lindane (0.1 ng/g lipid) set by the Ordinance of the Ministry of Health, 2007. This suggests the recent use of lindane for various purposes and its slow degradation rate in the environment. The increased percentage of DDE in the total of DDT value implies that no recent exposure of DDT was seen in the studied areas (Witczak et al., 2013).

In 2016, the milk samples from goat of two organic farms were analyzed for the presence of OCPs and positive result was obtained for the DDT and its metabolites, different isomers of HCH, endosulfan and methoxychlor among the other. The highest concentration among the HCH isomer was of ϒ-HCH (lindane) with the average value of 4.85 ng/g lipid. The highest DDT concentration was 14.76 ng/g lipid, and among its metabolites, p,p' DDE had the highest concentration value of 7.86 ng/g lipids. Among the endosulfan compounds, endosulfan sulfate had the highest concentration of 6.59 ng/g lipids. The entire detected residue in the goat milk samples under study were below the MRLs (Witczak et al., 2016).

In Germany, 525 breast milk samples from urban as well as rural areas were analyzed for the OCPs. The HCB, p,p' DDE and the β-HCH were found in almost all the samples with the median concentration value of 0.016, 0.063 and 0.006 mg/Kg lipid. The DDT concentration values were higher than the reference value of 0.5 mg/Kg lipid in 5% of the samples (Raab et al., 2011). Compared to the data of 2005, the levels of OCPs in breast milk showed a very slight decreasing trend. The concentration of β-HCH and ϒ-HCH in northern Germany was 26.8 and 3.7 ng/g lipid, respectively (Zietz et al., 2008).

In Czech Republic, samples of goat milk were treated and analyzed for different temperature conditions and at different time periods. As the treatment time progressed, the pesticide degraded and the content of pesticide in milk decreased (Bo et al., 2011).

The elimination and degradation of pesticides is also carried out by the sterilization process (Donia et al., 2010). The highest mean value of OC pesticide was obtained on heating the milk at the temperature of 63–65 °C for 30 min and was 0.073014 (w/w% of fat). The minimum OC pesticide mean value of 0.025086 (w/w% of fat) was obtained at 89–100 °C for 1 s. The presence of DDT, endosulfan, lindane, etc. confirms the use of OCPs in the region for insecticidal use (Tomovska, Hristova, Trajkovska, and Gjorgievski, 2013).

In Belgium, the breast milk sample was analyzed and all the 84 samples were found contaminated with HCB, p,p'-DDE (23.3 ng/g lipid), oxychlordane (1.3 ng/g lipid) and β-HCH (3.5 ng/g lipid). Comparing the data with WHO, the Belgium study, found that aldrin, endrin, endrin ketone, heptachlor, trans-heptachlor epoxide, some DDT metabolites (o,p'-DDD, o,p'-DDE and o,p'-DDT), toxaphene, endosulfan, α-CHL and ϒ-CHL, α-HCH, 4,4′-methoxychlor and pendimethalin not of any concern for Belgium population as they were not detected in any of the samples (Croes et al., 2012).

The primiparae breast samples collected from two regions of Croatia showed the predominant presence of p,p'-DDE and ϒ-HCH. The excessive presence of p,p'-DDE in the sample assures that there was no recent fresh application of DDT. The EDIs of these OCPs (total DDT-0.11 µg/Kg body wt./day: ϒ-HCH-0.22 µg/Kg body wt./day) were found not of urgent concern for the infant's health as it was way lower than the TDI (ΣDDT-10 µg/Kg body wt./day: ϒ-HCH-5 µg/Kg body wt./day) value given by FAO/WHO (Klinčić et al., 2014).

African countries

In Libya, the breast milk samples demonstrated the presence of seven among the initial dirty dozen OCPs. This included dieldrin, aldrin, endrin, CHL, heptachlor, DDT and HCB. The mean concentrations of these OCPs were higher than the MRLs, and thus, it suggests the necessity of periodic monitoring of milk samples in Libya.

In Northern Tanzania, the milk samples tested found positive for the presence of p, p'-DDE but the high DDE/DDT ratio suggested the previous exposure to DDT. The high level of dieldrin in breast milk (max 937 ng/g lipid wt. and in 66% of total sample) suggest the recent exposure of dieldrin in the area. The mean concentration of ϒ-HCH or lindane was 7.42 ng/g lipid wt. HCB was detected in incredibly low levels.

In agroindustrial zone of Upper Egypt, five OCPs, namely alachor, dieldrin, HCB, lindane and methoxychlor, were detected in the samples of raw buffalo milk. The tolerance level for the lindane set by the European Commission, crossed in 44% of total given samples. The average concentration for lindane was found to be 0.131 mg/Kg. The HCB (average concentration 0.028 mg/Kg) and methoxychlor (average concentration 0.46 mg/Kg) residue exceeded the MRLs in 88% and 66% samples, respectively. The alachlor and dieldrin did not cross the MRLs (Shaker & Elsharkawy, 2015).

On analysis of cow and human breast milk from three different regions of Ethiopia (Asendabo, Serbo and Jimma town), only DDT and its metabolite contamination were found. The three main metabolites of DDT detected in the samples were p,p'-DDT (55–71% of total DDT), p,p'-DDE (26–39% of total DDT) and p,p'-DDD (2–5% of total DDT). The DDT/DDE ratio value was 2.01, which was found higher than the values reported from the other countries and thus signify the recent exposure of DDT in the area. The mean EDIs (62.17 µg/Kg body wt./day) were alarmingly three times higher than the ADI value recommend by the WHO/FAO for DDT (20 µg/Kg of body wt.) (Gebremichael et al., 2013).

North American countries

In Mexico, the average concentration found in bovine milk sample for various OCPs were α-HCH and β-HCH (3.62 ng/g), ϒ-HCH/lindane (0.34 ng/g), heptachlor (0.67 ng/g), DDT and isomers (1.53 ng/g) and endrin (0.66 ng/g). The average concentrations for all the OCPs were below the permissible limit given by the FAO/WHO/Codex Alimentarius (Gutiérrez et al., 2012). Another study in 171 human breast milk samples was conducted, and the median concentration of OCPs (mg/Kg fat) was found as: HCB (0.009), β HCH (0.004), p,p'-DDE (0.760), p,p'-DDT (0.045) and o,p'-DDT (0.016). The lower value of these pesticides is because of more than 30 years of the OCP ban (Chávez-Almazán et al., 2014).

South American countries

Columbia scored lowest in terms of average p,p'-DDE concentration, according to the First Regional Monitoring Report for POP under the Stockholm

Convention. The mean value of p,p'-DDE was found to be 203 ng/g of lipid, and the maximum value was found to be 14,948 ng/g lipid (Rojas-Squella et al., 2013).

In Brazil (2012), among the 100 pasteurized bovine milk samples analyzed, aldrin was present in 44% samples, following which total DDT, mirex, endosulfan, CHL, dicofol, heptachlor and dieldrin were found in 36%, 34%, 32%, 17%, 14%, 11% and 11% of samples, respectively. The ΣDDT concentration was found to be below the given MRLs in all the samples. But 47% of samples exceeded the CHL MRL value (2.0 ng/g of fat), 14% samples exceeded the MRL value for aldrin and dieldrin (6.0 ng/g of fat), and heptachlor MRL value (6.0 ng/g of fat) exceeded in 30% of contaminated samples (Avancini et al., 2013).

Discussion

The various OCPs were used to increase agriculture productivity, and the later was used as vector control agent. Excessive and injudicious use resulted in the deposition of OCPs in the ecosystem. Their slow degradation rate played a big role in increased contamination of OCPs. The residues from agricultural and industrial sector accumulated in the soil, groundwater and air (Rêgo et al., 2019). The farm animals and the aquatic life accumulated these OCP residues through the diet (Tsiplakou et al., 2010). The bioaccumulation and biomagnification of these OCPs resulted as a consequence of passing on to the successive level in food chain became a greater risk factor for humans as they were the end consumers.

The lipophilic property of OCPs leads to their deposition in fatty tissues such as adipose tissue and breast tissue (Shahmoradi et al., 2019). This possesses a risk as the OCPs are then released into breast milk and are transmitted to the next generation. OCPs are capable of passing the placental barriers also, resulting in prenatal exposure to the fetus (Mishra & Sharma, 2011; Yalçın et al., 2015). The exposure is taken seriously because of its capability to pose several health hazards (Ezequiel, Miguel, Gustavo, and Nora, 2015). The ill effects on human and environment health caused by OCPs combined with its efficiency to last in the environment for several decades make them a great health risk factor and needs to be monitored periodically (Rêgo et al., 2019).

The OCPs are known to cause neurobehavioral, immunological, carcinogenic effects, apart from gastrointestinal, hepatic and neural disturbance on acute exposure. OCP possesses a higher risk of being carcinogen in people living in constant exposure of these compounds in the form of pesticides (Bedi et al., 2015). Malwa village of Punjab (India) reported 46% of the total 34,430 cancer deaths in the whole state as OCP was extensively used as pesticides in cotton farming in the area (Awasthi, and Awasthi, 2019). The most common form of cancer directly associated with OCP is the non-Hodgkin's lymphoma. OCPs have also been positively associated with increased pancreatic and liver cancer. It is reported that workers in the OCP manufacturing companies have a four- to fivefold increased risk of pancreatic cancer and significant risk of hepatic cancer (Attaullah et al., 2018). OCP is also associated with strong neurologic reactions. It has become evident that continuous exposure to OCP over long period of time increases the risk of Parkinson's disease. Adults aged over 50 years living in or around a farm where OCP is still used are found to be more susceptible to this disease. Parkinson's disease possesses a major threat in developing countries where majority of settlements are besides agricultural farms (Jia, & Misra, 2007; Sharma, Zhang, Barber, and Liu 2010). Neurologic symptoms such as elevated levels of stress, anger and even depression have also been reported in OCP exposed workers (Ezequiel, Miguel, Gustavo, and Nora, 2015).

The ban on use of various OCPs such as DDT and others started in late 1970s. The developed nations agreed for the full ban on production, use, trade of the OCPs, but the tropical developing countries signed for the partial ban only. The reason behind this step was unavailability of an alternative agent for vector control, as malaria and kala-azar diseases are common in the region and is responsible for large number of deaths annually. The Stockholm Convention that included the Dirty Dozen OCPs is responsible for ban and monitoring of OC pesticide residues in the environment (Rojas-Squella et al. 2013). Later various other OCPs were added in the initial list and the WHO proposed a detailed procedure manual for the OC pesticide residue monitoring in 2007.

After more than 4 decades of ban, OC pesticide is still found in the various milk samples from human as

Table 2 Global comparison of OCP range in variety of milk samples and their detection methods

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Belgium (Flanders)	84	Breast milk	SPE	DDTs	196 ng/g	100	(Ji et al. 2016)
			CALUX	HCB	9.6	100	
				Oxychlordane	5.6	100	
				HCH	8.9	100	
Brazil (Mato Grosso do Sul)	100	Bovine milk	GC ECD	Aldrin	0.1–1.86 ng/g	44	(Ferronato et al. 2018)
				DDTs	0.58–16.72	36	
				Endosulfan	0.28–12.2	32	
				CHL	1.49–6.57	17	
				Dicofol	2.75–9.61	14	
				Heptachlor	1.22–6.02	11	
				Dieldrin	0.98–14.73	11	
				HCHs	0.45–2.34	3	
				HCB	0.45–0.64	5	
				Endrin	3.91–3.91	1	
				Mirex	1.24–13.77	34	
China	1237	Breast milk	GPC GC-NCI-MS	DDTs	149.4–1755.3 ng/g	100	(Rêgo et al. 2019)
				HCHs	51.6–536.4	100	
				CHLs	0.0–17.8	75	
				HCB	18.4–56.8	100	
				Aldrin	ND	29.2	
				Mirex	ND-8.1	20.8	
China (Beijing)	65	Breast milk	GC/Ni-ECD	HCB	0.40–3.79 ug/Kg	100	(Bulut et al. 2011)
China (Beijing)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	1348.48 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	9.63	87	
China (Shanghai)	46	Breast milk	GC/u-ECD	OCPs	88.3–2532.9 ng/g lipid	100	(Tomovska, Hristova, Trajkovska, and Gjorgievski 2013)
Colombia	32	Breast milk	LLE/GC/μECD	DDTs	7781.5 ng/kg	51	(Gutiérrez et al. 2012)
				HCHs	814.2	34	
				CHLs	469	33	

Table 2 continued

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Egypt (Assiut)	45	Raw buffalo milk	GC/MS	Dieldrin	0–15 mg/kg	100	(Croes et al. 2012)
				HCB	0.019–0.033	100	
				Methoxychlor	0.013–0.2	100	
				Lindane	ND-0.192	66	
Germany (Bavaria)	525	Breast milk		HCB	0.003–0.140 ng/g	98	(Zhou et al. 2011)
				Lindane	0.002–0.034		
				Dieldrin	0.002–0.016		
				Oxychlordane	0.002–0.006		
				DDTs	0.009–2.980		
Greece	200	Sheep milk and goat milk	GC MS/MS & LCMS/MS	DDT	ND	–	(Pandit et al. 2002)
			ECD	HCH			
			QuEChERS				
India	22	Bovine milk	GC/ECD	DDTs	0.016–0.338 mg/kg	50	(Witczak et al. 2016)
				HCHs	0.001–0.023	30	
India	8	Milk powder	GC/ECD	DDTs	0.014–0.027 mg/kg		(Witczak et al. 2016)
				HCHs	0.014–0.027		
India (Dibrugarh, Assam)	101	Breast milk	GC/Ni-ECD	DDTs	2550–3430 ng/g	100	(Aslam, Rais, and Alam 2013)
				HCHs	2120–2480		
India (Haryana)		Raw bovine milk	GLC	DDTs	0.1199–0.9899 ug/ml		(Klinčić et al. 2014)
				HCHs	0.0037–0.3595		
India (Nagaon, Assam)	104	Breast milk	GC/Ni-ECD	DDTs	2870–3350 ng/g	100	(Aslam, Rais, and Alam 2013)
				HCHs	2280–3350		
India (New Delhi)		Breast milk		DDTs	430 ug/Kg		(Bedi et al. 2015)
India (New Delhi)		Buffalo milk		DDTs	ND-0.97 ng/g	80	(ul Hassan, Tabinda, Abbas, and Khan 2014)
				Endosulfan	ND–0.022	65	
				HCHs	0.0001–1.081	100	
India (Punjab)	312	Bovine milk	GC–MS	HCH	0.9 ug/Kg	7	(Pastor Ciscato et al. 2002)
				DDT	1.6	10.3	
				Endosulfan	1.2	9.3	
Indonesia (Bogor)		Breast milk		DDTs	1100 ug/Kg		(Bedi et al. 2015)

Table 2 continued

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Iran (Marivan)	30	Breast milk	GC/Ni-ECD	DDTs	70–10,550 ng/g	–	(Al Antary et al. 2015)
				HCHs	50–12,850		
				HCB	30–4120		
Jakarta		Breast milk		DDTs	640 ug/Kg		(Bedi et al. 2015)
Japan (Sendai)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	134.255 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	0.9	87	
Japan (Takarazuka)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	117.33 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	<0.1	87	
Japan (Takayama)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	110.48 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	1.485	87	
Jordan	100	Breast milk	GC	Endrin	0.56 ng/g	1	(Kampire et al. 2011)
			DFG	HCH	0.005–1.68	30	
				Heptachlor	0.08–0.14	2	
				DDTs	0.04–1.50	59	
Korea	206	Breast milk	HRGC/HRMS	DDTs	ND-392 ng/g	66	(Ezequiel, Miguel, Gustavo, and Nora 2015)
				HCHs	ND-107	98	
				CHLs	ND-28	99	
				HCB	ND-56.1	86	
				Heptachlor	ND-13.4	96	
Korea (Busan)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	143.995 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	1.465	87	
Korea (Seoul)	14 pooled sample (210 mothers)	Breast milk	GS-MS	DDTs	143.505 ng/g	100	(Anadón, Martínez-Larrañaga, Ramos, and Castellano 2011)
				Dicofol	2.68	87	
Lampung		Breast milk		DDTs	1000 ug/Kg		(Bedi et al. 2015)
Libya (urban)	40	Breast milk	GLC FP	BHCs	0.067 ng/g		(Shahmoradi et al. 2019)
			ECD	DDTs	0.047		
Libya (rural)	40	Breast milk	GLC FP	BHCs	0.078 ng/g		(Shahmoradi et al. 2019)
			ECD	DDTs	0.210		

Table 2 continued

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Mexico (Guerrero)	171	Breast milk	GC	HCB	0.001–0.074 mg/Kg	36.8	(Tutu et al. 2011)
				HCHs	0.001–0.123	36.3	
				DDTs	0.017–5.896	100	
Pakistan	20	Milk from local market	GC/ECD	DDT	0.05–15.61 ug/Kg	100	(Mishra & Sharma, 2011)
			GC–MS	Dieldrin	2.08–18.45		
				HCH	0.19–10.18		
				Endosulfan	0.75–297.1		
Pakistan (Punjab)	150	Dairy milk	HPLC	DDT	0.003–1.23 ug/mL	10	(Hajjar & Al-Salam, 2016)
				Endosulfan	0.1326	7	
				Aldrin	0.32–5.19	35	
Poland	15	Raw milk	GC–MS	HCHs	0.205–0.683 ng/g		(LaKind et al. 2009)
				Heptachlor	1.539		
				DDTs	0.133–1.96		
				Aldrin	1.92		
				Dieldrin	0.103		
				Endrin	0.136		
Poland	15	Raw goat milk	GCMS	HCHs	0.56–5.88 ng/g		(Ishaq & Nawaz, 2018)
				DDTs	0.081–5.54		
				Endosulfans	0.5–8.16		
				methoxychlor	ND–1.78		
Purwakarta		Breast milk		DDTs	1300 ug/Kg		(Bedi et al. 2015)
Spain (Canary Island)	16 (Fresh)	Bovine milk	SPE/GPC/GC/MS	DDTs	ND-30.22 ng/g	81.3	(Tian, 2011)
				HCHs	0.93–28.55	100	
				CHLs	0.75–12.69	100	
				HCB	0.39–10.06	100	
				Heptachlor	ND-7.77	87.5	
Spain (Canary Island)	10 (Organic)	Bovine milk	SPE/GPC/GC/MS	DDTs	ND-20.49 ng/g	80	(Tian, 2011)
				HCHs	0.68–2.45	100	
				CHLs	ND-6.04	90	
				HCB	0.92–5.64	100	
				Heptachlor	ND-1.23	70	

Table 2 continued

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Turkey	50	Buffalo milk	HPLC	HCH	0.47- 63.36 ng/g	64	(Fujii et al. 2011)
				Aldrin	2.48	8	
				CHL	0.21–1.51	6	
				Endosulfan	Nd-3.60	50	
				DDT	1.23–14.96	16	
				Methoxychlor	27.17	86	
Turkey	50	Cow milk	HPLC	HCH	Nd-91.32 ng/g	64	(Fujii et al. 2011)
				Aldrin	0.89	–	
				CHL	0.63–2.45	2	
				Endosulfan	ND- 7.25	24	
				DDT	ND- 16.48	20	
				Methoxychlor	24.99	42	
Turkey	50	Sheep milk	HPLC	HCH	6.47–122.98 ng/g	82	(Fujii et al. 2011)
				HCB	4.49	30	
				Aldrin	1.53	4	
				CHL	Nd-12.66	10	
				Endosulfan	Nd-4.19	82	
				DDT	Nd-16.34	42	
				Endrin	5.10	12	
				Methoxychlor	26.09	68	
Turkey (Ankara)	75	Breast milk	SPE/GC/ECD	DDTs	12.65.7 ng/g	89.3	(Cok et al. 2011)
				HCHs	427.6	70.7	
				CHLs	46	25	
				Heptachlor	120.4	34.7	
				Aldrin	230.6	58.7	
				Endosulfan	84.5	25	

Table 2 continued

Country	No. of samples	Sample type	Method	OCPs detected	Range	(%)	References
Turkey (Mersin)	47	Breast milk	HRGC-HRMS	HCHs	37.3 ng/g		(Pirsaheb et al. 2015)
				DDTs	338.38		
				CHL	0.001–0.002		
				Hptachlor	0.001–1.586		
				Aldrin	0.002		
				Dieldrin	8.559		
				Endosulfan	0.028–0.048		
				Methoxychlor	0.063		
				Mirex	0.073		
Uganda (Kampala)	54	Fresh cow milk	GC/Ni-ECD	Lindane	–0.086 ng/g	85	
				DDTs	0.018–0.152	64.8	
				Aldrin	0.002–0.018	7.4	
				Dieldrin	0.001–0.018	37	
				Endosulfan	0.001–0.004	7.4	
Uganda (Kampala)	47	Pasteurized cow milk	GC/Ni-ECD	Lindane	ND–0.066 ng/g	76.5	
				DDTs	0.012–0.088	63.8	
				Aldrin	0.005 – 0.008	36.1	
				Dieldrin	0.001 – 0.021	36.1	

ND Non-detectable, percentage of detectable samples (%), high-resolution gas chromatography/high mass spectrometer (HRGC/HRMS), gas chromatography/63Ni electron capture detector (GC/Ni-ECD), solid-phase extraction/gel permeation chromatography/gas chromatography/mass spectrometry (SPE/GPC/GC/MS), gas–liquid chromatography (GLC)

Fig. 1 Map depicting global footprint of OCPs in milk and dairy products

well as animals. The most common were DDT and its metabolites, HCH and isomers, HCB, lindane, dieldrin, etc. (Witczak et al. 2016). On the positive note, all the studies showed a declining trend of amount of OCPs in the sample over the years. This supports the successful worldwide OC pesticide ban and the increased awareness of its harmful effects among the nations, organization, health setups and common people.

The samples showed a higher level of OCPs in areas where malaria vector control and termite control were carried out using these pesticides. The bovine milk was found to be relatively more contaminated than the milk from sheep and goat because of its high fat content in comparison with the latter (Pastor Ciscato et al., 2002; Witczak et al., 2016; Berruga, Molina, Althaus, and Molina, 2016) The presence of OCPs in breast milk remains a big issue because of the sensitive nature of infants and secondly because of total dependence on mother's milk (Song, Ma, Tian, Tong, & Guo, 2013a, 2013b).

The human breast milk was found to contain OC pesticide residues in almost all the obtained samples around the world. Older women were found to have higher residue concentration because of longer time of OC pesticide accumulation. The mothers residing near the agriculture fields and industrial areas showed higher concentration of OC pesticide than the mothers from urban cities for obvious reason. Studies from China have shown the relation of higher OCPs in milk sample to the seafood diet. The samples from many regions in China and India showed alarming level of DDT and other OC pesticide residue, but nonetheless the declining trend was seen in these regions also (Zhou et al., 2012; Kaushik, Sharma, Gulati, and Kaushik, 2011). Korea, Turkey and other Asian and many European countries demonstrated successful OC pesticide ban to control its release in the environment. Sample from some countries such as Czech Republic confirmed the use of OCPs in the region for insecticidal use (Tomovska, Hristova, Trajkovska, and Gjorgievski, 2013). The North and South American countries also showed the similar result, where the OC pesticide residues were found in most of the samples but mostly below the level at which the total intake can become a factor for health risk. European countries showed the lowest amount of OC pesticide residue in the samples (Table 2) (Fig. 1).

The most concerning results came from African continent where harmful OCPs such as dieldrin, aldrin, endrin, CHL, heptachlor, DDT and HCB were found in the analyzed samples, and the concentration was remarkably high than the suggested values by the various global regulatory bodies.

Conclusion

The increasing demand of food for the increasing world population has resulted in various non-sustainable agricultural advancements and the nature is paying its price in the form of environment pollution. The pesticides have been a great concern for human and ecosystem due its tendency of bioaccumulation and persistence. Breast milk is of significant value to analyze the population OC pesticide burden as well as the extent of exposure to the next generation. The continuous use of OCPs around the world, especially in developing and underdeveloped nations, demands the continuous monitoring of OC pesticide residues and to maintain the proper regulation of steps taken to control or ban its use.

Failure to take urgent precautionary action may result in severe social, economic and health consequences. The *precautionary principle* states that in cases of serious or irreversible threats to the health of humans or ecosystems, acknowledged scientific uncertainty should not be used as a reason to postpone preventive measures. The preventive measures taken should aim to reduce and possibly eliminate the exposure of harm causing substances, activities and other conditions. The precautionary principle includes that chemicals should not be discharged into the environment until they are proved to be harmless. This is the opposite to the usual process of risk assessment, which consider that chemicals are safe and harmless until proved otherwise. Therefore, the implementation of precautionary steps avoids difficulties that may arise from limitations of assessing the toxic effects of chemicals on health. The precautionary actions that should be taken in case of OC substances are:

- Replacement of OC substances with less harmful alternatives.
- Re-evaluation of production technique, products and human activities to minimize the ill effects.
- Provision of information and education to the public to minimize the exposure to possibly harmful substances, such as OCs.
- Education and awareness generation about the ill effects OCPs and its and proper handling among the farmers.

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Data availability This is a review article, and no data were generated during manuscript preparation.

Declarations

Conflict of interest All the authors declare that there are conflicts of interest whatsoever.

Consent to participate No human samples were collected during the course of this study.

Consent to publications All authors have provided the consent to jointly publish this review article.

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