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Review

Global trends in pesticides: A looming threat and viable alternatives

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ABSTRACT

Pesticides are widely used chemical compounds in agriculture to destroy insects, pests and weeds. In modern era, they form an indispensable part of agricultural and health practices. Globally, nearly 3 billion kg of pesticides are used every year with a budget of ~40 billion USD. This extensive usage has increased the crop yield as well as led to significant reduction in harvest losses and thereby, enhanced food availability. On the other hand, indiscriminate usage of these chemicals has led to several environmental implications and caused adverse effects on human health. Epidemiological evidences have revealed the harmful effects of pesticides exposure on various organs including liver, brain, lungs and colon. Recent investigations have shown that pesticides can also lead to fatal consequences such as cancer among individuals. These chemicals enter ecosystem, thus hampering the sensitive environmental equilibrium through bio-accumulation. Due to their non-biodegradable nature, they can persist in nature for years and are regarded as potent biohazard. Worldwide, very few surveillance methods have been considered, which can bring awareness among the individuals, therefore the present review is an attempt to delineate consequences induced by various types of pesticide exposure on the environment. Further, the prospective of biopesticides use could facilitate the increase of crop production without compromising human health.

1. Introduction

The use of chemicals on a large scale has not been started long ago however this approach has brought havoc in the biosphere, leading to a decline in the quality of life (Pimentel, 2005). A variety of chemical compounds are continuously being used these days to eradicate unwanted weeds and insects with the most common among them being pesticides. According to the World Health Organization (WHO) pesticides are considered as a special class of chemical compounds used to kill a wide range of pests that include insects, weeds and rodents. These chemicals are used to enhance the yield as well as quality of crops. Pesticides are considered as potentially dangerous chemicals to human health and their consumption needs to be carefully monitored. Worldwide, the many fold increase in the demand of pesticides is mainly due to continuous attack of pests like insect larvae, which are responsible for destroying crops and huge monetary losses to the farmer communities (Cerda et al., 2017). Besides their role in getting rid of pests/insects in crop fields, they are also used to prevent the spread of vector-borne diseases in the environment. Pesticides like dichloro diphenyl trichloroethane (DDT) and its metabolic product dichlorodiphenyldichloroethylene (DDE) are used for indoor residual spraying (IRS) to control vector-borne diseases like malaria, dengue (WHO, 2012), leishmaniasis (Claborn, 2010), Japanese encephalitis (JE) (Dutta et al., 2011) and schistosomiasis (King and Bertsch, 2015). Further, pesticides

Abbreviations: CPF, Chlorpyrifos; CRISPR, Clustered Regularly Interspaced Short Palindromic Repeats; DDT, Dichlorodiphenyltrichloroethane; GABA, Gamma Amino Butyric Acid; OPs, Organophosphorus pesticides; PCBs, Poly Chlorinated Biphenyls; POPs, Persistent Organic Pollutants; RNAi, RNA interference; TRP, Transient Receptor Potential; WHO, World Health Organization

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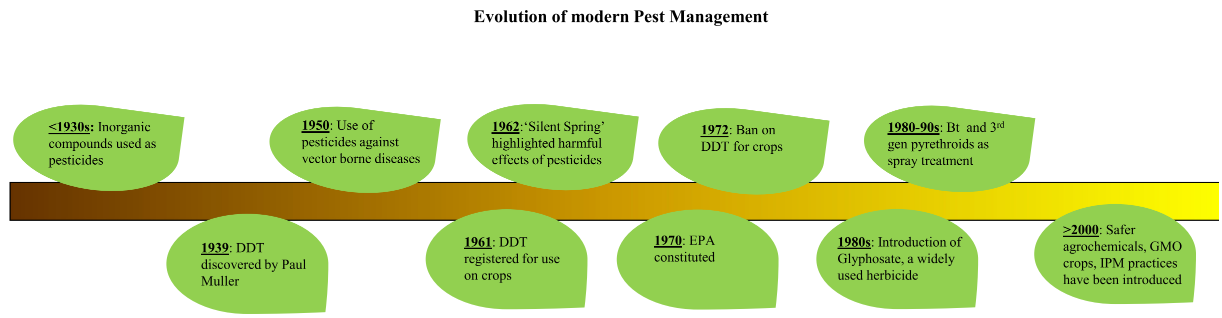


Fig. 1. Evolution of modern pest management. A timeline of pesticide uses since early 1930s. Important discoveries are indicated at with their year. Harmful effects of few pesticides over the years have been described herein.

should not only be carefully used and stored but also need to be disposed in a proper manner. In early 1986, Pimental and Lavitan found that only 0.1% of pesticides reach the target whereas, larger parts of them cause contamination of the environment (Pimentel, 1995). These pesticides have been classified under persistent organic pollutants (POPs) and their usage is strictly regulated across the world by the Stockholm convention on persistent organic pollutants (WHO, 2011) (Fig. 1).

Studies have shown that persistent exposure of these pollutants can lead to their accumulation in the tissues and induce harmful effects on growth, development as well as the metabolism of the body (La Merrill et al., 2013). The pesticides have been linked to several disorders, which are associated with cardiovascular (Obukhov et al., 2015), central nervous (Keifer and Firestone, 2007) and pulmonary system (Ye et al., 2013). These compounds have also been observed to be carcinogenic, mutagenic and teratogenic in nature (Baird et al., 2005; Parker et al., 2017).

Exposure to pesticides may either be acute or chronic: acute exposure to pesticides is considered when individuals are exposed with high amounts for a short duration. This type of exposure causes burning of skin, blisters or rashes, blindness, abdominal pain, diarrhoea and vomiting (Thundiyil et al., 2008) whereas chronic exposure has effects that appear months or years after pesticide exposure and include cancer, birth defects, reproductive abnormalities, toxicities and even death (Alavanja et al., 2004).

Due to their persistent nature, they have become a major threat to the ecosystems as natural resources like water and soil are constantly being affected by them (Kole et al., 2001). Keeping in view the ability of pesticides to affect human health through variegated sources, their permissible limits need to be carefully reviewed before application (Damalas and Eleftherohorinos, 2011). Here in this review, we try to discuss in detail about various aspects of pesticides such as their chemical composition, the target organisms and their routes of exposure (Fig. 2).

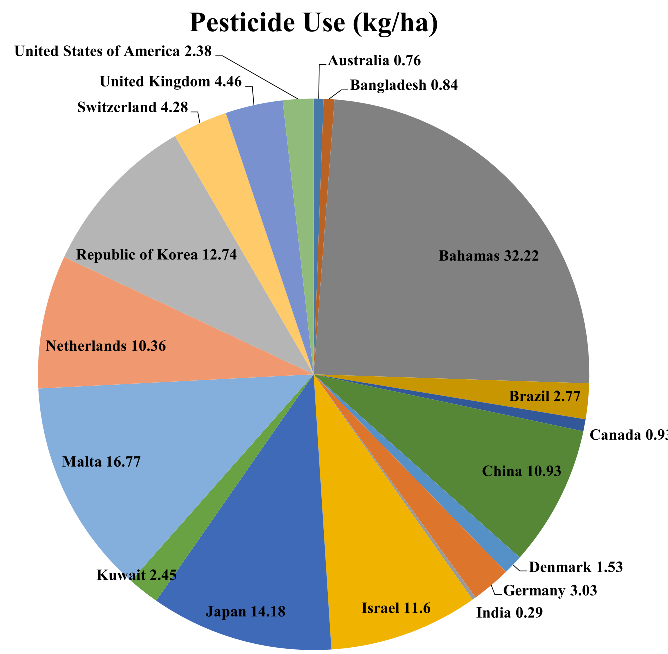


Fig. 2. Pesticide Use (kg/ha). Pie chart representing the average usage of pesticides per area of crop-land (kg/hectare) from 1990 to 2016 in different countries across the world is shown. Highest usage among the countries for which the chart is madehas been noted for Bahamas with average usage of 32.2 kg/ha while lowest for India with an average of 0.29 kg/ha. Data were taken from FAO website (http://www.fao.org/faostat/en/#data/EP/visualize).

2. Pesticide poisoning

According to the WHO, pesticide poisoning accounts for about 300,000 deaths every year worldwide (Gunnell and Eddleston, 2003). It is defined by a condition where a person consumes or inhales any pesticide above its threshold levels leading to detrimental consequences. This can further be classified into occupational or accidental. Occupational poisoning occurs among people who use these chemicals in their day to day life in agricultural fields or the ones who are engaged in manufacturing industries (Darçın et al., 2017; Gangemi et al., 2016). Human exposure to pesticides under this category may occur through various routes such as skin, inhalation, ingestion and contact (Calvert et al., 2008).

Accidental pesticide poisoning stems from relative unawareness among the people of harmful effects via ingestion/inhalation. Studies have revealed that women exposed to DDT during gestation period can get its traces in umbilical cord and even in breast milk (Debost-Legrand et al., 2016; Wolff et al., 2007). Association between pesticide exposure and changes in weight at the time of birth have also been observed (Kezios et al., 2013). It has been estimated that a large amount of pesticides are consumed deliberately by individuals for committing suicide (Gunnell et al., 2007).

3. Classification

Pesticides can be classified broadly on the basis of their origin as natural, synthetic and target organisms etc.

3.1. Natural pesticides

Pesticides isolated from natural sources such as plants or microbes are known as natural pesticides (Table 1). Such pesticides are non-toxic to mammals and are biodegradable in nature (Campos et al., 2016). The most commonly used natural pesticides are neem, pyrethrum, rotenone and nicotine (Duke et al., 2010).

Table 1
Different naturally occurring pesticides and their modes of actions.

Name of natural pesticide	Source	Target	Mode of action
Phosphinothricin	*Streptomyces hygroscopicus*	Weed	Irreversible inhibitor of glutamine synthetase (Duke et al., 2010)
Leptospermone	Bottle-brush plant	Weed	Inhibitor of enzyme hydroxyphenylpyruvate dioxygenase (HPPD). Involved in synthesis of tocopherols and plastoquinone in plants (Owens et al., 2013)
Spinosads	*Saccharopolyspora spinosa*	Insects	Affects the nervous system and causes severe damage (Araujo et al., 2019)
Milbemycin and Avermectin	*Streptomyces* sp	Insects	Potentiate glutamate and GABA gated chloride-channel opening (Merola and Eubig, 2012)
Azadirachta indica	Neem leaf and seeds	Insects, Fungus	Blocks synthesis and release of molting hormones (ecdysteroids) (Chaudhary et al., 2017)
Rotenone	Lonchocarpus root	Insects	Inhibits mitochondrial complex I in cells and induces apoptosis (Qi et al., 2014)
Sabadilla	Sabadilla lily	Insects	Works on voltage-sensitive sodium channels (Silver et al., 2014)
Nicotine	Aqueous tobacco extract	Insects	Interacts with nicotinic acetylcholine receptors (Millar and Denholm, 2007)
Capsain	Capsicum peppers	Insects and mammalian pests	Activates Transient Receptor Potential (TRP) channels and acts as an irritant (Salgado, 2017)

3.2. Synthetic pesticides

They are man-made pesticides and are formed by the modification of minerals or chemical compounds. These are the most extensively used pesticides in the world. Several studies have shown that synthetic organic and inorganic pesticides are very stable in nature and can accumulate over time, i.e., organochlorines, organophosphates, pyrethroids and carbamates (Jayaraj et al., 2016b). The synthetic pesticides can be further categorized on the basis of chemical nature namely organic and inorganic.

3.2.1. Inorganic compound pesticides

They are formed by modification of inorganic compounds. Investigations have shown that their usage should be restricted due to high levels of contamination and damage to environment (Shaban et al., 2016). Copper, boric acid, silicates, sulfur and arsenic are some of the pesticides that belong to this category (Gimeno-Garcia et al., 1996).

3.2.2. Organic compound pesticides

They are designed by regulating the organic structure of the compounds. These are chemically modified structures and considered as the most potent pesticides. Their mode of action involves blocking the key processes of the central nervous system (CNS), which eventually results in death of the organism (Abreu-Villaca and Levin, 2017).

3.3. Target organisms

Pesticides can also be differentiated on the basis of their target organisms (Table 2)–

4. Biopesticides- A boon in disguise

Biopesticides are used to refer to pesticides that are naturally produced by living organisms like microorganisms, herbs, plants etc. (Chandler et al., 2008). These are comparatively safer to use than man-made pesticides as have lesser toxicity towards living systems. Due to damage caused by pest infestations in agricultural fields, pesticide application is vital for a decent crop yield. The synthetic pesticides are very expensive and their continuous use is leading to the development of resistance among the pests, rendering these chemical compounds ineffective.

Among microorganisms *Bacillus thuringiensis* has been in use to fight against various insect pests (Bravo et al., 2011). In case of botanical products, *Azadirachta indica* has been found to be a potent pesticide and exhibits anti-carcinogenic properties (Chaudhary et al., 2017).

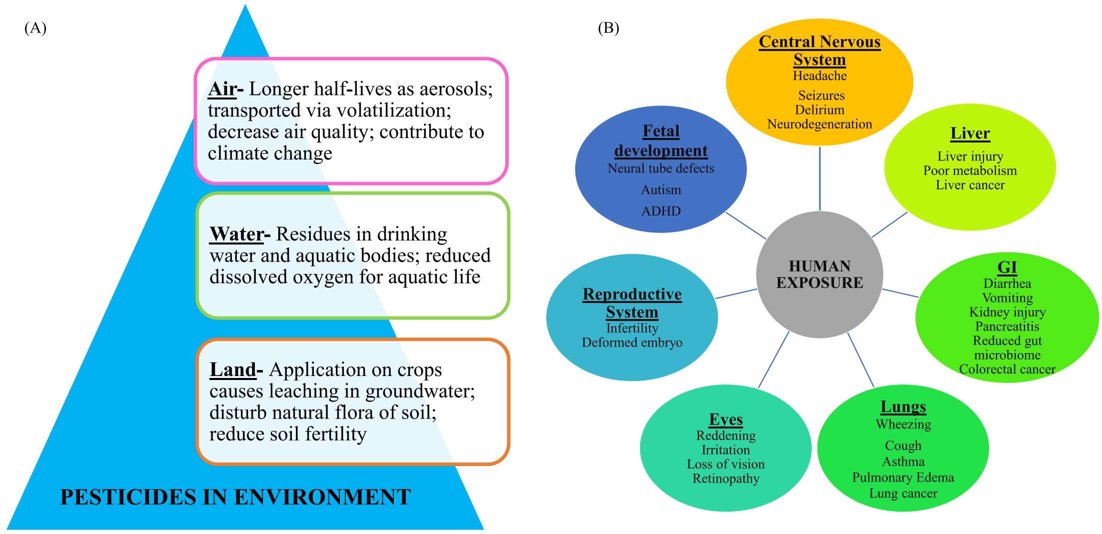
The biopesticides are biodegradable as these are not synthesized anywhere artificially. These natural substances efficiently remove the target pest and provide many other benefits as well (Gartia et al., 2019; Tamhane et al., 2005; Telang et al., 2005). They can augment the availability of nutrients in soil for the plants (Bae et al., 2009). Moreover, biopesticides can also help promote resistance to droughts in plants (Marasco et al., 2012). Thus, these form an important part of integrated pest management (IPM) practices (Chandler et al., 2011). Fungal species like *Beauveria bassiana* also used as bioinsecticide (Kanzok and Jacobs-Lorena, 2006; Sain et al., 2019). The use of these natural pesticides leads to minimum pollution.

5. Exposure

Human exposure to pesticides is mainly through food, water and air (Fig. 3). Due to their wide availability in the form of liquid, solid and gaseous, they can easily intrude the human physiology by skin contact,

Table 2
Classification on the basis of target organisms along with their examples.

NAME	TARGET ORGANISM	USES	EXAMPLES
Acaricide	Mites and ticks	Used to kill ticks and mites around homes	DDT, Dicofol, organophosphates, Carbamate
Avicide	Birds	To control birds in orchards	Strychnine, Fenthion
Algicide	Algae	For removal of algal growth from water reservoirs such as swimming pools and lakes	Benzalkonium chloride, Copper sulphate, Dichlone, Simazine
Bactericide	Bacteria	As disinfectants, antiseptics and antibiotics	Quaternary ammonium compounds, Silver nitrate, Mercury chloride, Hypochlorites, Lugol's iodine, Triclosan, Hexachlorophene, Salicylic acid, Fluoroquinolones
Fungicide	Fungi	In preventing plant diseases	Tea tree oil, Cymoxanil, aureofungin, Metalaxyl, Hexaconazole
Herbicide	Weeds	Managing turfs, for removing weeds	Atrazine, Paraquat, Oxadiazon, Glyphosate, Metoxuron, Sulfosulfuron, Linuron
Insecticide	Insects	Used to kill insect eggs and larvae	Azadirachtin, Malathion, Carbofuran, Chlorfenapyr, DDT, Lindane, Endosulfan, Thiacloprid, Clothianidin, Thiamethoxam
Molluscicide	Molluscs	Used for agriculture and gardening	Metaldehyde, Thiacloprid
Nematicide	Nematodes	As fumigant for crops	Chlorpyrifos, Phosphamidon, methyl bromide, Fenamiphos
Rodenticide	Rats	Managing invasive rodents	Zinc phosphide, Bromadiolone, Coumachlor, Coumatetralyl, Warfarin
Synergists	Several pests	Act to increase the toxicity of other pesticides	Piperonyl butoxide
Virucide	Viruses	To control the spread of viruses	Cyanovirin-N



(A) Effects of pesticides on environment (B) Effect of pesticides on humans

Fig. 3. Effects of pesticides on environment and humans. (A) Represents the modes of exposure of pesticides on the environment. (B) Depicts the effects of pesticides on human physiology.

Table 3
Classification of pesticide exposure on the basis of toxicity (Damalas and Koutroubas, 2016).

Toxicity	Package label	Respiratory exposure (mg/L)	Ingestion (mg/kg)	Skin contact (mg/kg)
Almost non-toxic	CAUTION	20 +	5,000 +	20,000 +
Mildly toxic	CAUTION	2.0–20	500 - 5,000	2,000–20,000
Medium toxic	WARNING	0.2–2.0	50–500	200 - 2,000
Extremely toxic	POISON	0–0.2	0–50	0–200

Table 4
Maximum residue limit (MRL) in drinking water for various pesticides (WHO, 2017).

PESTICIDE NAME	GUIDELINE VALUE	
	μg/l	mg/l
Aldicarb	10	0.01
Aldrin and Dieldrin	0.03	0.000 03
Atrazine and its chloro-s-triazine metabolites	100	0.1
Carbofuran	7	0.007
Chlordane	0.2	0.0002
Chlorpyrifos	30	0.03
Cynazine	0.6	0.0006
2,4 Dichlorophenoxyacetic acid	30	0.03
Endrin	0.6	0.0006
Hydroxyatrazine	200	0.2
Lindane	2	0.002
Methoxychlor	20	0.02
Simazine	2	0.002
2,4,5-Trichlorophenoxyacetic acid	9	0.009
Terbuthylazine	7	0.007
Trifluraline	20	0.02

inhalation or ingestion. There are several guidelines formulated by international agencies like WHO, USFDA and FAO in place to keep the contact with these hazardous chemicals to a minimum. Thus, a few of them are presented in this review (Tables 3–5).

Apart from maintaining maximum residue limits for different products for human consumption, the application of pesticides also depends on the weather conditions, like speed of wind, humidity etc. In-fact, food and agriculture organization of the United Nations (FAO) has issued guidelines, which dictate that pesticide should be sprayed only when the wind speed is between 3 km/h to 7 km/h (FAO, 1988). Otherwise, indiscriminate spraying has been shown to cause respiratory disorders among individuals (Damalas and Eleftherohorinos, 2011).

Pesticide exposure to individuals can be through two modes: Occupational and non-Occupational (Damalas and Koutroubas, 2016).

5.1. Occupational exposure

5.1.1. Dermal

Skin contact is the easiest and the most frequent form of pesticide interaction with human body. Here, liquid contamination by pesticides

Table 5
Maximum residue limit (MRL) in foodstuff for various pesticides (FAO, 2020).

Commodity (mg/kg)	Aldrin and Dieldrin (mg/kg)	Chlorpyrifos (mg/kg)	DDT (mg/kg)	Endosulfan (mg/kg)	Glyphosate (mg/kg)	Heptachlor (mg/kg)	Lindane (mg/kg)
Cereal grains	0.02	0.5	0.1	–	30	0.02	0.01
Eggs	0.1	0.01	0.1	0.03	0.05	0.05	0.001
Meat	0.2		5	0.2	0.05	0.2	0.01
Milks	0.006	0.02	0.02	0.01	0.05	0.006	0.001
Poultry meat	0.2	0.01	0.3	0.03	0.05	0.2	0.005
Fruits	0.05	0.5–2		0.5–2	0.05	0.01	
Vegetables	0.05–1	0.05–2	0.5	0.05–1	2–5		0.01

is considered as the most lethal form of exposure. Investigations have shown that dermal exposure of pesticides tends to occur during their handling, mixing and application. Reports have suggested that absorption through skin also depends on the type of solvent used. Their exposure in the form of organic solvents is able to induce more deleterious effects due to their faster absorption property (Damalas and Eleftherohorinos, 2011). It has been observed that pesticides in the form of aerosols, powders and minute solid particles can also affect the skin but their effects are minimal in comparison to liquid form of pesticides (Damalas and Koutroubas, 2016).

5.2. Inhalation

Gaseous pesticides tend to pose immense risk to individuals on inhalation. It has been observed that absorption through the respiratory tract is rapid and tends to affect multiple regions of the body. It can exhibit serious effects on lungs, throat and nose tissue. Pesticides applied as dilute sprays, foams, powders or even minute solid particles can also severely affect individuals respiratory system and skin (Damalas and Koutroubas, 2016). Studies have suggested that weather conditions such as stormy winds and high humidity in addition to pesticides can exacerbate respiratory conditions (Damalas and Eleftherohorinos, 2011).

5.3. Ingestion

Reports have suggested that pesticides are rapidly absorbed through ingestion in gastrointestinal tract (GIT) and can cause adverse effects among individuals (Eddleston et al., 2008; Paudyal, 2008). Further, residual amounts of pesticides can be ingested from contaminated bottles, food and hands (Rather et al., 2017). Therefore, it is essential to carefully wash hands, food and utensils after using pesticides.

5.4. Non-occupational exposure

It has been observed that the pesticides can induce lethal effects on normal population due to bioaccumulation. It is the phenomenon where increased accumulation of harmful chemical residues in the living organisms are observed (Achudume et al., 2009; Genuis and Kelln, 2015). It has been reported that weather conditions, biodegradability and distance from agricultural settings tend to play a major role in pesticide related hazards. Since synthetic pesticides are non-biodegradable, they can lead to contamination of ground-water. These are also responsible for polluting nearby water bodies via rainwater and pesticide run-off. Another source of exposure is through fruits as well as vegetables and if not processed properly, can cause ill effects on humans and the surrounding ecosystem (Damalas and Eleftherohorinos, 2011).

6. Pesticide handling and disposal

Worldwide, agricultural workers are prone to dire health implications due to acute and chronic exposure to pesticides (Damalas and Koutroubas, 2016). Several reports have suggested that, farmers are more susceptible to neurological, digestive, retinal, respiratory and reproductive disorders than general population, due to their close contact with these chemicals (Fuhrimann et al., 2019). Globally, pesticides are an indispensable part of normal farming practices and exposure to them is an inevitable occupational hazard for crop producers (Nankongnab et al., 2020). Thus, it is important to take certain precautions to minimize the hazardous impact of these toxic substances on individuals involved in agriculture. One of them is extensive usage of personal protective equipment (PPE), which includes gloves, masks, protective goggles, boots, hats and respirators. Also, the applicator used for pesticide spraying should be in a suitable working condition and free from leakages (Damalas and Koutroubas, 2016). After usage, washing of exposed body parts with soap is absolutely necessary to remove pesticide residues. Further, cans and bottles used for pesticide storage should be rechecked for leakage free before disposal or reusage (Damalas and Eleftherohorinos, 2011).

There have been guidelines suggested by the WHO for safe handling, storage and application of pesticides (WHO):

- Detailing the mode of application, precautions to be taken and hazardous warnings in local languages on the pesticide packaging.
- Storage of pesticides should be in dry and dark rooms, which are inaccessible to children.
- Polyethylene and rubber-based PPE to be used while working as the assimilation of pesticide residues is minimal in such fabrics.
- Thorough cleaning of pesticide containers after emptying is essential. They should be filled with water for 24hrs to remove the previous contents and minimize accidental exposure.

Other than handling, the disposal of pesticides is an issue of grave concern, which needs considerable attention. Many farmers from different regions of world have admitted disposing the unutilized pesticide on land. Such malpractices occur due to lack of awareness in rural populations. In certain cases, it has been found random disposal of pesticide containers in the fields after usage. Furthermore, many people use the empty pesticide cans for storage purposes at homes, while others burn, bury them and throw them freely in the fields. These practices contaminate other ecosystems too, for instance the traces of pesticides in the containers lying in fields reach the soil as well as water and affect the inhabiting organisms (PAN, 2010).

FAO has issued guidelines on disposal of empty pesticide cans and also on managing small quantities of unwanted and obsolete pesticides.

A pesticide law should have such provisions that ensure proper disposal by a national authority.

- Disposal should be in concordance with instructions received from the authority
- Any unexpected situation arising during disposal should immediately be reported
- Any unauthorized and unlawful dumping and dumping site should urgently be brought to notice

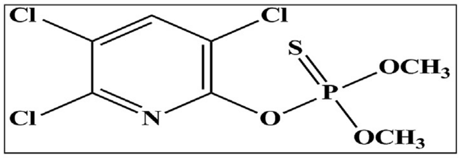
It should prohibit-

- Discarding pesticides directly in drains and water bodies
- Burying pesticide waste in landfill not meant for its disposal
- Burning of the waste, if not approved for incineration

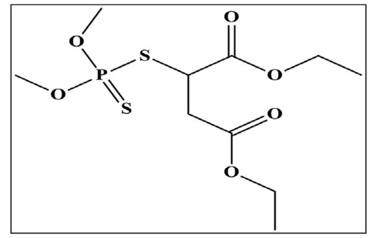
Additionally, pesticide manufacturing firms should lend support in the disposal of pesticides no longer in use and harmful for the environment. Any person in possession of pesticides, which is no longer in use should immediately inform the concerned authority about the quantity and type of the product so that their disposal should take place according to legislation and norms of the country. Particularly in developing countries there are many difficulties associated with disposal due to lack of proper facilities. The Basel and Stockholm conventions had provided direction in this matter on how such hazardous waste must be dealt (FAO and WHO, 2015).

Further, FAO suggests complete cleaning of empty container of pesticides is mandatory and all the pesticides that are diluted before use should at least be triple rinsed, while dry pesticides should be utilized completely before disposing. All such containers should then be punctured so that these cannot be reused for any other purpose. Worldwide, burial of the pesticide waste is prohibited as it may cause leakage of residual pesticides, if any, that may further pollute soil and water. Similarly, burning causes release of toxic gases, which can cause serious difficulties if inhaled besides polluting the air (FAO, 1999).

Organophosphorus pesticides



Chlorpyrifos



Malathion

Scheme 1. Chemical structure of common Organophosphorous pesticides.

7. Common pesticides: Impact on human health and ecology

Due to high efficacy and affordability of synthetic pesticides, they are considered as the most prevalent pesticides across the world (Aktar et al., 2009). They are routinely used in agricultural sectors but also have implications on humans and environment. Initial exposure can cause headache, nausea, convulsions, diarrhoea, irritation in eyes and breathing discomfort (Costa, 2018; Hoppin et al., 2017; Jaga and Dharmani, 2006; Kamel and Hoppin, 2004). It has been observed that pesticides exposure can lead to neurological disorders, respiratory distress, retinopathy, gastrointestinal dysfunction an cancer under certain conditions (Mamane et al., 2015; Abolhassani et al., 2019; Abreu-Villaca and Levin, 2017; Jaga and Dharmani, 2006). The most commonly applied synthetic pesticides can be categorized into four types (Schemes 1–4):

1. Organophosphorus
2. Organochlorines
3. Carbamates
4. Pyrethroids

In this review, we will primarily be focusing on organophophosorus pesticides (OP) and organochlorine pesticides (OC) as they are most abundantly utilized pesticides across the world (Kaur and Kaur, 2018).

7.1. Organophosphorus pesticides

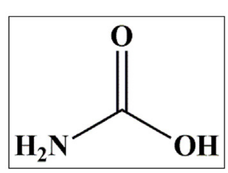
Organophosphorus pesticides (OPs) are esters of phosphoric acid and their derivatives. They are comprised of a central phosphorus atom (P) and the characteristic phosphoric (P=O) or thiophosphoric (P=S) bond and a leaving group, a molecular fragment, which departs with a pair of electrons after bond cleavage. Its primary mode of action is through inhibition of acetylcholine esterase (AChE), which is an important enzyme of cholinergic system (Fig. 4). Due to this property, they are known to inhibit the cascade of nerve impulse. Studies have shown this situation can result in rapid twitching of voluntary muscles leading to paralysis/death (Jokanovic, 2018). The rate of AChE inhibition by the OP is dependent on the leaving group present in the chemical structure of the pesticide i.e. a higher tendency of leaving of the particular group results in higher affinity of the inhibition of acetylcholine esterase (Fukuto, 1990). Research suggests halogen (ca. fluorine) containing organophosphates to be highly toxic as fluorine possesses higher tendency for hydrolysis and can result in significant inhibition of AchE (Makhaeva et al., 2009). Reports have indicated that organophosphates induce toxicity by metabolization of the pesticide via cytochrome P450 (CPF) enzymes (Ellison et al., 2012). The most commonly used OPs are chlorpyrifos (CPF), methyl parathion (MPT), and malathion (MLT) due to their highly toxic nature (Mangas, 2016).

7.2. Effect of Organophosphates on human physiology

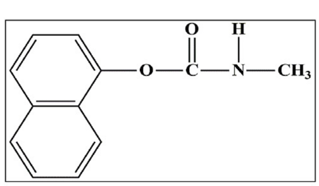
7.2.1. Brain

Evidences have revealed that organophosphates like CPF and diazonin act by inhibiting the activity of acetylcholine esterase in neurons leading to accumulation of acetylcholine, which further induces severe neurotoxicity and cognitive impairments (Abreu-Villaca and Levin, 2017; Judge et al., 2016). It has been observed that chronic exposure to pesticides like CPF can result in altered glutamatergic metabolism in brain through reduction of GABA and glutamate levels (Abreu-Villaca and Levin, 2017). Additionally, the acetylcholine accumulation

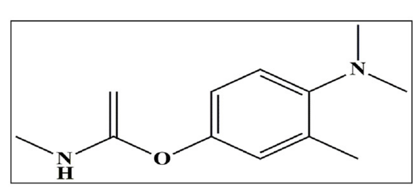
Carbamates



Carbamic acid, fundamental constituent of Carbamates



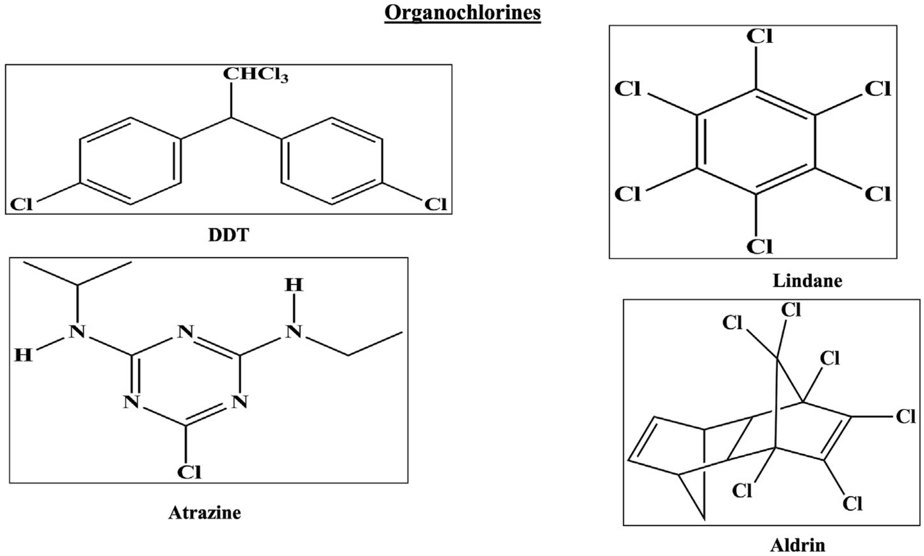
Carbaryl



Aminocarb

Scheme 2. Chemical structure of common Carbamate based pesticides.

Organochlorines



Scheme 3. Chemical structure of common Organochlorine based pesticides.

mediated by OPs can lead to reduced uptake of serotonin from the synapses, which is a prominent cause of depression and mood-related disorders in adults (Judge et al., 2016). Unfortunately, infants and children are also not spared from the hazardous implications of these pesticides. Reports have suggested that neuro-transmission perturbations caused by OPs can result in neuro-behavioral and neuro-developmental abnormalities in new-borns (Abreu-Villaca and Levin, 2017; Bjorling-Poulsen et al., 2008). Further, it has also been demonstrated that exposure to OPs contributes to progression of ADHD (attention deficit hyperactivity disorder) among children too (Ito et al., 2020).

Apart from utilizing acetylcholine esterase as a target, OPs have been shown to attack another enzyme in central nervous system called NTE (neuropathy target esterase), which can result in the onset of a disorder called organophosphate-induced delayed polyneuropathy (OPIDP). The initial symptoms of this affliction include ataxia, sensory loss, muscle weakness and tingling sensation in hands and feet. On a cellular level, it can lead to disintegration of neuritic segment and myelin sheaths (Costa, 2018). Other than the above two enzyme targets, there are also organophosphorous herbicides like Glyphosate, which attack pathways in weeds that are not present in mammals but still are neurologically toxic to humans. It has been reported that Glyphosate can result in reduction of GABAergic and dopaminergic neurons in *C. elegans*, which can lead to development of Parkinson's disease like symptoms. Moreover, Martinez and group in 2019 discovered that exposure to glyphosate can alter glucose metabolism in the brain by crossing the blood-brain barrier, which can be the reason for the decline of neurons in brain.

7.2.2. *Respiratory system*

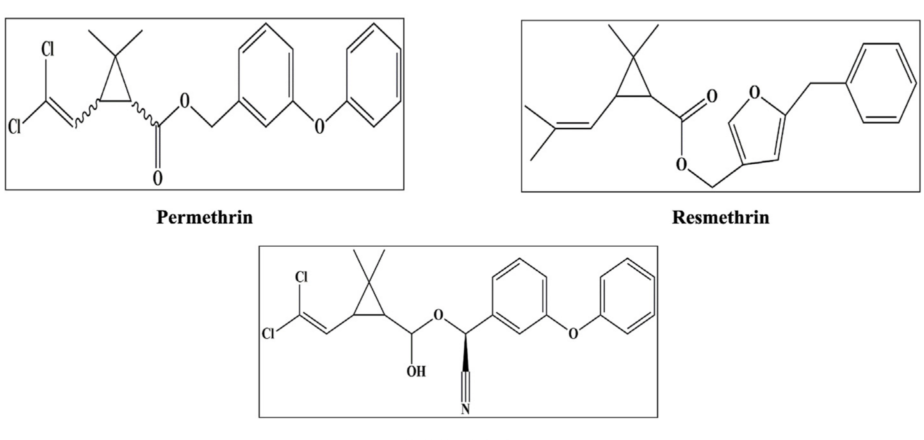
Organnophosphorous pesticides like CPF and glufosinate are known to have detrimental effects on the respiratory system and initially cause symptoms like wheezing and asthma. Hoppin et al., in 2017 illustrated that pesticide exposure increases airway hypersensitivity in farmers by reducing the efficacy of muscarinic receptors in lungs (Hoppin et al., 2017).

It has been observed that OPs can cause weakness of respiratory muscles, interstitial edema (i.e. buildup of pathological fluid in lungs) and total respiratory failure due to excessive accumulation of acetylcholine at neuromuscular junction. Moreover, numerous studies have reported that chronic exposure to OPs results in lung cancer (Alavanja and Bonner, 2012; Giyanwani et al., 2017).

7.2.3. *Ocular system*

It has been discovered that OPs such as fenthion can cause

Pyrethroids



Scheme 4. Chemical structure of common Pyrethoid based pesticides.

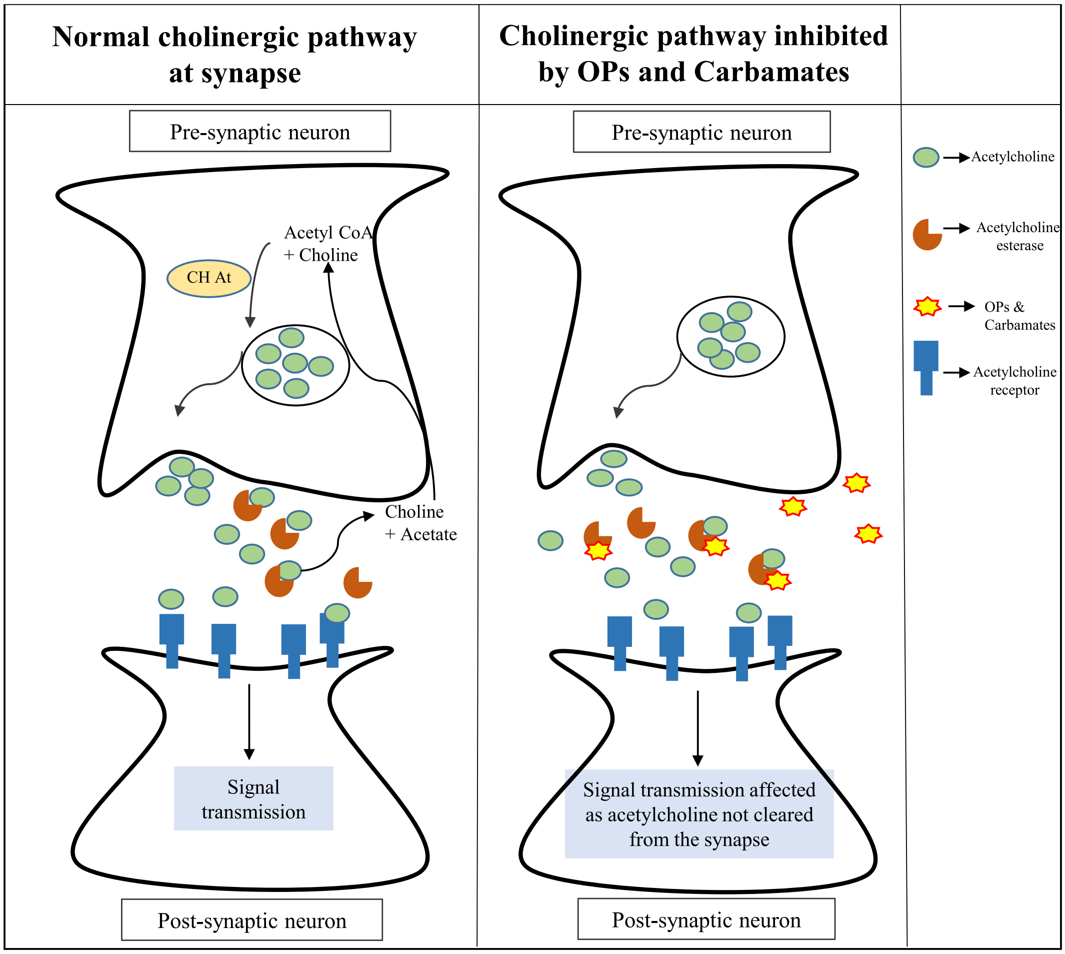


Fig. 4. Mechanism of action of Organophosphates and Carbamates. Part (A) illustrates the acetylcholine neuro-transmission under normal conditions. Acetylcholine released in the synapse is taken up by post-synaptic neuron and signal is transmitted. To regulate neuro-transmission, extra Acetylcholine is cleaved by Acetylcholine Esterase into choline and acetate. Further, choline is taken up by neuron and converted to Acetylcholine through addition of Acetyl CoA by Choline Acetyltransferase. Therefore, neurotransmission is regulated and over-excitation of neurons doesn't occur. Part (B) shows the effect of pesticides on signal transmission. The OPs and carbamates inhibit the activity of Acetylcholine Esterase. Thereby, it leads to over-stimulation of neurons and ultimately neuronal death.

reddening and irritation in eyes on initial exposure. In certain cases, they can also result in eye-related disorders such as myopia, pupillary malfunction, optic disc edema, blurred vision and optic nerve atrophy. Further, if untreated, prolonged exposure to OPs leads to retinopathy and sometimes can cause loss of sight among individuals (Jaga and Dharmani, 2006; Pham et al., 2016). Scientists have also revealed that OP's are responsible for altering the cell turnover, which further contributes to the ocular damage (Sanyal and Law, 2019).

7.2.4. Digestive system

Studies have shown numerous implications of OPs on digestive system (Manfo et al., 2020; Peter et al., 2014). It can severally affect liver physiological functions (Karami-Mohajeri et al., 2017). In certain cases, they are known to cause liver and colo-rectal cancers (Abolhassani et al., 2019; Costa, 2018). Selmi and group have also studied their correlation in kidney injury and pancreatitis (Selmi et al., 2018).

It has been observed that the OPs can greatly alter the gut microbiome (Costa, 2018). A number of changes are induced by pesticides in the gut, which includes alterations in the composition of bacterial species of the gastrointestinal tract, bile acids and dysfunction of metabolic parameters associated with gut microbiome (Gao et al., 2017).

7.2.5. Reproductive system and fetal development

It has been reported that exposure to OPs can result in male infertility (Neghab et al., 2014). They can induce oxidative stress in the body, which ultimately affects the semen motility and semen quality in men (Mehrpour et al., 2014; Wang et al., 2014). Additionally, it has been observed that OP exposure also results in reduced testosterone levels, which further contributes to male infertility (Ghafouri-Khosrowshahi et al., 2019). Moreover, several animal studies have found that OPs adversely effects female reproductive system and are responsible for infertility in females, as well (Fei et al., 2010; Guerra et al., 2011). They can cause dysfunctional estrous cycle, inhibition of follicle cells and reduction of steroid hormones like estrogen (Hu et al., 2018). In fact, Hu et al. (2018) reported that prior exposure to OPs resulted in decreased fertility of Chinese couples (Hu et al., 2018).

Pre-natal exposure to OPs has also been considered as highly detrimental for the fetus, thereby resulting in poorer cognitive functions, emotional and social development in grown children (Bjorling-Poulsen et al., 2008). Moreover, it has been observed that poor reflexes, learning disabilities and disorders like ASD or ADHD are common diagnosis for children exposed to pesticides at prenatal stage (Hertz-Picciotto et al., 2018).

7.2.6. Effect of Organophosphates on ecology

Organophosphorous pesticides (OPs) are regarded as less toxic and harmful to the environment than organochlorine pesticides (Triassi et al., 2019; Zheng et al., 2016). They are more bio-degradable by air, sunlight and water in comparison to OCPs (Jayaraj et al., 2016b). But organophosphates are known to accumulate in water bodies and riverine system due to their high solubility in water (Triassi et al., 2019). In nature, it has been observed OPs such as glyphosate, limit plant growth by interfering with photosynthesis, plant metabolic pathways and disturbing the concentration of bacteria in root nodules of leguminous plants (Gomes et al., 2017; Lushchak et al., 2018; Zobiole et al., 2011). Further, these pesticides have been shown to reduce organic nutrient content of the soil and thereby, adversely affect the soil fertility in the treated area. They can also form resilient complexes with metal ions prevalent in soil, which reduces their uptake by plants (Kaur et al., 2017).

The impact of OPs on non-target terrestrial and aquatic organisms is quite, as well (Long et al., 2006; Watson et al., 2014). It has been discovered that OPs are toxic to various fish species of fresh water reservoirs such as catfish, carps and trouts (Islam et al., 2019; Maryoung et al., 2014; Wang et al., 2015). It has also been found that the quantity of algae, which is prevalent in aquatic bodies and form an essential part of their ecosystem, are reduced in presence of these pesticides (Sun et al., 2015). A study by Hill et al. (2017) helps delineate the deleterious impact on non-target species by organophosphates. They reported that OPs like CPF and methidathion were instrumental in destroying the local non-target slug-eating beetle population in a canola field. This cross-toxicity was shown to cause an upsurge in the number of slugs present in the area and eventually invertebrates preyed on the canola crop and reduced crop yield. Therefore, it is essential to curb the application of OPs for the welfare of environment and wild animals.

7.3. Organochlorine pesticides

It has been estimated that about 40 percent of the pesticides commonly used are Organochlorine compounds, pointing to their prevalence and indispensability in the environment. This class includes potentially toxic pesticides like Endrin, Dieldrin, Heptachlor, Endosulphan, Isodrin, Isobenzan, Aldrin and Pentachlorophenol besides others that may show slightly lesser toxicities. Even though most of these organochlorine pesticides are insecticides, there are proven detrimental effects for human health (Jayaraj et al., 2016a).

These are chlorinated hydrocarbon compounds with five or more chlorine atoms. They have low aqueous solubility, high persistence, high lipid solubility and low polarity. Organochlorines induce toxicity mainly via stimulating regions of the central nervous system. Studies have shown that organochlorines act like gamma-aminobutyric acid (GABA) antagonists and thereby inhibit activity of ion channels (Jayaraj et al., 2016b). A lot of well-known pesticides come under the organochlorine category i.e., DDT, lindane, endosulfan, aldrin, dieldrin and chlordane. Jayaraj and group have reported that they are extensively used in developing countries owing their low cost and efficacy against a wide range of pests (Jayaraj et al., 2016b). These compounds are impervious to microbial degradation. Due to this property, they can persist in environment for a longer duration and are responsible for disturbing the natural flora and fauna. Further, it has been observed that chronic exposure can lead to adverse health effects like endocrine disorders, neurodevelopmental defects, hepatic diseases and even cancers like breast cancer and colo-rectal cancer (Nicolopoulou-Stamati et al., 2016; Park et al., 2014) (Abolhassani et al., 2019).

7.4. Effects of organochlorine pesticides on human physiology-

7.4.1. Brain

A metabolite of heptachlor (a commonly used insecticide) called heptachlor epoxide has been linked with the formation of “Lewy bodies” in brain (Ross et al., 2019). It has been discovered that OCPs like chlordane, dieldrin and lindane are present in considerable amounts in the brain samples of Parkinson's disease affected patients (Ross et al., 2019). In a study carried out on rats, it has been found that even low exposure of lindane before birth crosses the placental barrier and up-regulate the synthesis of enzymes of cytochrome P family in the brain (Srivastava et al., 2015).

7.4.2. Respiratory system

Organochlorine pesticides have been implicated with upper and lower respiratory tracts illnesses among the children (Dallaire et al., 2004; Sunyer et al., 2010). In a meta-analysis Gascon and co-workers observed that DDE exposure to mothers during pregnancy may lead to asthma besides other respiratory disorders like wheezing in kids (Gascon et al., 2012, 2014). Exposure to DDE early in life reduces growth among children, especially height and weight, which are considered to be critical indicators for normal pulmonary functions (Balte et al., 2017). Agricultural workers using DDT in farms have also been found to suffer from chronic bronchitis (Hoppin et al., 2007).

Lindane in combination with lipopolysaccharide (LPS), which is an important constituent of bacterial membranes, causes inflammation of the lungs in mouse models (Tewari et al., 2017). As a consequence of this, the immune system gets activated, producing several chemokines and cytokines like Interleukins, Tumor Necrosis Factor (TNF) α, cells like neutrophils, macrophages etc. in the body (Tewari et al., 2017).

7.4.3. Hepatic system

Methoxychlor (MXC), another insecticide from organochlorine family is known to target cytochrome P450 enzymes of the liver, thus is responsible for altering the detoxification potential of liver. These enzymes are also involved in the process of drug metabolism and their dysfunction may thus result in diseases like testis cancer, cryptorchidism etc. (Chen et al., 2015). It has been found that p,p' dichlorodiphenyldichloroethylene (p,p'DDE) and hexachlorocyclohexane (β-HCH) have tendency to get deposited in adipose tissues, which ultimately contributes to high fatty acid concentration in liver. In addition, they cause dys-functioning of liver mitochondria, disturb β-oxidation of fatty acids, and change the activities of proteins related to TCA cycle (Ji et al., 2016; Liu et al., 2017).

7.4.4. Female reproductive system and fetal development

In a recent study it has been found that higher levels of pesticides such as Hexachlorobenzene (HCB), Hexachlorocyclohexane (HCH), Dichlorodiphenyldichloroethane (DDD), DDE and DDT in blood plasma may increase the concentrations of homocysteine, which indicates their involvement with the folate dependent mechanism (Yin et al., 2020). Pesticides such as DDT and α-HCH are linked with complications in pregnancy that may lead to neural tube defects (Ren et al., 2011). This also stresses the need for women to take proper folic acid supplements during pregnancy to protect them against OCP's toxicity (Ueland et al., 2001). Furthermore, organochlorine pesticide exposure also increases the risk of endometriosis among women (Cooney et al., 2010).

7.4.5. Endocrine system

Reports have indicated that DDT exposure affects the functioning of the endocrine system (Mangochi, 2010; Patisaul and Adewale, 2009) and is linked to risk of breast cancer (Cohn et al., 2015). It modulates the thyroid functions by exerting inhibitory effects on the thyroid stimulating hormone (TSH) receptor (Rossi et al., 2018).

Studies on NES2Y cell lines clearly reflected the adverse effects of organochlorine pesticides exposure on insulin production (Pavlikova et al., 2015). A prolonged exposure to DDT and DDE has been shown to affect protein production by the β cells (Pavlikova et al., 2015). The proteins which mainly gets affected are cytoskeleton proteins that transport insulin across the body and α enolase, an enzyme catalyzing the conversion of 2-phosphoglycerate to phosphoenolpyruvate in glycolysis (Pavlikova et al., 2015).

7.4.6. Effects on ecology

Evidences have shown that DDT can induce many adversative effects on the environment (Woodwell et al., 1971). Due to long persistence of its residues in the environment and excessive accumulation in successive trophic levels, it has been considered as a serious cause of concern for the ecosystem (Di et al., 2017). The contamination of soil with organochlorine pesticides not only affects plant growth, but also the natural flora (Ramani, 2011). Their residues continue to persist for a long period, thus posing bigger threat for crops to be grown in the soil (Mishra et al., 2012). The unabated use of organochlorine pesticides has antagonistic effects on the phosphate solubilizing bacteria (PSB) of the soil. The activity of rhizobacteria has also been found to be greatly affected, which helps to solubilize the phosphorus present in soil for plants and promote their growth (Rani et al., 2018; Tripti et al., 2015). Researchers have found a large amount of residues of lindane, dieldrin, DDT in drinking water that raises concern over their indiscriminate use in the environment (Agarwal et al., 2015; Fosu-Mensah et al., 2016). Endosulphan, a persistent organic pollutant used extensively on crops in many parts of the world is toxic to life forms as well as a contaminant of soil and water (Weber et al., 2010). Traces of its presence have been detected in tree barks as well as on vegetation (Weber et al., 2010).

To reduce the effects of organohlorine pesticides on land, bioremediation has been proposed to be an effective alternative. Recently, this method has been implemented by Raimondo and co-workers, where they used lindane contaminated soil samples and treated them with cocktail of acinetobacteria that further boosted the renewal process by increasing the microbial flora (Raimondo et al., 2020). In another study, lindane contaminated soil was improved with a mixture of different strains of *Streptomyces* with fungi like *Fusarium solani*, *Trametes versicolor* and *Trichoderma atroviridae* (Saez et al., 2018). Several studies have revealed that the genus *Streptomyces* has been shown to degrade a variety of pesticides and the fungi's are used to enhance the process of degradation (Briceño, 2016; Ruiz-Hidalgo et al., 2014).

7.5. Other pesticides

Apart from OPs and OCPs, pyrethroids and carbamates are prominently used pesticides (Fig. 5) in agricultural activities. Pyrethroids are synthetic analogs of naturally occurring pyrethrins found in flowers of pyrethrum (*Chrysanthemum cinerariaefolium*) (Kaviraj and Gupta, 2014), examples include permethrin, cypermethrin and deltamethrin (Soderlund, 2012). They are effective insecticides, biodegradable and have low toxicity to mammals as compared to OPs and OCs (Kaviraj and Gupta, 2014). Pyrethroids act by regulating sodium voltage channel present in the nerve cells of insects (Xu et al., 2018). On the other hand, pesticides derived from carbamic acid are known as Carbamates. The structure of carbamates primarily consists of an amide-ester bond (Ghosh and Brindisi, 2015). They are highly potent insecticides due to their action as cholinesterase inhibitors. Commonly used carbamates include carbaryl, carbofuran and aminocarb (Jayaraj et al., 2016b).

In brain, carbamates and pyrethroids can cause toxic yet reversible side effects/adverse effects in humans as compared to OPs and OCs (Bjorling-Poulsen et al., 2008). Newly discovered insecticide Neonicotinoid, which is being used as a replacement for organophosphates and carbamates, has also shown associations with neurodevelopmental disorders like autism, anencephaly and memory loss (Cimino et al., 2017). Researchers have found that developed adult brain is more robust than a developing brain against pesticide induced toxicity. It has been observed that matured neural networks and post-mitotic cells tend to develop a certain resistance to toxic metabolites. Therefore, the deleterious effects of pesticides are more pronounced in developing brain of children as compared to a fully developed adult brain (Comfort and Re, 2017).

A large number of respiratory problems have been reported upon pesticide exposure such as wheezing, airway irritation, dry/sore throat, cough, breathlessness and chest tightness. These compounds can further result in damage of lung functions and finally, alter the lung volume as well as rate of gaseous exchange (Hoppin et al., 2017; Ye et al., 2013). Pesticides accumulation in the body is associated with development of respiratory disorders like bronchitis, asthma, chronic obstructive pulmonary disease (COPD) (Hoppin et al., 2007; Mamane et al., 2015; Ndlovu et al., 2014). Further, studies have shown that exposure to arsenic-based pesticides, carbamate insecticides and phenoxyacetic acid herbicides increase the risk for development of lung cancer (Alavanja and Bonner, 2012).

Digestive system of the body is also greatly impacted by pesticides. One of the regions severely impacted by these chemicals is the GIT microbiome. The gut is home to more than 30,000 species of bacteria (Frank et al., 2007). Wide variety of microorganisms inhabit the gut and immensely benefit the host via production of vitamins, amino acids (Spanogiannopoulos et al., 2016). Persistent organic pollutants (POPs) enter the digestive tract through diet; hence their interaction may lead to impairment in the functioning of the gut microbiome (Defois et al., 2018). This may further affect the immune system, cause poor absorption of nutrients and may lead to the production of metabolites toxic to the body (Jin et al., 2015). Zhang et al. in 2015 found that treatment with tetrachlorodibenzofuran (TCDF) changed the gut microbiota population and cause inflammation of the gut (Zhang et al., 2015). It has also been studied that exposure of the mouse gut to polychlorinated biphenyls (PCBs) led to a decrease in the population of Gram-negative bacteria and altered the metabolic activities in the gut (Choi et al., 2013).

POPs have been shown to cause toxicity in the liver, as well (Lee et al., 2014). It has been studied that pesticide exposure can lead to an increased risk of liver cancer (VoPham et al., 2017). Metabolism of pesticides takes place in the liver and this is responsible for accumulation of carcinogenicity through various mechanisms like oxidative stress, genotoxicity, changes in cell adhesion etc. (Gomaa et al., 2008; Jin et al., 2014a, 2014b) Apart from liver, a direct correlation has been shown between pesticides and increased incidence of ColoRectal Cancer (CRC) too (Abolhassani et al., 2019). Pesticides have also been reported to affect organs like the stomach, pancreas, and spleen and are responsible for inducing cancers like leukemia, myeloma and non-Hodgkin's lymphoma (Alavanja and Bonner, 2012).

It has been observed that Pre and postnatal exposure of pesticides is associated with pediatric cancers, neurological deficits, fetal death, intrauterine growth restriction, preterm birth and many congenital abnormalities such as cardiovascular and neural tube defects. For example, maternal exposure to DDT, DDE and endosulfan results in neural tube defects (Kalliora et al., 2018). Maternal pesticide exposure in the developmental window of 3 to eighth week of pregnancy is said to have highest impact on fetal deaths. The timing of paternal pesticide exposure is also critical and exposure to phenoxy herbicides even as early as 3 months before conception significantly increase the risk of spontaneous abortions (Greenlee et al., 2004). Mouse studies show that exposure to agrochemical pesticides such as atrazine, methoxychlor, permethrin and ammonium nitrate result in impaired blastocyst development, reduced cell number and increased cell death (apoptosis) in the developing embryos (Amstislavsky et al., 2003; Greenlee et al., 2004). Further, the exposure to insecticides such as imidacloprid results in many developmental defects such as head enlargement, limb defects, ectopia viscerale, reduced body length and teratogenic effects in vertebrate embryos (Hussein and Singh, 2016).

8. Molecular targets for pesticides

DDT and pyrethroids primarily target the sodium channels of insects while the organophosphates like Malathion, Chlorpyrifos and methylcarbamates inhibit Acetylcholinesterease (AChE) considered important for the conduction of nerve impulse (Colovic et al., 2013; Silver et al., 2014). Herbicides like Pinoxaden are known to act against the enzyme Acetyl CoA Carboxylase (ACCase) in plants. It is involved in fatty acid biosynthesis, which has several important roles to play for the organism such as membrane formation, polyketide synthesis, besides serving as

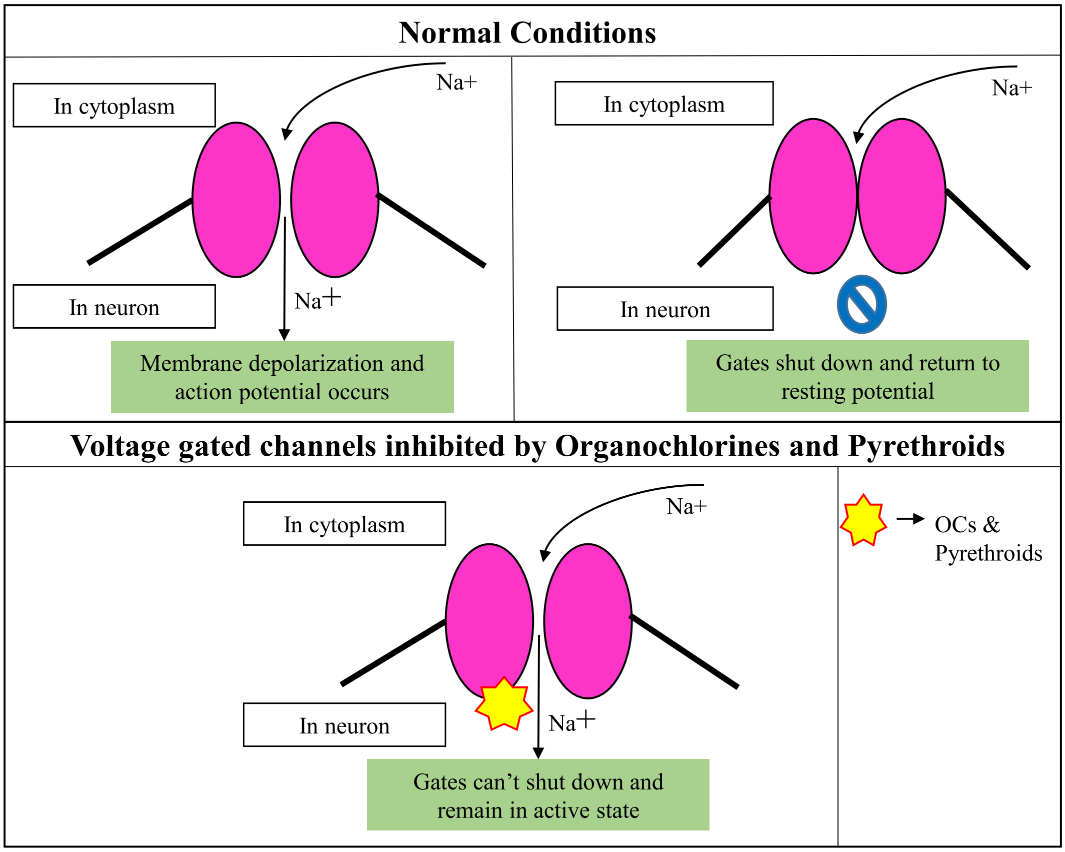


Fig. 5. Mechanism of action of Organochlorines and Pyrethroids. In part (A) & (B), normal condition of voltage gated channels is depicted. Sodium enters the voltage gated channels and membrane depolarization takes place, which results in conductance of an action potential. Once voltage has increased, the membrane returns to resting potential by closing the voltage channels and stopping the influx of sodium ions. Part (C) demonstrates what happens in presence of pesticides. Membrane repolarization is inhibited by Organochlorines and Pyrethroids. Therefore, the voltage gated channels remain in stimulated state and lead to neuronal dysfunction.

energy reserve (Kukorelli et al., 2013; Pyne et al., 2019; Yu and Jez, 2008). While other herbicides target the enzyme Acetolactate synthase that leads to the synthesis of amino acids isoleucine, leucine, and valine (Zhou et al., 2007), herbicides like glyphosate inhibit the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) involved in the synthesis of aromatic amino acids (Zulet et al., 2013).

Other neurological targets of pesticides include GABA and glutamate gated channels (Ffrench-Constant et al., 2016). A number of cyclodienes like aldrin, dieldrin and endrin target GABA receptor (Bloomquist, 1993). Glutamate gated chloride channels are exclusive to insects and mediate inhibitory neurotransmission in invertebrates (Wolstenholme, 2012). Lactones like Avermectins and Milbemycins exert their effect through these channels (Ffrench-Constant et al., 2016). They are effective for pesticidal action against nematodes and mites too (Wolstenholme, 2012).

It has been suggested that rotenone acts as the inhibitor of NADH dehydrogenase, thus is responsible for blocking ATP synthesis and high production of reactive oxygen species (Chiaradia et al., 2019). Rotenone also interferes with the levels of aldehyde dehydrogenase that may further contribute to the development of features of Parkinson's disease (Goldstein et al., 2015). G protein coupled receptors (GPCR) have been thought to play a role in the development of new pesticides. These belong to a family of proteins most extensively found on the cell surface and hence, are found on the surface of insect pests (Audsley and Down, 2015).

Majority of the pesticides have adverse effects not only on the target pests, but they also affect the metabolism of non-target organisms like humans. Conazole fungicides that include hexaconazole, tebuconazole etc. interfere with endocrine functions in the human body (Yu et al., 2013). Besides this, most of the organophosphorus pesticides (OPs) are responsible for development of insulin resistance among humans (Lasram et al., 2014).

Apart from targeting enzymes and neurotransmitters, pests can be targeted on a genomic level using gene disruption tools; RNAi and CRISPR/cas9 can be utilized to inhibit insects (Ngai and McDowell, 2017). They make pests targeting very specific and restrict growth of insects even at larval stage (Hall et al., 2015; Ulrich et al., 2015). Further, these techniques will have reduced toxicity to humans and non-target species.

9. Environmental impact

POPs are the pesticides or chemical compounds exhibiting high degrees of stability and are resistant to environmental degradation. Due to their ability to accumulate in the living systems, they pose a serious threat to mankind and other inhabitants of our planet. These Persistent Organic Pollutants include some key chemical compounds- Aldrin, Chlordane, Dichlorodiphenyltrichloroethane (DDT), Dieldrin, Endrin, Heptachlor, Hexachlorobenzene, Polychlorinated biphenyls (PCBs) and Polychlorinated dibenzofurans, Toxaphene, Polyaromatic hydrocarbons (PAHs) (Ashraf, 2017; Jones and de Voogt, 1999).

Natural habitats are being converted to agricultural lands to meet the demands (Dudley and Alexander, 2017) and pesticides are being used on a large scale to increase the yield from crops to cater to the growing needs of the ever-increasing population. These consequences are causing loss of biodiversity as after being applied to the crops, pesticides ultimately find their way to soil and groundwater reserves, air and water which are important resources for living beings (Aktar et al., 2009; Schafer et al., 2012). Several factors that play a key role in determining the effects pesticides have on water resources include-half-lives, solubility, rate of application of the pesticide and disposal (Agrawal et al., 2010).

Research has demonstrated that approximately ninety per cent of chemical pesticides applied in agriculture end up having consequences which can be deleterious to the ecological system. This leads to detrimental impact on the environment and living organisms which are not the primary targets of these chemicals. So far it has been discovered that adversity caused by pesticides is exacerbated by their non-biodegradability and toxicity. Till date few microbial communities have tried to reverse the effects of the pesticides to some extent by means of remediation but nothing concrete has been revealed (Castelo-Grande et al., 2010; Morillo and Villaverde, 2017).

Many studies suggest that water bodies near agricultural fields are contaminated by pesticides via simple drifting, percolation through soil, run-off or even spillage. Not only this, the aquatic ecosystems have also been found to be seriously disturbed (Moss, 2008). Further, these consequences make water unfit for human and animal consumption. On the other hand, spray-based pesticides and volatile compounds can spread across distances, which can further make environment vulnerable. Further, aerial spraying through aircrafts can cause severe damage to living organisms. It has also been observed that volatile organic compounds are released from pesticides meant to fumigate soil; they can act as major air pollutants when they reach the troposphere (Squillace et al., 2002).

It has been reported that excessive application of pesticides causes reduction in organic matter of soil which also lowers its water retention ability. This leads to a decline in soil fertility as the microbial load and diversity of the soil reduces. Consequently, the total organic matter present in the ground lowers considerably. Therefore, it makes the area more prone to droughts. Thus, serious measures should be taken on a global scale to tackle the problem of environmental pollution due to pesticides (Fig. 6). The Rotterdam Convention has most of the UN member nations committed to ensure fair trade in hazardous chemicals whereas the Stockholm Convention, signed in 2001 by 90 countries, aims to restrict the usage and production of POPs.

9.1. Future implications

Indiscriminate usage of pesticides has led to severe implications for the environment. The deleterious effects of these chemicals has been scientifically reported and documented. A conscious campaign to create awareness in normal population is essential. In this direction, efforts have been made to generate more knowledge among general populace about the ill effects of pesticides. Consequently, farmers have slowly started taking up organic farming to limit chemical application. Therefore, this has led to an unprecedented rise in organic produce. Apart from organic farming, Integrated Pest Management (IPM) can also help in considerable reduction of chemical application. These practices protect harvest and don't cause extensive damage to non-target organisms. Though introduced in 1970s, IPM has been adopted by agriculturists fairly recently and can easily be applied for various crops. Another alternative for conventional pesticides is Bio-pesticides. These are biological compounds produced by plants or microbes which have insecticidal activity. Due to their biodegradable nature and less toxicity to humans, they can help reduce pest damage without causing extensive damage to surrounding environment. These alternatives to harmful pesticides can assist in changing the face of agriculture and make it more sustainable for future generations.

10. Conclusions

The use of pesticides is a pertinent aspect of modern agricultural activities. These chemicals protect crops from a variety of insects, pests and even weeds. Thus, their application has risen dramatically in recent times and resulted in an overwhelming increase in food production all over the world. Moreover, it has also led to a significant drop in prices thereby, making nutrient-rich food accessible to a larger population. It would have been difficult to accomplish this feat without the use of pesticides. On the other hand, excessive pesticide usage is leading to severe detrimental effects on the environment and humans with passage of time. Since majority of pesticides are toxic and non-biodegradable in nature, environmental implications are immense due to incessant consumption of pesticides. Investigations have shown that pesticides are a major cause of pollution in water, air and soil. In the human body, these chemicals can cause a range of disorders in different organs and are especially harmful at a developing state. Consequently, many harmful pesticides like DDT have been banned in developed nations but several middle- and low-income nations are still dependent on them due to their high efficacy and low cost. Despite the hazards posed by rampant usage of pesticides, their utilization continues unabated in developing countries as viable and practical alternatives are lacking. Globally, several acts have been passed and laws are implemented to tackle the pesticide menace but success has been limited. Hence, better measures are required to ensure minimum pesticide consumption and to look for economical alternatives. Biopesticides have emerged as feasible alternative to conventional pesticides. They are effective and

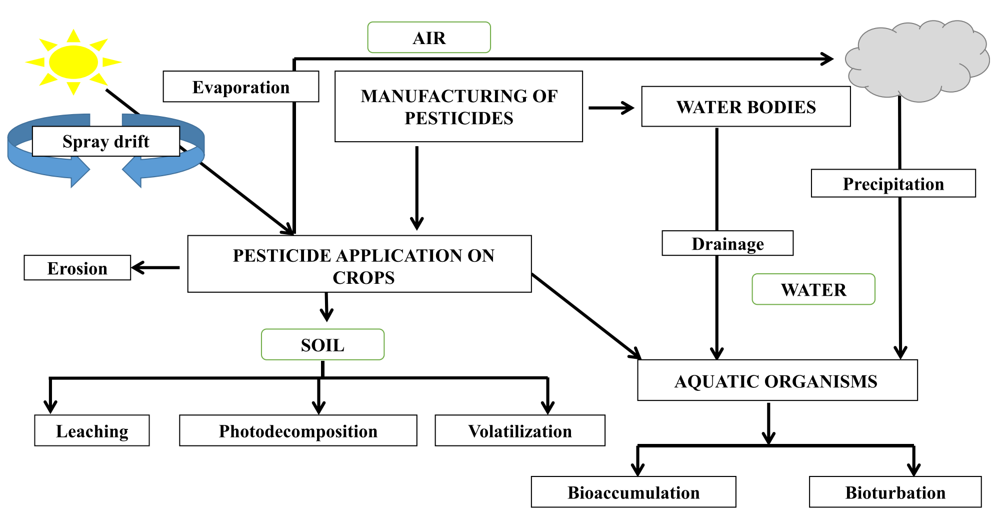


Fig. 6. Different ways of Environmental exposure of pesticides. Flow chart showing environmental exposure of various life forms to pesticides through natural resources like air, soil and water involving processes of evaporation, erosion, bioaccumulation etc. via action of sunlight and rainfall.

have minimal negative implications for the surrounding ecosystems. The initiatives either to optimize the use of pesticides or to increase biopesticides' dependencywill be vital to conserve environment and protect living organisms from highly deleterious effects posed by them at large.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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