Review

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Review

Economic Impacts of Viroids

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Abstract: Plant diseases are responsible for over 10% loss in global food production and have serious impacts on world-wide food security across several countries. Amongst these diseases, those caused by viroids are highly significant, accounting for extensive damage to crops every year and pose a major economic threat to agricultural crops. Combined infections with viroids, plant viruses and their satellites further exacerbate the situation. Vector transmission of viroids necessitates the use of pesticides, thus incurring high costs in addition to eliciting several detrimental effects on the ecosystem due to the noxious outcomes of pesticide use. The current review addresses the major economic impacts of viroids on crops, costs to the world economy and impacts on regions, farmers and consumers in addition to describing remediation measures to mitigate the losses caused by these subviral agents. Also described are issues relating to the pros and cons of pesticide use, the compelling need towards sustainable agricultrual practices while reducing pesticide use. In particular, the role of RNAi and genome editing technologies towards amelioration of agricultural loss is discussed.

Keywords: viroids; diseases; economic impacts; farmers; consumers; mitigation measures; resistance; decontamination; detection; NGS; CRISPR

Introduction

With the ever-prevalent rise in population, the world is increasingly facing malnutrition or hidden hunger particularly in the developing countries. To address this predicament, food crops and cash crops must be successfully cultivated considering that they form the foundation of all of our societies. In the light of such compelling need to produce more food for the human populace, we still face the threat of damage to crops on a global scale caused by plant viruses, viroids and satellites [1]. Efforts to reduce or remove plant pathogens range from using agricultural inputs such as pesticides and antimicrobials, to the development of plants which confer resistance to specific pests. Viroids may be specifically challenging to overcome; unless they are carried by an insect pathogen, they cannot be treated with the available assortment of pesticides we have today. Reduction of contamination by viroids includes decontamination measures, early detection using sensitive techniques such as PCR and culling of symptomatic plants in addition to the development of resistant crops using conventional or new plant breeding techniques, such as transgenesis or genome editing technologies. While the latter methods have some merit, they may be more challenging from a regulatory standpoint than the use of chemical inputs. Thus, viroids alone impose significant economic losses to global crop production. World-wide, viroids have been considered as quarantine pathogens to preclude the risk of transmitting viroids to countries free of viroid diseases, and there is an urgent, compelling need to formulate potent antiviroid measures. Viroids are characterized by the presence of a population of sequence variants, accounted for by the low fidelity of the RNA polymerases associated with their transcription and replication, leading to high frequencies of mutations. Hence, viroids occur as quasispecies that enable them to replicate in a wide range of crops including both monocots and dicots. Host plants for viroids include economically valuable crops such as citrus, potato, tomato and fruit trees such as avocado and peach.

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In the following review, we discuss the economic impacts of viroids, how viroids affect countries, regions, individual farmers and consumers. Importantly, vector transmission of viroids and employment of pesticides in combatting crop diseases, impacts of climate changes on pest proliferation, advantages and disadvantages of pesticide use, the regulatory, environmental, defensive and human health costs of the use of chemical pesticides, growth in the market for pest control and finally the newly emerging biological pest control technologies are addressed. Sustainable agricultural practices to induce resistance to viroids while decreasing pesticide use are discussed. Our review also covers the mechanisms by which viroids elicit symptoms in their host plants and how viroid diseases can be managed using thermotherapy, decontamination measures and mRNAi or the modern CRISPR technologies.

Discovery of Viroids

Earlier when viroids were yet to be identified, they were recognized only by the destruction that they wreaked. In the 1920s, growers in the USA and other regions were impacted by an unknown pathogen that caused decreased quality and quantity of potato crops. Some areas of China and Ukraine were also affected by the seemingly same disease in the 60s and 70s. Scientists initially thought of it as a viral disease and it was only in 1971, Diener identified that these diseases were caused by a sub-viral article composed of a minuscule circular RNA having no capsid protein and therefore not an authentic virus. He named it “viroid” [2]. Viroids are the simplest among infectious agents targeting plants. There are about 300 viroids identified to be capable of infecting plants. They show remarkable selectivity, and each viroid type infects only a particular type of plants occurring within the same genus. Viroids have been deemed as an agriculturist’s most dreadful nightmare (Hazeltine, Forbes magazine, 2023). Viroids are minuscule, closed circular RNAs that range in size between 246-463 nucleotide bases wherein they form a rod-like structure due to internal base pairing [3]. They are incapable of encoding any proteins and are devoid of protein coat unlike viruses. All viroids identified so far are plant pathogens and all of them affect angiosperms. Viroids affect at least 33 species of angiosperms and their wide host range accounts for significant damage to the economy.

Economic Impacts of Viroids

Potatoes

Potatoes are our staple food consumed by the majority of the human population and are among the most essential crops following rice, maize and wheat. Over 300 million metric tons of potatoes are produced annually the world over. As high as 64% of the potato yield has been decimated by the potato spindle tuber viroid (PSTVd, Figure 1) [4]. In the saco potato variety, even mild PSTVd strains reduced the yield by 24% while in the case of more severe PSTVd strains, as much as 60% of the potato yield has been impacted [5]. Additionally, as low as 4% of the infected potato crop could result in 3% yield loss as per an investigation conducted in the USA [6]. Therefore, it not surprising that PSTVd has been deemed as an agricultural pest in several countries. This is aggravated by impediments in eradicating this viroid once it has infested the field as it is spread through contaminated pollen, seeds and farming equipment. Only stringent quarantining measures, and in the worst instances, complete elimination of infected potato crops have been shown to be successful. Some nations such as the USA and Canada have succeeded in completely eliminating PSTVd infection in potato crops. But nevertheless, the major four potato producers including India, China, Ukraine and Russia continue to struggle with PSTVd infestation.

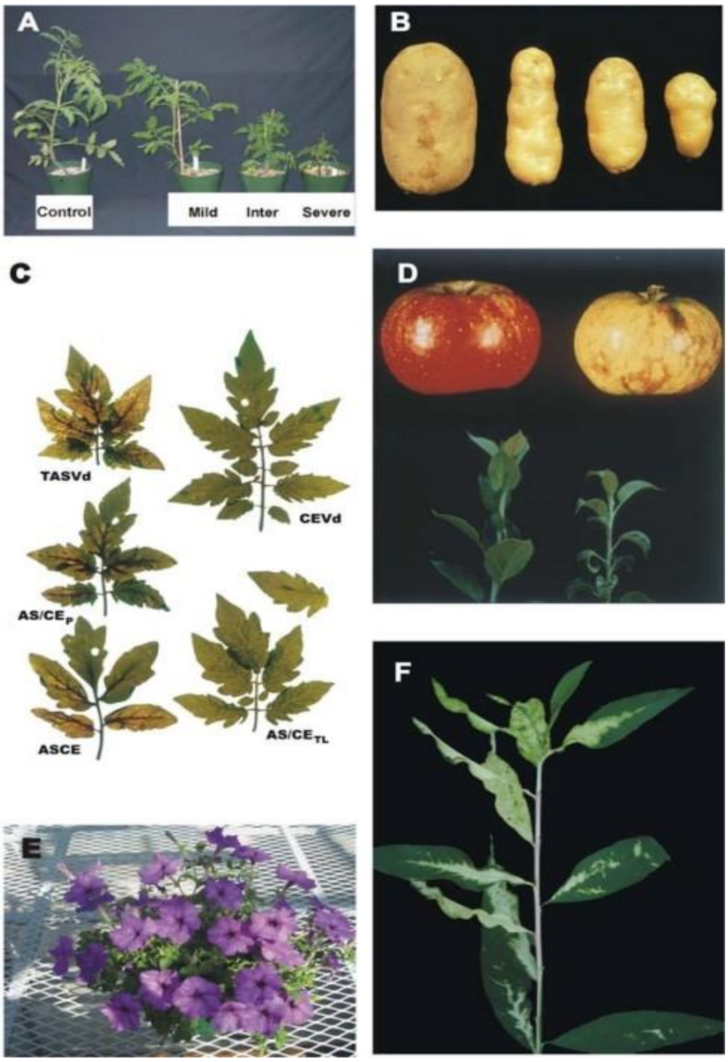

Figure 1. Symptoms caused by viroids. (A, C) PSTVd infection of tomato cultivars that are sensitive or infection with related viroids such as TASVd and CEVd cause stunting, veinal necrosis and epinasty wherein leaves undergo downward curling. Importantly, there are differences in the severity of symptoms between various PSTVd strains (A) or different viroids (C). (B) PSTVd symptoms in the natural host, potato; the healthy tuber towards the left is from an uninfected plant. (D) Woody host plants such as plum or apple develop fruits exhibiting color breaks or abnormal pigmentation; towards the left is healthy uninfected apple; towards the left is apple infected with Apple scar skin viroid (ASSVd). (E) Several plants infected by viroids, particularly herbaceous ornamental plants such as petunia infected with Tomato chlorotic dwarf viroid (TCDVd) are likely to show no visually detectable symptoms. Such plants infected latently with this viroid when vegetatively propagated, result in dramatic enhancement of the number of infected plants, thus increasing the chances for accidental dissemination to other sensitive plants growing in the vicinity. (F) Peach infection by some of the variants of PLMVd causes chlorophyll loss from the large areas of the leaves and severe chlorosis. Clone ASCE indicates a viroid construct encompassing the left side of the TASVd and the right portion of the CEVd, while AS/CE-P and AS/CE-TL represent TASVd whose P or TL domains have been substituted by the corresponding regions of the CEVd. (Reproduced from Owens, R.A.; Hammond, R.W. Viroid Pathogenicity: One Process, Many Faces. *Viruses* **2009**, *1*, 298-316. https://doi.org/10.3390/v1020298; citation credited and no permission needed).

Avocados

Avocado crops are widely consumed across the USA, specifically consumption of over 3000 million pounds of this fruit has been reported in 2021 [7]. Further, this fruit is on demand in East Asia particularly in South Korea. However, avocado crop has been impacted by the avocado sunblotch viroid (ASBVd). ASBVd is the smallest among viroids and is capable of causing substantial damage including fruit discoloration such as yellowing, whitening and redness along with scarred skin, scarred fruit and smaller fruit size, otherwise called dwarfing. Some of the trees show no symptoms which poses hazard for spread of this viroid unwittingly by handlers or farmers who may transmit the viroid to healthy, uninfected trees. Similar to PSTVd, removal of ASBVd from avocado orchards poses a major challenge often requiring complete eradication of all the trees within the orchard followed by a total restart of the cultivation process. ABSVd is relentless in decimating avocado crops. For instance in Mexico, the largest avocado producer, symptomatic trees of Hass avocado showed 75% decrease in fruit total weight [8]. A worse 83% fruit yield reduction was observed in Mendez avocado trees. Even trees that were asymptomatic showed yield loss ranging from 30% to 58% based on the avocado variety.

Coconut & Oil Palms

Palm oil, the universally used vegetable oil for cooking in addition to its incorporation in several cosmetics makes it an important product [9].This oil is obtained from the African palm tree and these trees are affected by the dreadful viroid called the coconut cadang-cadang viroid (CCCVd). Symptoms caused by this viroid include orange spotting, stunting of growth and decrease in yield. Palm trees impacted by orange spotting generate only 25-50% of the normal fruit yield [10] that lead to losses of $25.6–256.2 million USD yearly in Malaysia, a country that is one of the primary cultivators of palm trees.

Further, the CCCVd infects coconut palms in which it is lethal and devastating. Over the last 10 years, the cadang-cadang disease has lethally affected 40 million coconut palm trees in the Philippines which resulted in an estimated loss of $4 billion USD [11]. The CCCVd has been reported to cause a yearly loss of nearly 22,000 tons of copra or dried coconut kernels in the Philippines [12], thereby resulting in an annual loss of $10.6 million USD considering roughly $480 dollars per ton [13]. CCCVd transmission occurs mainly through non-sterile agricultural tools in addition to transfer of infected pollen to healthy palms resulting in viroid-infected progeny [13].

Hemp

Hop latent viroid (HLVd) infects hop plants on a global scale. It has also affected the cultivation of hemp crops [14]. Cannabis cultivation is rapidly growing in the USA and its worth was shown to be $26.5 billion USD in the year 2022 [15]. The demand for cannabis is estimated to soar by about 4% yearly, likely reaching as high as 70 million USD by 2030. While the rising demand warrants adequate supply, the hemp crop producing cannabis is susceptible to viroid infections. The hop latent viroid (HLVd) infects hemp crops causing symptoms such as decreased growth, poor yield, brittle stems and leaf discoloration. This negatively impacts the yield of cannabis in addition to causing decreased crop quality such as dullness of smell and diminished oil content in the cannabis flowers resulting in the so-called "dudding disease".

Out of 90% of the hemp cultivation fields, HLVd infection was shown to impact 33% of these sites leading to an annual loss of $4 billion USD for hemp farmers [16]. Dr. Bryce Falk of the University of California, Davis has proclaimed the HLVd as the biggest hazard to the cannabis industry in the USA [17]. This viroid causes latent infection and by spreading undetected it decimates the commercial worth of cannabis. Therefore, in order to realize its prospects as a commercially viable crop, testing for HLVd has to be conducted on a large-scale along with rigorous treatment regimens.

The rates of infection of cannabis plants with Hop latent viroid has escalated in Canada and the USA. In California alone, a survey conducted in 2021 involving 200,000 plant tissue tests showed that nearly 90% of the hemp crops had already been affected by HLVd infection [18]. This viroid has also spread rampantly into countries such as Europe and South America, further exacerbated by globalization.

Even as HLVd mostly causes asymptomatic infection in hop plants, research has shown that the contents of terpene and alpha-bitter acids in hop cones is greatly decreased, thus impacting its economic value. A similar situation is observed with hemp plants infected by HLVd wherein poor

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quality and yields have been reported due to HLVd infection. This is accounted for by 50% reduction in terpenes and cannabinoids in the infected hemp plants. Flowers are tinier and less compact with reduced aromas and lower trichome development, resulting in tremendous economic losses. A report from the Dark Heart Nursery Research has estimated that HLVd infection in hemp crops causes losses as high as 4 billion USD annually [19].

It is important to know that by the time we detect the viroid symptoms, it might be too late to save the infected plant, but nevertheless, this would save the remainder of the crop. HLVd moves systematically through the phloem tissue of the infected plant in roughly over 6 weeks. By the time leaves develop symptoms, the roots of the hemp plant have already been infected resulting in extensive infection through the entire plant, thus precluding early detection. Nevertheless, the most notable symptoms to distinguish are weaker plants with dwarfed growth, reduced internodal spacing, brittle and less vigorous stems, smaller or under-developed leaves accompanied by chlorosis in areas impacted by the spread of the viroid in addition to poor uptake of water and nutrient leading to decreased development of the plants. HLVd infection becomes notably obvious at the flowering stage, however it becomes too late for the infected plant. In comparison to the vegetative stage, the flowering stage shows higher concentrations of the viroid, likely due to added plant stress. The flowers of HLVd-infected hemp plants are smaller and accompanied by unexpected leaf yellowing close to the buds in contrast to that of healthy plants.

Economic Impacts of Crop Losses Incurred by Regions, Farmers and Consumers due to Viral and Viroid Diseases

Evaluation of the incidence of diseases and crop losses is a vital factor associated with the economic facets of plant disease management. Preclusion of crop loss economically justifies plant pathology and epidemiology. Assessment of yield decrease for a given crop and pathogen combination could be catastrophic. Some of the plant viruses, viroids and satellites destroy all parts of plants such as roots, stems, leaves, flowers, and seeds wherein the degree of loss will primarily depend on the crop value in either or both quantitative or qualitative terms. In instances of quantitative loss, the loss of crops would concern crop number or weight while for qualitative loss, this concerns reduced product size in addition to distortion of taste, flavor, and chemical constitution. Decreased size and malformation of the commodity, in case of flowers with smaller sizes and color breaking while for root crops with decreased size, negatively impacts market values for vegetables and fruits [20].

Losses of crops are typically measured in yield units such as bushels, kilograms etc. in addition to the per cent decrease in 'potential' yield as estimated for the corresponding healthy crop. Further, it can be expressed in terms of monetary units dependent on fluctuating market valuations. In the context of the open market, the association between financial loss and weight loss for individual farmers is further exacerbated by the issue of whether other cultivators supplying to the same markets have incurred equivalent losses. Also, if farmers do not deliver well, it will affect the buyer-producer relationship or even stop. Provided losses occurring due to plant diseases are moderately evenly disseminated, rise in prices would tend to recompense. Economic losses to certain cultivators could be much higher in instances when only a few of the growers are impacted.

Plant virus infections or virus-like diseases in fruit crops such as banana, grapes, avocado, citrus or any other commercially significant perennial crops cause crop loss every year. This is further complicated by loss in time and expense in developing trees to the stage of bearing and forfeiture of other crops that could have been cultivated on the same land during that period of time and variations in land value with or without a fruitful orchard.

Disease associated crop losses impact both the farmer and the consumer. When plant diseases circumscribe production on account of heavy infections and lead to paucity of crop yields, then the prices would show typical increase [20]. For fruit crops, in order to evaluate the economic outcomes, the following factors are of primary importance. Every fruit tree contains two varieties, the scion and the root stock which differ notably in their responses to infection by a given virus or viroid. Also, these infectious organisms occur in a diverse array of strains frequently varying from highly virulent

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to those inducing no symptoms. Further, the viruses and virus-like infectious agents could interact i.e., a given virus could significantly influence the impact of another virus in the same plant wherein this influence could be synergistic and could augment the symptom severity or antagonistically be protective. These factors affect the outcome of virus infection in a specific tree to the degree that no prediction could be made with any surety in the absence of information regarding the identity of the root stock and scion variety, the virus strain under consideration and the extent of underlying infections with the other viruses.

Typically, only one of the above factors is known. Some viruses affecting only the fruit can be estimated by considering the number of virus-infected trees and the ratio of fruit rendered unmarketable. A majority of viral diseases impact the growth and productiveness of the tree, nevertheless, as observed with apple infection that causes decreased color and fruit size which are of tremendous importance at the market level. Among stone fruit trees, infection due to viruses influence scion survival, especially of bud grafts at the nursery. Such an effect has not been shown for pome fruits, yet many viruses (e.g., apple mosaic, rubbery wood, and pear vein-yellows) decrease scion growth and hence the percentage of first grade trees. Nursery personnel could counteract this effect by holding the smaller trees in the nursery for growth for a second year, however, this clearly augments the production cost.

Knowledge of crop losses significantly varies in precision and is an arduous task to undertake because the disease severity varies primarily with factors such as the crop variety, virus / viroid strain severity, vector activity, locality, crop season and crop nutritional status. Younger plants are more susceptible to virus infection. Figures of crop losses vary depending on the inoculum load. Also, the consequent losses in terms of crop economics changes with distinct viruses as well as virus-like agents in addition to the virulence of the given virus / viroid strain. Regarding losses incurred due to viruses, milder virus strains are less destructive compared to virulent strains. Singh et al., 1971 described that three mild strain isolates of PSTVd decreased the yield in var. 'Saco' respectively by 17, 24 and 24% whereas the severe strain diminished the yield by 64% [5]. Experimental evidence shows that combined infections with two or more viruses further causes greater, more serious losses compared to infection by a single virus.

The degree of crop losses varies between places and countries. In some regions, an individual grower or a group of farmers could lose the whole crop in terms of yield weight as well as incur financial loss due to destructive viral diseases. Concomitantly, other farmer(s) at another location could obtain a better harvest depending on supply and demand in addition to the infecting virus strain, phase of infection and better management practices. As not all farmers will be affected equally, the financial loss for certain farmers could be intense for the same crop loss. Therefore, all losses of crops are just estimates based on individual occurrences and investigations of such losses with respect to the world market is futile.

Variation of produce quality is a primary factor in determining the economics of losses due to virus disease. In a given crop harvested over a season, and further where the crop product is graded, the period at which the crop losses take place and the impact of the virus infection on crop quality are significant. Fruit tree viruses could render the fruits small, often disfigured and poorly flavored which affect their acceptability. The coconut Cadang-Cadang viroid disease has destroyed over 15 million trees in Philippines. Yet another important disease of coconuts is Lethal yellowing, which is a phytoplasma disease shown to be destructive in the USA and Central America. The above examples demonstrate the compelling and urgent need to preclude such catastrophes in the future. Crops including sweet potatoes, potatoes, sugarcane, yam, taro, citrus, bananas and cassava that are propagated vegetatively will gather different viruses / viroids and ultimately incur severe losses.

For perennial crops, in addition to the high levels of immediate loss, the expense of replacement is equally high if not higher than that observed with annual crops. The concentrated monoculture of today's crops invites the spread of several virus diseases on an epidemic scale. Expeditious vegetative propagation practices and a thriving international trade have rendered matters even worse. Therefore, it is obvious that crop loss estimates due to diseases caused by virus and virus-like agents vary in range from 0-100% based on several factors.

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One of strenuous problems in plant pathology is that of precisely evaluating disease incidence in crops and accurately measuring losses in finances and crop yield. Both crop losses and the agent of disease vary from time to time in a given location. Experimental evaluations must be conducted for at least 3-4 years at numerous locations. Such knowledge needs to be up-dated conceivably every five years, due to quickly fluctuating agricultural practices, introduction of novel plant varieties and use of agricultural chemicals. Total values of losses incurred because of a single infectious agent are always hard to discern as in most instances the same crop would be infected with other pests and pathogens like insects, bacteria, and fungi. Of these, insects can be contained to a certain extent by means of the use of agrochemical sprays while it would be more difficult to control microbial pathogens.

Some estimates of crop losses where the impacts are very low and compounded with lack of knowledge, can give the erroneous impression that the plant disease is not of economic significance while overestimates could lead to concentration of limited resources on a distinct disease while neglecting other more devastating infectious agents. Nevertheless, fruitful results can be acquired from well-designed and appropriately conducted experiments at the field level. This is vital to the grower to consider monetary losses incurred due to these destructive agents, warranting the trouble and cost of exercising respective control measures. Monetary losses incurred due to pathogenic diseases and the expense of containing them are transmitted to the consumer by means elevated retail prices and government subsidies provided to the farmer, such that all of the users of any agricultural produce would be severely affected.

Typically, experiments on crop losses have been conducted solely on the basis of yield reduction. Loss assessments must also include decrease in the crop market value and crop quality due to pathogenic infections. Changes in market standards from region to region preclude a uniform strategy to confront the problem of reduced quality. Towards accessing information on local conditions and to provide guidance on the generation and application of appraisal methods for crop losses, consultations or workshops must be undertaken in various locations by organizations such as the EPPO and FAO. Rigorous research is necessary towards developing new appraisal methods for crop losses.

Vector Transmission of Viroids

Discerning viroid transmission modes such as vectors, mechanical damage, asexual propagation by vegetative means, sexual transmission through pollen or seeds are essential to determine the epidemiology of viroid diseases and to develop effective containment measures against these diseases. Biological vectors identified hitherto include goats, parasitic plants and certain insects, in addition to some fungi [21].

The ACFSVd (apple chlorotic fruit spot viroid) was shown to be transmitted by two of the aphid species and by the codling moth larvae after directly feeding on viroid-infected, symptomatic apple trees [21,22].The green peach aphid, Myzus persicae was demonstrated to transmit PLMVd (peach latent mosaic viroid) under experimental conditions albeit at a low rate indicating minor significance under natural conditions in peach orchards [23,24]. Macrosiphum euphorbiae, an aphid was shown to transmit PSTVd in a non-persistent mode [25].The green peach aphid was able to persistently transmit PSTVd when the latter was encapsidated within potato leafroll virus (PLRV) particles [26–28]. In potato, Datura stramonium and Physalis floridana, the encapsidated viroid was shown to be transmitted by this aphid species despite the latter being not a major vector for PSTVd transmission alone. Based on the cultivar of potato used, the PSTVd transmission efficiency by the green peach aphid upon co-transmission with PLRV was shown to range from 0-55% [29]. Reportedly, the TPMVd (tomato planta macho viroid) was transmitted effectively by the green each aphid [30]. Efficient transmission of TCDVd (tomato chlorotic dwarf viroid) [31] and TASVd (tomato apical stunt viroid) [32] by bumblebees has been demonstrated in tomato plants. The Bombus ignitus bumblebees have been shown to transmit TCDVd [31] and TASVd [32].

Other aphids such as Myzus persicae and Dysaphis plantaginea have been shown to transmit ACFSVd [22], while PSTVd [26–28] TPMVd [30] and PLMVd [23] were reported to be transmitted by

M. persicae. Cydia pomonella, the codling moth efficiently transmits the viroid ACFSVd [22]. The greenhouse whitefly, Trialeurodes vaporariorum adversely impacts major crops wherein it acts as the vector for ASSVd [33] enabling its transmittance to other herbaceous plants. The T. vaporariorum small heat shock protein sHsp22.98 has been implicated in association with the ASSVd RNA which has an important role in viroid transmission. In the Netherlands, TASVd is the most prevailing among pospiviroids in ornamental plants, that may lead to outbreaks of infection in tomatoes [34]. The greenhouse whitefly successfully transmits ASSVd (apple scar skin viroid) from herbaceous hosts like cucumber and bean that have been infected with ASSVd to plants such as pea, tomato, bean and cucumber [35]. The cucumber phloem protein 2 was shown to enhance the transmission of ASSVd to cucumber wherein this protein forms a stable complex with ASSVd RNA in infected plants [35].

Mistletoe (Viscum album subsp. Album), a hemi-parasitic plant is often found to grow in apple orchards wherein it comes into direct contact with the apple trees via their haustoria. During this process, it could become infected with the viroid ACFSVd systemically and transmit it from infected to healthy uninfected trees [22].

Further, HSVd (hop stunt viroid) and CEVd (citrus exocortis viroid) viroid transmission has been reported due to domesticated goats (Capra hircus) and additionally when the horns of these goats rubbed against trees that are infected with viroids such as PLMVd [36,37].Such goat-mediated transmission could have resulted in long-range dissemination of viroids amongst wild and cultivated plants and reciprocally in addition to amongst plants that are graft-incompatible.

Use of Pesticides to Control Pests and Pest-Associated Diseases

The pest control market is estimated to reach as high as USD 32.8 billion by the year 2028, from the value of USD 24.9 billion in 2023, at a compounded annual growth rate of 5.7% in terms of worth during this forecast period [38]. The integrated global economy and goods movement across the borders has caused pest spread to new regions. This process has necessitated comprehensive strategies for pest management to preclude the introduction and induction of invasive pest species. Besides, changes in climatic conditions due to global warming, influence the behaviour, population dynamics and distribution of pests. Even as these pests acclimatize to new conditions, they could become stronger and more challenging to contain. Therefore, there is an increasing demand for services and products that determine the management of pest control.

Globally, the pest control market involves various services and industries committed to the management and elimination of pests that cause adverse effects on agriculture, environment, property, human and animal health. This market is critical for the maintenance of hygiene, preclusion of damage to property and protection of crop and livestock safety. The use of services and products towards pest control is driven by many factors reflecting the emerging requirements and priorities of industries, businesses and individuals. Increasing awareness of health risks due to pests and pest-associated diseases has prompted great demand for aggressive pest management towards ameliorating virus and viroid-induced diseases. Additionally, the increase in population density and urbanization in several regions globally, have caused an environment contributive to pest infestations that necessitate effective pest control measures.

Increased scale of agricultural productivity is essential for sustenance of the world population, considering the current growth rates of the human populace. Between the years 1960-2000, Green revolution augmented global food generation by 2-3-fold [39]. Nevertheless, the strategies used to enhance food production caused damage to several ecosystems, making them more susceptible to pests. The containment of these pests is of vital importance in order maintain high productivity levels essential for meeting the current demand for food. In addition to increase in the world population, there is increased preference to promote the quality and duration of human life. With denizens living lengthier lives and in improved health, demands for food have enhanced, necessitating efficient pest control [40].

Climate Change Impacts on the Proliferation of Pests

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Changing climates could impact pest behavior, population dynamics and distribution. As pests begin to adapt to new environments, they could become more difficult to control, escalating the demand for efficacious pest management. Climate change is an important factor contributing to the growth and evolution of the pest control market. As pests occur predominantly in warmer climatic conditions, global warming changes the pest population dynamics and their respective ecosystems. FAO (2021) [41] reports that plant pests devastating economically important crops are becoming increasingly destructive due to the impacts of climate change and therefore pose a rising risk to the environment and food security. About 40% of the annual global crop productivity is currently lost due to pests and every year pest-related diseases cost the world economy more than USD 220 billion [38].

Hence, to ameliorate pest impacts on crops and human health, appropriate pest management strategies must be enforced. Many significant factors are increasing the requirement of pest control products and associated services at the global level. Rising realization of health risks due to pests and associated diseases transmitted by pests is driving farmers and businesses to seriously consider measures to preclude and control these pests. This has fueled the demand for services related to pest control.

Pros and Cons of Pesticide Use

Organisms detrimental to humans, environment and food production can be contained in many distinct ways. Among these, pesticides function as one of the most efficacious, widely used tools for pest control. Pesticides include substances such as chemicals, biological agents and biopesticides. The majority of pesticides under use worldwide are chemical pesticides. There are 3 principal types of chemical pesticides namely, fungicides, insecticides and herbicides. Additionally, there are also other types called biocides inclusive of rodenticides and nematicides. Millions of people pursue agriculture and a majority of them apply pesticides to safeguard their livestock and crops. Despite being expensive, pesticides are extensively favored for use due to the advantages they provide. Sales of pesticides have increased tremendously in recent times. Chemical pesticide use is widespread because of their efficacy, easy availability, stability, simplicity of use and their low cost. Also, some of these chemical pesticides afford broad spectrum control, thus effectively and simultaneously controlling multiple pest species. This can be especially beneficial in circumstances involving diverse pest species. Also, in certain scenarios pesticides have enhanced human health, for instance, by destroying vectors harboring human pathogens, and improving the quality of human life [42]. These above factors drive the demand for chemical pesticides in the pest control market. Pesticide applications have proved to provide notably positive benefits on agriculture [42–45] as well as on human health [42]. Nevertheless, they cause serious deleterious outcomes on human health and the environment, incurring many types of costs. Chemical pesticides are likely the most detrimental pesticides for both humans and the environment.

Costs Incurred due to Chemical Pesticide Use

Apart from the increase in the amounts of pesticides, farmers apply stronger concentrations of these pesticides in addition to augmentation of the frequency of pesticide use, especially in developing countries [40]. Further, they increasingly combine many pesticides together to confront resistance to pesticides by the pests inclusive of insects, bacteria, fungi, plant viruses, viroids and satellites [46,47]. Such pesticide application practices are especially found to occur in Africa and in Asia.

In developed countries, herbicides form the bulk of pesticides under use whereas in the developing countries, the majority of pesticides applied are insecticides which result in pest resistance to the insecticides predominantly wreaking disastrous impacts on human health [48]. Moreover, insecticides under use in developing nations frequently consist of organophosphates (methamidophos, parathion, monocrotophos), organochlorines (dieldrin, lindane, endosulfan, DDT) and carbamates (maneb, thiodicarb, carbofuran) which have recognized toxic properties [48]. Notably, carbamates and organophosphates are less tenacious compared to organochlorides,

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however, they are more noxious to field workers and farmers, particularly upon misuse [49]. Insecticides such as pyrethroids can be administered at much lesser frequencies and are effectual against a majority of foliar insects. Additionally, they exhibit lower acute toxicity which have rendered them safe for farming personnel and consumers. Pesticides such as parathion, DDT, methamidophos and monocrotophos have already been banned from use or are greatly restricted, although they are illegally used, often because they are not under patent protection and therefore are less expensive than newly formulated pesticides [48].

Initially, pesticide use was seen to be highly effective in decreasing pest infestations as well as augmenting agricultural productivity. Nevertheless, with the passage of time, the targeted pests have built-up pesticide resistance which necessitates increase in pesticide applications or lead to increasing rise in pest populations or both. Resistance to pesticides occurs when the concerned pests develop the capability to withstand the effects of the pesticides, leading to the inefficacy of pesticide treatments over time. Therefore, the pest population initially declines, but then starts to increase again later upon development of pest resistance to chemical use accompanied by the decimation of beneficial predators that elicits a disequilibrium at the field level [50]. After a certain period of time, pest resistance may develop to such a scale that pesticide application may no longer be effective and therefore be detrimental from an economic point of view. And once pesticide application is stopped, the pest population may climb to great levels higher than those predating the application of pesticides. Also, they may persist permanently at levels higher than that prior to pesticide use. This can take place due to the elimination of beneficial pest predators.

Infestations of pests are commonplace in agriculture. Several pests have proliferated to outbreak levels in apples, cotton, onions, rice, tobacco, potatoes and soybeans [50,51]. Augmented use of pesticides has led to enhanced virulence in many pest species because non-target species such as parasites and natural pest predators are destroyed in the process [52–54]. Additionally, pesticide applications result in loss of agricultural productivity due to decrease in insect pollination of agricultural crops [53]. Reportedly, the stipulated insecticide dosages applied on crops have inhibited the yield and growth of strawberry and cotton (Instituto Centro Americano de Investigacion Tecnologia Industrial (ICAITI), 1977) [55]. Oka and Pimental (1976) have shown augmented susceptibility of corn to insects as well as diseases following the use of herbicides such as 2,4-D [56].

As per the FDA 1990 report, roughly 35% of foods procured by consumers had recognizable amounts of pesticide residues and about 1-3% of foods contain pesticide levels higher than the legal tolerance limits [57]. Babies and children have been shown to be more susceptible to carbamate and organophosphate elicited cholinesterase inhibition and associated effects [58]. Crop contamination with aldicarb has led to extensive outbreaks of toxicity due to food-borne pesticides [59]. Furthermore, water has also been polluted by pesticides which negatively impact consumers. Typical pesticides in ground water in the USA are the insecticide, aldicarb and the herbicides, atrazine and alachlor [60]. US EPA (1990a) has reported that rural domestic wells and community wells contain identifiable levels of pesticides [61]. Endosulfan, a highly toxic insecticide organochlorine applied on cotton crops has impacted beef production and beef exports in Australia [62]. In the USA, milk, eggs and beef have been contaminated [53].

Moreover, some pesticide residues persisting in the soil have affected crop rotation [63]. Such persistence can preclude growers from the use of crop rotation that could impel them to grow the same plants [64]. Also, drifting of pesticides into neighboring fields, even many kilometers away can lead to crop losses [65]. This problem is further exacerbated upon spraying of pesticides from aircraft [66].

Other detrimental impacts of pesticides include soil contamination that could result in toxicity to the ecosystem as naturally occurring organisms such as earthworms, bacteria, fungi, protozoa and arthropods are affected [53]. Pesticides gain entry into aquatic ecosystems through water runoff, wind, soil erosion and leaching [50,67]. Once they enter the aquatic ecosystem, they could destroy fishes, fish fry having high susceptibility, important fish foods such as invertebrates and insects in addition to the depletion of dissolved oxygen in the water caused by accompanying aquatic plant decomposition [47]. Pesticides also tend to pollute drinking water as well as food crops, particularly vegetables and fruits subjected to the highest pesticide exposure which pose adverse health risk to consumers [53]. Of course, every impact on the environment and eco-system affects the economy.

In developing nations, the counts of humans impacted by pesticide poisoning could be higher than that reported because of under-reporting, misdiagnosis and lack of data [68]. The seriousness and incidence of ill-health due to pesticide use is far more substantial in developing countries due to direct contact with the pesticides, increased use of insecticides with more potency and augmented frequency of pesticide application [48]. The protective gadgets worn by personnel in developing countries is ill-maintained or inadequate due to unaffordability issues in procuring standard high-quality protective gear and lack of enforcement regulations requiring the employment of protective equipment during pesticide use. Farmers regularly spray the pesticides, especially in hot tropical climates, leading to enhancement of the severity and incidence of health impacts [47]. Besides, lack of education among farmers, inadequate training and no regulatory enforcements lead to haphazard use, over-use, and accidents. Medical intervention access is circumscribed, and a majority of farmers rely on remedies that are home-made, hence leading to increase in illness morbidity and duration. Additionally, malnutrition and poor health are other factors contributing to increased impacts of pesticide use. Pesticide contaminated water, poor quality living conditions and non-existent or inadequate storage facilities also negatively impact human health in developing countries. Even in developed nations, in spite of the administration of safer pesticides and stricter regulations, occupational exposures could be significant [48].

Pesticides form an integral part of economically important high yielding crop varieties, for instance the Green Revolution varieties, without which it may not be possible to sustain high yields. Further, chemical industries selling pesticides also promote and advertise their products creating proclivity in favor of their application. Additionally, in a majority of instances, the short-term health outcomes emerging from pesticide use could be underestimated by the farming personnel. This is due to the fact that the effects of pesticide exposure only accumulate over lengthy time frames which creates time costs. Inadequate medical facilities also exacerbate this situation. Lack of proper diagnosis on account of pesticide exposure frequently ignores the perils of pesticide use and instead, poor health is attributed to other causes. The long-term association between pesticide dose and effect is complex and on account of the timeframe involved, it is more difficult to prove [50]. Yet another reason is that growers in developing nations have no facile options in place of subsistence farming, which requires very few skills and little capital. Subsistence farmers produce for their home consumption, which incurs a major portion of their filial expenditure. Hired farmhands applying the pesticides may not be aware of the true impacts of pesticides on human health until adversely affected. In this context, in Latin America, it has been shown that attempts by workers to assert their civil rights have met with censure and dismissals as replacement workers are readily available [48].

The following Table 2 shows the types of costs associated with pesticide use.

Table 2. Types and classification of costs generated due to pesticide use (adapted from [40])**.**

Cost category	Impact of pesticides
Regulatory costs	Public investigation, communication, capability studies on pesticides
	Regulations, edicts and laws
	Obligatory pesticide handling and disposal
	Decontamination of water, on-going containment
Environmental costs	Resistance to pesticides
	Degradation of soil
	Decrease in pollination
	Reduction of natural enemies
	Diminished productivity of plants due to the application of herbicides
	Bee renting
	Debilitation of farm environment and surroundings
	Health impacts on livestock, domestic animals
Human health costs	Preventative medicine, annual medical checkups

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Defensive costs	Health implications for farmers and the public Procurement of masks, glasses and protective clothing Procurement of bottled water and organic food

High Registration Costs and Interminable Time for Pest Control Product Approval

Stringent and intensive regulatory requirements within the environmental protection division are obligately pertinent to the manufacturers and users of pest control products. These regulations vary according to policies stipulated by each country. Typically, it takes high investment and long time periods to develop a new pesticide and the production of these pesticides involves strict guidelines, slow-paced processes and enormous costs which impede the advancement of the pest control industry.

Moreover, the process of adherence to pesticide regulations, which involves the execution of safety studies, procuring approvals and ensuring regulatory compliance, are exorbitant. These expenses are frequently borne by manufacturers of the pesticides, which can result in elevated prices of crop produce for consumers in addition to increased financial stress on smaller crop companies.

Pest Control Market Growth

The industries involved in pest control have exhibited steady growth which is projected to continue in the future. Stringent regulations associated with pesticide applications and environmental issues have resulted in the generation of more sustainable, eco-friendly pest control strategies and products. Advanced technologies including data analytics, remote monitoring and Internet of Things are being implemented by the pest control organizations to augment their efficiency. Integrated pest management methods focusing on long-term, preventive solutions are being developed instead of solely depending on chemicals, thus aligning with the demand for increasingly sustainable practices for pest control. There is elevated demand for organic, natural products for pest control, reflective of broader trends towards solutions that are environmentally friendly. Services and software offered by the agricultural companies play an important part in formulating digital pest control measures that help better monitoring as well as early identification of pest infestation, remote pest management solutions amid several other benefits.

The major players in the market for pest control include Corteva Agriscience (US), FMC Corporation (US), Bell Laboratories (US), Rollins Inc. (US), Ecolab Inc. (US), Bayer AG (Germany), BASF SE (Germany), Rentokil Initial Plc (UK), PelGar International (UK), Fort Products Ltd. (UK), De Sangosse (France), Anticimex (Sweden), ATGC Biotech Pvt. Ltd. (India), Syngenta AG (Switzerland), and Sumitomo Chemical Co., Ltd. (Japan). Bayer CropScience, Bayer AG's agricultural division has established partnership with Crystal Crop Protection Ltd., in June 2023 to launch and advance pioneering solutions for pest control towards benefiting paddy farmers across India. This constitutes a crucial turning point in the effort to augment farm yields and promote crop protection technologies in India. Corteva Agriscience established a seed research and crop protection laboratory in Eschbach located in Germany in June 2023. This would help advance innovations and drive sustainable solutions for agricultural personnel. Fox Pest Control was acquired by Rollins Inc. in April 2023 through its brand, the HomeTeam Pest Defense and is projected to enhance the company's long-term growth across the US market. Syngenta crop protection company collaborated with Gamaya SA, a Swiss agricultural startup in September 2022 for the launch and development of a digital technology to identify detrimental nematodes via satellite images. This constitutes a fiscal digital prognosis and mapping solution for detecting pests.

Advances in pest control methods and technologies have promoted the precision, sustainability and efficacy of treatments that make them more attractive to consumers. The pest containment industry is experiencing great innovations involving the adoption of faster and more precise technologies like CRISPR. The CRISPR technology is self-limiting, safe and scalable depending on the genetic population of distinct pest species. Advantages include accurate targeting of pest species, diminished environmental impacts and decreased evolution of resistance among pests. Companies

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including Monsanto, Bayer and Dupont have endorsed license agreements with biotechnology organizations for the application of CRISPR within their products for pest control.

Emerging biological pest control measures

In comparison to chemical pesticides, biological pest control has few or no side effect impacts on human health and is gaining increased acceptance by providers of pest services. Principal factors affecting market growth comprise resistance development among pests and changes in the regulations. In Europe, for instance, there is a ban on the use of neonicotinoid pesticides demonstrating the acceptance of biological pest control solutions.

Several companies are increasingly focused on initiating biological pest control. In 2022, BioPhero, a pheromone research and manufacturing company based in Denmark was acquired by the FMC corporation, whereupon the FMC introduced biologically synthesized pheromone insect containment technology into the market for pest control. This expanded its product investments and strengthened its status as a major player within this market. Such initiatives by businesses contribute to promoting the biological control strategy against pests offering several benefits ranging from decreased chemical use to environmental sustainability towards augmenting long-term strategies for pest management.

The serious concern of growing resistance to pesticides impedes the development of the pest management sector. Due to the evolution and adaptation of pests to chemical interventions, the efficiency of conventional pest control measures decreases, resulting in diminished control over pest infestations. While this undermines the pest control efficacy, it further necessitates the development of more potent, novel, and frequently more expensive formulations of pesticides. The use of plant-based chemicals, adherence to integrated pest control practices and employing the services of professionals involved in pest management can constructively decrease the risks of pesticide resistance.

Technologies to Elicit Resistance to Virus and Virus-Like Pathogens while Diminishing Pesticide Dependency through Sustainable Agricultural Practices

In temperate countries, horticulture plays a critical role in driving their economies. However, horticultural crops are impacted by many diseases, disconcerting the farmers in terms of economic returns. In this reality, augmented crop protection measures requiring close synergy between farmers, seed companies and the research scientists need to be adopted towards fulfilling consumer needs for high quality, environmentally friendly, healthy products. The drastic impacts of pesticide use on animals, plants, and water quality as well as their association with several detrimental outcomes on human health, inclusive of short-term malaise and many types of cancers, necessitates adoption of strategies such as precocious identification, prompt elimination of infected plant material and crop rotation [69]. Additionally, the use of certified plant propagation material, application of resistant varieties and chemical prophylaxis measures to combat insect vectors would be beneficial in the containment of pathogenic infection coupled with diminished pesticide use. Several innovative measures for pathogen control need to be practised on a global basis to enable the transition towards viable agricultural practices and sustainable lifestyles founded on the inputs of lower pesticides and decreased food waste and food loss. Propitious strategies further include the administration of novel cultural measures and innovative sources of lighting in order to optimize crop growth. Particularly, LED-based technologies are favorable for indoor farming of horticultural crops, inducing both biochemical and photomorphogenic traits in addition to physiological reactions appropriate for countering pathogen attack [70].

RNA interference or RNA silencing can be used in order to develop crop resistance to virus or virus-like pathogens [71]. Novel engineering technologies have also been developed such as Host-induced gene silencing (HIGS) in which RNAi-derived gene constructs are used to initiate stable resistance in the plants by eliciting PTGS. Such engineered constructs encompass short, inverted gene sequences that show homology to genes of the pathogens wherein these gene sequences are separated by a non-coding sequence, preferably an intron. These hairpin constructs (hpRNA) are typically

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under the control of specific gene promoters as well as terminators [72,73]. Lately, a novel technique called Spray-induced gene silencing (SIGS) has been invented wherein small RNA molecules are topically applied on plants [69]. SIGS has proved to be efficient and innovative for defense of crops against different pests and pathogens. It is also foreseen to raise lesser political / public concerns compared to that of plants genetically engineered to express hpRNA constructs, because it does not change the genetic structure of the crop. Following initial work reported by Tenllado and Díaz-Ruíz, 2001 wherein successful use of exogenous dsRNAs was shown to confer resistance against three distinct viruses, several investigations have been performed to generate resistance to plant viruses having disparate genomic structures [74,75].

Recent genome editing techniques such as the CRISPR/Cas system are being increasingly used to engineer resistance against virus and virus-like pathogens. These systems mutate the host susceptibility genes associated in specific molecular interactions with the infectious pathogen or directly target the genome of the pathogen [76,77]. CRISPR/Cas techniques are rapid, highly versatile, cost-efficient, and primarily successful, indicating stakeholder acceptance. This technology in association with omics technologies could play a principal role in the generation of plants resistant to pathogens and abiotic stresses as well as cultivars with improved yields, after circumnavigating legislation constraints [78]. In terms of cost efficiency, for a similar crop improvement, conventional GM crops would need a 15–25-fold higher market area to be profitable, when compared with gene editing [1]. Thereby, GM crops require on average $140–150 million and 12–13 years compared with $10 million and 5 years for gene edited crops for their development and commercialization [79].

Recent advancements in synthetic biology and next generation sequencing have opened new frontiers for detection and diagnosis of infectious plant pathogens in crops. These rapid diagnostic measures combined with high-tech, sustainable agricultural practices could offset the economic fallouts in these crops. Additional procedures to counteract climate change involve the use of preferred cultural methodologies such as altering the sowing and the harvesting calendar in addition to the choice of species / cultivars having a brief cultivation period and with genetic traits conferring resistance or tolerance to several abiotic stresses such as drought, high salinity, and high temperature. Furthermore, technical practices influencing soil erosion and conservation of rainwater could be exercised.

Besides, economic measures via the introduction of several financial incentives for the farmers and other appropriate political decisions [80] could help offset the adverse outcomes of climatic changes and pathogenic infections. This will enable better disease management combined with classical prophylactic and curative control schemes.

Proposed Mechanism of Viroid Activity in Symptom Elicitation in Host Plants

Viroids are an inscrutable conformation of pseudo-life incurring in economic damage ranging from millions to billions of dollars annually impacting the agricultural sector. They deform potatoes, decimate coconut palms and diminish the quality of avocados and hemp crops and in spite of several years of investigations conducted by scientific studies, their mechanism of action has yet to be established. This renders treatment of vrioid infections challenging, most often requiring elimination of the infected plants in addition to quarantining of plants surrounding these plants to stop the infection cycle.

Despite being unable to code for proteins they elicit symptoms in host plants. It has been proposed that they can be attacked by Dicer-like RNases by virtue of being composed of single-stranded, highly structured RNAs which assume the shape of double-stranded RNAs due to their internal base pairing [3,81]]. As a result, it leads to the production of small RNAs that exhibit strong structural homology with sRNA generated by the plants as silencing signals. The sRNAs bind to the argonaute (AGO) proteins present in the RNA-induced silencing complex (RISC) and recognize the target to be silenced or cleaved based on the extent of sequence match between the target strand and the loaded sRNA [82,83]. An ideal match leads to cleavage of the target strand whereas a partial match interacts with the RISC proteins making it unavailable for protein translation [82]. It has been proposed that the sRNA derived from viroids functions in a similar manner by targeting and silencing host plant mRNAs coding for proteins that may be detrimental to the viroid [84]. Further, the above phenomenon could influence other signaling pathways the host plant needs to sustain homeostasis and therefore such mechanisms could cause the symptoms due to viroid infections. This has been proven by a study in which when the RNA-directed RNA polymerase 6 (RDR6) responsible for generating sRNAs and causing RNA silencing was absent, this precluded the Hop stunt viroid from eliciting symptoms [85].

Precluding Viroid Infection

The first step in preventing viroid infection is to inspect all the incoming plants and plant products in the plant farming facility for probable viroid contamination. Quarantine implementation for a 30-day period or more on plants received newly to detect potential pathogens such as viroids and satellites is the next step. Viroids mainly spread by mechanical means, contaminated farming equipment and cuttings. A solution of 10% bleach must be applied to wipe out the viroids on any tools, and a sterile cultivation environment has to be maintained to decrease the hazard of viroid spread. Due to the lack of any cure for viroid infections, prompt identification and culling of the infected plants are critical. Considering the absence of any visually identifiable symptoms, cultivators face a great challenge in effectual containment of these viroids.

Can a Plant Ever Be Cured Following Viroid Infection?

Regrettably, viroids cannot be eliminated like pests. Viroids are not capable of being killed and the only route to clear the infection is to destroy any infected plant and plant material such as flowers, seeds or cuttings obtained from the infected plants in addition to disinfection of all farming equipment and other materials in the farm. Staying knowledgeable and practising strict preventive measures is vital to protect crops against increasing viroid threat. Exercising a proactive strategy and adhering to the above guidelines can enable fortification of farming practices and establish a fruitful healthy harvest. Screening of mother stocks for infection using detection techniques as facile as a quick PCR test should be conducted prior to use [86]. Also, subjecting meristem tissue cultures to cold treatment of the infected plant has been proved to eliminate viroids effectively [87]

Conclusions and Future Directions

Viroids are responsible for significant economic damage to crops and the world economy. In fact, viroids were discovered due to their ability to cause serious plant diseases in major food crops such as potato spindle tuber viroid (PSTVd) in potato, coconut cadang-cadang viroid (CCCVd) in coconut and citrus exocortis viroid (CEVd) in citrus. The economic impacts of viroids can be direct or indirect wherein direct impact is particularly associated with losses incurred due to reduction in quality, vitality and growth as well as additional production costs due to extra hygienic procedures. Indirect impact is associated with price changes and impacts on international trade. Viroids have both types of impacts on ornamental crops such as chrysanthemum, in addition to food crops and cash crops. Additionally, viroid-induced diseases in ornamentals are economically significant as they function as inoculum source for further infection of valuable food crops that may be drastically affected due to severe viroid disease. Grapevine and other fruit trees are major horticultural crops that greatly influence the global economy and are responsible for several billions of dollars every year in the world market while being the main income source of growers and related businesses. Losses incurred due to viroid infections in these crops are difficult to evaluate unless the infected host plants exhibit visible damage. At times, viroids might reside latently in some host plants while at the same time having adverse effects which are often overlooked. Viroid infections account for great economic losses in these plants irrespective of whether they exhibit visibly detrimental effects or do not elicit noticeable symptoms. The cadang-cadang disease caused by the Coconut cadang-cadang viroid (CCCVd), has threatened the coconut industry by rampantly spreading in coconut-growing areas in the Philippines. This disease is responsible for depletion of the lamina and the rapid deadly decline of coconut palms, called ‘brooming’.

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This review has sought to define the economic consequences of viroid infections, vector-mediated spread of viroids, the beneficial effects of pesticide use in the containment of viroids, the compelling need to reduce dependency on pesticides, in addition to shedding light on viroid detection techniques and mitigation measures. An up-and-coming technology to address these sorts of infections could be the development of genome edited crops which are resistant or in the least can tolerate exposure to such subviral particles. While the research in this regard is in its infancy, initial results hold great promise [88]. Thus, modern breeding techniques, such as CRISPR-Cas9, may turn the tide of viroid diseases, and reduce the economic consequences for years to come.

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