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Review

An extensive review on the consequences of chemical pesticides on human health and environment

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ABSTRACT

Pesticides are contributing in current agriculture to fulfil the need of raising population. Uses of pesticides are not limited to agriculture, but they are also used to control over domestic pests, disease insect vectors and home gardening. But they are very toxic in nature and pose acute risks on the human health and the environment. They negatively affected the agricultural workers and trigger social conflicts when employed extensively and without safety measures. Further, they also have adverse effects on the neighboring communities. Chiefly, agriculture workers meet with both direct and indirect exposure with these chemicals. Common man comes in contact with these chemicals by skin contacting which is due to leaking and drifting of pesticides during mixing and causing serious threat to human health such as diabetes, reproductive disorders, neurological dysfunction, cancer and respiratory disorders. In this review, we discussed classification, mechanisms, benefits and adverse effects of the pesticides on both human beings and the environment. We had also discussed some remedial measures to mitigate their toxicity. In future, research is needed to develop innovative ideas in current farming which are able to decrease the application of chemical pesticides.

Contents

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E-mail addresses: arun.srivastav@chitkarauniversity.edu.in, arunitbhu2009@gmail.com (A.L. Srivastav).

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0959-6526/

1. Introduction

Pests are any plants, animals or microorganisms which deal with foodstuff, health or console. According to Environmental protection agency (EPA), pesticides are the group of chemical substances which are being used to control and repel the pest population. Pesticides also defined as chemical as well as natural agents applied to control or kill the harsh pests like creatures, organisms causing plant diseases and weeds. It also used to control other living organisms, for example nematodes, arthropods expect from insect and vertebrates which destroy our food sources and cause many health problems. Pesticides may be summarized as chemical substances which are used in the broad area of crop to protect from insects, weeds, and pests for nourishing and increasing the yield and efficiency of crop. Besides, these pesticides have other benefits like save man's power, time and high efficiency (Igbedioh, 1991; Boxall, 2001; Narayanasamy, 2006; Cooper and Dobson, 2007; Schreinemachers et al., 2017; Wang et al., 2017). Many studies have documented that plants take up pesticides from soil (Fantke et al., 2013; Florence et al., 2015). According to the United States EPA report, in 2012 the worldwide expenses at the manufacturing stage were 5600 crore dollars. During 2008–2012; herbicides accounted for the top most expenses (45%) trailed by the expenses on insecticides, fungicides and other types of pesticides. The term 'pesticide'is not an innovation. It is being used from the ancient times; Sumerians, Greek, and the Romans were applying diverse chemicals to kill insects including sulphur, mercury, copper and plant extracts. But the consequences were not good because of ancient chemistry and lack of the application strategies. After the second world war, the use of pesticides became popular by the commencement of dichlorodiphenyltrichloroethane, 2,4-dichlorophenoxyacetic acid, benzene hexachloride, aldrin and dieldrin. All these synthetic chemicals were extensively used because of their high efficiency, simple to use and low cost. But after the continuous use of pesticides, some pests have no effect of pesticides, although other non-target pests were hazardous and pesticide residues found in that place where its presence is very harmful for the environment. The book published in 1962, 'Silent Spring' portrayed this argument that pesticides have deadly effects on ecosystem. The report was significantly analysed and it was found that danger of pesticides is more than actual which guides the researcher to find out the way of cropping with minimum use of pesticides (Gour et al., 2012). A trend of research publication on pesticides has also been explored (in Fig. 1) to understand the importance of this subject based on the data available on the webpage of PubMed.

Fig. 1 represents year wise trends in research documents published on pesticides in between 2011 and 2020. From Fig, it can be seen that in last ten years, total 71,979 research documents were published as per the PubMed electronic data base. It is a very important area of research as every year the counts of published research papers have been remarkably increasing. For example, in 2011, the publication count in this area was 7,745, which got increased up to 8291 by the year of 2012 only. From the above

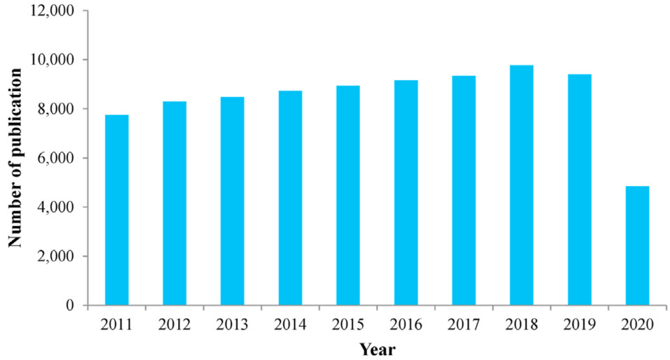


Fig. 1. Trend of research paper publication on the pesticides and their application (Source: PubMed, Accessed on Aug. 31, 2020).

diagram, increasing trend was found to increase from 2011 to 2018; however, in 2019 total count was less as compared to 2018. Moreover, in 2020 till now (August 2020), total 4842 research documents have been already published. The objective of the present review is to analyze the negative impacts of the chemical pesticides on the environment, human beings as well as on the animals. Moreover, the authors have presented thorough frameworks for their remedial steps along with the preventive measures.

2. Classification of pesticides

Pesticides can be broadly categorized on the basis of applications, target organism and chemical nature. On the basis of application, pesticides can be grouped as agriculture (used to protect the crop pest, insects and weeds), public health (used to kill vector which causes diseases) and domestic pesticides (used to kill insects like cockroach, bacteria, protozoa, mice etc). Based on the target organism pesticides can be categorized as insecticides (chemical which is used to kill the insects), fungicides (chemical which is applied to inhibit or to kill the fungus), herbicides (chemicals which are used to control or kill the weeds), rodenticides (pesticides used to kill the rodents), fumigants (they are gaseous pesticides used to kill or control the pest like bedbug) and insect repellents (which are applied on the skin or cloth to keep insects away from the skin and cloth). On the basis of chemical nature, pesticides can be categorized as organochlorines, organophosphates, carbamates, pyrethroids, phenyl amides (carbanilates, acylanalides, toluidines and acetamides), phenoxyalkonates, trazines, benzoic acid derivatives, benzonitriles, phtalimide derivatives, dipyrids and miscellaneous category (Table 1) (Jayaraj et al., 2016).

3. Mechanism of pesticide action

Pesticides are used from the ancient times. Now pesticides used in every part of the world very frequently. It is essential to know the modes of action of pesticides to recognize the health issue caused to human and non-target organism so facilitate the outline of more successive remedial assess. Mode of action also helps to give hints to the improvement of resistance in pests thus opposing assesses would be worked out. It can be illustrated by discussing three pesticides (Wang et al., 2017; Schreinemachers et al., 2017).

3.1. Insecticides

Insecticides mainly active on the 3 target sites in the nervous system: the acetylcholine receptor (neonicotinoids), acetylcholinesterase, an enzyme which plays an important role in the mediation of nerve impulse (organophosphorus and carbamates), voltage-gated sodium ion channels crossways the nerve membrane (pyrethroids and DDT) (Rajashekar et al., 2016; Nauen et al., 2006; Elbert et al., 2008; Yu, 2011). Some faddy insecticides for example, juvenile hormone mimics (fenoxycarb and pyriproxyfen), which inhibit the synthesis of ecdysone agonists and chitin (diflubenzuron) act on insect-particular targets that interrupt reproduction and development (Ishaayaand Degheele, 1998; Ishaaya, 2001; Hemingway et al., 2002; Chandler et al., 2011). Further on the basis of their mode of action insecticides are classified into three categories (Sparks and Nauen, 2015; Jayaraj et al., 2016).

3.1.1. Nerve and muscle active site

3.1.1.1. Cholinesterase inhibition. This type of inhibition was shown by carbamate and organophoshate insecticides which produce overstimulation in the nervous system of the insects. The consequence of this leads to death of the insect.

3.1.1.2. Acetylcholine receptor stimulation. Neurotransmitter acetylcholine action was shown by spinosad mimic and neonicotinoid insecticides. They bind to the acetylcholine receptors, which cause long time stimulation and ultimately kill the insect. They have shown no effect on the cholinesterase.

3.1.1.3. Chloride channel regulation. Chloride channel can be activated by three major pathways: inhibition of gamma-aminobutyric acid (GABA) receptor (organochlorine insecticides), agonists of the GABA-gated chloride channel (bifenazate) and activation of chloride channels.

3.1.1.4. Sodium channel modulator. This kind of mode of action shown by pyrethrins and pyrethroids insecticides, they ~~are~~ bind to the sodium channels, resulting in fixing of insects in the open state that result in tremor and is responsible for killing of insects.

3.1.2. Growth and development targets

3.1.2.1. Inhibitors for synthesis of chitin. Some hormonal substances block the chitin synthesis inside the insects which cause killing of insect at the initial phase at the time of embryonic growth.

3.1.2.2. Regulators of insect growth. Endocrine system affected by insecticides which directly is responsible for the production of the growth hormones. Insects poisoned by insect growth regulators do not receive the signal to metamorphose. Some of them were designed to mimic effects of juvenile hormone necessary to enter metamorphosis.

3.1.3. Energy production targets

3.1.3.1. Electron transport inhibition. In this mode of action energy supply to the target organism is crooked by hindering the electron transport and this type of mechanism has been shown by aliphatic type of organochlorine insecticides.

3.1.3.2. Interruption of oxidative phosphorylation. Mitochondrial electron transport chains are blocked by organotin miticides; on the other hand pyrroles uncouple electron transport and oxidative phosphorylation. Therefore, the production of ATP blocked, which leads to death of insects (Colovic et al., 2013; Sparks and Nauen, 2015; Jayaraj et al., 2016; Thapa et al., 2017).

3.2. Fungicides

Fungicides are used to inhibit or kill the fungicides. Fungicides are active on the weak sires in the metabolic and chemical process and produce toxic effect. On the basis of mode action fungicides are

Table 1
Chemical classification of pesticides (Jayaraj et al., 2016; Kim et al., 2019).

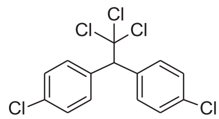
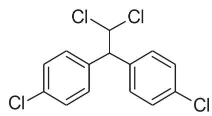
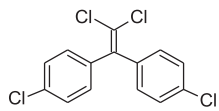
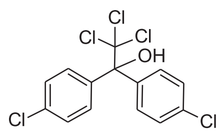
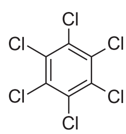
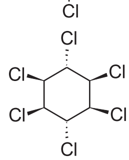
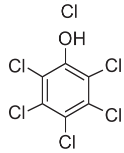
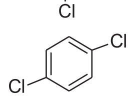
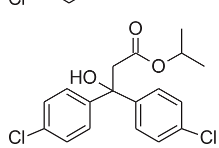
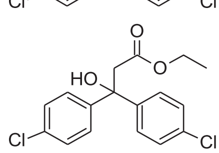
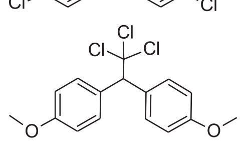
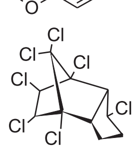
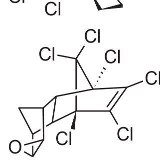
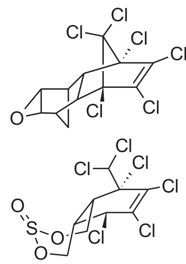
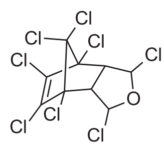
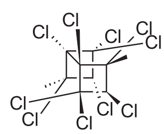
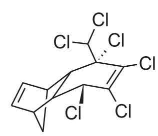
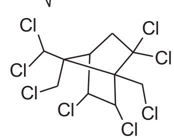
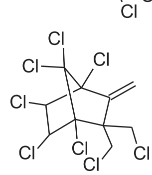
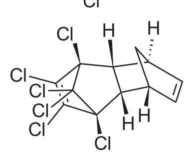
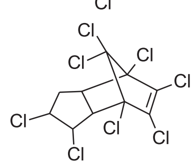
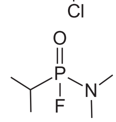
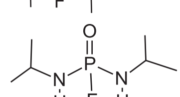
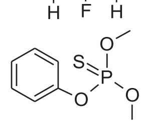
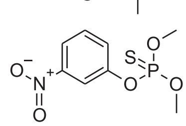
Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
Organo-chlorines	Dichlorodiphenyltrichloro-ethane (DDT)		Insecticide	Nausea temeros seizures	Banned
	Dichlorodiphenyldichloro-ethane (DDD)		Insecticide	–	Banned
	Dichlorodiphenyldichloro-ethylene (DDE)		Insecticide	Negative effect on serum and adipose tissue	Banned
	Dicofol		Acaricide	Skin disease, nausea	Banned (Norway, Netherlands)
	Benzene hexachloride (BHC)		Insecticide	Damage of CNS, Seizures	Banned (U.S.)
	Lindane		Insecticide Rodenticide	Effect on immune system, damage of CNS	Banned
	Pentachlorophenol		Herbicide	Damage kidney, liver and CNS	Banned (U.S.)
	1,4-Dichlorobenzene		Rodenticide	Failure of liver and respirator system	–
	Chloropropylate		Acaricide	–	–
	Chlorbenzylate		Acaricide	Nausea, weight loss and sever cases leads tocoma	Restricted (U.S.)
	Methoxychlor		Insecticide	Damge reproductive system	Banned (U.S.)
	Heptachlor		Insecticide	Produce irritation in eyes	Banned (U.S.)
	Endrin		Insecticide	Nausea, damage of CNS	Banned (South east Asia)
	Dieldrin		Insecticide	Vomiting, disorder in muscle movement	Banned (South east Asia)

Table 1 (*continued*)

Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
	Endosulfan		Insecticide Acaricide	Damage CNS	Banned (India)
	Isobenzan		Insecticide	_	Not registered (EPA)
	Mirex		Insecticide	Damage liver, CNS and reproductive system	Banned (U.S.)
	Aldrin		Insecticide	Mayoclonic Jerk, dizziness	Banned (South east Asia)
	Camphechlor		Insecticide	Failure of kidney, liver and CNS, carcinogenic	Banned
	Toxaphene		Insecticide	Disorder of CNS	Restricted (Argentina, Columbia)
	Isodrin		Insecticide	_	_
	Chlordane		Insecticide	Breathing problems, stomach pain	Banned (South east Asia)
Organo-phosphates	Dimefox		Insecticide		Banned (U.S.)
	Mipafox		Insecticide		Used
	Methyl parathion		Insecticide Repellant	Repiratory disorder, deffect in eye side	Restricted (U.S.)
	Fenitrothion		Insecticide Acaricide	_	Used
	Dicrotophos (Bidrin)		Insecticide Acaricide	Diarrhea, nausea	Banned (U.S.)

(*continued on next page*)

Table 1 (*continued*)

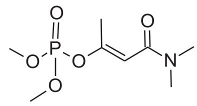
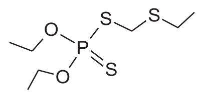
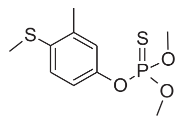
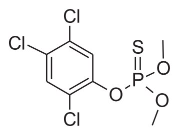
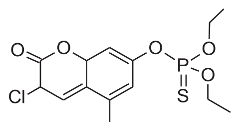
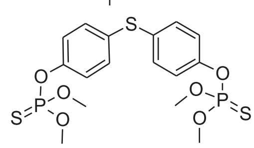
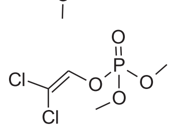
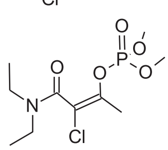
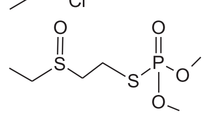
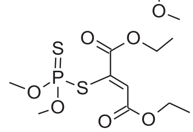
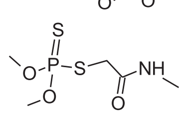
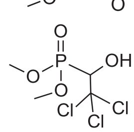
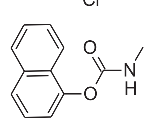
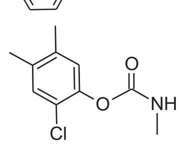
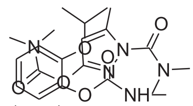
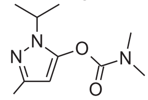
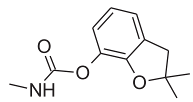
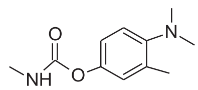
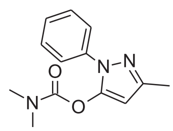
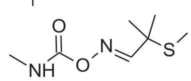
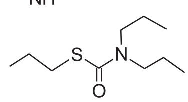
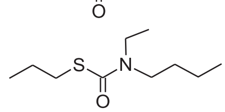
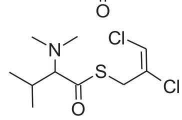
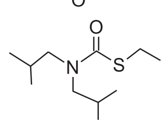
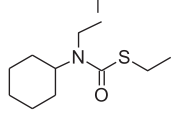
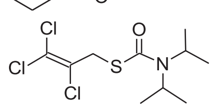
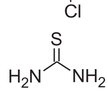
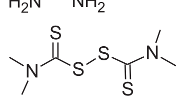
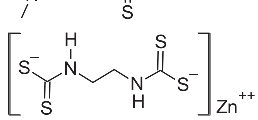
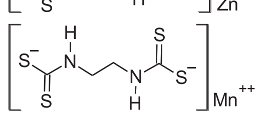
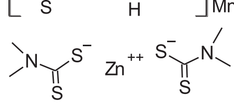
Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
					
	Phorate		Insecticide Acaricide	Disorder of heart rate and respirator rate	Banned (U.K.)
	Fenthion		Insecticide	_	Banned (Greece)
	Ronnel (Fenchlorfos)		Insecticide	_	_
	Caumphos		Insecticide	_	_
	Temefos (Abate)		Insecticide	_	_
	Dichlorovas		Insecticide	Diarrhea, blurred vision	Used
	Phosphamidon		Insecticide Acaricide	Repiratory disorder	Used
	Oxydemeton-methyl		Insecticide Acaricide	Cardiovascular disease	Used
	Malathion		Insecticide Acaricide	Diarrhea, blurred vision respirator disorder	Used
	Dimethoate		Insecticide Acaricide	Diarrhea, blurred vision respirator disorder	Not produced (U.S.)
	Metrifonate (Trichlorfon or Diptrex)		Insecticide	_	Banned (Argentina)
Carbamates	Carbaryl		Insecticide	Diarrhea, blurred vision	Used
	Carbanolate		Insecticide Acaricide	_	Used
	Propoxur		Insecticide	Diarrhea, loss of cprdination	Used

Table 1 (*continued*)

Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
	Dimetilan		Insecticide	Vision defect, respirator disorder	Banned
	Isolan		Insecticide	_	used
	Carbofuran		Insecticide Nematicide Acaricide	Hypertension vision defect, respirator disorder	Used
	Aminocarb		Insecticide	_	Used
	Pyrolan		Insecticide	_	_
	Aldicarb		Insecticide Nematicide Acaricide	_	Used
	Vernolate		Herbicide	_	Used
	Pebulate		Herbicide	_	Used
	Diallate		Herbicide	_	_
	Butylate		Herbicide	_	Used
	Cycloate		Herbicide		_
	Trillate		Herbicide	_	_
	Thiourea		Rodenticide	Bone marrow damage, carcinogenic	_
	Thiram		Fungicide	_	_
	Zineb		Fungicide	Nausea, fatigue, reproductive disorder	Banned (U.S.)
	Maneb		Fungicide	Weight loss, nausea, dermatitis, reproductive disorder	_
	Ziram		Fungicide Repellant	_	_

(*continued on next page*)

Table 1 (*continued*)

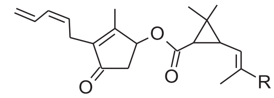
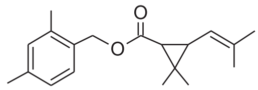
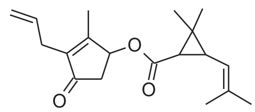
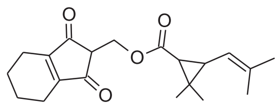
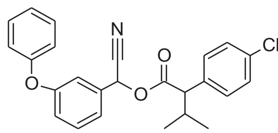
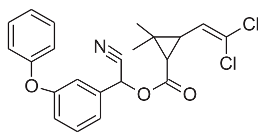
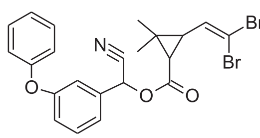
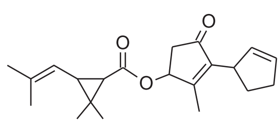
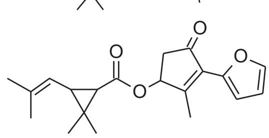
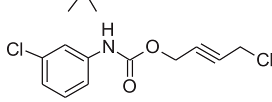
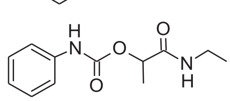
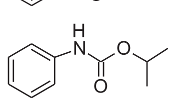
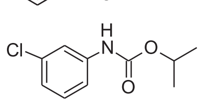
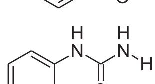
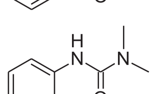
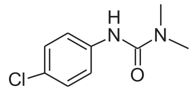
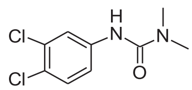
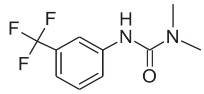
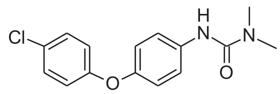
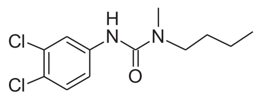
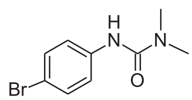
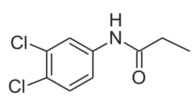
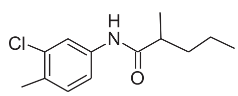
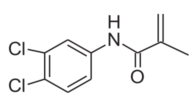
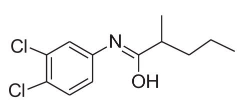
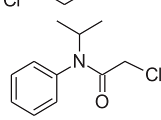
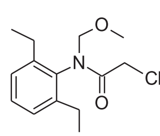
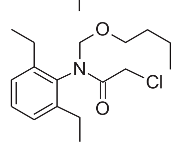
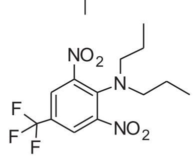
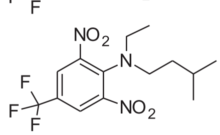
Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
Pyrethroids	Pyrethrin		Insecticide	–	–
	Dimethrin		Insecticide	–	–
	Allethrin		Insecticide Anti-microbial agent		
	Tetramethrin		Insecticide	Carcinogenic, mutagenic effect, adverse effect	–
	Fenvalerate		Insecticide Acaricide	–	Banned (U.S.)
	Alphamethrin (Cypermethrin)		Insecticide	–	–
	Decamethrin		Insecticide	Neurotoxin, paraesthesia	–
	Cyclethrin		Insecticide	–	Used
	Furethrin		Insecticide	Respiratory disorder, damage of CNS	–
Carbanilates	Barban		Herbicide	–	–
	Carbetamide		Herbicide	Hypoglycemia, anorexia	used
	Propham		Herbicide Plant growth regulator	–	–
	Chlorpropham		Herbicide Plant growth regulator	Kidney and liver failure	Used
	Phenyl urea		Herbicide	–	Used
	Fenuron		Herbicide	–	Banned
	Monuron		Herbicide	–	–

Table 1 (*continued*)

Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
					
	Diuron		Herbicide	Anemia, bone marrow damage, abnormal blood pigment	Used
	Flumeturon		Herbicide	Cancer, kidney failure	_
	Chloroxuron		Herbicide	_	_
	Neburon		Herbicide	_	Not approved (U.S.)
	Bromuron		Herbicide	Skin rahes, dizziness, nausea	_
Acylanalide	Propanil		Herbicide	_	_
	Pentanochlor (Solane)		Herbicide	_	Not approved
	Dicryl		Herbicide	_	_
	Karsil		Herbicide	_	_
	Propachlor		Herbicide	Respiratory disorder	Not approved (EU)
	Alachlor		Herbicide	Thyroid, cancer, mutagenic effect	Not approved (EU)
	Butachlor		Herbicide	_	Not approved (EU)
Toluidines	Trifluralin		Herbicide	Nausea, irritation in eyes, skin disease	_
	Benefin (Benfuralin)		Herbicide	_	_
	Oryzalin		Herbicide	skin disease	_

(*continued on next page*)

Table 1 (*continued*)

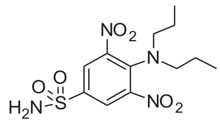
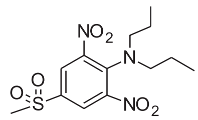
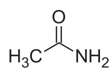
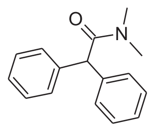
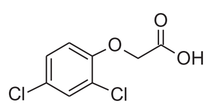
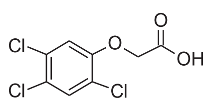
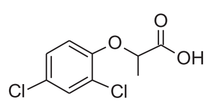
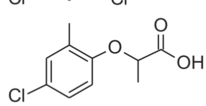
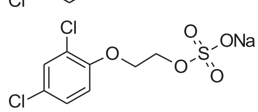
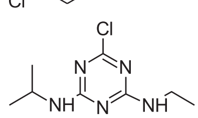
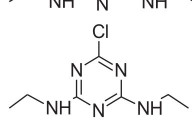
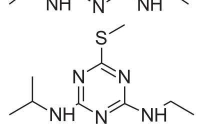
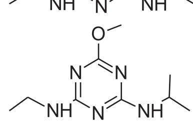
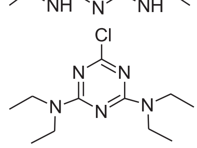
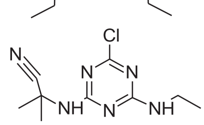
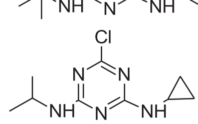
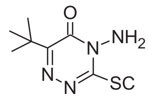
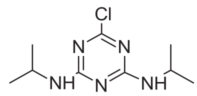
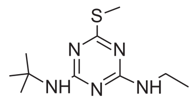
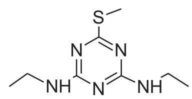
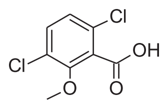
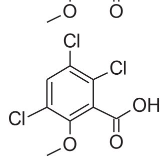
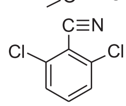
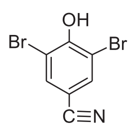
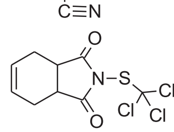
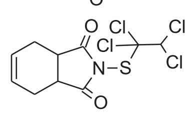
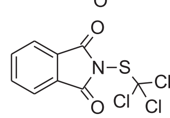
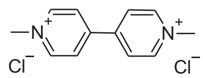
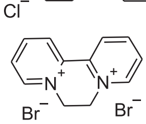
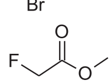
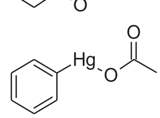
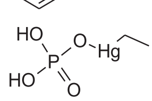
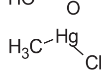
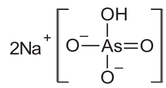
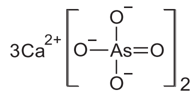
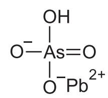
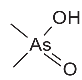
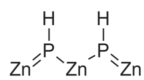
Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
	Nitralin	 	Herbicide	–	Not approved (EU)
Acetamides	Acetamide		Flavoring Agent	CNS disorder	Used
	Diphenamid		Herbicide	dermal irritation, dermal sensitization, inhalation toxicity	Used
Phenoxy alkonates	2,4-Dichlorophenoxyacetic acid		Herbicide	Nervousness, headache, dizziness	–
	2,4,5-Trichlorophenoxyacetic acid		Herbicide	Damage of liver	Not approved (EU)
	Dichloroprop		Herbicide	Reproductive disorder	Not approved (EU)
	Mecoprop		Herbicide	Low blood pressure, rooling	Not approved (EU)
	Sesone		Herbicide	–	–
Triazines	Atrazine		Herbicide	Kidney failure, congestive heart failure	Not approved (EU)
	Simazine		Herbicide	Reproductive disorder, kidney failure	Not approved (EU)
	Ametryn		Herbicide	Liver damage and heart failure	Not approved (EU)
	Atratone		Herbicide	–	–
	Chlorazine		Herbicide	–	–
	Cynazine		Herbicide	–	–
	Cyprazine		Herbicide	Constipation, nausea, dizziness	Used

Table 1 (*continued*)

Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
	Metribuzin		Herbicide	–	Used
	Propazine		Herbicide	Anemia	Used
	Terbutryn		Herbicide	–	Not approved (EU)
	Simetryn		Herbicide	–	–
Benzoic acid derivatives	Dicamba		Herbicide	Damage to CNS, heart failure	–
	Tricamba		Herbicide	–	–
Benzonitriles	Dichlorobenil		Herbicide	–	–
	Bromoxynil		Herbicide	Vomiting, urinary disorder	Used
Phthalimides	Captan		Fungicide	Respiratory ailment	–
	Diflotan (Captafol)		Fungicide	–	–
	Folpet		Fungicide	Brain ailment, skin disease	Used
Dipyrids	Paraquat		Herbicide	Failure of kidney	Not approved (EU)
	Diquat		Herbicide Desiccant	Skin disease	–
Miscellaneous	Fluoroacetate		Rodenticide	Cardiac ailment, disorder of kidney and respiratory system	–
	Phenylmercuric acetate		Herbicide Fungicide Insecticide	Reproductive and kidney disorder	–
	Ethylmercuric phosphate		Fungicide	–	–
	Methylmercuric chloride		Fungicide	–	–
	Sodium arsenate		Anthelmintic	Diarrhea, ulcer	–

(*continued on next page*)

Table 1 (*continued*)

Chemical class	Pesticide name	Chemical structure	Uses	Side effects	Current status
					
	Calcium arsenate		Insecticide Molluscicide	–	Banned (UK)
	Lead arsenate		Insecticide	–	–
	Cacodylic acid		Herbicide	Carcinogenic, reproductive disorder	–
	Aluminium phosphide	Al≡P	Acaricide	–	–
	Zinc phosphide		Rodenticide	–	

two types one single-site which attack only at one site in the metabolic pathway. Other is multisite which are active on multiple sites in the metabolic pathway in the fungus. This can be illustrated by fungicides which prevent the sterol biosynthesis mainly ergosterol that is the chief sterol in fungi. Carboxamides are precise preventer of succinate oxidation in the mitochondria. Benzimidazoles are efficient anti-microtubule agents for the fungi (Perez et al., 1991; Carr et al., 2005; Sioud et al., 2009; Aponte et al., 2010; White et al., 2010). There are some common mode actions involved in the action of fungicides as discussed below.

3.2.1. Inhibitors of ergosterol biosynthesis

Ergosterol is the vital part of the cell membrane of the fungi, whose synthesis is inhibited by the canazoles. Firstly, they blocked cytochrome P450 (CYP-51) or lanosterol-14α demethylase, which is the single components of the cytochrome family, which are present in fungi, prokaryotes, plants and animals. They have been shown broad spectrum antifungal activity, therefore employed in pharmaceuticals to cure systematic and tropical fungal infections (Bolognesi and Merlo, 2011).

3.2.2. Inhibitors of protein biosynthesis

The insecticides dithianon play a role of a multisite inhibitor of protein formation modifying the sulfhydryl groups of many proteins. Further the protein inhibition obstructs the spore germination and germ tube growth. Benzimidazoles, for example, suppress the reassembly of depolymerized spindle microtubule division. Although these compounds exhibit specific efficiency against fungal organisms, they also target mammalian microtubule assembly dynamics (Bolognesi and Merlo, 2011; Oruc, 2010).

3.2.3. Mitochondrial respiration inhibitors

The inhibition of Electron transfer at the quinone "outside" site of the cytochrome *bc*1 complex between cytochrome *b* and cytochrome *c*1 referred to as the Ubiquinol oxidizing by the Azoxystrobin, which block the mitochondrial respiration that leads to the blockage of mitochondrial respiration and energy production (Balba, 2007; Casida and Durkin, 2017).

3.2.4. Multisite fungicides

Some fungicides are targeting multiple sites of the targeted fungi, which affected various biochemical processes. It involves the inhibition of suppression of respiration, antioxidant enzymes to disturb the redox balance in cells (Lushchak et al., 2005), and some of them also inhibit the nuclear factor-kB (NF-kB) signaling cascade (Rath et al., 2011).

3.3. Herbicides

Herbicides are the chemical agent applied to control or kill the weeds. They are used in place of the mechanical method used to remove the weeds. Herbicides action is withdrawing the benefits of plant metabolic pathway such as photosynthesis, plant hormone action, regulation of cell division, synthesis of amino acids such as an antidote and graminicides prevent monooxygenase (De Roos et al., 2005; Pretty, 2008; Thrall et al., 2011). Herbicides can be categorized based on various factors, including site of action, mechanism of action, chemical nature, period of usage, translocation and selectivity (Varshney et al., 2012; Torrens and Castellano, 2014). Herbicides associate themselves with active site before killing the targeted herbs. They can influence different sites insides the plants and at the sites of action. Every herbicide possesses distinct mode of action, which are discussed below:

3.3.1. Growth regulators

Broad leaf weeds can be killed or control by these kind herbicides, they mainly impact on the growth hormones of the plants such as 2,4-dichlorophenoxiacetic acid and mechanism involve behind their action is based on their auxin-like capacity (Jablonkai, 2011).

3.3.2. Seedling growth inhibitors

Thiocarbamates and acid amides herbicides serve as potent inhibitors for both root and shoot. They interrupt the growth of the plant, mainly at the growth point.

3.3.3. Photosynthesis inhibitors

These types of herbicides interfere with the biomembranes by highly active molecules which lead to the inhibition of photosynthesis. Ultimately, plants get killed due to increase in highly reactive molecules which damage cell membranes. For example, triazine herbicides, which used to kill the broad leaf weeds (Sathiakumar et al., 2011).

3.3.4. Lipid biosynthesis inhibitors

There are some herbicides, which block the production of lipid, which results no biological membrane, fluazifop, sethoxydim are the example of these herbicides.

3.3.5. Amino acid biosynthesis inhibitor

Biosynthesis of some amino acids can be inhibited by these types of herbicides. Roundup herbicide has glyphosate [N-(phosphonomethyl)glycine] as an active constituent which inhibit the biosynthesis of the aromatic amino acids such as tryptophan, phenylalanine and tyrosine. in addition to this there are different compounds which act as powerful inhibitors of glutamine synthase that catalyzes incorporation of ammonia onto glutamate (Jablonkai, 2011; Tarazona et al., 2017).

3.3.6. Inhibitors of pigment biosynthesis

Clomazone herbicides block the biosynthesis of photosynthetic pigments, biosynthesis of photosynthetic pigments recognized as carotenoids. These pigments play an important in the protection of chlorophyll from the light and if carotenoids not present in the plant then chlorophyll will be damaged, which make plants unable to perform photosynthesis (Corniani et al., 2014).

4. Advantages of pesticides

Pesticides are extensively employed in greatest zones of crop, making to diminish infestations due to the pests and thus protect crops from the possible harvest losses and decrease in product quality (Damalas, 2009). There are big variety of encouraging consequences after use of different types of pesticides. Decreased crop loss subsequent of spraying fungicides is an apparent advantage, nevertheless, few are less apparent either as they happen in the medium or long term, or delicate or minor incremental assistances dispersed over a great zone. The effects are the instant consequences of pesticide usage. Three major consequences of the pesticides include controlling farm pests and plant ailment vectors; controlling vectors of human and livestock ailments and annoyance creatures; and averting or controlling creatures that damage other human actions and constructions. The primary advantages are the result of the pesticide's action; the straight gain anticipated after using them. From the 3 major consequences, 26 primary advantages were identified extending from the safety of recreational surface to protection of human lives. The advantages which are less immediately or apparent and consequences of the primary advantages are known as secondary advantages and 31 secondary advantages (Fig. 1) were recognized, extending from healthier persons to preserved bio-diversity (Cooper and Dobson, 2007). The interrelation between the harmful effects and the advantages of pesticides remains complicated and not easy to conform forever (Aktar et al., 2009; Abhilash and Singh, 2009; Damalas, 2009; Maksymiv, 2015; Bonner and Alavanja, 2017; Zhang, 2018).

4.1. Increase productivity

Indian economy depends upon the terrific benefits of the pesticides, and has been an initiative for the usage of pesticides for community well-being, forestry, and domestic province as well as in agriculture segment. This high productivity can be attained by selecting the high-yield seeds, innovative irrigation methods and agriculture chemicals. Pesticides play a vital role in the process of decreasing the debts due to disease, weeds and insects which are responsible for the considerably decreased crop productivity. Strangely, the economic loses could be due to not using pesticides and use of pesticides could result in notably raised crop yield (Webster et al., 1999). However, maximum pesticides in the environment go through photochemical reaction conversions that are comparatively non-toxic for both environments as well as human beings (Kole et al., 1999). The crop production could be enhanced by high yielding seed selection, better soil and water management, fertilization and some other cultivation approaches. Greater susceptibility to pest damage enhances productivity of crop (Oerke et al., 1994; Oerke and Dehne, 2004; Aktar et al., 2009). Globally, pre-harvest pest, pre-processing, storing, dispensation, packing, promotion and bowl left-over losses contribute for majority of loss. It is very important to prevent waste throughout the entire length of the food chain so that crop losses would be moderate (Oerke, 2006; Popp, 2011). Weeds can decrease productivity of dry land up to 37—79%. Critically, a huge number of weeds in the beginning level of crop; contribute for a 40% decline in the crop yield (Behera and Singh, 1999; Samant and Prusty, 2014).

4.2. Controlling vector diseases

The diseases which originate from the vectors can be prevented by killing the vectors. Only by using the insecticides is the feasible way to restrain the insects which cause the mortal diseases. For example, malaria is the bigest cause for about 5000 deaths every day (Ross, 2005). According to Bhatia et al. (2004), 'malaria is one of the foremost reasons of morbidity and mortality in the developing countries and a principle civic health issue in India'. Lindblade et al. (2015) claimed that applying insecticides-treated bed nets decreased incidences of malaria infection also the infant mortality. Deltamethrin treated bed-nets remarkably decreased in-house resting frequency, light trap catches, biting, human-being obtained bulge rate and degree of malaria contamination. The malaria occurrence was lowered 59% in deltamethrin-treated net, 35% in untreated net and 9% in no net cases (Yadav et al., 2001). Usage of insecticide-treated bed nets significantly decreased the infectious bites per individual (Curtis et al., 2006). Insecticide usage portrays a crucial part in the deterrence and management of infectious ailments, including malaria, dengue and filariasis (World Health Organization, 2006).

5. Consumption of pesticides

Every year about 20 lack tons of chemical pesticides are being used all over the world, out of which 24% is used in the United States and 45% in the Europe (Abhilash and Singh, 2009). The data showed that the rate of pesticides uses is very high in the developed countries; North Western Europe, Japan and the United States used three by four of the total pesticide employed worldwide (Alavanja, 2009). In these countries mostly herbicides were used which has low acute poisoning as compared to insecticides. The amount of pesticides applied in the developing countries was lesser than the developed countries (US EPA, 1998; Wilson and Tisdell, 2001). The annual consumption of pesticides in India and neighboring countries in last 5 years is presented in Table 2.

In general, the pattern of pesticide application in India is unlike to that of the world (Fig. 2). In India, highest used pesticide (76%) is insecticide in contrast to that of the world (44%). The usage of herbicides (10%) and fungicides (10%) is compatibly very low which is totally different from the world in which 30% herbicides and 21% fungicides were used (Mathur and Tannan, 1999).

6. Risk of using pesticides

The exposure to the chemical pesticides is extremely destructive for the flora, fauna and the environment.

6.1. Human health

The labors working in the pesticide manufacturing

Table 2
Annual consumption (tons) of pesticides in the neighboring countries of India from 2013 to 2017 (Source: https://www.fao.org/faostat).

Country	Year				
	2013	2014	2015	2016	2017
Austria	3108.6	3380.7	3787.1	3662.1	4655.3
China	1811605.3	1815730.5	1772403.9	1772369.3	1773634
France	66497.29	74909.6	66531.02	71951.22	70588.7
Germany	43756.1	45836.29	48131.97	46920.98	56641
India	45620	60280	56120	50410	52750
Italy	55633	59422	63322	60259	56641
Japan	52794.3	53543.7	54171.16	51006.46	52248.52
Netherlands	10720.17	10665.55	9999.3	9999.3	8494.74
Thailand	8190.5	21800	21800	21800	35287
United Kingdom	17673.46	18392.45	18302.28	19277.79	19843.94
United States	407779.2	407779.2	407779.2	407779.2	407779.2
Argentina	170964.45	207706	207706	207706	196008.93

*Data are available till 2017 only.

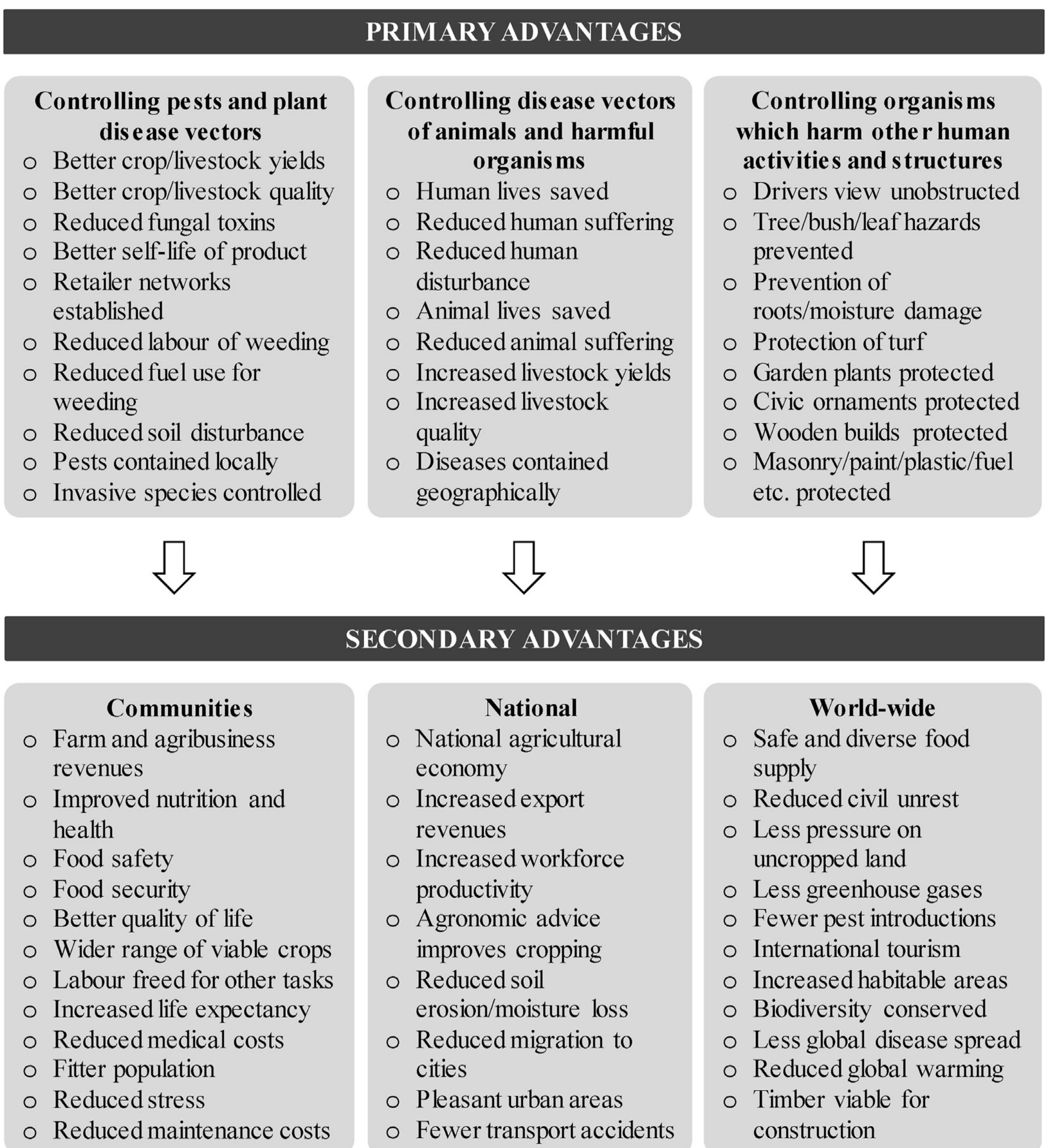


Fig. 2. Major primary and secondary advantages from the use of pesticides (Cooper and Dobson, 2007).

organizations, in fields, assassinating of household pests and green house are mostly affected due to pesticide exposure. The greater chance of exposure in the working area of the pesticidesis at the time of production and formulation because in this practice risk is very high. In manufacturing site probability of danger is high as they deal with several hazardous chemicals including pesticides, crude materials and harmful solvents (Maroni et al., 1999, 2006; Wilson and Tisdell, 2001; Pimentel, 2005; De Roos et al., 2005; Tariq et al., 2007; Atreya et al., 2008; Aktar et al., 2009; Soares et al., 2009; Martníez-Valenzuela et al., 2009; Damalas, 2009; Damalas and Eleftherohorinos, 2011; Mittal et al., 2014; Tago et al., 2014; Damalas and Koutroubas, 2016; Nicolopoulou-Stamati et al., 2016; Gangemi et al., 2016; Grewal et al., 2017). Various types of health problems, including cancer, diabetes mellitus, respiratory disorders, neurological disorders, reproductive (sexual/genital) syndromes and oxidative stress are caused due to the direct exposure, handling of pesticides or pesticide residues present in the food stuffs.

6.1.1. Cancer

The direct exposure to the pesticides is the foremost reason of cancer globally. This issue becomes globally concern and currently attracting the researcher throughout the world (Samanic et al., 2008). Out of the 43 investigations (agricultural health study), 12 investigation reports suggested that there is no considerable relation between the direct contact of pesticides to the farmers and enhanced danger of malignancy (De Roos et al., 2005; Lynch et al., 2006; Greenburg et al., 2008). On the other hand, remaining 31 investigation reports confirmed the strong relationship between the direct contact of some specific pesticides and the danger of cancer (Alavanja et al., 2003; Beane et al., 2005; Lynch et al., 2006). Some proof provided from agricultural health study in context of raising the risk for cancer of prostate, breast, bladder, lungs, colon, leukaemia and multiple myeloma due to continuous exposure of some pesticides (Alavanja et al., 2004; Lee et al., 2004; Rusiecki et al., 2004; Lee et al., 2004a; Bonner et al., 2005; De Roos et al., 2005; Engel et al., 2005; Hou et al., 2006; Beane et al., 2006; Rusiecki et al., 2006; Mahajan et al., 2006; Mahajan et al., 2006a; Mahajan et al., 2007; Purdue et al., 2007; van Bemmel et al., 2008; Koutros et al., 2009; Alavanja and Bonner, 2012; Huang et al., 2019). 'International Agency for Research on Cancer' (IARC), evaluated on cogenic risks of pesticides to human beings which is extensively used to pinpoint environmental carcinogens and assist the government to direct formation of policy for shielding of the public from the chance of cancer owing to food, environment and working cancer-causing agents. IARC had put two pesticides (arsenic, pesticides and 2,3,7,8-tetrachlorodibenzene-p-dioxin) into the category of carcinogens (IARC, 1991). A cohort study on 57310 people of the United State suggested the existence of positive relations between the danger of bladder cancer and contact of the pesticides including imidazolinone; imazethyper and imazaquin herbicides (Koutros et al., 2015). Further, a study on 953 cases including, 881 control cases on the agriculture, male workers suggested the enhanced risk of bladder cancer via contact of pesticides with odd ratio (OR) of 1.68 (Amr et al., 2015). According a report of hospital-based control investigation on the 462 glioma and 195 meningioma sufferers in the United States, women with exposure of herbicides have greater risk of meningioma than the women who were not in contact with herbicides even single time with OR of 2.4 (Samanic et al., 2008). The outcomes obtained from an investigation on women from Jaipur indicated that levels of the residues of organochlorine pesticides were importantly advanced in all of the persons suffering from cancerin contrast to the control cluster (Mathur et al., 2008). Health risk assessment recommends that day-to-day nutritional organochlorine pesticide contact through herbal feeding was advanced for children than adults. The hazard quotient and lifetime malignancy danger assessed from nutritional exposure of these vegetables were more than the tolerable edge (Chourasiya et al., 2015).

6.1.2. Diabetes

The consequences of various studies confirmed the correlation between the exposure of pesticides and diabetes. With continuous contact with the pesticides amplified the danger of diabetes. Positive correlation between the organochlorine compounds and diabetes was observed and similar correlation with organophosphate was also with the risk of type 2 diabetes (Cox et al., 2007; Montgomery et al., 2008a,b; Azandjeme et al., 2013; Evangelou et al., 2016; Velmurugan et al., 2017). In addition, the real dataset has significant drawbacks as the maximum studies cross sectional studies. From the finding of the few studies it was suggested that the significant correlation between the chances of type 2 diabetes and exposure of organochlorine pesticides with different population (Everett et al., 2007; Turyk et al., 2009). A study on 11273 women to investigate the association of contact of pesticides with the incidence of gestational diabetes showed that the resident women who were using the pesticides in the garden and home had no risk of gestational diabetes during the pregnancy. Women who were on life time agriculture contact with the herbicides and insecticides had the highest risk of gestational diabetes during the pregnancy (Saldana et al., 2007). Further, a cross-sectional study was done in the Bolivia amongst 116 pesticide sprinklers and 92 non-exposed controls; and it was examined that unusual glucose control as 6.1% for the sprayer individual's comparative to 7.9% of non-exposed persons (Hansen et al., 2014). Increased levels of the pesticides DDT and heptachlor epoxide in the human blood were associated with the occurrence of diabetes and diabetic nephropathy (Everett and Thompson, 2015; Everett et al., 2017). Increasing evidence has associated obesity with persistent the pesticides including DDT and its metabolite DDE (Cano-Sancho et al., 2017). A case-controlled investigation on the population in Bang Rakam, proposed increased risk for occurrence of diabetes due to pesticide exposure (Juntarawijit and Juntarawijit, 2018). The imazamox-based herbicide preparation decreased the size of the β-islet cells and stimulated an increase in blood glucose and calcium (Sevim et al., 2018). Evidences from human as well as experimental studies supported the fact that endocrine-disrupting chemicals (such as DDE) could be involved in the development of diabetes (Lind and Lind, 2018; Ruiz et al., 2018). A case-control investigation carried outongroup of adults from two cities in India suggested that levels of pesticide DDE in Delhi were exceptionally high, but there was no significant association amongst DDE and type 2 diabetes (Jaacks et al., 2019). Studies demonstrated an association between contact with the organophosphates and metabolic dysregulations in rodent models as well as humans (Joshi and Sukumaran, 2019). Malekirad et al. (2013) performed a cross-sectional study, which was based on the questionnaire to found out the relationship between occupational exposure of organophosphorus insecticides and hyperglycemia. They observed that a positive association between exposure of organophosphorus insecticides and hyperglycemia. Further increased the risk assessed approximately 1.6, 1.6, 1.6, and −9 due to exposure of fonofos parathion, trichlorfon, and phorate organophosphorus insecticides, which was evaluated by two different cohort studies based on questionnaire (Montgomery et al., 2008a,b; Starling et al., 2014). Further Starling et al. (2014) demonstrate that the positive association between the occupational exposure of phenoxy herbicides and increased occurrence of diabetes (HR; 1.6), beside this a positive relationship was observed in ecological and cross-sectional study assessed about an Ors of 2.7 and 1.04 respectively amongst Korean Vietnam veterans (Kim et al., 2003; Yi et al., 2014).

6.1.3. Respiratory disorders

Lung diseases, including asthma, bronchitis, organic dust lethal condition, over-sensitivity pneumonitis, silo filler's disorder and neuromuscular respiratory failure amongst farm labors can result from exposures to organic dusts, chemicals and toxic gases (do Pico, 1992; Kirkhorn and Garry, 2000). Many studies supposed presence of positive relationship between the asthma and contact to pesticides. Pesticides exposure can cause the development of asthma with impatience, swelling, endocrine disruption or immune suppression (Balluz et al., 2000; Linaker and Smedley, 2002; Omland, 2002; Langley, 2011). Evidences showed that agricultural contact to pesticides was related with advanced incidences of lung, indication particularly when the contact is more than 2 days every month (Faria et al., 2005). A study on wheeze in farmers and commercial applicators supported a role for organophosphates in respiratory disorders (Hoppin et al., 2006). The agricultural health study proposed that pesticides could lead to atopic asthma, but not nonatopic asthma, in females working in farm (Hoppin et al., 2008). Farm residents in Colorado showed a positive relationship in pesticide poisoning and respiratory symptoms (Beseler and Stallones, 2009). Contact to pesticides could lead to augmented danger for rhinitis (Slager et al., 2009, 2010; Mamane et al., 2015). A cross sectional investigation was carried out in northern India revealed that pesticides cause different respiratory ailments, including dry cough, wheezing, blood in sputum and irritation of the respiratory system (Fareed et al., 2013). An investigation on 926 adult pesticide applicators with active asthma suggested that use of glyphosate and paraquat may contribute to exacerbation of asthma among individuals with allergies (Henneberger et al., 2014). Pesticide exposure could upsurge the danger of lung disorders, as well as the morbidity and mortality problem (Buralli et al., 2018). Occupational exposure among crop farmers was related to a higher occurrence of the pulmonary indications including lung dysfunction, and an advanced occurrence of enduring respiratory ailments (Stoleski et al., 2019). Meng et al. (2016a, b) carried an out a study to evaluate the level of pesticides in indoor dust and blood sample collected from cases of asthma and controls. They were published in two different case control studies which showed that the occurrence of asthma positively associated with the exposure of alpha-hexachlorocyclohexane (α-HCH) and (OR of 1.06) DDE (ORs 1.02 and 1.8). Further Henneberger et al. (2014), performed an agriculture health cohort study to found out the association of the application of pesticides and asthma. Authors observed that a positive relationship found between the exposure of pesticides pendimethalin having an OR about 2.1 and aldicarb having an OR about 10.2. In addition to this Yi et al. (2014) demonstrated that positive relationship between exposure of a cohort of Korean Vietnam veterans to Agent Orange and chronic bronchitis (OR: 1.05).

6.1.4. Neurological disorders

Exposure to pesticides plays contributory role in the growth of neurological syndromes. Evidences had revealed an association of pesticide contact and occurrence of the neurological illness. Most common diseases related to the neurotoxic impact of the pesticides are Parkinson's and Alzheimer's disease (Baldi et al., 2003; Kamel and Hoppin, 2004; Keifer and Firestone, 2007; Rastogi et al., 2010; Mostafalou and Abdollahi, 2013; Thany et al., 2013; Faria et al., 2014; Khan et al., 2014; Li et al., 2014).

6.1.4.1. Parkinson's disease. Parkinson's disease (PD) is related with the depletion of dopaminergic neurons of the substantia nigra that results in occurrence of symptoms including rigidity, akinesia and tremors; and harshness of the disease progressively increases over the years. Previous studies had established the role of pesticides on the instigation of PD (Priyadarshi et al., 2000; Shimizu et al., 2003; Firestone et al., 2005; Brown et al., 2006; Hatcher et al., 2008). Rotenone recognized as a broad-spectrum herbicide is the main cause of degeneration of nigrostriatal dopaminergic neurons via impeding mitochondrial complex I that results in motor dysfunction (Tanner et al., 2011; Goldstein et al., 2015). Benomyl (a fungicide) via its thiocarbamate sulfoxide metabolite, inhibited aldehyde dehydrogenase resulting in buildup of 3,4-dihydroxyphenylacetaldehyde (active metabolite of dopamine), leading to deterioration of dopaminergic neurons (Fitzmaurice et al., 2013). Major danger of PD was associated with paraquat and rotating crops (Brouwer et al., 2017). Data from meta-analysis also revealed the role of pesticides in gene alteration that contributed towards PD pathogenesis which includes multidrug resistance mutation 1, paraoxonase 1 and glutathione transferases (Ahmed et al., 2017). An investigation in California on the 36 generally used pesticides demonstrated a robust association between pesticides and prevalence of idiopathic PD (Betarbet et al., 2000). Rotenone and paraquat are well known pesticides for developing toxin-based PD animal model as they induce neuroinflammation and loss of dopaminergic neurons. Swiss albino mice treated with rotenone developed PD due to deterioration of dopaminergic and dihydroxyphenylalanine decarboxylase-rich neurons (Taetzsch and Block, 2013; Mitra et al., 2015). C57BL/6 mice injected with paraquat every week for 4, 8, 12 and 24 weeks showed dose and age reliant degeneration of dopaminergic neurons, suggesting that single dose didn't give any damaging effect as compared to repeated treatment (Baltazar et al., 2014). Upbeat association was detected between the pesticide exposure and PD on the basis population control study on 133 cases and 128 controls on the French population (Moisan et al., 2015). Similarly, it was observed that the danger of PD was enhanced by 3% by each 1.0 μg pesticide per litre of ground water in 'Colorado medicare beneficiary database' (James and Hall, 2015). In Netherland, an investigation showed a positive relationship between the deaths due to PD and work-related contact with the pesticides (Brouwer et al., 2015). A strong relationship was observed for PD in people with nitric oxide synthase (NOS) genotypes exposed to commonly used organophosphates. This supported role of NOS2A genetic variants in PD vulnerability in organophosphate exposed people (Paul et al., 2016). In disagreement, PD and farm living, ingesting well-water, agriculture and the usage of pesticide chemical; the association was less persistent compared to cigarette smoking (Breckenridge et al., 2016). Evidence suggested that lifelong contact with pesticides might contribute to the progression of neurodegenerative ailments, but the results were controversial. The 5- and 10-years pesticide contact was linked with a 5% and 11% augment in the danger of PD (Yan et al., 2018). Tanner et al. (2009) studied the association between the PD and 2, 4-D herbicide. It was found that occupational exposure of 2, 4-D herbicide increase risk of PD approximately 2.6 times. Further exposure to β-HCH increased PD risk about 4.4 times and in another case control study it was observed that β-HCH more likely present in the blood of PD as compared to the control (Richardson et al., 2009).

6.1.4.2. Alzheimer's disease. Alzheimer's disease (AD) is a form of dementia that results in progressive memory damage and retaining power due to neurodegeneration in cerebral cortex. Several reviews have linked exposure of pesticides with neurological disorders. Men have been reported with greater pesticides exposure as compared to women due to difference in their working activities (Kamel and Hoppin, 2004; Keifer and Firestone, 2007; Rastogi et al., 2010; Li et al., 2014). With respect to the neurodegenerative disorders, Hernandez et al. (2017) reported that alteration in mental function in school children is due to prenatal exposure to organophosphates (Muñoz-Quezada et al., 2013; González-Alzaga et al., 2014). Other studies also showed that maternal or prenatal and post-natal exposure of organochlorines developed cognitive, motor and autism disorder in children. Pesticide exposure damaged cholinergic neurons of basal forebrain that caused memory, motor and sensory dysfunction. The US armed forces were exposed to sarin and cyclosarin during the Gulf war in 1991 and later suffered from neurological disorders (Carles et al., 2017). In 1995, Tokyo was affected with sarin gas due to Japanese terrorist attack. Some victims died, many recovered, but mental disabilities still persisted for years. These chronic mental health problems either due to accidental or suicidal organophosphate poisoning results in the loss of many productive life (OECD, 2002). A study on residents of the agricultural community of Cache County showed that contact with pesticides (organochlorines) had greater chance of having dementia and AD in the late-stage of life (Hayden et al., 2010). Evidence recommended that lifelong cumulative contact with the pesticides may generate long-lasting damage on the brain and contribute to the development of AD. A direct relation observed between pesticide contact and AD in a meta-analysis confirmed the theory that pesticide contact is a dangerous aspect for AD (Yan et al., 2016). Two different case-control studies carried to assessed exposure of pesticides associated with Alzheimer disease and matched their controls. The consequence of the first study showed that risk associated with pesticides an OR approximately 1.1. Second study informed that there was a positive association between the increased level of DDE in blood and Alzheimer disease with an OR approximately 4.2 (McDowell et al., 1994; Richardson et al., 2014).

6.1.5. Reproductive syndromes

The relationship between environmental and occupational pesticide contact was extensively analysed and several investigations have confirmed that contact with pesticides could produce fertility disorders in females as well as males (Hanke and Jurewicz, 2004; Kumar et al., 2004). Endocrine-disrupting chemicals (EDC) have ability to influence the hormone signaling including estrogens, thyroid and androgens which are essential part of usual embryonic growth. EDC examples are bisphenol (present in the baby bottle), diethylstilbestrol and specific pesticides like vinclozolin and atrazine (Jeyaratnam et al., 1990; Kavlock et al., 1994; Toppari et al., 1996; Crisp et al., 1998; Mylchreest et al., 1999; Damstra et al., 2002; Czene et al., 2002). Moderately increased danger of premature abortions for preconception was observed for contact with phenoxyacetic acids and triazines. Postconception contact was mostly related to the late-stage spontaneous abortions and elderparentalphase was the biggest risk factor for the spontaneous abortions (Arbuckle et al., 2001). The high risk of delayed abortion was directly associated with thiocarbamate and glyphosate type pesticides (Jurewicz et al., 2008). In contrary to this, a study carried out on females working in the greenhouse, did not show any considerable connection of pesticide contact with the incidents of natural abortion, pre-mature delivery and natal faults. Exposure of males to pesticides can influence blood, sex hormone, sperm (morphology, concentration and motility), semen quality or the gonad's structure. Reduction in the sperm count was observed in men working in the green house for more than ten year (Jurewicz and Hanke, 2007; Bretveld et al., 2007; Roeleveld and Bretveld, 2008; Jurewicz et al., 2008; Perry et al., 2011; Saadi and Abdollahi, 2012). A study on a population of randomly chosen couples showed greater incidence of major infertility, along with incessant still birth and spontaneous abortion with those working in the farm (Neghab et al., 2014). Exposure to pesticides (environmentally or occupationally) could be related to reduce sperm well-being (Martenies and Perry, 2013). Mehrpour et al. (2014) features of semen are evaluated fertility of male. Authors observed a positive relationship between exposures of pesticides and decreased semen quality. Further, the people those are contact with abamectin have been detected decreased in sperm maturity and motility (Celik-Ozenci et al., 2012). Beside this Burdorf et al. (2011) observed that the occupational exposure of pesticides to pregnant women leads to lower weight birth having an ORabout 2.4 evaluated by a JEM-based cohort study. A case-control study based on questionnaire had demonstrated that the pesticides exposure to pregnant women increased the imperfection of neural tube two times. Another study has compared the cases with control level of organochlorines in the placenta studied the motherly contact with DDT and α-HCH was positively associated with imperfection of neural tube with an OR approximately 5.2 and 3.9 (Brender et al., 2010; Ren et al., 2011). A JEM based case control study has demonstrated about double occurrence of spina bifida with occupational exposure to motherly (Makelarski et al., 2014). Brucker-Davis et al. (2008) carried out a JEM-based cohort study amongst the sons of mothers those who are working in the horticulture and farming and evaluated a cryptorchidism HR of 1.3. Furthermore another imperfection Gastroschisis has been found in the parental exposure to pesticides assessed by a JEM-based case-control study an OR of approximately. Waller et al. (2010) observed that the occurrence of gastroschisis elevated in young those mothers lived in region where the level of atrazine was present in the surface water.

6.2. Environment

Pesticides could pollute soil, water, grass as well as other flora. In addition to assassinating insects or weeds, pesticides could be poisonous to the other creatures such as birds, fish, useful insects and non-target vegetation. Insecticides are usually the further most intensely poisonous type of pesticides, but herbicides could also pose dangers to the non-target creatures (Van der Werf, 1996; Jeyaratnam, 1985; Igbedioh, 1991; Aktar et al., 2009; Abhilash and Singh, 2009; Chanda, 2014; Mahmood et al., 2016).

6.2.1. Surface water quality deterioration

Employing of pesticides in the farming could contaminate surface water through draining, drift, runoff and leaching. The contaminated surface water has adverse effect on the living organisms (Forney et al., 1981; Leonard et al., 1988; Miyamoto et al., 1990., Mulla et al., 1981; Bachmat et al., 1994). In the developing countries surface water serve as main source of drinking water (Mandl et al., 1994). The consequence of a series of investigations done by the U.S. geographical survey (USGS) in the early mid of the 90s on the main river basin throughout the country had given surprising results. The sample water and fish from all stream consisted above 90% of one or more pesticides (Kole et al., 2001). The sample collected from the rivers with mixed agriculture and urban land use was found to contain pesticides in the all the samples. The USGS established that level of the insecticides in the urban stream generally above the guideline for security of the aquatic life (U.S. Geological Survey, 1999). The aquatic life standards in the U.S. assess the ecological risk for the pesticides which is evaluated by the USEPA office of pesticide programs (USEPA, OPP) and Environment Protection Agency. In Europe, the predicted-no-effect content is dependent upon EU pesticide directive 91/414/EEC. The water quality requires further evaluation, if pesticide levels are more than 1/100 of the severe LC_{50} of the fish or Daphnia (Hester et al., 1998; Brock et al., 2006). Continuously pesticides including alachlor, acetochlor, simazine, metolachlor and atrazine were identified in water ways of cornbelt in U.S. (Sullivan et al., 2009). In California, rivers were contaminated with prometon, diuron, chlorpyrifos, diazinon and 2,4-dichlorophenoxyacetic acid (Zhang et al., 2012; Anderson et al., 2018). Further, several other countries also studied pesticide residues and found 76 pesticide residues intop soils of Europe. It was found that in 83% of the soils contained one or more residues and 58% of samples consisted of two or more residues. The highest levels of glyphosate and its metabolites were identified regularly. Existence of several pesticides in the surface water, river and lakes throughout Europe were revealed which may cause probable risk for the aquatic organisms (Loos et al., 2009; Brown and Beinum, 2009; Proia et al., 2013; Silva et al., 2019).

6.2.2. Ground water quality deterioration

The ground water pollution caused due to pesticides became a global issue and the major risk toward exposure of human beings to the pesticides exists in the water. Earlier the USEPA (Environmental Protection Agency) had provided information that general agriculture usage had caused existence of 46 pesticides in the groundwater and 76 in the surface water (US EPA, 1998; Larson et al., 1997). In accordance with USGS, minimum 143 distinct pesticides and 21 metabolites were observed in ground water, including pesticides from each main chemical group. The findings over last 2 decades observed the presence of pesticides in the 43 states (Waskom, 1995). A survey in India showed presence of organochlorine more than US EPA standard in 58 percent of drinking water samples collected from several wells and hand pumps near to Bhopal. In India, above 90 percent of aquatic and fish samples from every stream were bearing at least one pesticide. By the testing of the drinking water across India, it was found that metabolites of DDT; endosulfan and hexachlorocyclohexane were present at prominent levels (Rehana et al., 1995; Bakore et al., 2004; Sankararamakrishnan et al., 2005; Singh et al., 2005; Purkait et al., 2009; Samanta, 2013; Agarwal et al., 2015; Dwivedi et al., 2018).

6.2.3. Aquatic species

The contamination of pesticides in water cause greatest risk to the water bodies, mainly by lowering levels of dissolved oxygen in water. They can influence the aquatic species at numerous trophic levels, from algae to fish. The various studies comprise the turf concern pesticides have been observed in surface water and waters sources for example streams, lakes and ponds. Massive usage of pesticides could result in decreased number of fishes (DeLorenzo et al., 2001; Helfrich et al., 2009; Scholz et al., 2012). Aquatic animal gets exposure of pesticides by 3 modes; dermally (direct absorption through skin), breathing (uptake by means of gills through breath) and orally (intake by drinking contaminated water). The oxygen level decreases rapidly due to killing of the aquatic plants by usage of herbicides which finally lead to suffocation in fishes and decreased fish production. The reproductive capability of aquatic species was also affected owing to herbicide usage nearby weedy fish nurseries (Helfrich et al., 2009). Pesticides arrive in the ground water via leaching of polluted surface, by chance spill and leak and in appropriate disposal. Atrazine showed adverse effects on few fish species and impacted immunity of few amphibians. Over exploitation and habitat loss of amphibians was due to pesticide contaminated water (Forson and Storfer, 2006; Rohr et al., 2008; Rowley et al., 2010). Carbaryl adversely affected many amphibian families and glyphosate (herbicide) increased mortality frequency of tadpoles and young frogs (Relyea, 2005). Malathion altered the profusion and composition of periphyton and plankton resulting into disturbed tadpoles (Relyea and Hoverman, 2008). Chlorpyrifos and endosulfan also produced serious damage to amphibians (Sparling and Feller 2009).

6.2.4. Impact on soil health

Pesticides are being used extensively in the agriculture sector. Only 0.1% of used pesticides getting to the target and the residual volume pollute the soil environment (Pimentel, 1995; Carriger et al., 2006). With rising usage of pesticides in the present-day farming, problem of exposure of these compounds on the composition of soil microorganisms and route they lead has subjected more interest (Andrea et al., 2000; Baxter and Cummings, 2008). Pesticides can damage the native microorganism, interrupt soil flora and fauna and they entering into the food chain, show negative impact on human health (Niewiadomska, 2004; Ingram et al., 2005; Wang et al., 2006; Littlefield-Wyer et al., 2008).

6.2.4.1. Soil enzymes. Pesticides have adverse actions on the enzymes of soil which are vital biocatalysts to edict the soil quality, to manage nutrient cycle and involved in fertilization. Pesticides affect the activity of enzymes related to carbon, nitrogen, sulphur and phosphorus cycles such as acid phosphatase, phosphatase, dehydrogenase, fluorescein diacetate hydrolase, β-glucosidase, urease, aryl-sulfatase and alkaline phosphatase (Riah et al., 2014; Md Meftaul et al., 2019). Enzyme activities mainly depend on soil parameters including moisture, organic matter level and temperature (Bergstrom et al., 1998; Lalande et al., 1998; Tscherko et al., 2001). Metabolic activities of enzymes can be interrupted by accomplishment of pesticides into the soil (Engelen et al., 1998; Hussain et al., 2007). In the literature, harmful effects of pesticides on the soil biocatalysts such as oxidoreductases, hydrolases and dehydrogenases were broadly documented (Perucci and Scarponi, 1994; Sahid et al., 1998; Malkomes and Dietze, 1998; Monkiedje and Spiteller, 2002; Menon et al., 2004; Sukul, 2006; Cáceres et al., 2009). Evidence showed that few pesticides enhanced the enzyme action and ATP levels (Megharaj et al., 1999). There is a relationship between ATP content and particular enzyme actions and could provide important information about trend in alteration of enzymes in soils (Kanazawa and Filip, 1986).

6.2.4.2. Soil microbial diversity. On the basis of chemical nature of pesticides and characteristics of the soil, they can go through number of breakdown, adsorption and desorption (Weber et al., 2004; Laabs et al., 2007). Pesticides can modify the biochemical and physiological behavior of soil microbes and their metabolic events (Singh and Walker, 2006; Supreeth et al., 2016). Biomass mass serve as key signal of microbial actions and give straight evaluation of the relationship amongst microbial actions and transformation of nutrients (Schultz and Urban, 2008). Several contemporary reports showed the hazardous outcome of pesticides on the soil breathing and soil biomass (Pampulha and Oliveira, 2006; Lo, 2010; Ataikiru et al., 2019; Sharma et al., 2019). Normally, reduced soil respiration imitates decrease in microbial biomass (Chen et al., 2001; Wardle et al., 1994; Haney et al., 2000). The usage of pesticides decreased the microbial diversity while enhancing the functional variety of microbial groups and occasionally exhibits the affinity of rescindable stimulatory/inhibitory influence on the soil microbes (Wang et al., 2006; Pampulha and Oliveira, 2006). The usage of herbicides slaughtered or blocked the action of specific fungi species (Chen et al., 2001; Harding and Raizada, 2015). Likewise, heterotrophic psychrophilic aquatic bacteria as well as mesophilic and culturable phosphate-solubilizing microbes were enhanced in lake water samples after treatment with simazine (López et al., 2006).

6.2.5. Impact on the ecosystem

Pesticides have extreme influence on the non-target organisms and also influence the animal as well as plant biodiversity (Aktar et al., 2009). Majewski and Capel (1996) gave a statement that"-around 80−90% of the used pesticides be able to vitalize in shorter time periods of utilization". As pesticides, being volatized in nature can easily mix with the air and cause damage to the non-target creatures. Herbicides that volatilize the treated plant and vapors are enough to produce acute harm to non-target plants (Straathoff, 1986). The consequence of unrestrained applying of pesticides is decrease in various aquatic and terrestrial plants as well as animal families. Pesticides are also a threat to the endurance of few infrequent species, including peregrine falcon, osprey and bald eagle (Helfrich et al., 2009)**.** Natural ecosystem can be contaminated by pesticides in two different ways based on their solubility. The pesticides which are dissolved in water enter into the ground water, rivers, lakes and streams and may cause damage to the non-target creatures. On the other hand, the fat-soluble pesticides go into the bodies of animals by means of bioamplification resulting in the longer existence in the food chain. Bioamplification disturbs the entire ecosystem, particular at high trophic levels the species will die because of larger toxicity in their bodies. This results in the increased number of secondary consumers and decreased number of primary consumers (Katagi and Tanaka, 2016).

6.2.6. Risk to biodiversity

The risk related with the extensively applying of these toxic chemicals cannot be ignored. Contemporary there is an urgent need to think about the effect of pesticides on the number of terrestrial and aquatic animals, birds and plants. Persistence of pesticides in the food chain is the utmost bother since it mainly influences the predator and raptors. Indirectly existence of pesticides may bring reduction in magnitude of shrub, weeds and insects on which higher order animals feed. The falling off the rare species of the animals and birds also has been associated with the spray of insecticides, fungicides and herbicides. Furthermore, the regular and prolonged use of pesticides may result into bioaccumulation (Isenring, 2010; Brühl and Zaller, 2019; Schäfer et al., 2019).

6.2.7. Terrestrial species

The exposure of pesticides could also show mortal impact on the earthly vegetations in addition to damage untargeted plants. Migration or evaporation of phenoxy herbicides could harm neighboring trees and shrub (Dreistadt et al., 2004). The vulnerability of plants to diseases increased and seed quality decreased due to glyphosate (Brammall and Higgins, 1988; Locke et al., 1995). Similarly, herbicides caused destructive effects on the production non-targeted crops, wildlife and natural plant community (Fletcher et al., 1993). Wild birds are principle part of the ecosystem. The decreased in the population of birds act as a signal for environmental effluence. Frequently application of pesticides is one of the principle reasons for the reduced number of birds. The chemical impact of pesticides on adult birds include deaths, sub-lethal strain, reduction in fertility, egg-shell shrinking, inhibition of egg formation, damaged incubation and chick rearing behaviors (Gilman et al., 1979). Wide-ranging pesticide like carbamates, organophosphates and pyrethroids can reduce the population of the valuable insects such as bees and beetles. The population of insect has been seen to be higher in organic farms than the non-organic farms. Synergistic influences of pyrethroids and triazole or imidazole fungicides are hazardous to the honey bees (Pilling and Jepson, 2006). The neonicotinoids insecticides (imidacloprid and clothianidin) were harmful to bees (Yang et al., 2008). Herbicides caused significant harm to the fungal species of soil, for example trifluralin and oryzalin prevented the evolution of symbiotic mycorrhizal fungi which assist in nutrient uptake (Kelley and South, 1978). Oxadiazon had reduced population of fungal spores and triclopyrwas harmful to specific species of mycorrhizal fungi (Moorman, 1989; Chakravarty and Sidhu 1987). Earthworms show significant part in enhancing fertility of soil. Pesticides negatively influenced the earthworms and the later was exposed to the former primarily through polluted soil water. Insecticides and fungicides were neurotoxic to earthworms and were physically injured post prolonged contact (Schreck et al., 2008). Neonicotinoids in the soil lead to killing of earthworm's species like *Eisenia fetida* (Goulson, 2013).

7. Diagnosis of pesticides

In modern-day pesticides have become vital parts and share of agriculture. Without pesticides the life of flora and fauna will endanger. They are used not only in agriculture but also used in non-agriculture area. The massive use of pesticides polluted our water, soil and food; hence endanger our welfare. Numerous prolonged pesticides and their degrade products enter into the plant tissues or remain in soil and water. Uncontrolled application of pesticides has resulted into pollution of several grades, thus regular inspection of environment and food is most essential. Pesticides have been detected by several traditional as well as modern-day techniques including spectrometry, chromatography, immunoassays, electrophoresis, biosensors and solid phase extraction. Massive research has been done on the analysis of pesticides in the food stuffs and environment. The various methods used for estimation or detection of pesticides or pesticide residues in food stuffs and the environment are summarized in Fig. 3 (Rekha et al., 2000; Ye et al., 2009; Hsu and Whang, 2009; Guan et al., 2010; Wong et al., 2010; Kanrar et al., 2010; Zhang et al., 2011).

Gas chromatography (GC) is the furthermost used approach for the diagnosis of the pesticides and this technique is applied for the estimation of non-polar and volatile derivatives. Pesticides can be analysed by GC commonly coupled with a particular detector such as a flame photometric detector, electron capture detector, flame ionization detector and nitrogen phosphorus detector (van der Hoff and van Zoonen, 1999; Vela et al., 2007; An and Shin, 2011; Moawed and Radwan, 2017; Słowik-Borowiec et al., 2015; Blankson et al., 2016; Farajzadeh et al., 2016; Mahpishanian et al., 2015). To obtain high sensitivity and selectivity, GC can be coupled with mass spectrometer (MS), called as GC-MS (Zou et al., 2016; Xu et al., 2017; Xu and Liu, 2017; Han et al., 2018; Tankiewicz and Biziuk, 2018). Distinctive types of detector are employing to identify distinctive pesticides, with different merits and demerits (Alder et al., 2006; Hernández et al., 2013; Grimalt and Dehouck, 2016). Liquid chromatography (LC) or coupled LC is used with variety of detector like ultra-violet, fluorescence and diode detectors (Tadeo et al., 2010 Beceiro-González et al., 2012; Pérez-Lemus et al., 2019). High performance LC (HPLC) is an admirable approach to detect broad range of pesticides including polar and heat-unstable pesticides (Lambropoulou et al., 2007; Li et al., 2010; Bidari et al., 2011). The combination of MS with LC is the utmost sensitive and selective method for the detection of the pesticides. For example, diagnosis

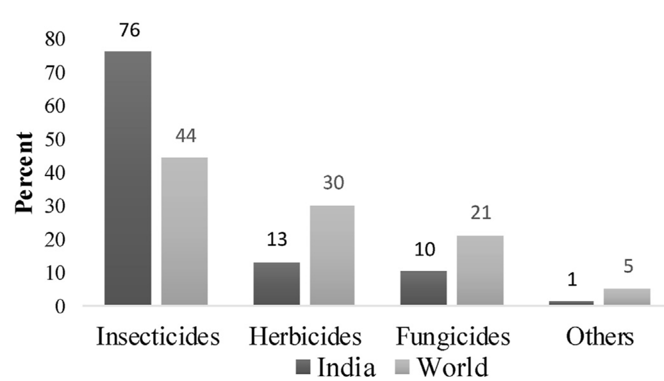


Fig. 3. Comparison of the pattern of pesticide application in India with the world (Mathur and Tannan, 1999).

of pesticides and pesticide residues in vegetable and fruit samples using LC-MS (Sannino et al., 2004; Zamora et al., 2004; Sannino and Bandini, 2005; Sannino, 2007; Crnogorac et al., 2008; Wong et al., 2010; Qin et al., 2016; Jallow et al., 2017; Hadian et al., 2019). Analytical technique ELISA is beneficial for the rapid and cost-effective separation as well as detection of pesticides. This technique has good sensitivity and selectivity for particular kinds of pesticides on the basis of their antigen-antibody interactions. The main benefit of this detection operation is that it involves very simple preparation of sample (Aga and Thurman, 1997; Watanabe et al., 2001; Ahn et al., 2011). The other beneficial analytical technique is capillary electrophoresis which is employed for several practices. This approach has some benefits such as fewer quantities of reagents and sample is required, high separation capability and requires lesser time. Capillary electrophoresis suffers from few shortcomings specifically in term of identification and detection due to smaller inner diameter (50–75 μm) of the capillary, which allows only little amount of sample to be used in the system. Due to the small sample injection amount into the capillary system, capillary electrophoresis has been coupled with extremely subtle sensors including MS and can be integrated with online or offline pre-concentration techniques (Malik and Faubel, 2001; Juan-García et al., 2005; Picó, 2006; Sánchez-Hernández et al., 2014; Chang et al., 2016; Malik et al., 2016).

The above-mentioned methods are sensitive and selective at lower diagnosis limit, but these approaches are time consuming, high cost and not simply. The alternate way to overcome these limitations is the use of advanced methods for the diagnosis of the pesticides, which are based upon the principle of 'biosensor' (Songa and Okonkwo, 2016). Zheng et al. (2015) gave a statement that "the diagnosis limit of the sensor, specifically biosensor (based on enzyme) cannot have been reached to the same level as the traditional techniques". In these approaches conventional chromatographic techniques are combined with some selective detectors for diagnosis of the pesticide. The chromatographic approaches are precise, certain and valid. But they take a long time, costly, not simple, and utilize large volume of organic solvent make them inappropriate for selection of large amounts of sample. However, several countries particularly developing nations still do not have facility to use advanced techniques (Van Dyk and Pletschke, 2011). The main advantages of the advanced techniques are simple and fast apply, cost effective and provides appropriateness for in-situ monitoring. Also, they give adequate outcomes in terms of sensitivity and selectivity in the diagnosis of pesticides (Liu et al., 2013; Verma and Bhardwaj, 2015; Songa and Okonkwo, 2016; Zhao et al., 2015; Bucur et al., 2018).

8. Preventive steps for pesticide management

The execution of suitable remedial measures facilitates to reduced incidents of pesticide toxicity and other health issues linked to usage of pesticides. Indian government is worried of the adverse actions of pesticides on well-being and has executed several measures, such as; banned most toxic pesticides, national implementation plan, integrated pest management and limiting the use of toxic chemicals (Yadav et al., 2015).

8.1. Integrated pest management (IPM)

Human health hazards and ecological imbalance is mainly owed to the progress of pest resurgence, pest defense, existence of pest residue in air, water, soil and the outburst of the secondary pests. Government of India has planned and implemented an IPM technique to strengthen and modernize the pest management techniques to decrease the chronic danger due to pesticides. Usually it employs mechanical, cultural and biological method; allows use of chemical pesticides only when there is requirement of it; if possible, bio-pesticide usage, bio-control and indigenous advanced possibility (Yadav et al., 2015). Swaminathan (1975) at first developed IPM technique for the two crops (rice and cotton) through research project (Indian Council of Agriculture Research (ICAR)), which facilitated the creation of location-specific methods for these two crops (Peshin et al., 2009, 2014). From 1981, Indian government has implemented IPM to decrease requirement of chemical for pest control. The 'Central Institute of Cotton Research'in 2002 projected the insecticide resistant management (IRM) program in 10 states farming cotton, selecting districts that were utilizing 80% of insecticides on cotton crop (Russell, 2004; Kranthi and Russell, 2009). These ecological techniques were actively developed by the Food and Agriculture Organization for the crop control. Consequently, government of India has adopted numerous IPM local programs in 3 levels. The first level of the program stressed on validation of IPM methods and the increase of pilot extension actions with farmers. The next level was related to the development of human resource and initiation of a permanent training program for farmers called as 'IPM farmer's field school (FFS)'; and this tactic was most common amongst Indian farmers. The third level stressed on the institutionalization of the IPM technique into the government system. Currently, 31 central IPM cores are working throughout India. Various functions are being played by the IPM including delivering of bio-control agents and production, monitoring of diseases, pests and bio-pesticides, and conservation of bio-control agents. IPM developed package to control pest and disease for 77 main crops and adopted in all state of India (Yadav et al., 2015). The contribution of the existing policies and management methods to pesticide control in India, compared to the global control strategy as shown in Table 3.

8.2. Rational use of pesticides

The term, rational usage of pesticides (RUP) was invented in the label of a book written by Brent and Atkin (1987). RUP (Fig. 4) mainly emphasized on the sub-set of IPM and integrated crop management (ICM), which efforts to moderate the harmful influences of pesticide usage through better specificity and accuracy in pesticide usage with space as well as time of the products themselves. The advantages of RUP are enhanced by a mixing of all three, and the promising advantages including decreased expenses (for pesticides as well as labour), decreased environmental influence (by additional efficient application of sprays and usage of the selective compounds including biopesticides), and better safety (Boardman, 1986; Mancini et al., 2008; Abhilash and Singh, 2009; Gupta et al., 2010) (Fig. 5).

8.3. Organic farming

One of the substitutes to the usage of chemical pesticides is 'organic farming'. 'Organic farming' practices are being extensively employed in the advanced countries (Grewal et al., 2017). The crucial feature of organic farming is to inspire and increase organic cycles with in agriculture structures to preserve and enhance extended soil fertility, to minimalize all types of hazards caused due tothe fertilizers and pesticide usage and to harvest food of to psuperiority in adequate amount. Though, this method is expensive, labor concentrated, and in certain condition sun successful (Abhilash and Singh, 2009). Prevalence of the detectable pesticide remainders was four times greater in crop obtained by non-organic farming compared to that of organic farming (Barański et al., 2014). Organic food ingesting can decrease contact to the pesticide residues in diet (Smith-Spangler et al., 2012). Organic crops have higher content of

Table 3
Pesticides control policies in India and globally.

Country	Policy and Management	References
India	For every type of pesticides: Registration is mandatory before production and marketing etc. Demand and supply to the Indian states is monitored a top-level committee of Indian government. Moreover, data compilation, production & use along with export and import are also monitored by the Indian government. Standards are formulated by Bureau of Indian Standard. Promotion of integrated pest management practices. Including all the activities as mentioned above, without license any kind of pesticide trade has become an offence which includes 3 years imprisonment and/or a fine of ~Rs. 40 lacs except personal apliaction in gardening, home etc.	Indian Insecticides Act 1968; BIS, 2019/2012; Devi et al. (2017); Srivastav (2020) Tiwari (2020)
Global	Consumption of pesticide in Indian is observed very low as the data given below: China (13.06 kg/ha), Japan (11.85 kg/ha), Brazil (4.57 kg/ha) India 0.29 (kg/ha) Latin American countries	FAOSTAT, 2017; Subash et al. (2017)
Global	Major guidelines include: Regulatory provision for pesticide application to reduce the threat on human health. Help in developing policy for the pesticide management in all the countries.	WHO (2010)
India	Need of strict food safety standards for the use of pesticides in food items along with challenge identification.	Halstead et al. (2018); Elahi et al. (2019); Rajput et al. (2020)
England	Adopted the standards of EU to regulate the level of pesticides (alone and total) in drinking water should not increase than 0.1 μg/l and 0.5 μg/l, respectively.	Ibrahim et al. (2019)
40 East African countries	South-East Africa Regulatory Committee on Harmonization (SEARCH) formulated in the year of 1996 to make the safe use of agrochemicals in 40 African nations in the compliance of International regulatory authorities. The crops were taken in account like maize, cotton, and sugarcane. This effort has been found quite successful.	Loha et al. (2018)
European union	Started campaign to make aware the farmers regarding use of pesticides and their behavioural change. The main policies were determined the maximum use chemicals, spoke about the banned chemicals, taxation, subsidy provided by the government. Assessment of environmental depletion due to pesticides was under provision. Many chemical pesticides have been completely banned. All the stakeholders of pesticide (including private, government and farmers) trade and application were trained about the technical knowledge regarding its management. 25 years were spent on the policy research regarding wise use of pesticides to reduce the economic burden along with enhancing food security.	Falconer (1998); Skevas et al. (2013); Bocker and Finger (2016); Storck et al. (2016); Salazar-Morales (2017); Giomi et al. (2018); Lee et al. (2019)
USA	For the safeguards of environment and human beings from the pesticides, USEPA has launched OPP (Office of Pesticide Programs). In USA, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) is responsible for the approval of pesticide trade, application etc. They have also categorized the pesticides for food useable and non food useable pesticides. Huge budget was provided ($200–300 million) for the monitoring, human health risk assessment, path of exposure etc.	Craig et al. (2019)
China	Chinese government took seriously pesticide residues being an agricultural country for the trade. Also, updated chinese food safety standard on maximum residue limits for 3650 pesticides in terms of maximum residue limits.	Zeng-long et al. (2015)
Global	Suggested that world should focus on the use of biological pesticides (naturally occurring) instead of chemicals through awareness, public participation, policy makers, experts etc.	Lengai et al. (2020)
Greece	Many monitoring programs were in practice to assess pesticide residues in the river water. Suggested that surface water reservoirs should also be considered during policy decisions to make them free from the chemical pesticides.	Tsaboula et al. (2019)
World and South Korea	Experimental models were developed in USA, UK and The Netherland to predict pesticide residues in the crops through calculating bio-concentration factors.	Hwang et al. (2018)
Vietnam	Some pesticides (like organochlorines and organophosphates) were excluded to protect environment and public health. Studied mostly chemicals kept in class II and III by WHO which are relatively less harmful	Toan et al. (2013)

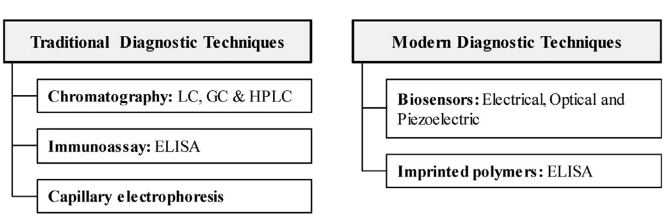


Fig. 4. Analytical techniques for detection of pesticides in the foodstuffs and environment.

antioxidants and increased consumption of antioxidant rich diets shield against enduring ailments, such as cardio vascular disorders, cancer and neuro-degenerative ailments (Wahlqvist, 2013).

8.4. Awareness of agriculture workers

The farmers are familiar with the risks of critical pesticide poisoning, still the urgent requirement is to emphasize on the chronic effects which may pose several neurological diseases. Indian farmer are not so familiar with the use modern approaches for pesticides spraying. Root of the problems is that the modern technology presented in the India and adopted by some educated farmers, most of the farmers are not in position to execute these technologies; may be because of lack of awareness or resources. Now a day there is an urgent requirement to train the farmers by the crop production companies since they are major users of the products. This awareness helps in development of local training

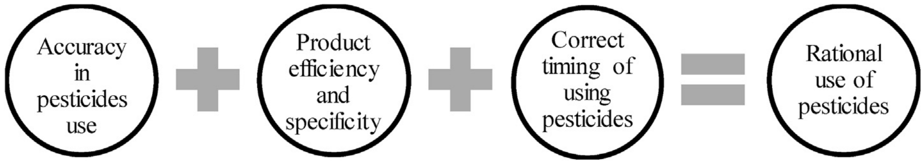


Fig. 5. Benefits of the 'rational use of pesticides' to decrease effects of pesticides on the environment.

according to the requirement of the farmers. Farmers in their target to managing pests and enhancing productions dispense with the problems of health and environment hazard (Nair, 1991; Flaconer and Hodge, 2000; Gadgil et al., 2002; Pemsl et al., 2004).

8.5. Techniques for remediation of pesticides from environment

Remediation techniques can be divided into 4 groups: (a) Removal (contaminates or contaminate medium are eliminated from the spot with no requirement to separate from the host medium); (b) Separation (elimination of contaminants from the host medium such as water or soil); (c) Destruction (more toxic chemicals are transformed into less toxic products by degradation or neutralized chemically or biologically); (d) Containment (interference or inactivate surface and subsurface passage of the contaminates). Removal, separation and destruction is the process in which contaminates are eliminated or decreased from the host medium. Containment is an approach used to control the passage of contaminates to perceptive receptors with no reducing or eliminating contaminates. These approaches were employed for the remediation of the soil, ground water, sludge, solid matrix waste and sediments (Suthersan, 2001). The remediation techniques can be also classified into 3 categories namely biological process, physical process and chemical process (Bollag and Liu, 1990; Gavrilescuet al., 2002; Gavrilescu et al., 2004). The conversion of complex organic compound into simple products like H_2O and CO_2 is known as biological process or bioremediation. This remediation can be carried out in three ways: with microorganism, remediation with advance natural attenuation, bio-augmentation and bio-stimulation (Helbling, 2015; Nwankwegu and Onwosi, 2017). The physical process of remediation is carried out by physical way such as clay, activated carbon, Zeolite and polymeric materials. The co-chemical inversion of the more toxic material into less toxic material by the chemical reaction is known as chemical process of remediation (Hamby, 1996). Frequently this technique combined withphysical process (Brooks et al., 2003; Dhal et al., 2013). There are many methods which are related to chemical process like advanced oxidation processes zero valent iron (Shea et al., 2004; Gavrilescu et al., 2005).

Also, various types of remediation techniques are being used to overcome the pesticide problems from the contaminated environment. At first, by spreading awareness in the society, some problems due to pesticides can be prevented at the source of their application. Different stakeholders such as environmental protection organizations, academia, research organizations, farmers, health officials, pesticides manufacturers, and government authorities have to come forward to find some suitable solution to this problem. Collaboration of these people will definitely reduce the risks of pesticide toxicity on the living creatures as well as on the environment. It is our moral duty to take necessary steps for the efficient management of pesticides by making strict laws for pesticide sues and its toxicity regulations. The quantity of pesticides should be developed with precision and accuracy along with better safety profile so that their negative impact on the environment and human beings can be reduced. Some significant processes of pesticide management or remediation are discussed below:

8.5.1. Biological process

Bioremediation is an important technique for the removal of pesticides from the contaminated sites. It has been considered as eco-friendly and economically feasible process of environmental cleanliness. Moreover, it does not generate any toxic byproducts. Different types of microorganisms have been employed for the degradation of the pesticides. Generally, during bioremediation process, microorganisms are helpful to convert the pesticides into non-toxic products and because of this reason, their extensive application have been reported for the onsite breakdown of contaminants present in the environmental systems. The microorganisms, which have the capacity of insecticides degradation, can be usually isolated either from the sludge, soil or aqueous solutions. In addition to these, isolation is also possible from the resistant insects and/or fermented foods (Sharma et al., 2016; Zhu et al., 2016; Tian et al., 2018; Han et al., 2018). Moreover, biodegradation of pesticides has also been achieved by employing different fungal strains and bacteria (Maqbool et al., 2016). In Bio-augmentation exogenous, microorganisms are added to the polluted sites along with certain catabolic abilities or into a bioreactor to begin bioremediation process (Perelo, 2010). This technique has been proven as very efficient in case of non-availability of local microbes for enhanced degradation of pesticides at contaminated sites, whereas in case of biostimulation, appropriate physiological conditions and nutrients have to be provided for the proper growth of locally available microbes. Consequently, metabolic activity of microbes would get increase, which will facilitate the fast degradation of onsite pollutants (Trindade et al., 2005). Modifications can also be carried out by using co-metabolic substrates and enzyme-inducers for the pesticide degradation in environment (Robles-Gonzalez IV et al., 2008; Plangklang and Reungsang, 2010). Table 4 is the compilation of various types of microbes, which have been used in the degradation of pesticides from the soil as well as water.

From Table 4, it can be seen that many types of microbial species can be applied to degrade the pesticides present in water as well as soil environment.

8.5.2. Adsorption

Adsorption is one of the best techniques for the removal of pesticides because of its eco-friendly nature, low production of by-product waste and cost-affectivity. Different types of adsorbents like clay, activated carbon, biochar and nanoparticles have been used for the adsorption of pesticides from the polluted environment. The mechanism of the adsorption may be chemical bonding through ion-dipole interactions, weak Van Der Waals, forces, dipole-dipole, cation exchange and strong covalent bonding or physical adsorption (Rashed, 2013). The physisorption requires lower enthalpy during adsorption, whereas chemisorption needs greater enthalpy because of covalent bonding in between adsorbent with pesticides (Sims and Kanissery, 2019; Vidal and Moraes, 2019). Activated carbon can also be employed for the removal of the

Table 4
Microbial species employed for the degradation of pesticides from the soil as well as water.

Target pesticides	Medium	Microorganism	Efficiency	References
SOIL				
Myclobutanil, tetraconazole and flusilazole (fungicides)	Soil	Bacillus strains, namely, DR-39, CS-126, TL-171, and TS-204	85% (after 20 degraded days)	Salunkhe et al., 2015
Organochlorine pesticides	Soil	Endogenous flora Biodegradation		
Chlorpyrifos (herbicide) Laboratory	Soil	CS2 strain	55% (degraded after 6 days	Singh et al., 2016
Diuron	Soil	Micronutrients, sewage sludge mixed with pruning wastes, urban solid residues, hydroxypropyl-β-cyclodextrin	46.5% mineralized after 140 days	Rubio-Bellido et al. (2015)
Carbofuran	Soil	Ligninolytic fungus *Trametes versicolor*, compost	100% (degraded after 48 days)	Madrigal-Zúñiga et al. (2016)
Methoxychlor	Soil	Actinobacteria	60% (degraded after 12 h)	Fuentes et al. (2014)
WATER				
Molinate Simazine Pyriproxin	Water	*C. vulgaris*	85.6% 86.3% 88.2%	Mishaqa et al. (2017)
Prometryne	Water	C. reinhardtii	66% (degraded after 6 days)	Jin et al. (2012)
Malathion	Water	S. platensis	54% (20 days)	Ibrahim et al. (2014)
Malathion	Water	N. muscorum	91% (degraded after 20 days)	Ibrahim et al. (2014)

pesticides because of greater surface area, porous structure and higher adsorption capacity (Abraham et al., 2018; Ligneris et al., 2018). Shao et al. (2018) investigated the adsorption capacity of powdered activated carbon mixed with gravity-driven membrane and found that the adsorption capacity was 28.5% greater than activated carbon under similar experimental conditions. Biochar is a carbon rich substance (~80%) produced by pyrolysis of biomass under oxygen free environment (Yuan et al., 2019). Biochar possess unique characteristics like higher pore volume, larger surface area and high environmental stability (Graber et al., 2012; Wang et al., 2018). It was also used to remove pesticide (96% triazine removed) using biochar with help of modified biochar (Suo et al., 2019). Zhao et al. (2013) investigated the adsorption capacity of the biochar derived from the corn stalk for the removal of atrazine and found that the rate of removal of atrazine was quite high. Further, some other materials like clay, zeolite applied were also used for the removal of pesticides from the polluted environments.

8.5.3. Advance oxidation processes

Advanced oxidation processes have also shown higher potential for the removal of pesticides from the contaminated soils. Examples of the advance oxidation processes are plasma oxidation, Fenton process ozonation and photocatalysis. In this process, pesticides degraded up to less quantity or changed into any non-toxic compounds such as carbon dioxide, water and inorganic compounds. This technique has attracted researcher of the world for the removal of pesticides from the contaminated environments due to its working feasibility under ambient temperature and pressure (Cheng et al., 2016). However, the research on the oxidative processes is still in initial stage and this approach is limited to laboratory scale. Operating conditions and cost of this technique has not very much optimized yet (https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-83582019000100302, Morillo and Villaverde, 2017). Therefore, it could be an area of further exploration for the researchers.

9. Concluding remarks

Pesticides have several applications including to increase crop yield, to control over vector diseases and to kill or inhibit the hazardous pests. However, the harmful effects of pesticides cannot be unseen. As they are significantly harming environment as well as human beings, they are damaging the quality of water and soil, which leads to the hazardous effect on the animals, birds, plants and human beings. Pesticides also disturb the biodiversity and the continuous direct or indirect exposure to pesticides can cause serious threats to human health. They can cause acute health problems such as cancer, diabetes mellitus, reproductive disorders, respiratory disorders and neurological disorders. Now a day, there is need to control the use of pesticides and to find their substitute; as well as to aware people about safety measures to be employed during application of pesticides; and to encourage the farmers for organic farming, so that usage of pesticides can be reduced**.** In future, investigation is needed to develop innovative ideas in current farming which will be able to decrease the usage of pesticides. Various remediation techniques have been reported for the remediation of pesticides from the contaminated environment such as adsorption, bioremediation, advanced oxidation etc. However, adsorption and bioremediation are reported as the best techniques due to environmentally friendly nature, cost effective and producing less toxic byproducts. Environmental protection organizations farmers, health officials, pesticides manufacturers and Governments should take joint initiatives to reduce the risk of pesticide poisoning. Necessary actions should be taken for the efficient management of pesticides by imposing strict laws and toxicity regulations. Integrated pest management can be helpful in managing the pesticides application as well as control of pesticides. Pesticides should be produced with due precision and accuracy along with better safety profile so that their negative impact on the environment and humans beings should be less. In addition to these, future research should be directed to develop relatively safe chemical for the same.

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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