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REVIEW

Progress in the development and application of plant-based antiviral agents

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Abstract

Plant virus disease is one of the major causes of biological disasters in agriculture worldwide. Given the complexity of transmission media and plant disease infection mechanisms, the prevention and control of plant viral diseases is a great challenge, and an efficient green pesticide is urgently needed. For this reason, when developing candidate drug leads to regulate plant viruses, pesticide experts have focused on characteristics such as low pesticide resistance, eco-friendliness, and novel mechanism. Researchers have also theoretically investigated the molecular targets of viruses infecting agricultural crops. Antiviral screening models have been constructed based on these molecular targets, and the mechanisms of commercial drugs and high-activity compounds have been extensively investigated. After screening, some compounds have been applied in the field and found to have good commercial prospects; these drugs may be used to create new green antiviral pesticides to control plant viruses. This paper reviews the screening, mode of action, development and application of recently used plant-based antiviral agents.

Keywords: research progress, antiviral agents, screening model, action mechanism, drug development and application

1. Introduction

Plant viruses are commonly known as “plant cancer” (Palukaitis and Zaitlin 1997), and they are completely dependent on their host for energy and other resources (Lewsey and Carr 2009). Viral infections greatly reduce the quality and quantity of crop yield; moreover, viral diseases are extremely difficult to prevent and control (Oerke and Dehne 2004; Leigh and Proud *et al.* 2015). Pesticide experts have performed various studies aimed at finding methods to control plant viral diseases, and the methods mainly employed in these studies are biological (Laceya *et al.* 2015) and chemical prevention and control (Roger *et al.* 2014). Given its simple operation and high effectiveness, chemical prevention and control is widely applied in the field. But chemical control will become resistant to insects and pesticide residues can exceed standards. Thus, there is an urgent need to create efficient and low-toxicity pesticides, and the development of effective and environment-friendly synthetic antiviral compounds has become the focus of recent studies (Wu and Song 2016). Considerable improvements in synthetic antiviral compounds have been made. For example, antiviral compounds, such as dufulin (Song *et al.* 2009), antofine (Yao *et al.* 2001), GU188 (Lv *et al.* 2007),

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Jiasaiyouan (JSYA) (Liu *et al.* 2010) and 3-acetonyl-3-hydroxyoxindole (AHO) (Li *et al.* 2008), were synthesized through modification of the structure of natural compounds. Screening models for these drugs have been established based on their molecular and protein targets. Moreover, the mode of action of these compounds has been studied, new lead compounds have been discovered, and dufulin and JSYA have been patented and applied in agriculture.

2. Establishment of screening models for antiviral drugs based on their molecular targets

The use of a biological screening model is a key approach in studying new antiviral pesticides. Although some traditional models, such as using half leaf methods to screen anti-tobacco mosaic virus (TMV) compounds, have been widely used, some problems in their accuracy and precision have been noted (Yu *et al.* 2013). Moreover, a biological screening model has not yet been employed to screen antiviral pesticides targeting newly discovered plant viruses. Thus, researchers have conducted a series of studies on methods used to screen biological activity, such as the polyethylene glycol (PEG)-mediated method (Yu *et al.* 2013). Recently, there has been considerable progress in developing screening systems.

2.1. Development of a screening system for anti-southern rice black-streaked dwarf virus (SRBSDV) compounds

Yu *et al.* (2013) constructed a screening model for antiviral compounds targeting SRBSDV using a PEG-mediated method. This model can be used to screen anti-SRBSDV compounds rapidly and effectively (Fig. 1).

2.2. Development of a screening system for anti-TMV compounds

A modified TMV expression vector carrying a GFP gene downstream of the TMV coat protein (CP) sgRNA promoter that can systemically infect and express GFP in *Nicotiana benthamiana* plants was used to monitor the replication of the TMV in whole plants (Shivprasad *et al.* 1999). Li *et al.* (2014) constructed a screening model for anti-TMV compounds based on TMV-GFP that can be used to screen anti-TMV compounds directly and with high-efficiency (Fig. 2).

3. Studies of protein targets and the mode of action of antiviral compounds

Replication, assembly and disassembly of plant virus proteins play important roles in the viral infection process and thus have recently become hot topics for research. Studies on the treatment of plant virus infection have shown the importance of controlling the assembly and disassembly of infective plant viruses and that overexpressing CP in plants can lead to resistance against viruses. However, there have been few studies on the targets of plant viruses. Given that the infectivity of most plant viruses is realized through assembly and disassembly of plant viral proteins, the key to discovering antiviral compounds is to study the mechanism of action of CP.

3.1. TMV CP assembly and replication as a target of ningnanmycin (NNM) and seco-pregnane steroids

CP protects viral nucleic acids and plays an important role

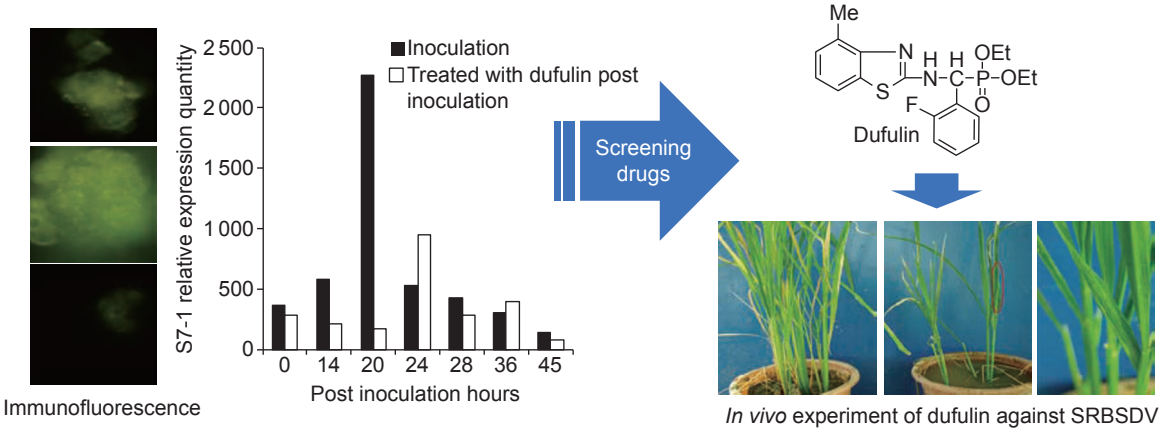

Fig. 1 Development of the screening system for anti-southern rice black-streaked dwarf virus (SRBSDV) compounds (adapted from Yu *et al.* 2013). Rice suspension cells infected with SRBSDV by polyethylene glycol were used in screening antiviral drugs.

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