REVISÃO

Is the best resistance strategy against begomoviruses yet to come? A Comprehensive Review

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ABSTRACT

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The worldwide spread of Geminiviruses and its vector has been attributed to the high rate of recombination, mutation, presence of alternate hosts, transport of plant material, global human activity along with global trade, new agricultural practices and climate change; therefore, the most severe viral diseases among crops have grown in almost all regions of the world, including cassava viral diseases in Africa, cotton leaf curl disease in Pakistan, and multiple diseases related to tomatoes, legumes and cucurbits in India and all over the world. Begomovirus is the major and largest genus of Geminiviridae which has shown a worldwide increase in its variations and distribution by affecting previously unaffected plants. The increasing population has augmented the demand for a sustainable agriculture boost, but begomoviruses have become a continual threat to the world's agriculture. Numerous control strategies have been used for the viral invasion of the world as pathogens but begomoviruses continually overcome the control methods, and this has generated a need to end this competition between researchers and begomoviruses. The present review summarizes all strategies used against begomoviruses and provides a comprehensive comparison among all control methods, their drawbacks, and future insights.

Keywords: geminiviruses, begomoviruses, control strategies, host resistance

RESUMO

Ishfaqe, Q.; Shafiq, M.; Ali, M.R.; Haider, M.S. Resistência é a melhor estratégia contra begomovírus? Uma revisão abrangente. ***Summa Phytopathologica,*** v.48, n.4, p.151-157, 2022.

A disseminação mundial de geminivírus e seu vetor tem sido atribuída à alta taxa de recombinação, mutação, presença de hospedeiros alternativos, transporte de material vegetal, atividade humana e o comércio globalizado, novas práticas agrícolas e mudanças climáticas. Portanto, as doenças virais mais graves cresceram em quase todas as culturas e regiões do mundo, por exemplo as doenças virais da mandioca na África, doença do enrolamento da folha do algodão no Paquistão e várias doenças em tomateiros, legumes e cucurbitáceas na Índia e em outras partes do mundo. O begomovírus é o principal gênero de Geminiviridae que tem apresentado aumento mundial em suas variações e distribuição afetando plantas anteriormente não afetadas. A população mundial crescente aumentou a demanda por uma agricultura sustentável, mas os begomovírus tornaram-se uma constante ameaça à agricultura mundial. Numerosas estratégias de controle têm sido usadas para este vírus em várias partes do mundo, mas os begomovírus superam continuamente os métodos de controle. A presente revisão resume todas as estratégias utilisadas contra begomovírus e fornece uma comparação abrangente entre os métodos de controle, suas desvantagens e futuras percepções.

Palavras Chave: geminivirus, begomovirus, estratégias de controle, resistência

Geminiviridae is the leading family of insect-transmitted single-stranded circular DNA plant viruses comprising more than 450 species (57). Over the last several years, geminiviruses have gained the attention of researchers due to their ability to cause infection in cultivated, non-cultivated monocotyledonous and dicotyledonous vegetation worldwide (2). Extensive geographic distribution of insect vectors and alternate host planting material due to inadequate quarantine measures around borders made geminiviruses a major limiting factor in the production of important agronomic crops of economic value, such as cotton, pepper, tomato, beans and cassava (81, 87). Economic losses caused by geminiviruses to these crops have been estimated at around USD 5 billion for cotton in Pakistan, USD 140 million for tomato in Florida, USD 1300–2300 million for cassava in Africa, and USD 300 million for grain legumes in India (62). Geminiviridae family is divided into 14 genera of plant viruses (Becurtovirus, Begomovirus, Capulavirus, Curtovirus, Eragrovirus, Grablovirus, Mastrevirus, Topocuvirus, and Turncurtovirus, Citlodavirus, Maldovirus, Mulcrilevirus, Opunvirus, and Topilevirus) based on insect vectors, genome organization, and host range and phylogeny. The whitefly (Bemisia tabaci G.) transmits wide-reach geminiviruses belonging to the largest genus Begomovirus; approximately 409 species make it a diversified genus of Geminiviridae family. Begomoviruses with one-molecule genomes are known as monopartite, and those with two-molecule genomes are known as bipartite. Irrespective of whether the genome is mono or bi-partite, the size of each genomic DNA molecule is 2.8 to 3kb (75, 94). In the establishment of infection in plants, the satellite molecules associated with begomoviruses also play an important role; these known subviral molecules are betasatellites, alphasatellites, deltasatellites or non-coding satellites (31). The introduction and blowout of begomoviruses and their vectors around the world provide threatening circumstances for the cultivation of vegetables and other economically significant crops, since tomato yellow leaf curl virus (TYLCV) is widely known to have emerged as a serious concern for tomato production worldwide, and these viral diseases of vegetable crops have ultimately posed serious threat to food security (39, 32, 33). Recombination and mutation have resulted in new variants, which are favored by climate changes, global agricultural trade, poor quarantine measures and cropping systems, and have increased their host range and geographic distribution around the globe, making their control more complex. Since the identification of begomoviruses as deadly plant pathogens, different methods have been adopted to control the disease or minimize the infection (3, 8, 19).

CONTROL STRATEGIES USED AGAINST BEGOMOVIRUS INFECTION

Managing begomoviruses is difficult on a global platform due to the high incidence of economically significant diseases caused by these viruses. Integrated pest management (IPM), which includes actions before, during and after the growing season, is the most efficient technique for management, regardless of the type of agricultural practices (77).

Cultural and phytosanitary practices

Every country is following some quarantine measures and has created special quarantine departments to stop the introduction of exotic pests (79). The purpose of plant quarantine measures is to safeguard a country's or a region's agriculture against the potential effects of dangerous pathogens and pests (79). These measures are especially crucial and pertinent for states whose economies are heavily focused on agriculture. In addition to reducing the threat posed by exotic pests, quarantine also aims to eradicate and stop the spread of pests and pathogens (both native and imported) with restricted dispersal within the territory or the country; this is known as domestic quarantine (59). However, poor quarantine measures have resulted in the introduction of numerous devastating pests into new countries (90). The Irish Famine in the 1840s, which was brought on by Phytophthora infestants imported from Central America, is one example of introduced pest causing epidemic and pandemic with severe effects on food production, way of life, and environmental biodiversity. Banana bunchy top virus outbreak in the sub-region of West Africa due to the virus spread through planting material from sub-regions of Central Africa, as well as cassava mosaic disease invasion in East Asia caused by Sri Lankan cassava mosaic virus (SLCMV) which was introduced from South Asia, are two recent examples of devastating outbreaks caused by trans-boundary pest introductions (50, 43). Strong and strict quarantine measures can stop the introduction of pests, which can cause epidemics. This is the first step towards control strategies (42). Over the years, weeds have become the reservoir of plant viruses (51). Cultural practices, including roguing, removal of alternative host plants, disposal of residues, rotation with unrelated and non-host crops, balanced fertilizer usage, deep burial of infected plants, and time of cropping (24), can not only reduce the insect vector population, but also lower the disease pressure (45). Physical barriers like UV-absorbing plastic sheets and fine mesh screens have been demonstrated to be helpful against whiteflies, but this method also causes issues with shadowing, overheating and inadequate ventilation, and is not such a common practice in underdeveloped countries (91). In rural areas of Pakistan, the farmers are not much educated about integrated pest management and are following the conventional mono-cropping methods. Mono-cropping and poor field sanitation have increased the insect pest population, and there is a dire need to stop these practices in underdeveloped countries (1, 54, 6).

Vector management through Insecticides

Begomoviruses are spread by whiteflies, and this small monster has wreaked havoc on agricultural crops all over the world where farming is practiced or possible (25). A traditional and hypothetically easier approach to control viral infection usually involves the interruption of transmission through vector control, which is led by the application of chemical insecticides/pesticides (63). Pesticides are used to boost agricultural output; however, they accumulate over time in components of plant, soil, water, biota and remains suspended in the air. Pesticides contaminate the environment, reside in the crops and eventually invade the food chain, risking the human and animal health (88, 41). Around 2 million tons of agricultural-related chemicals are used worldwide, of which 17.5% are fungicides, 29.5% are insecticides, 47.5% are herbicides, and 5.5% are other pesticides. China, the United States, Argentina, Thailand, Brazil, Italy, France, Canada, Japan and India are the top ten pesticide-using countries on the planet (83). Judicious application of insecticides is essential (76), since a non-judicious and unnecessary use of pesticide has developed resistance in insect pests. Bemisia tabaci is the fifth most insecticide-resistant species in the world out of the top 12; therefore, the control of whitefly has become a global concern due to readily developing resistance against each new introduced insecticide (46). Indiscriminate use of insecticides against whitefly can only be stopped by the proper and timely pest scouting. Pesticide usage causes serious consequences and this control significantly adds to the production costs, but chemical pesticide application is still chosen over all other options for preventing crop yield loss by farmers. (37)

Development of resistant varieties

Development of plant resistant cultivars through breeding techniques is the inviting and cost-effective approach to prevent plant virus diseases (77). Conventional breeding has extensively used natural sources of resistance to generate virus-resistant plants (74). Because this method does not require additional resources to control viral vectors, virus-resistant crops boost breeders' profitability. The introduction of new geminivirus strains as a result of continuous recombination and changes in farming techniques is the only flaw and failure of this method (40, 49). Another problem is when two or more viruses co-infect a crop plant (29). When the vector is present in the field and the environmental conditions favor the disease development, there are chances that new resistance breaking viral strains emerge, since viruses change their genome through recombination and mutation under pressure and a new more destructive strain evolves (53, 52, 20). In 1967, a village close to Multan, Pakistan, reported the first case of cotton leaf curl disease (CLCD) brought on by begomoviruses, but it kept unnoticed until early 1990s (73), when it became pandemic and caused financial losses of up to 5 billion USD to the Pakistan' economy between 1992 and 1997 (12). At that time, researchers in Pakistan focused on the development of resistant varieties of cotton, by breeding locally cultivated susceptible varieties with resistant sources; resistant cotton variants were developed, and the resistance in the recently released cotton cultivars held firm until the appearance of a Burewala viral strain in 2001 in Punjab District of Vehari. The newly developed resistance-breaking strain infected all resistant cotton cultivars. Cotton leaf curl Burewala virus (CLCuBuV) is the name of this strain, which has sequences of other two strains: Multan and Khokhran. So far, there is no resistant cotton variety available in Pakistan against Burewala strain (35, 65).

Cross Protection

Cross-protection is another disease management method that was defined more than 70 years ago for plant viruses. McKinney originally identified this method in 1926; numerous examples of cross-protection have been identified thereafter (27). According to this method, by injecting a mild isolate of a virus into a plant, the symptoms of the severe strain are inhibited or delayed in expression when the plant is subsequently inoculated with a severe isolate of the same virus (95). Previously, it was believed that cross-protection could only be used to identify whether a plant virus belonged to the same strain or a different species. Another term used for cross-protection is "plant immunization" (66). Cross-protection entirely depends on a viral strain that causes either no symptoms or mild symptoms with low viral capacity, and this strain is called primary virus (52). The primary virus is classified as attenuated and therefore acts as a vaccine (67, 96). Citrus tristeza virus, zucchini yellow mosaic virus, papaya ring-spot virus and tomato mosaic virus have all been successfully controlled by this method (89). Early research revealed that severe strains of cassava mosaic disease (CMD) viruses might infect plants that were previously infected by moderate strains. Due to their poor disease-causing ability, primary viruses or strains cause no impacts on plants due to no or mild disease symptoms and therefore generate bearable yield losses (54, 26, 34). As demonstrated by the managing of two important plant viruses, Citrus tristeza virus (CTV) or pepino mosaic virus (PepMV), cross-protection against plant viruses can be a very effective strategy. However, in order to use cross-protection against plant viruses, it is compulsory to assess mild strains that are similar to the severe strains. It may be sufficient to use cultural practices and keep insect vector populations at a minimum level to lessen the spread of pathogenic viruses; however, cultural practices are not sufficient to lower the disease incidence (72). There are several drawbacks to using the cross-protection technique. Transmission to a new and different host, mixed infections with other viruses, mutation or recombination between different strains or viruses, and even a more serious disease can result from infection by the mild strain (28). As a result, cross-protection should be employed only after other protective measures have failed, and the procedure should be constantly monitored (15).

Resistance through RNAi

Gene silencing is described as the epigenetic process used to regulate the genes; it can be transcriptional or post-transcriptional (23). The mechanism of RNA silencing was first observed in tobacco plants in 1928 by Wingyard when he observed the discovery of new leaves from tobacco ring spot viral infection (36, 9) but, at that time, the mechanism was unknown. In 1989, it was again found in Nicotiana benthamiana (22). In 1990, Napoli and Jorgensen reported gene silencing in petunia (80). Post-transcriptional gene silencing (PTGS) or RNA interference (RNAi) involves cutting of double-stranded ribonucleic acid (dsRNA) strands, when recognized by the plant defense mechanism, into small strands of approximately 21-26 nucleotides. The dsRNA is cut by dicer protein into short interfering RNA. Then, the dsRNA is unwound to make single-stranded ribonucleic acid (ssRNA) molecules and are known as small interference RNA (siRNA). The siRNA interrelates with RNA-induced silencing complex (RISC). Whenever RISC finds a complementary strand to its associated siRNA, it binds to it and the dicer cleaves the dsRNA, thus preventing gene expression (7, 93). RNA interference is actually a naturally occurring mechanism to regulate transposons and other endogenous genes, as well as to counteract the invading genes (21, 60). Nowadays, it has been used by scientists to study functional genomics and to develop improved crop plants and disease resistant plants (61). Against geminiviruses, RNAi has been adopted to develop resistance to cotton leaf curl Multan virus (CLCuMV) in cotton (64), African cassava mosaic virus (ACMV) in cassava (70), cucumber mosaic virus (CMV) in tomato (68), rice dwarf virus (85) and cotton leaf curl Multan virus-Rajasthan strain (CLCuMV-Raj) in elite Indian cotton (Gossypium hirsutum) (48), bean golden mosaic virus in common bean (Phaseolus vulgaris) (11), chili leaf curl virus Pakistan isolate Varanasi, and tomato leaf curl New Delhi virus-isolate chili and chili leaf curl Vellanad virus tested in Nicotiana benthamiana (84).

Host plant resistance

A more effective option to manage diseases, particularly those that are primarily introduced by geminiviruses largely over a specific length of time, is the host plant resistance phenomenon (4). Resistance (R) genes are often involved in triggering downstream signaling response during plant disease resistance. Based on structural motifs, leucine-rich repeat domains, coiled-coil domains, interleukin-1 receptor domains, transmembrane regions and nucleotide-binding site resistant proteins can be divided into various super-families. Generally, nucleotide-binding site leucine-rich repeat (NBS-LRR) genes are the two most dominant R-genes found in plants; these two R-genes are further sub-grouped based on N-terminal coiled coil or toll/interleukin-1 receptor (TIR) domain (17). Plants use a variety of defense mechanisms against pathogenic attacks. A defense response known as systemic acquired resistance (SAR) stimulates a hypersensitive system to an avirulent pathogen, which exhibits a normal part of plant resistance to virulent pathogens. The SAR is considered to be responsible for the activation of various related genes such as non-expressor of pathogenesis-related genes 1 (NPR1) and its paralogues NPR3 and NPR4. Exogenous application of certain chemicals to the plant, such as salicylic acid (SA), -2,6dichloroisonicotinic acid and benzo 1,2,3 thiadiazole-7-carbothioic acid S-methyl ester, stimulates the SAR; in the signal transduction pathway(s), coupling the hypersensitive response (HR) with the onset of SAR endogenously produces SA after some hyper response (13). The SA-signaling pathway is considered an important system that requires the plant for immunity against the pathogen (38, 30). The NPR1 and its paralogues (NPR3 and NPR4) are bona fide SA receptors that play a vital role in local and systemic immunity for SA-mediated regulation (10). Plants are very complex in nature and have effective innate immune systems to combat bacteria, fungi, viruses, etc. Characterization of the SAR mechanism especially depends on the induction of pathogenesis-related gene bundle, SA accumulation, and long-term resistance properties against plant diseases. Due to the long-term resistant property of SAR, AtNPR1 has been used as a resistance engineering tool in most agronomic crops against bacterial, fungal and viral attacks. Overexpression of BjNPR1 in Brassica juncea increased immunity against fungal pathogens like Alternaria brassicae and Erysiphe cruciferarum (5), while overexpression of MuNPR1 (of Mulberry) in Arabidopsis displayed increased resistance against Pseudomonas syringae PV. tomato DC3000 (PstDC3000) (92). In a similar pattern, knockdown of tomato NPR1-like gene (18), tobacco NtNPR1 (56), and barley HvNPR1 (78, 58) showed a hike in susceptibility to Ralstonia solanacearum, tobacco mosaic virus (TMV) and powdery mildew fungus, respectively. Two interrelated branches constitute the plant innate immunity: PTI, or pathogen-associated molecular pattern (PAMP)-triggered immunity, is initiated when the pattern recognition receptor (PRR), present on the plant surface, recognizes the molecular signs of pathogens and a signal is mediated and further triggered downstream to mitogen-activated protein (MAP) kinase cascades and defense genes; and ETI, or effector-triggered immunity, is initiated when the plant disease resistance proteins (major R gene products) directly or indirectly recognize specific pathogen-derived effectors. Both PTI and ETI activate the SAR and are controlled by phytohormones, especially jasmonic acid (JA) and SA (71). The pathogen-inducible transcription factor CaWRKY2 is known to have a role in early defense responses to biotic and abiotic stresses in chili pepper (69).

CRISPER/Cas9

A holistic genome-editing approach, well known as clustered regularly interspaced short palindromic repeats and CRISPR associated protein 9 (CRISPR/Cas9), is the most adaptable and defined method currently used to produce virus-resistant cultivars. CRISPR/Cas9 was initially found to be an adaptive immune defense mechanism in bacterial cells to protect against invading DNA (86). Due to its fascinating features, the Cas9 genome editing system has developed into a versatile method to achieve specific gene targeting, gene replacements, gene insertions/deletions, and single base-pair alterations. As a result, this tool has become a crucial component of contemporary plant breeding (82). Cas9 technique has advanced the plant breeding programs and has made resistant cultivars possible even with transmissible resistance against plant viruses. This system includes the complex of Cas9 endonuclease and single-guide RNAs (sgRNAs), which target specific parts of the virus or plant genome sequence by either interposing the cleavage of viral sequence or altering the plant genome, meanwhile they reduce the replication ability of the virus. This technique can act in two ways: it can detect and degrade pathogenic genes of viruses, making them less virulent or non-virulent, or it can be used to develop crops with resistance genes against viruses. Therefore, this approach has created a buzz in reforming the research against viruses due to its sequence-specific nuclease proficiency (82, 55, 47). CRISPR-Cas9 system has been engineered to confer resistance to various human viruses and plant geminiviruses (91). The bean yellow dwarf virus (BeYDV) and the beet severe curled top virus (BSCTV) were targeted in the first experiment using CRISPR to develop viral resistance in N. benthamiana and A. thaliana (4). The highest level of resistance to leaf curl disease and decreased viral infections are demonstrated by transgenic tobacco plants that produce dual gRNAs targeting the C1 (Replication-associated protein) and IR sections of cotton leaf curl Multan virus (CLCuMuV) (93). Targeting numerous regions of the viral genome at the same time would prevent the virus from using the non-homologous end joining (NHEJ) repair pathway; then, cleaved molecules would eventually be tainted. A catalytically inactive Cas9 would be predicted to stop viral replication and eventually result in viral interference if it were to target an intergenic region that is essential for binding and replication start. However, while developing CRISPR/Cas9-based approaches for long-term viral interference and resistance, leading to higher agricultural production, there are several crucial considerations to take into account (93, 44, 40, 14).

CONCLUSION

Controlling and managing begomovirus infections has become difficult due to the dynamic and rapid evolution of new viral strains. Several researches have contributed significantly to the development of resistant plants through the expression of viral and non-viral proteins, host-resistant (R) genes, and gene silencing by RNA interference against begomoviruses, but different researchers keep finding ways and discovering pathways to better understand and manage plant-virus interactions. In the previous years, RNAi technique was considered the best method for resistance against begomoviruses of the cotton crop; however, cotton leaf curl in Pakistan still prevails and causes losses every year. All control strategies discovered so far, when applied against begomoviruses, create pressure on the viral genome, and this survival pressure changes the viral genome to appear as strong as before to break this pressure. Burewala strain of cotton leaf curl virus is a clear example of this mechanism. Due to recombination and mutation, begomoviruses have been changing their genome and spreading as new strains and becoming more devastating by infecting new plants and breaking host resistance. The present review suggests adopting a method that does not create conditions for the virus to undergo recombination and mutation or emerge as a more devastating strain; however, the host should have enough strength to tolerate the disease. Natural defense is a more economical and environment-friendly method, since it does not create any pressure on the virus. There are numerous insights in the plant genomes that are still hidden from the eye of the researcher and need to be explored before begomoviruses take over the agriculture of the world. The current study aimed to provide a comprehensive comparison among all control methods used all over the world to control begomovirus infection; despite all control methods, the viruses continue spreading, still uncontrolled, and agriculture is still threatened, which has arisen a question for researchers: is the best strategy against begomoviruses yet to come?

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