Toxicity of pesticides to plants and non-target organism: a comprehensive review

Mohd Amir Shafeeque[1], Farhan Ahmad[2] and Aisha Kamal[1]*

1. Department of Bioengineering, Integral University, Lucknow, India-226026
2. Department of Biotechnology, Ashoka Institute of Technology and Management, Varanasi, India-221002

Abstract

Pesticides are agrochemicals used to increase agronomic production and higher economic profit. However, these chemicals could be persistent in soil and water, collective in silt or bio-aggregates in biota relying upon their dissolvability, prompting various kinds of natural contamination. These pesticides have also shown detrimental effects such as phytotoxicity, genotoxicity, and cytotoxicity on target plants along with alteration in their antioxidant system. The demerits continue as they also affect non-target species such as humans, birds, animal, and other aquatic organisms. The higher accumulations of pesticides are also responsible for the generation of ROS that leads to oxidative stress and finally cell demise. Thus, in this review the toxicity of pesticides will be discussed in detail at a cellular and molecular level linked with the response of the plant defense system. Besides, various strategies that have been commonly used worldwide to remediate the toxicity have also been highlighted in the later section. The study will help plant researchers and chemical engineers to understand the gap between the research and a novel, innovative, and cost-effective technique/ procedure will be outlined for healthy environments.

Keywords: pesticides; cytotoxicity; antioxidant system; phytohormones

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Introduction

In ancient times, the introduction of natural compounds or synthetic pesticides to increase agricultural crop productivity for the rapidly growing global population had been proved an effective strategy against the adverse climatic condition, coupled with biotic and abiotic stress (Kumar and Verma, 2018). Beside this, rapid population growth also led to introduction of new component of pesticides in modern agricultural system viz organochlorine, organophosphate, carbamates, pyrethroids, phenoxy herbicides, benzoic acid herbicides, triazines, and urea as insecticides, fungicides, herbicides, rodenticides, and nematicides for improved agricultural output and productivity yield by protecting crop from various pest, insect, and other possible threats (Mieldazys et al., 2015; Fatma et al., 2018). Ideally, a pesticide must have a deadly effect on only unwanted growth or pest that affect productivity but no lethal effect on non-target species, including man. But disappointingly, this is not the situation, as it affects nearly all non-specific targets and causes other serious consequences along with major environmental issues thus, the

*Corresponding author
E-mail address: aishakamal04@gmail.com
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uses of pesticides are always contradictory (Aktar, 2009). The adjustment and resistance developed by pests to these synthetic substances further increases the demand for a new formulation of pesticides to protect the crop and further increases the cost of food production (Parween et al., 2016). It was also presumed that only a small part of pesticides (<0.1%) of total applied pesticide concentrations reached to the active site while major portion run-off or accumulated on off-target sites. These excess pesticides should also be removed from the environment with modern equipment and techniques and these practices also rise the expenditure on crop production cost (Parween et al., 2016). However, after making the maximum effort to remove or minimize the level of residual pesticides, only a little or non-significant result is achieved. As pesticides degradation is the sequential process of chemical reaction, arrangement of chemical moieties and metabolic product of pesticides is subject to abiotic natural conditions (temperature, dampness, soil pH, and so forth.) and pesticide chemical composition (hydrophilicity, pKa/b, Kow, etc.) (Ahemad and Khan, 2012). The other most unacceptable fact is that pesticide application (over or higher doses/ repeated uses) shows a detrimental effect on a host plant that is being protected by these pesticides. The end product or pesticide residual incorporate into the host plant and consequently damage important biomolecules in the plant when enters into the metabolic pathway and thus leads to ROS production (Faize et al. 2011; Mahmood et al., 2014). Sufficient literature is available revealing the negative effects at cellular/genetic level, cytotoxic, genotoxicity, chromosomal abnormalities, DNA damage, and increased rates of mutation induction associated with pesticides usage (Anitha and Savitha 2013; Fatma et al., 2018) but their detailed mechanism of action is still unclear. Pesticide toxicity has been usually assessed by means of phytotoxicity symptoms in plants, changes in photosynthetic pigment, plant growth and development, alteration in the antioxidant system, and specific molecular changes (Chris et al. 2011; Horbowicz et al., 2013). The detrimental effects of pesticides are not only limited to plant but their excessive application also contaminates soil and water, kills beneficial insects and microorganism, birds, fish, and non-target plants, and negatively affect the environment and human health (Nicolopoulou-Stamati et al., 2016). These chemical pesticides are also associated with dermatological, gastrointestinal, neurological, cancer-causing, respiratory, regenerative, endocrine, and other health issues in humans (Sanborn et al., 2007; Hutter and Moshammer, 2018). As the application of harmful chemical pesticides affect the entire environment, there is an urgent need to develop innovative ideas/ approaches in the farming sector with the eco-friendly modern technique used to avoid these lethal chemical moieties. Also, the exploitation of some biologically active components extracted with natural resources should also be taken in the active mode of agricultural practices. Thus, this review will critically discuss different pesticides and their effect on the plant from the early stage of seed germination to maturity and highlight the suitable methods or strategies to nullify the exceeded concentration than permissible limits. Before discussing the alternative approach, it is worth to discuss the correlation of different pesticides in growth, development, and physiological response in plants.

Morphotoxicity, phytotoxicity, cytotoxic, and genotoxicity effect of pesticides

Pesticides, above permissible dose severely affect cell development, photosynthesis, biosynthesis, and molecular responses at various stages of plant life (DeLorenzo et al., 2001; Shakir et al., 2016). Excessive and repeated application of these chemical pesticides exhibit reduced germination, retarded growth of vegetative and reproductive organs, and severely affect various morphological and physiological efficiencies in several important crops (Tort et al., 2005; Rio et al., 2012; Aksoy et al., 2013; Kilic et al., 2015; Shakir et al., 2016). The visible morphological symptoms that are frequently used to assess the effect of pesticide usages on crops are poor germination, retarded growth, yellowing and curling of leaves, poor reproductivity and yield. Common herbicide acifluorfen, a diphenyl ether utilized on numerous harvests, such as soybean, bean, pea, wide bean, cotton, and spinach causes leave injury (Saladin and Clément, 2005) and in some cases chlorosis, necrosis, wilting, and shrinking of leaves have also been reported. In another study, exogenous application of insecticides such as dimethon-S-methyl (organophosphate), dimethoate (organophosphate), pirimicarb (carbamate), dicofol (diphenylethane) to wild tamarind plant affect dry matter, leaf area, and leaf number and decrease or inhibit photosynthetic machinery (Dalzell and Mullen, 2004, Saladin and Clément, 2005). Furthermore, in vitro developed grapevines treated with the fungicides pyrimethanil (anilinopyrimidine) and fludioxonil (phenylpyrrole) at field focus or at a lower rate showed a decreased rate of photosynthesis, low carotenoid and chlorophyll contents, sucrose, and hexose content along with overproduction of secondary metabolites (Scarponi et al., 2002; Saladin et al., 2003). Besides this, net CO_2 absorption also reduced along with changes in stomatal conductance and intercellular CO_2 concentration in *Malusdomestica* and *Cucumissativus* after fungicide application (Untiedt and Blanke; 2004; Xia et al., 2006). The use of a non-systemic fungicide, fludioxonil, in *Vitis vinifera* caused a reduction in net CO_2 absorption and in intercellular CO_2; however, stomatal conductance was not influenced (Petit et al., 2008). Another research carried out by Saladin and Clement, (2003), revealed that use of a similar fungicide, fludioxonil, and pyrimethanil with in vitro developed plants and fruiting cuttings of *Vitis vinifera* showed advanced distinctive physiological reactions: in vitro plants, the two fungicides diminished net CO_2 absorption, transpiration rate, stomatal conductance, and intercellular CO_2 focus; however in the fruiting cuttings, the fungicides did not influence CO_2 trade either transpiration rates (Dias, 2012). The herbicide glufosinate (phosphinic acid) applied to tomato plants caused ammonium accumulation and ethylene generation as a marker of both stress and bright senescence (You and Barker, 1997). The treatment of pea plants with herbicide imazethapyr (imidazolinone) enhanced absolute free amino acid content but decreased protein content demonstrating protein hydrolysis (Royuela et al., 2003). Besides herbicides, fungicides (phenylpyrrole anilino pyrimidine) also reported to decrease amino acid content; enhance protein hydrolysis, and stress protein accumulation in grapevine (Llorens et al., 2000). Hence, it was reported that both carbon and nitrogen metabolism showed abnormal pathway regulation but the alteration in metabolism depends upon the type of crop and duration of pesticide exposure. Extensive studies about the deleterious effect of pesticides on plant growth, development, seed germination, flowering, pollen germination, and pollen tube growth have already been done very precisely. Recently, it was found that application of mancozeb, imidacloprid, and sulfentrazone, on model plant *Allium cepa* showed cytotoxic and genotoxic effects by inducing different types of chromosomal abnormalities, likely sticky, disoriented and fragmented chromosomes, abnormal DNA condensation, and chromosome coiling by spindle inactivation and thus reduced mitotic index (Bianchi et al., 2016; Fatma et al., 2018). The detailed list of commercially available pesticide and their mode of action in various crops are listed in Table 1. In addition to these parameters, the literature is very scary on the pesticides' effect on antioxidant modulation, plant defense mechanisms, pathogenesis-related proteins (PRP), and alteration of secondary metabolites and phenolic compounds. Thus, an attempt has been made to explore the modulation of the antioxidant system, and relation component to detoxify the negative effect of pesticides in the next section.

Pesticides-induced oxidative stress and modulation of the antioxidant system

Highly regulated mechanisms are involved in maintaining the equilibrium between ROS formation and their detoxification during normal growth and metabolism. But unfavorable condition such as water scarcity, higher accumulation of salts, ions, and toxic metal coupled with climatic changes are responsible for excessive ROS production that disturbs the equilibrium and causes oxidative stress (Khan et al., 2015; Ahmad et al., 2017). Although, ROS are short-lived, toxic molecules, they degrade important biomolecules such as lipids and

Table 1
Inhibitory effects of pesticides and their mode of action on several important crops

Sl. No	Plants/ species	Pesticides	Nature/ Chemical Family	Toxicity	References
1.	*Allium cepa L*	Endosulfan	Insecticide/ Organophosphate	Irreparable chromosomal damage	(Khan and Damalas,2013)
2.	*Lens culinaris L*	Mancozeb	Fungicide/ Dithiocarbamate	Morphological and anatomical	(Bashir et al., 2007)
3.	*Zea mays L*	Omethoate (OM)	Insecticide/ Organophosphorus	Yellowing of leaf, distortion of stomata and, loss of chloroplast mitochondrial structure and function	(Wen et al.,2017)
4.	*Phaseolus vulgaris L.*	Butachlore	Herbicide/ Acetanilide	Inhibit photosynthesis, protein synthesis, RNA synthesis, lipid Synthesis	(Chang et al 1985)
5.	*Vigna radiata L.*	Chlorpyrifos	Insecticide/ Organophosphate	Decreasing root and shoot length	(Parween, et al. 2011)
6.	*Vicia faba*	Fenthion	Insecticide/ Organophosphate	DNA damage, program cell death including chromatin condensation, cytoplasmic vacuolization, nuclear shrinkage, condensation of the protoplast, fragmentation with apoptotic-like corpse formation	(Cortés-Eslava et al. 2018)
7.	*Phaseolus vulgaris L.*	Atrazine	Herbicide/ Triazine	Effects on fine Structure of Chloroplasts	(Ashton et al., 1963)
8.	*Cucumis sativus L.*	Carbendazim	Benzimidazoles/ Fungicide	It affects the anti-oxidant system in different plant tissues	(Zhang et al., 2007)
9.	*Triticum aestivum L.*	Malathion	Insecticide/ Organophosphate	Higher concentration of malathion inhibits the production of primary metabolites, seed germination and photosynthetic pigments.	(Kumar& Sharma, 2017)
10.	*Solanum lycopersicum*	Pirimicarb	Insecticide/ carbamate	Morphological parameters are affected such as germination and growth	(Chahid et al., 2013)

proteins, membrane disruption, along with denaturation of nucleic acids, leading to cell death (Anjum et al., 2011; Ahmad et al., 2018). A similar effect is also caused by pesticide-induced stress in plants that are being protected by the application of pesticides and also to non-target plants by altering cell metabolism, biochemical and other physiological responses. In a recent study, application of emamectin benzoate, alpha-cypermethrin, and imidacloprid pesticides at prescribed level or high level of dosage to tomato seedlings, disturbed cell viability, cell injury coupled with alteration in SOD, CAT, POD activity, increment of GR antioxidant, accumulation of proline, and increased content of MDA level (Shakir et al., 2018). Besides this, the toxicity of mancozeb and chlorpyrifosin, a dose-dependent manner, enhanced the antioxidant system (CAT, POD, and SOD) in *Allium* to tolerate morphotoxicity of the pesticides but failed beyond the precise limit (Fatma et al., 2018). In addition to this, histochemical detection by NBT methods carried out by Kamal and co-worker pointed out that application of different fungicides and insecticides on mung bean showed an enhanced level of ROS generation and disturbance in the equilibrium of redox hemostasis pathway (unpublished data). The pesticides also interfere with the photosynthetic pathway and bind to (QA) D1 protein and inhibit electron transport by acting as a non-reducible analog of plastoquinone and block the PQH_2 for example. Paraquat, a commonly known herbicide, interferes with photosynthesis via the generation of free radical $O^{2,-}$. Free radicals disturb the electron gradient system, thus, affecting the transport of electron to the final molecule and hindering the process of energy generation (Laskay and Lokas, 2011). To overcome pesticides prompted oxidative stress, plants themselves have created viable safeguard systems, for the most part, alluded to as the inner tolerant component through which plants get by against oxidative strain by means of expanding the action of antioxidant enzymes (Weisany et al., 2012). The antioxidant enzyme activities in plants determine their scavenging ability (Xu et al., 2011). A wide range of antioxidant enzyme response has been discussed in the literature in the context of the application of the pesticide. For instance, enhanced activity of catalases and isoenzymes was reported to minimize the level of H_2O_2 in wheat and tomato plants when exposed to a higher level of insecticides pentachlorophenol 2, 4-dichlorophenol (Michałowicz et al., 2009; Shakir et al., 2018). However, different parts of the plant showed a slight variation in antioxidant responses e.g., root and shoot showed differential responses in POD activity upon application of chlorotoluron herbicide (Song et al., 2007). Besides this, GST is a multifunctional enzyme that activates the ascorbate-glutathione cycle which regulates the conversion of herbicide/ ROS to GSH thus providing tolerance to these chemical pesticides (Edwards et al., 2000). The induced level of GST activity was reported in *Arachis hypogaea* and *Triticum aestivum* plants in response to glyphosate and prometryn, respectively (Singh and Prasad, 2018). Moreover, the most important osmolytes, proline, has been considered as the signal of biotic or abiotic stress as its concentration elevated in stress conditions (Ahmad et al., 2017). Proline is the only organic solute that has been shown to protect plants against singlet oxygen and free radical-induced damage that is why proline is able to stabilize proteins, DNA, and membranes (Matysik et al., 2002). Almost every treatment of pesticides enhances the proline level in plants indicating the level of stress in crop plants. To understand the proper mechanism induces by pesticides, extensive scientific research should be carried out and the most appropriate and possible pathway should be given. In the next section, various outcomes of pesticide effect or more specifically, insecticides on non-target organisms will be critically discussed.

Mode of collateral toxicity induced by pesticides to human and non-target organisms

Despite all the sufficient scientific information collected and the facts revealed in this area, little effort has been made to give a complete assessment on the danger dimensions of a wide range of pesticides to the different non-target taxa. The lethality and toxicity of pesticides are a result of their biochemical strategy for cell or physiological responses in life forms. The toxicity caused by pesticides is associated with various human disease such as astrointestinal, respiratory, endocrines, reproductive as well as neurodegenerative diseases (Mostafalou and Abdollahi, 2013). The major chronic diseases are Parkinson (Van Maele-Fabry et al., 2012), Alzheimer (Parronet al. 2011), diabetes (Thayer et al., 2012), cardiovascular diseases (Zamzila et al., 2011) and chronic nephropathies (Siddharth et al., 2012) and most lethal cancer disease are more prone to population where excessive pesticide has been used and either most of these diseases are not curable or the available drugs show severe

Table 2
Pesticides responsible for human disease

Sl.No	Pesticides	Chemical Nature	Site of action	Symptoms	Chronic disease
1.	Chlorpyrifos, Lindane, Methoxchlor	Chlorinated Hydrocarbon	Kidney, Liver	Aplastic anemia, hyperesthesias	Leukemia, Parkinson disease, Prostrate cancer
2.	Phenoxy derivative	2,4-D and 2,4,5-T	Respiratory and GI tract	Diarrhoea, metabolic acidosis	Lung cancer, gall bladder cancer
3.	Diquat, paraquat	Dipyridyls	Kidney, Liver, GI tract	Nausea, vomiting, Jaundice	Stomach cancer
4.	Captofol	Fungicides	CNS, lungs, liver	Chronic cough, Pulmonary edema	Pancreatic and lung cancer
5.	Chlorpyrifos	Organophosphate	Neurotoxins	Muscular cramps, fatigue, asthma	Leukemia, and colorectal cancer
6	Methylbromide	Organobromine	Neurotoxins	Headache, memory loss	Neurological effects
7	Toxaphene	bicyclic chloroorganic compound	lungs, nervous system, and kidneys	Not specified	bronchial carcinoma in
8	Pendimethalin	Dinitroaniline	Skin, Eye	Skin, eye and respiratory irritations	Rectum cancer
9.	Oxychlordane	Organochlorine	adipose tissues, Liver	migraines, respiratory infections, anxiety, depression, blurry vision	Non-Hodgkin's Lymphoma

side effects (Table 2). The molecular machinery related to the disease is very specific and involves different modes of action. However, the oxidative generation has been considered as the primary reason for all these chronic diseases which involve various caspases, suppression of immune and autophagy system, and formation of defective protein (Kaur and Kaur, 2018). Besides, this epigenetic alteration involves the acetylation, methylation, and also involves modifications to histone protein at the gene level and these alterations are heritable to the next generation (Mostafalou and Abdollahi, 2013). Sometimes, these modifications mimic DNA repairs system and also induce lethal mutation.

The pesticide toxicity is not limited to humans but influences other terrestrial and aquatic invertebrate species. well-known effects of pesticides range from organismal toxicology and behavioral effects at population level. While poisonous quality is constrained by the internal bit required to cause the end of a living thing (paracelsus), the distinction depends upon the biochemical or physiological frameworks centered by the pesticides, which can either change essentially among taxa (for instance explicit bug sprays showers) or be similar for every single living being (for instance wide range creepy-crawly splashes) (Jayaraj et al., 2016). Obviously, broad range insects' splashes are risky to a wide scope of life forms, paying little heed to whether their destructive doses are in a general sense higher for humans and other creatures than for little bugs (Katagi, 2010). Life shapes weak to this kind of poisons join all arthropods, vertebrates, night crawlers, marine worms, mollusks, and distinctive living creatures with a made neuronal structure. For example, Acetylcholinesterase (AChE) inhibitors include the organophosphorus (for instance chlorpyrifos, dimethoate and 60 others) and carbamate (for instance aldicarb, methomyl, pirimicarb, and 25 others) pest showers are the sweeping extents and risky poisonous substances, especially to bumblebees, warm-blooded creatures and feathered creatures (Sanchez-Bayo, 2012). The avermectins (for instance abamectin) are agonists of these receptors (Casida and Durkin, 2013), and are particularly deadly to all arthropods (for instance scroungers, bumble bees, and 8-legged animal), and they are the most unsafe pest sprays to an aquatic organism.

Possible strategy to reduce toxicity of pesticides

Phytohormones-mediated mitigation of pesticides toxicity

Modern agricultural practices have been known for the excessive utilization of synthetic chemicals known for their capacity to decrease physiological efficiency of the plant and negative impact on human health, and degrade the natural environment. Therefore, a crucial, premeditated line of the plan is required to limit the practices of these agrochemicals, and cost effective and innovative methodology should be implemented for sustainable agricultural production. Furthermore, current farming practices need to explore ecologically competent practices with few or no risk of environmental threat and sustain yield and productivity of crops that provide stability to agricultural business (McBratney et al., 2005; Watcharaanantapong et al., 2014). Thus, in this context, we will emphasize the best possible strategy either adopted by the plant itself or scientifically opted approaches to reduce the toxicity caused by pesticide application on growth and development of the plant.

Plant overall growth and development metabolism is well-coordinated by phytohormones for normal growth and development of crop (Wani et al., 2016; Ahmad et al., 2017). Full-on literature has also been documented to prove phytohormones as an efficient method to reduce the various abiotic stresses such as drought, salinity, heavy metal toxicity, radiation, and also many biotic stress (Khan et al., 2015; Ahmad et al., 2018). Recently, the involvement of phytohormones has gained more attention due to their potent efficiency against various pesticides applied to agricultural crops (Fatma et al., 2018). In this context, salicylic acid (SA), important plant signaling molecules and a well-known growth regulator, has been reported to regulate local defense and systemic resistance response to various pathogen attack (Klessig and Malamy, 1994; Ahmad et al., 2019). Previous studies showed that 0.1 mM SA applied to *Brassica napus* seeds reduced the napropamide levels (herbicides) and also improved the growth parameters by decreasing the abundance of O^{2-}, H_2O_2 as well as activities of superoxide dismutase, catalase, and ascorbate peroxidase, and increased activities of guaiacol peroxidase (POD) and glutathione-S-transferase (GST) in napropamide-exposed plants (Cui et al., 2009). Pre-soaking treatment of salicylic acid (1 mM) before the application of Mancozeb pesticides reduced the phytotoxicity effect by regulating the level of detoxifying enzymes and photosynthetic efficiency in *Vigna radiata* (Fatma et al., 2018). Moreover, exogenous application of brassinosteroids increased the activity of various components of antioxidant defense system comprising of SOD, CAT, GPOX, GR, DHAR, and MDHAR, and increased the tolerance against pesticides application on rice by accumulating the proline and other stress combater under chlorpyrifos (CPF) and imidacloprid pesticide exposure **(**Sharma et al., 2015; Kumar et al., 2016; Sharma et al., 2017). The treatment significantly enhanced the expression of P450 (P450 monooxygenase), GST, and MRP (multidrug resistance-associated protein) genes responsible for pesticide detoxification in plants (Sharma et al., 2018).

Nowadays, nitric oxide (NO) is extensively used as a suitable candidate for stress signaling under abiotic stress (Yadu et al., 2017). Keeping in mind the role of NO carried out study by application of 100 µM SNP as a treatment against mancozeb and chlorpyroios and found enhanced antioxidant activities, increased growth parameters such vigor index and reduced phytotoxicity effect on model plant *Allium cepa* (.

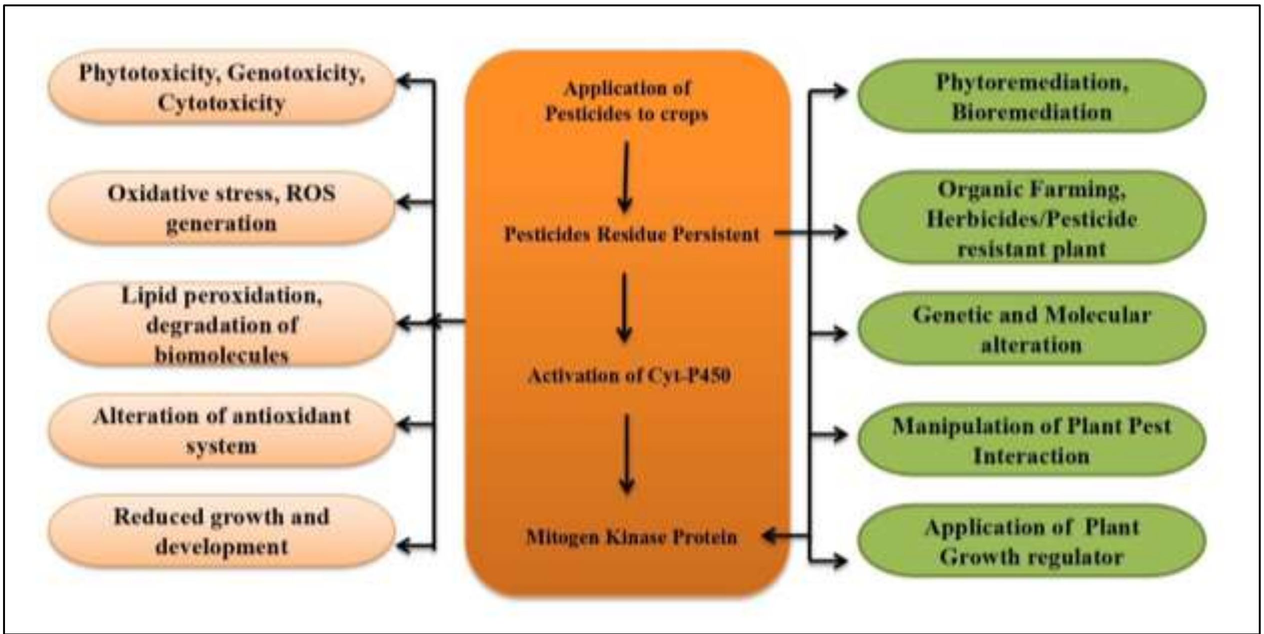

Fig.I. Possible mechanism involved in application of phytohormones and bioremediation process in reducing pesticide toxicity; the (pink part) shows the pesticide-induced cytotoxicity and phytotoxicity responsible for excessive generation of ROS and producing oxidative stress that leads to degradation of biomolecules and reduces plant growth. The green part shows the possible strategies to overcome the toxicity caused by pesticides

In another study, it was reported that mitogen-activated protein kinase (MAPK) and nitric oxide (NO) play an essential role in BR-mediated pesticide detoxification (Yin et al., 2016). Hence, the synergistic effect of the application of phytohormones could be an efficient method to achieve the best amelioration effect. The possible underlying mechanism has been outlined in Fig. I. Recently, JA seed treatment resulted in the significant recovery of chlorophyll content and seedling growth and reduced content of superoxide anion, hydrogen peroxide, and malondialdehyde were enhanced with IMI application. JA seed treatment up-regulated the expressions of *RUBISCO,* NADH-ubiquinone oxidoreductase (*NADH),* carboxylesterase (*CXE)*, and *P450* under imidacloprid (IMI) toxicity in *Brassica juncea* plants (Sharma et al., 2018). The detailed mechanism of mitigation of toxicity by salicylic acid, nitric oxide, and jasmonic acid requires extensive scientific research. However, salicylic acid is associated with activation of mitogen kinase protein when higher production of ROS takes place which in turn accumulates and is linked with activation of the full component of Cyt-P450. The works of literature regarding the prominent role of other plant growth regulators is very scanty and provide plant researcher and broad level of research that should be carried out in very precise manner.

Use of pesticides/herbicides-tolerant plants

The toxicological impacts of herbicides are major issues for human wellbeing and environmental assurance organizations (Sunohara et al., 2010). The production of commercially approved herbicides with specificity to specific weeds and effective in low dosage is essential in controlling unwanted growth without affecting another non-target organism. Apparently, lessening herbicide decisions may result in significant monetary and ecological outcomes to farming. The assessment of herbicide-safe weeds includes mind-boggling and exorbitant techniques. Due to cross-resilience, consistent determinations have to be done to minimize the herbicide blockade (Mahmood et al., 2014). The regular course for creating herbicide-resistant crops (HRCs) was first completed by conventional reproducing techniques. Later on, genetic manipulation proved an efficient method to develop HRCs, yet the innovation has been under investigation for its advantages and other ethical issues. Genetically modified HRCs crop are

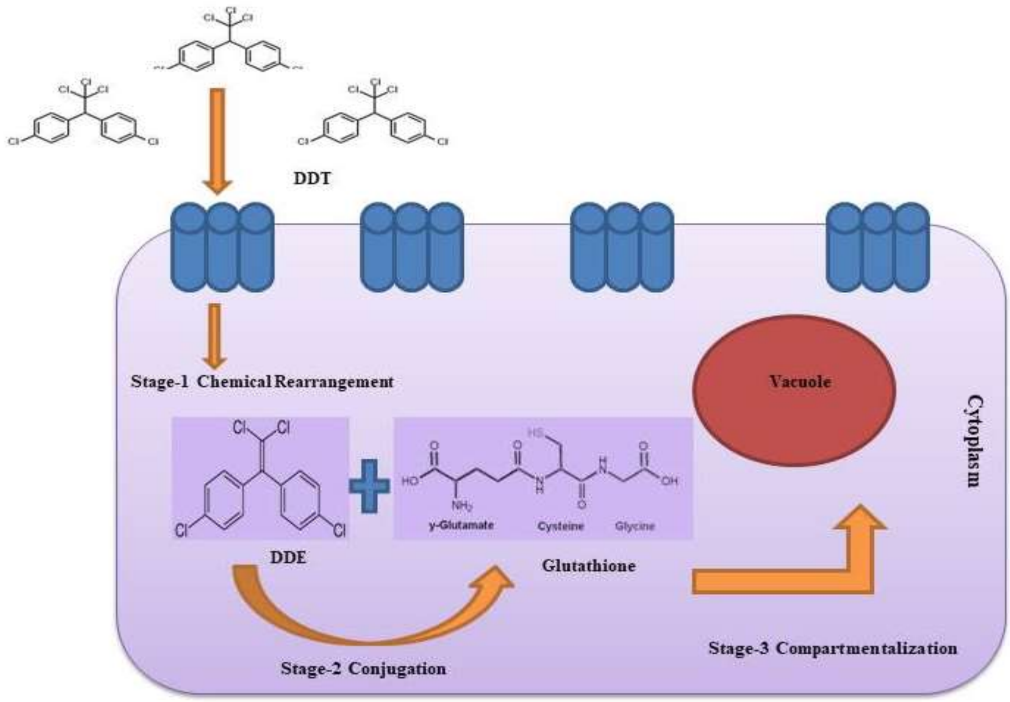

Fig. II. Steps involved in plant driven phytoremediation in plant cells (adopted from Sandermann, 1994); detailed mechanism has been discussed in text.

generally outcomes of cross breeding such as *Brassica rapa*, Glyphosate-tolerant soybean crops, and most common HR rice varieties (Carpenter and Gianessi, 2001; Madsen and Streibig, 2013). The primary machinery involved in resistance against pesticides in plants is a muddled procedure including various parts, for example, phytochromes, plant cell reinforcement hardware, glycoproteins, and communication of different metabolic framework (Mizutani and Ohta, 2010; Mahmood et al., 2014). The activity found in Cyt P450 in plants has a significant capacity in detoxification, which is very like an animal model system that intervenes with the actuation of a few organophosphates, most widely utilized pesticides. Most of the organophosphates are detoxified through Cyt P450 monooxygenases to accomplish herbicide obstruction; diminished actuation may also be involved with the procedure and it is proved to be a common resistance pathway. Besides extensive environmental studies, it is still unclear what route is opted by plants to treat different contaminants from soil and water. But in some studies it was found that pesticides specifically targeting biologically active compounds lost their functionality due to overexpression or overstimulation of the specific proteins thus plants may use molecular strategy to protect them with specific pre and post-translation modification (Singer et al., 2003; Mahmood et al., 2014).

Plant-associated remediation

Phytoremediation has been considered as the most efficient, innovative, and economical technique used to degrade pesticide residual by using a plant rhizosphere system (Hussain et al., 2009). However, the whole process is very complicated and multistep process comprises of various bio-physiochemical reactions in a systematic manner such as hydrolysis, reduction, and chemical conjugation; physical rearrangement takes place both inside and outside of plant (Hoagland et al., 2000). Numerous plants have been reported to tolerate the higher accumulation of pesticides significantly. The reaction catalyzed during plant-mediated phytoremediation in the cell is represented in Fig. II. These plants are regularly considered for phytoremediation in light of their high number of cultivars because of their significance in horticulture and crop improvement, just as their excellent aggregation capability of a broad scope of natural contaminants (White, 2010**).** Organic farming is characterized as the arrangement of creations that are fit for maintaining a strategic distance from or significantly obstruct the utilization of pesticides and artificial composts; domesticated animals' feed adds substances and development regulators. To a vital degree, adaptable natural cultivating framework depends upon crop residues, green manure, pest weeds, crop rotations, off-farm organic wastes, legumes, aspects of biological pest control insects, animal manures. Strategies for organic harvesting are utilized broadly in developing countries, significantly in view of financial elements and fewer assets of synthetic substances. However, they are rising as generally endorsed ideas in the created nations because of long stretches of destructive industry synthetics.

Use of Bio-pesticide over conventional pesticides

Bio-pesticides are naturally occurring substances extracted from plant isolates, fatty acids, or pheromones that control pests by non-toxic mechanisms. The bio-pesticides are broadly categorized under microbial pesticides, plant-incorporated-protectants (PIPs), and biochemical pesticides. The main advantage of bio-pesticides is that they specifically affect the target and related species and do not affect other non-target organisms, are required in low quantity, and are environmental friendly as they are decomposed very speedily by themselves and thus side-stepping the contamination problems caused by a conventional type of pesticides.

The most widely known microbial pesticides have been obtained from bacterium *Bacillus thuringiensis*, which produces a protein that is harmful to specific insect pests and protects crop insect attacks (Greenplate et al., 2003). The commercial mycoinsecticide 'Boverin' is based on *B. bassiana*in combination with a lower dose of trichlorophon to suppress the second-generation epidemics of *Cydiapomonella* (Ferron, 1971). It was also reported that *B. bassiana* and sublethal concentrations of insecticides increased mortality rate when applied to Colorado potato beetle (*Leptino tarsadecemlineata*), recognizing complex synergism between two agents. Recently, genetically modified (GM) crops have been exploited to express genes encoding insecticidal toxins to reduce the damage caused by arthropod pests. Azadirachtin, a tetranortritarpinoid, is a main active component well-known to interrupt the metamorphosis of insects (Sharma and Malik, 2012). Besides this, meliantetyraolenone and odoratone have also exhibited insecticidal activities against *Anopheles stephensi* (Siddiqui et al., 2003). Peptidomimetics are a non-peptide network and have a strong affinity towards the target site in insectophore and interfere with functional moieties due to similar structures and are considered for the potential in the development of novel insecticides which helps in penetration in insect's guts. The development of a peptidomimetic insecticide is likely to be challenging since non-critical residues determined in insect toxicity bioassays may be vital for averting vertebrate toxicity, via steric hindrance. In addition, these non-critical residues maybe essential for providing insect target subtype selectivity (Nicholson et al., 2007).

Future prospective

A different class of pesticides has been made by overall agrochemical associations, which generally controls overall sustenance creation, applying new engineered substances with pesticide properties and complete biotechnological advance, thus veering from standard rural strategies. Besides, current rural practices depend on the wide utilization of chemical pesticides that have been related to adverse effects on human wellbeing, untamed life, and typical habitat. These chemical pesticides are a major threat to the environment. Their resistance in soil and plant and slow degradation naturally makes them enter into food chain and therefore, they are a major issue of health risks for humans and other organisms. Pesticides are mainly used for proper growth and good yield of a crop by protecting them from pests, insects, and additional unwanted growth but due to inadequate knowledge of the environment and unskilled hands that fail to maintain the prescribed level of the dose especially in developing countries the outcomes of these higher doses and application of non-specific pesticides are responsible for the negative effects on plant growth at various morphological, physiological, cellular, and molecular levels. The major consequences caused by these pesticides at the morphological, genetic, and cellular level and associated antioxidant defense system have been discussed in the earlier section of the study. The main aim of this study was to critically review the most appropriate information available regarding pesticides and plant interaction in the natural environment. Besides, various strategies have also been examined such as regulating the defense system, maintaining proper signaling pathway linked with phytohormones, using herbicide-tolerant plants, and the application of pesticides and organic farming. However, there is very little information regarding molecular approaches that have been available. Thus a detailed and extensive effort is still required to dissect molecular and genetic approaches to develop pesticide tolerant plants.

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