Vol. 2 Issue-12, August 2022 (e-ISSN: 2582-8223)

Antiviral Drugs: A Nascent Approach to Plant Viral Disease Management

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ARTICLE ID: 009

Introduction

Climate change coupled with the world's burgeoning population poses a great threat to global food security in the twenty-first century. There is a paradigm shift in plant disease scenario keeping pace with climate change and a plethora of biotic (bacteria, mollicutes, fungi, algae and some phanerogamic parasites) and mesobiotic agents (virus, viroids and virus-like pathogens) are responsible for causing deadly diseases which greatly diminish crop yield and quality. Out of such biotic and mesobiotic pathogens, the virus alone causes losses of several billion dollars every year.Some of the plant viral diseases such as Rice tungro, Banana bunchy top, and Citrus tristeza have already created pandemics in recent years. The situation will worsen in near future due to global warming and a lack of effective management strategies. Management of plant viral diseases is a tedious job, as the pathogen is nonliving outside of the host.Some prophylactic measures like avoiding exporting or importing viral diseased plant materials to disease-free localities through quarantine law certification and inspection, selection of viral disease-free seeds and planting materials, cultivation of trap crops (Marigold in Okra), destruction of weeds that serve as a reservoir host for the virus during the off-season, cultivation of resistant varieties are the existing feasible option to manage plant viral disease right now. In addition, the most commonly used measure to manage plant viruses in field conditions is by applying insecticide as mostly plant viruses are transmitted by insect vectors. Off late, antiviral drug therapy has emerged as a modern approach to the management of plant viruses. It is still in its nascent stage and its large scale application can act as a game changer for the farming community.

Antiviral Drugs

Antiviral medications, unlike most antibiotics, do not kill their target pathogen; instead, they prevent its development. Lists of Anti-viral drugs for animal and human viruses are well documented and used at the commercial level, but for plant viruses, most of the drugs are at the experimental trial level and very few are commercialized. There is an urgent need for the development and use of anti-viral drugs for plant viral disease management as cultural practices are not being fully effective, regular breaking of host resistance and more importantly development of insecticide resistance in insect vectors. In addition, some anti-viral drugs have a potent role in plant growth and development in addition to checking viral infection in plants. As viruses replicate in the host's cells, it's tough to develop safe and effective antiviral drugs and this makes it difficult to develop pharmacological targets that will interfere with the virus without disrupting the cells of the host organism. Despite such difficulties, some anti-viral drugs are developed to check viral infection in plants. Some of such potent chemicals are described below: -

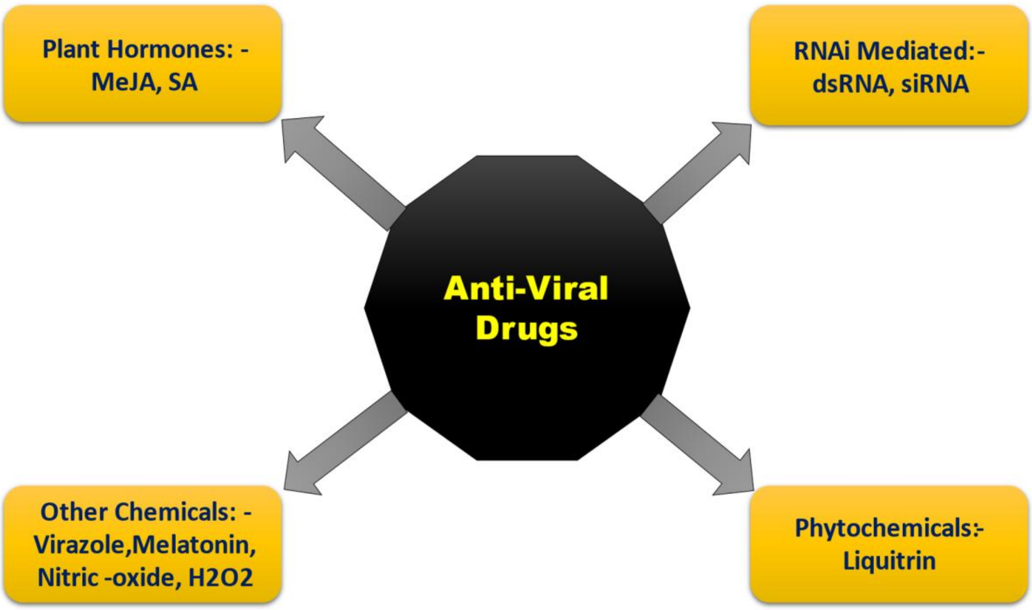

Figure 1: - Types of different anti-viral drugs used in Plant virus management. (**MeJA**- Methyl Jasmonate, **SA**- Salicylic acid, **H2O2**- Hydrogen peroxide)

Methyl Jasmonate (MeJA) and Salicylic acid (SA)

Exogenous application of different concentrations of MeJA resulted in decreased levels of malondialdehyde with higher membrane stability index values in MYMIV susceptible *V. mungo*, suggesting the protective role of MeJA through restoring the membrane stability (Chakraborty, N., &Basak, J. 2018).Applying 0.06 mM JA and then 0.1 mM SA 24 h later, enhanced resistance to *Cucumber mosaic virus* (CMV), *Tobacco*

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mosaic virus (TMV) and *Turnip crinkle virus* (TCV) in Arabidopsis, tobacco, tomato and hot pepper. The inhibition efficiency of virus replication is usually achieved up to 80–90%.SA promotes major changes in the induction of resistance in tomato plants and suggests that treatment with exogenous SA could be considered to reduce the infections caused by PVX (Shang et al., 2013).

Double-stranded RNA (dsRNA)

In general, dsRNA is the precursor molecule in achieving gene knockdown employing RNAi or through post-transcriptional gene silencing. But, restricting viral or any biotic stress in plants through transgenic RNAi is less accepted and has a high cost. So, an alternative means of RNA interference is the exogenous delivery of dsRNA on plants which will knock down viral genes in infected plants. There are some experimental proves to show the effectiveness of dsRNA in combating viral existence in the host plant. This antiviral drug is effective against both RNA and DNA viruses of the plant. Functional foliar application of dsRNAs targeting the plant viruses, *Pepper mild mottle virus* (PMMoV), *Alfalfa mosaic virus* (AMV) and *Tobacco etch virus* (TEV), was first reported by Tenllado and co-workers in 2001 (Tenllado and Diaz-Ruiz, 2001). Konakolla et al., 2021, reported that upon mechanical inoculation of in vitro transcribed 237-bp dsRNA targeting the TMV p126 showed antiviral protection in tobacco. A single spray application of cocktail dsRNA (mixing equal volume of dsC2, dsV2 and dsC4 with 0.1% celite) upon *N. bentamiana* resulted in the reduction of disease incidence up to 70% caused by *Chilli leaf curl virus* (ChiLcV) (Singh et al., 2021).

Virazole

Virazole (Ribavirin), an antiviral medication used to treat RSV infection, hepatitis C and some viral hemorrhagic fevers in humans has been successfully used against tomato spotted wilt virus (TSWV) in tomato and tobacco plants. In the case of tomato, the most efficient concentration to control TSWW was 500 mg/l while in tobacco, concentrations of 100 mg/l were sufficient to control systemic infection (De Fazio et. al., 1980).

Melatonin, Nitric Oxide and Hydrogen Peroxide

Exogenous application of melatonin, nitric acid and hydrogen peroxide act as resistance inducers in plants against different biotic and abiotic stresses of plants. There are so many reports of successful inhibition of plant virus infection on the treatment of exogenously applied antiviral drugs. Pretreatment with exogenous H_2O_2 and NO on the upper

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leaf led to increased *RDR1* expression and systemic TMV resistance. The function of melatonin (MT) and Nitric oxide (NO) in the response of rice to virus *Rice stripe virus*, plants were pre-treated with exogenous MT and NO and they found that MT and NO could both reduce the disease incidence in a concentration-dependent manner, with the largest effects at 10 μM of MT and 100 μM of SNP (a specific NO donor), resulting in 30.00 and 25.78% disease incidence reduction, respectively (Liao et al., 2013).

Liquitrin

Liquiritin is a kind of flavonoid isolated from the root of *Glycyrrhizauralensis* that attenuated rheumatoid arthritis via reducing inflammation, suppressing angiogenesis, and inhibiting the mitogen-activated protein kinase signaling pathway. Foliar application of liquiritin (200 ppm) effectively suppressed the development of Cucumber Mosaic Virus (CMV) symptoms by not less than 40% compared with the control in cabbage plants in both greenhouse and field trials along with the significant increases in the marketable yield and nutritional quality of cabbage (Akram et. al., 2021).

Conclusion

In the battle of host and pathogen, no one is the all-time winner which means one dominates over the other for a while and vice versa. With the continuous emergence and re-emergence of viral strains and new viruses and the development of insecticide resistance, management of such plant viral diseases is quite difficult with the existing strategies. Hence these potent antiviral drugs can be an alternate approach and hopefully going to be a path breaking find in plant virus management. Besides such antiviral drugs, modern innovative approaches for plant virus management should be discovered.

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