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Toxins in Plant Disease: Study of Toxins their Role and Mechanisms in Pathogenesis

Kantikeshwar Jaiswal*[1]

[1] Department of Botany, Government Naveen College, Sonakhan - 493 335, District Balodabazar -Bhatapara, Chhattisgarh, India

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Abstract

Thus, this paper analyses the importance of toxins to plant diseases and also assesses measures in preventing the effects of toxins on agriculture. Bacterial, fungal and viral toxins interfere with plant cell metabolism and defense mechanisms resulting to huge crop losses. In this paper, we discussed the current methods of identification and measurement of toxins such as high- performance liquid chromatography, mass spectrometry, and enzyme-linked immunosorbent assays. Nevertheless, these methods have some drawbacks, for example, sensitivity, specificity, matrix effects, etc. This paper also investigated plant defense mechanisms with reference to the genetic level involving detoxification and activation of resistance genes. Breeding techniques, both conventional and those involving the use of biotechnology, seek to improve toxin content in crops through the use of transgenic techniques and marker assisted selection. Also, we evaluated the use of toxin management techniques, including toxin-inhibitors and genetic engineering techniques which have the potential of decreasing the reliance on chemical pesticides and increasing the resistance of crops. They help in practice of sustainable agriculture by encouraging the use of environmentally friendly practices and enhancing crop yield. Therefore, the present study calls for further research in toxin detection, resistance mechanisms, and application of the biotechnology for enhancing the sustainability of agriculture and food security.

Key words: Toxins, Plant diseases, Analytical techniques, Toxin detection, Genetic

Diseases affect plants in a myriad of ways and are a major thorn in the side of world agriculture since they greatly reduce the yield and quality of crops [1]. These diseases are mainly due to a number of pathogens such as bacteria, fungi, viruses and nematodes which interferes with the normal physiology of the plant [2]. Plant diseases are developed through a series of processes starting with the pathogen's attack on the host plant in which the pathogen adapts different ways and means to penetrate, proliferate, and feed on the host. Of all these strategies, the synthesis of toxins occupies a strategic position in the infection process and increasing the pathogenicity of the pathogen. Knowledge of the processes of plant pathogenesis, especially with regard to toxins, is essential for the prevention of diseases and the preservation of agriculture sustainability [3]. The process of plant disease development, known as pathogenesis, generally follows a series of well-defined steps: inoculation, penetration, infection, colonization, reproduction, and dissemination. During these stages, pathogens deploy various strategies to establish and maintain infection, with toxins playing a crucial role in increasing their virulence.

Toxins are complex chemical substances that are secreted by the pathogens and which can either directly or indirectly harm the plant tissues, disrupt metabolic processes and erode the plant defense system [4]. These toxins can be categorized into two main types: Non host specific toxins (non-host) and host specific toxins (HST) are the two main classes. They are molecules produced by the pathogen which have an affinity for the host plant, and it is with these molecules that one can define the host specificity of the pathogen [5]. Non-host-specific toxins, in contrast, have less selective action and can produce harm to a large number of plant species. These toxins are usually essential in defining the intensity of the disease symptoms and the general effectiveness of the infection [6-7].

The role of toxins in plant diseases cannot be overemphasized since they are usually the main effectors that help pathogens to overcome plant resistance and become established. These toxins act as primary effectors, helping pathogens bypass or weaken the plant's natural resistance mechanisms. For example, some toxins cause the death of cells in the host plant, leaving regions of tissue that are dead and which, therefore, supply the pathogen with nutrients. Some may affect some cellular processes like protein synthesis, cell membrane structure and function, and photosynthesis which disrupts the physiological processes of the plant. Often, the virulence of a pathogen depends on the ability of the pathogen to produce toxins which are specific to a particular disease, and therefore these compounds are significant targets in disease management [8].

Moreover, the analysis of toxins in plant diseases helps to understand better the ongoing coevolutionary battle between pathogens and plants. There are several ways that plants have developed to detoxy or neutralize the effects of toxins such as the manufacture of detoxifying enzymes, the onset of signaling pathways in order to activate the immune system and alteration of the target site in order to minimize the toxin's ability to bind to it [9]. Knowledge of these interactions at the molecular level

***Correspondence to:** Kantikeshwar Jaiswal, E-mail: kantikeshwar@gmail.com; Tel: +91 9301103616

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can help in the creation of resistant crop types, as well as help in the design of new agrochemicals that can counteract or block toxin action [10].

Type of toxin in plant diseases

In the context of plant diseases, toxins produced by pathogens are classified into two primary categories: The two categories are the host-specific toxins (HSTs) and the non-host-specific toxins (non-HSTs). These toxins are diverse in terms of how they work, where they focus, and the part they have to play in the disease. It is important to know these distinctions in order to design specific strategies for dealing with plant pathogens and enhancing the plant resistance [11].

HSTs are different from the other toxins in that they are very specific in their action in as much as they only affect certain plant species or in some cases only certain varieties of a given species. These toxins are in many times responsible for the host specificity of the pathogen, that is, the ability of the pathogen to infect a given plant species. HSTs act on certain receptors or molecular targets in the host plant to cause cell injury, interference with normal cellular functions, and expression of disease symptoms. For instance, T-toxin of *Cochliobolus heterostrophus* that infects the southern corn leaf blight (SCLB) only affects the maize plants with the Tcms Texas male-sterile cytoplasm. This toxin interferes with normal function of the mitochondria in susceptible maize plants and results in cell death and serious damage to the leaves. The specificity of HSTs is thus a disadvantage since the host plant can be consider fully susceptible whenever the genetic factor is present.

On the other hand, non-host-specific toxins (non-HSTs) are active on a large number of plant species including the host plant and other plant species irrespective of the differences in their genetic makeup. These toxins are thought to be general virulence factors making many pathogens more pathogenic [12]. Non-HSTs are usually toxic to normal plant cell processes that are common to most plants, for example protein synthesis, membrane stability or ion transport. A classic example of a non-HST is the toxin produced by a fungal pathogen Botrytis cinerea, which causes gray mold disease in many crops. This toxin affects plant cell membranes thus causing loss of cellular contents, cell death and necrotic lesion formation. This is so because non HSTs are designed to affect basic cellular processes with the plant cell which are inherent to many species of plants hence a blanket effect on the plant is achieved thus leading to losses in agriculture.

Differences between HSTs and non-HSTs affect plant breeding and disease management in a number of ways as well. In crops that are affected by HSTs, breeding approaches are directed to the removal of genes that make the plant vulnerable to the toxin. In the case of the non HSTs, resistance breeding may involve improving on the general defense mechanisms of the plant e.g. increasing the rate of production of detoxifying enzymes or making the cell walls thicker so as to hinder penetration by the toxins.

Table 1 Summarizes chemical nature and mode of action of important toxin

Toxin	Organism	Host	Chemical nature and structure	Specificity	Mode of action
Lycomarasamin	*Fusarium oxysporum lycopersici*	Tomato	Amino acid derivative	Non-specific	Injures permeability of leaf cell. Causes strepogenin deficiency
Fusaric acid	*Fusarium oxysporum, F. heterosporum F. lycopersici F. cubense F. moniliforme*	Tomato, Rice, Cotton	5-n-butylpyridine carboxylic acid	Non-specific vivotoxin	Affects permeability of plant membrane and water balance. Depresses respiration and polyphenol oxidases. Chelates Fe
Pyricularin	*Pyricularia oryzae*	Rice	Emprical Formula C18H14N2O3	Non-specific	Increase respiration growth at low concentration and inhibits the enzyme peroxidase, catalase, cytochrome oxidase and ascorbic acid oxidase.
Victorin	*Helminthosporium victoriae*	Oat	Polypeptide	Host specific toxin	Damages plasma membrane permeability. Loss of electrolytes from host cells, disruption of chloroplast
Alernaric acid	*Alternaria solani*	Potato, Tomato	Dibasic acid Alternaric acid	Non-specific Phytotoxin	Wilting, necrosis and Chlorosis. (Role in disease doubtful)
HC-Toxion	*Helminthosporium carbonum*	Corn	Cyclic polypeptide	Host specific toxin	Effect on nitrate uptake, reduction of corn tissues
HS-Toxin	*Helminthosporium sacchari*	Sugar cane	Glycoside helminthospoeiside	Host specific toxin	Disruption of chloroplast lamellae, Plsmalemma disruption
HM-Toxin	*Helminthosporium maydis*	Corn	Not yet established	Host specific toxin	Swelling of mitochondria and loss of respiratory control
Amylovorin	*Ervinia amylovora*	Apple and Pear	Galactose in polymeric form and protein	specific Phytotoxin	Disrupting cellular permeability
PC-Toxin	*Periconia circinata*	Sorghum	Polypeptide	Host specific toxin	Interference with membrane function. Increased respiration

Mechanisms of toxin action

Toxins that are secreted by plant pathogens have numerous ways through which they cause plant diseases and these include interference with important cellular processes, triggering of plant cell death and evasion of plant defense responses [13]. These actions also help in the colonization and movement of pathogens from one plant to another and further dictate on the severity of the symptoms exhibited by the affected plant.

The major way of toxic action is the interference with crucial biological processes in the host plant. Toxins can act as inhibitors of various biochemical processes for instance photosynthesis, respiration and synthesis of proteins hence disrupting the normal physiological processes of the plant. For instance, some toxins interfere with the enzymes that are essential for chlorophyll synthesis or with the electron transport system of chloroplasts, thus causing a decrease in the efficiency of photosynthesis and chlorosis in the affected tissues. Other toxins can interfere with the plant's protein synthesis apparatus either by means of ribosome inactivation or by altering key proteins thus affecting the plant's ability to synthesize key enzymes and structural proteins. These disruptions can reduce the general health of the plant and therefore is more vulnerable to the further invasion of pathogen and diseases [14].

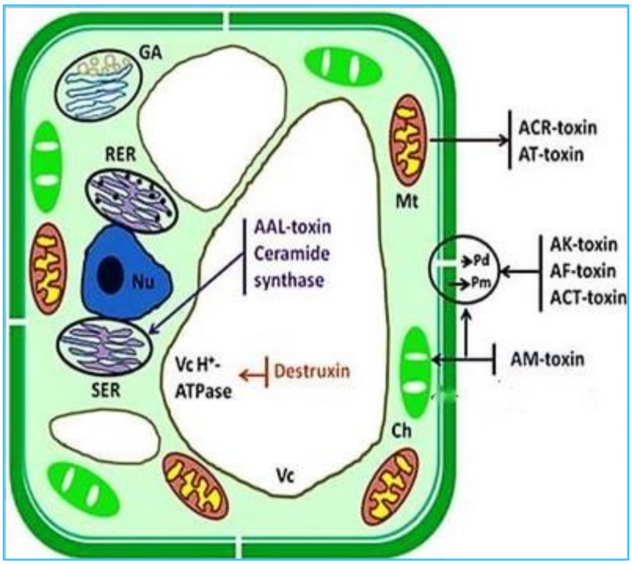

Fig 1 Schematic Presentation of target sites of some important toxin

Ch, (chloroplast), Mt (Mitochondria), SER (Endoplasmic reticulum), Pm (Plasma membrane), Pd (Plasmodesmata), Vc (Vacuole), Nu (Nucleus), GA (Golgi apparatus)

Another essential process that pathogens use to manifest the disease is through the use of toxins which cause cell death. Some of the toxins cause PCD or necrosis in the plant tissues resulting in dead or dying cells which in return become a source of nutrition to the pathogen. This cell death may be through plant apoptosis like mechanism where the toxin caused the release of ROS that resulted to oxidative stress and cell death signals. For instance, the victorin toxin secreted from *Cochliobolus victoriae* affects the PCD of susceptible oat plants through binding to a particular protein that is associated with apoptosis. The resulting necrotic lesions provide a favorable environment for the pathogen to proliferate, as the dead tissue offers an abundant supply of nutrients and reduces the plant's defensive capabilities. By inducing cell death, toxins help pathogens establish a foothold in the host plant and facilitate the spread of the disease.

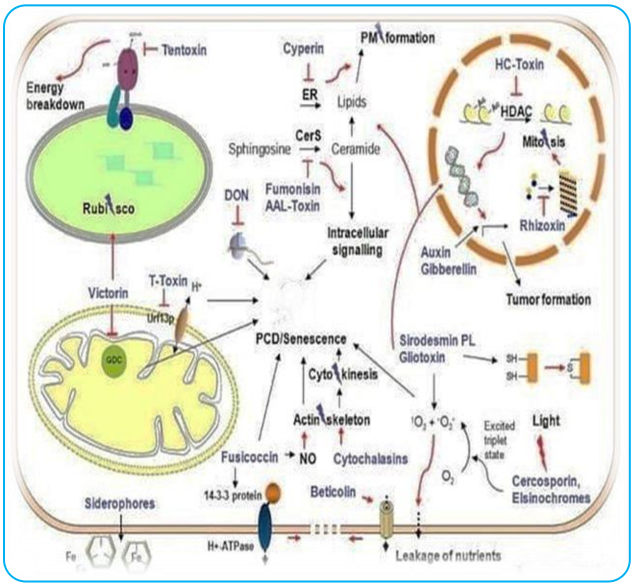

Fig 2 Overview of the mode of action of several fungal pathotoxin

Toxin production by pathogens

Toxins are synthesized by plant pathogens via biosynthesis pathways that are specific to the production of these toxic substances. Such pathways consist of a sequence of enzymatic reactions in which simple precursors are transformed into complex toxin molecules. For instance, polyketide synthases and non-ribosomal peptide synthetases are the enzymes responsible for the production of many of the fungal toxins, such as those produced by Aspergillus and Fusarium species. These enzymes build toxins through the stepwise polymerization and post-polymerization modifications of small molecular precursors giving rise to the complexity of chemical structures seen in plant pathogenic toxins [15]. The biosynthesis pathways involved are usually very specific and define the structure and function of the toxins encountered by the pathogen and can thus influence its capacity to cause disease. Further, some pathogen microorganisms can synthesize toxins as products of secondary metabolism, which is different from the regular metabolic processes of the organism, though not necessarily necessary for the reproduction of the pathogen. Some of these secondary metabolites may elicit strong biological activity on the part of the plant, thereby enhancing the pathogen's virulence and host specificity.

The synthesis of toxin in pathogens is very much coordinated and frequently associated with signals such as environmental conditions, life cycle and host-pathogen interphase. The timing and quantity of toxin production are often tightly regulated by environmental cues, the pathogen's life cycle, and interactions between the host and pathogen. Bacteria and viruses have to secrete toxins at the appropriate time and in the correct concentration to cause the maximum amount of damage to the host but at the same time have to be energy efficient. This regulation is done through multiple layers of genetic and epigenetic regulations [16]. For example, in fungi, the genes that are involved in the synthesis of toxins can be controlled by general factors that are sensitive to conditions like pH, temperature or availability of nutrients. These factors make sure that toxins are produced when the pathogen is in a right environment for infection. Furthermore, there exists the quorum sensing, which is a process of communication among the pathogens depending on the number of organisms present; this is important for controlling the production of toxins among bacteria. In response to increasing cell density, bacteria can upregulate the production of virulence factors, including toxins, to enhance their collective ability to infect the host.

Case study

Jain and Khurana [17] stated that plant growth and development come across abiotic and biotic stresses including drought, cold, salinity, heavy metals and pathogen attacks. As a result, plants turned on genes that encodes effector, receptors and protective molecules the pathogenesis related (PR) proteins are particularly important. These proteins were crucial to the plants' defence against pathogens and accumulated in infected and distal parts of the plant [18]. Since the PR proteins were induced in a variety of plants, it suggested that their overall function was in the response to stress. Furthermore, PR proteins were also associated with the defence mechanisms of HR and SAR against infection. Jain and Khurana [17] have also described the structure, biochemistry, regulation and the defense related characteristics of these proteins. Nazarov *et al*. [19] have also pointed out a recent rise of diseases due to bacterial, fungal, and viral infections impacting plants at the different production phases. In silage crops the disease can affect 70 to 80% of the plant population with yield losses ranging from 80 to 98% based on the weather and crop condition. Plants have a basic form of cellular immunity but some phytopathogens can overcome it. The article analyzed phytopathogens – viral, fungal, bacterial – and modern approaches to protecting plants, including chemical, biological and agrotechnical tools, as well as detection techniques for phytopathogens.

Kwiecinski and Horswill [20] described Staphylococcus aureus as an opportunistic pathogen that is usually found in the human anterior nares, but is frequently responsible for severe bloodstream infections including sepsis and endocarditis. In their review, they concentrated on the pathogenesis of these invasive infections, with regard to the strategies used by *S. aureus* to avoid the host immune response, to seize control of host defense and coagulation mechanisms, and how it interacts with the endothelium of blood vessels. They also examined the regulatory systems employed by *S. aureus* during invasive infections; with the identification of new therapeutic targets in bloodstream infections.

Sharma *et al*. [21] described Alzheimer's disease (AD) as a progressive neurodegenerative disorder and one of the leading causes of dementia in the elderly; it is a major global health concern. They underlined the necessity of invention of new therapies and the comprehension of large sets of data to reveal the molecular basis and pathophysiological processes of AD. The review described several pathological processes such as cholinergic dysfunction, amyloid-beta deposition, abnormalities in tau protein, and oxidative stress, though pointing out controversies and contradictory findings with regard to them. Other issues like cost benefit analysis of cholinesterase therapy, selectivity of AChE over BChE, and BBB permeability of BACE-1 inhibitors and problems with vaccination and immunization. This review also discussed the possible treatments, structural data of traditional and new targets, and the use of computational techniques in synthesizing target selective inhibitors.

Sher Khan *et al*. [22] have also discussed the importance of natural antimicrobial peptides including defensins in the immune defense of plants and in animals, as part of their adaptive immunity. Defensins show a lot of action against different types of pathogens, viruses, bacteria, fungi and have a broad-spectrum action in different organisms ranging from human to plants. Plant defensins are known to primarily exert their biological activity through the association with membrane lipids. The use of these antimicrobial peptides has been proved to be beneficial for increased disease protection in plants, and the genes of defensins have been incorporated into plant genomes to produce transgenic crops with increased disease resistance.

Ghorbanpour *et al*. [23] presented the effects of plant diseases on ecosystems and the transition from the poisonous synthetic fungicides to the safe and favourable fungi. Trichoderma species, arbuscular mycorrhizas and non-pathogenic strains of pathogens have been found to have strong bio-control potential through competitional mode, mycoparasitic mode, antibacterial mode, by using mycovirus cross protection and by inducing systemic resistance mode. Advances in genetics and biotechnology now enable the enhancement of biocontrol traits in fungi and plants, including the incorporation of antimicrobial genes into plant genomes and the development of hypovirulent fungal strains. The review emphasized the practical applications and benefits of these biocontrol mechanisms in sustainable agriculture.

Detection and quantification of toxins

Detection and, in particular, quantitative analysis of toxins in various situations, the presence of which in plant pathogens, environmental samples, or clinical practice has been identified, is essential for assessing the consequences of their action and controlling them. There is an important and significant role of analytical techniques in the identification and accurate measurement of toxins though the difficulties and issues of toxin detection are still the barriers.

The general approaches to toxin identification and their concentration are the presence of several rather complex and effective methods. HPLC is popular because of its effectiveness to analyze joint mixtures and its exactness in measurement of toxins [24]. High performance liquid chromatography coupled with mass spectrometry (HPLC-MS) provides more data about the molecular weight and structure of toxins making identification more precise. ELISA tests are used for their specificity and sensitivity and antibodies are used to identify and quantify specific toxins. Another method is gas chromatography-mass spectrometry (GC-MS), which is suitable in case of volatile and semi-volatile toxins [25]. They offer accurate information on the toxins and their levels, which are useful in research and in everyday life, for instance, in food inspection and ecological surveys.

But there are several factors that make toxin identification challenging. One of the major challenges is the matter of selectivity, because most toxins are in very low concentrations in mixtures, and in addition, the compounds are very similar to each other. Also, matrix effects, interferences from other compounds in the sample, can also be an issue to detection and quantification. For example, the presence of large and complex matrix in plant samples or environmental samples may cause interferences and suppress the signals of target toxins and thus demands much time for sample preparation and method development [26]. Another difficulty is the fact that pathogens produce toxins in different amounts and this influences the reliability of the results obtained. Moreover, some of the toxins can be metabolized or alter in the environment and the analytical techniques used should consider these changes.

These problems can be solved more effectively by devising the finer kind of analytical methods and by refining the sample preparation process in order to achieve high sensitivity and selectivity. Advances in technology, such as the integration of biosensors and portable detection devices, offer promising solutions for real-time and on-site toxin analysis. Overall, while current analytical techniques provide powerful tools for toxin detection, ongoing efforts are needed to overcome the inherent challenges and improve the accuracy and reliability of toxin quantification [27-28]. The integration of biosensors and portable detection devices is a game-changer for real-time toxin analysis in agriculture, offering more accessible, faster, and cost-effective solutions. These technologies allow for immediate responses to plant diseases and contamination, potentially saving crops and minimizing economic losses. However, to fully realize their potential, ongoing research is needed to improve their robustness, accuracy, and affordability.

Plant resistance to toxins

There is a complex of genetic factors and breeding techniques concerned with plant resistance to toxins, whether they are pathogen-derived or abiotic, and the general goal of such resistance is to decrease the negative impact of toxins on plants [29]. Plant resistance to toxins, whether produced by pathogens or as a result of abiotic stresses (like heavy metals or pollutants), is a vital aspect of plant breeding and genetic research. Developing toxin-resistant plants is crucial for sustaining agricultural productivity, reducing losses due to diseases, and enhancing resilience in environments prone to abiotic stress. This resistance involves a complex interplay of genetic factors, biochemical pathways, and plant defense mechanisms that minimize the harmful effects of toxins on plant health.

Genetic resistance mechanisms: Following are some of the genetic mechanisms that plants have developed to combat the effects of toxins: One of the gross strategies is the synthesis of enzymes that either inactivate the toxins or alter their properties so that they are harmless. For instance, glutathione S-transferases (GSTs) and cytochrome P450 enzymes which are involved in metabolism of xenobiotics and secondary metabolites. Another mechanism implies the activation of specific resistance (R) genes which code proteins capable to recognize the toxins produced by pathogens and to initiate defense reactions. Some of these R proteins can induce localized cell death or other defense reactions which prevent the spread of toxins. Also, the stress tolerance can be modulated at the biochemical level through various biochemical pathways in plants. For example, enhancement of the production of defensive molecules such as flavonoids and phenolics may assist in reducing the effects of toxins that cause oxidative stress. Knowledge of these genetic resistance mechanisms helps in the isolation of genes and pathways that are involved in toxin defense [30-35].

Breeding for toxin resistance: Breeding strategies focuses on the attempt to introduce resistance traits into crop varieties to enhance the level of resistance towards toxins. The conventional breeding techniques in practice entail the use of plants with natural resistance and then mating them in order to develop plants with resistance genes in the subsequent generations. Molecular breeding tools including marker assisted selection, genomic selection have given a boost to the breeding of toxin resistant crops. MAS in this case employs molecular markers associated with resistance genes; this helps in selecting and propagating resistant varieties. In contrast, genomic selection focuses on the prediction of breeding values of plants from its whole genome so as to select for traits related to toxin resistance. Genetic engineering is also used in breeding for toxin resistance by either inserting or altering genes that are associated with metabolism or defense. For instance, transgenic plants expressing genes encoding detoxifying enzymes or protective proteins can be developed to enhance resistance to specific toxins. These advanced breeding approaches, combined with traditional methods, offer promising strategies for developing crops with improved resistance to harmful toxins and enhancing agricultural resilience [36-38].

Potential applications in agriculture

Toxin-inhibitors as plant protectants: It is becoming clear that toxin-inhibitors have great potential for use in agriculture in helping to safeguard plants from toxins that may be synthesized by pathogens or are naturally occurring in the environment. These inhibitors work in the way that they either bind to the toxins and thereby decrease their adverse impacts on the plant health. For instance, chemicals that counter act on predetermined toxins enzymatic activities can be sprayed on crops to reduce damage. Also, the use of biologically derived inhibitors that can be peptides or proteins resulting from microorganisms can be used to counteract pathogen-produced toxins [39]. The inclusion of these inhibitors in our crop protection programs will improve plant resistance and minimize the application of the traditional chemical pesticides to control diseases.

Engineering toxin resistance in crops: Genetic engineering can be considered as a strong tool to increase toxin resistance in plants through the alteration of the plant's DNA. Strategies include transgenic expression of detoxifying enzymes or resistance proteins to ''neutralize'' specific toxins. For instance, engineering genes which produce enzymes capable of degrading or transforming toxins can assist crops to endure pathogen toxins. Another approach is the integration of resistance genes that give signals that lead to defense in plants when exposed to toxins, hence preventing destruction. Due to recent improvements in the CRISPR/Cas9 and other genome editing tools, plant genomes can be modified systematically to create crops that are more resistant to toxins and are generally more resistant [40-41].

Implications for sustainable agriculture: This paper also shows that the use of toxin-inhibitors and toxin resistant crops in the agricultural setting has effect on sustainable agriculture. These approaches are more sustainable because they downplay the extent to which farmers have to rely on chemical pesticides while at the same time enhancing the crops' resistance to pests. There are also possibilities to reduce the effect of chemical treatments on other species and the environment with the help of toxin inhibitors and genetically modified crops with high resistance to toxins reducing the frequency of pesticide application [42-43].

CONCLUSION

Thus, this research has discussed the various functions of toxins in plant diseases and their significance to crop yield and wellbeing. Bacterial, fungal and viral toxins play a huge role in the increased disease severity by interacting with plant cellular processes and its defense mechanisms. We have also highlighted the different analytical methods used in the detection and quantification of toxins to appreciate the improvement in high-performance liquid chromatography, mass spectrometry and enzyme-linked immunosorbent assays. However, there are still some significant problems like sensitivity, specificity, and matrix effects which make the toxin analysis difficult. On exposure to toxins the plants employ complex genetic resistance mechanisms including biosynthesis of enzyme and gene activation. Conventional and novel breeding techniques have been aimed at improving resistance to toxins, be it by selection or genetic modification. This is where the advancement in technology like the production of transgenic crops and the use of marker assisted selection to properly incorporate the resistance traits. The possibility to extend the use of toxin management strategies in agriculture seems rather great. Various toxin-inhibitors are useful in plant protection as they counter toxic effects in one or another way, whereas genetic engineering is a rather powerful approach to develop plant varieties with toxin tolerance. Apart from increasing the plant's robustness, these innovations equally support the use of efficient and environmentally friendly practices such as minimal use of chemical pesticides and increase production of crop yields.

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