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How can Plants help Fight COVID-19?

Sachi Sharma* and Lynetta Binger

Phoenix Country Day School, Paradise Valley, USA

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***Corresponding author:** Sachi Sharma, Phoenix Country Day School, Paradise Valley, AZ 85253, USA

Abstract

COVID-19 is a disease caused by SARS-CoV-2. The virus is highly contagious and is passed by human contact, and in severe cases it was found that COVID-19 was causing pneumonia and ultimately lung or multisystem organ failure. Vaccine development is a high priority for COVID-19. The main goal of vaccine development is to achieve herd immunity throughout the world. Various approaches are being utilized to accelerate vaccine development. One approach is called molecular pharming, which refers to the recombinant expression of pharmaceutically useful proteins in plants. Several unique steps have been followed for molecular pharming for vaccines in plants. These steps include expression of antigens in plant based systems, the creation of Virus Like Particles (VLPs), a VLP based vaccine in influenza, a SARS-COV vaccine using molecular pharming, and finally the creation of a COVID-19 vaccine from plant sources. Molecular pharming is advantageous and has an unprecedented opportunity for vaccine development for pandemic diseases because of rapid and low-cost production and recombinant technology.

Keywords: COVID-19; SARS-CoV-2; Molecular pharming; Vaccine; Plant-based vaccine; Virus; Virus-like-particles; Recombinant; Coronavirus

Abbreviations: COVID-19: Coronavirus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2 of the genus betacoronavirus; VLP: Virus Like Particle; SARS-CoV: Severe acute respiratory syndrome coronavirus; MERS-CoV: Middle East respiratory syndrome-related coronavirus of the genus Betacoronavirus; RNA: Ribonucleic Acid; CoV-2: Coronavirus 2 of the genus betacoronavirus

Introduction

COVID-19 is a disease caused by SARS-CoV-2. In January of 2019, the disease was first identified in Wuhan, China, the capital of the Hubei Province. The virus is highly contagious and is passed by human contact. The outbreak of COVID-19, nicknamed coronavirus, has impacted every continent severely [1]. SARS-CoV-2 is an enveloped RNA virus that was first discovered in Wuhan, China, the capital of the Hubei Province. Like previous coronaviruses, SARS-CoV-2, now known as COVID-19 causes respiratory, hepatic, and neurological diseases [2]. Coronaviruses spread quickly, as seen with the 2002 outbreak of SARS-CoV in China or the 2012 MERS-CoV outbreak in the Middle East [3,4]. In most patients, COVID-19 will mimic common cold symptoms.

However, in severe cases, it was found that COVID-19 was causing pneumonia and ultimately lung or multisystem organ failure [2,5]. COVID-19 has been linked to the Huanan Seafood Wholesale Market in Wuhan, China. The market sells an array of live animals including bats, snakes and marmot. Most healthy people exposed to COVID-19 could range from being entirely asymptomatic to mild symptomatic. Mild symptoms include dry cough, sore throat, and most commonly fever. However, in older or high risk patients, symptoms can be severe including severe pneumonia, pulmonary edema, septic shock, or multisystem organ failure.

Males appear to be more susceptible to infection from COVID-19. Approximately 54.3% of infected people are male with an average age of 56 [6-8].

The Need for Vaccines for Covid-19

Vaccine development is a high priority for COVID-19 [9]. The main goal of vaccine development is to achieve herd immunity throughout the world. Various approaches are being utilized to accelerate vaccine development. Scientists have identified a protein known as the 3C protease that is necessary for all viral replication [10]. Spike protein of the COV-2 virus is a key antigen that is being utilized in gene based or protein based approaches for vaccine development [9]. The fastest approaches to develop vaccines are recombinant vaccines followed by inactivated or attenuated protein based vaccines [11]. Several challenges have been pointed out. Firstly, it is not clear what antigens will produce the most effective neutralizing antibodies. Secondly, there is a concern if the antibody titres are universally protective. Thirdly, there are instances where vaccines may paradoxically increase lung disease. And finally, vaccine development is an expensive and often commercially unviable process [9,11]. Several biotechnology companies including Moderna, CanSino and University of Oxford with AstraZeneca have entered clinical trials [12].

Molecular Pharming for Vaccines in Plants

Molecular pharming refers to the r ecombinant expression of pharmaceutically useful proteins in plants. In recent years, molecular pharming has been of particular interest because of the discovery that plants can be developed as bioreactors for the rapid production of candidate proteins through transient expression.

Because plants can produce recombinant proteins at high levels and low cost, there is a large potential for this technology to be applied to development of recombinant vaccines [13].

Several unique steps have been followed for molecular pharming for SARS-COV-2 vaccine in plants:

1. Expression of antigens in plant based systems: The first challenge is to express the transgene for the antigen in plant cells. The time-tested method for this is to infect plant cells with genetically modified Agrobacterium [14,15]. This technology has been optimized to achieve large biomass and yield.

2. Virus Like Particles (VLPs): VLPs are attenuated plant viral particles that lack infectivity. They express viral coat proteins and can be modified to express candidate vaccine genes. A Canadian biopharmaceutical company Medicago studies plant-based technology that utilizes VLPs. A VLP is an easier system than Agrobacterium and has the potential to produce a large biomass of vaccines [16]. Amazingly, the virus like particles can form enveloped structures that bud off the intracellular membranes. These VLPs have a distinct advantage over isolated antigens because they present multivalent structures that mimic the original virus. This technology has been demonstrated to work for various viruses preclinically including Hepatitis B, Norwalk virus and Influenza [17-19].

3. VLP based vaccine in influenza: Using technology that included H5 strain Medicago scientists developed a preclinicaly active vaccine in three weeks [17]. A quadrivalent vaccine developed by this company is currently in Phase 3 clinical trials.

4. SARS-COV vaccine using Molecular Pharming: In preclinical studies, M and N structural proteins were utilized to develop vaccines during the Severe Acute Respiratory Syndrome (SARS) virus using potato virus and agroinfiltration systems [20]. Another study demonstrated expression of the S protein using agroinfiltration in tobacco plants [21].

5. COVID-19 vaccine from plant sources: Medicago has announced that the Canadian government has agreed to provide $ 7 million in funds to develop its COVID-19 vaccine, and VLPs have been produced in 20 days. A subsequent press release also claims that positive antibody responses have been seen in animal models.

Future Potential for Molecular Pharming for COVID-19

One of the potential advantages of the plant based approach is that robust expression of antigen in plants can be directly administered to humans without antigen purification. Such a technological revolution would have several advantages:

1. Possibility of administering plant based oral vaccines that could be rapidly produced at low cost and deployed rapidly esp. in developing countries.

2. Enhanced mucosal immunity that can be obtained by oral route that cannot be obtained by parenteral routes. This is especially important for respiratory pathogens like CoV-2 because they use respiratory epithelium as an entry point [22,23].

Conclusion

Molecular Pharming has an unprecedented opportunity for development of vaccines for pandemic diseases because of rapid and low-cost production and recombinant technology. In the future, advances in this area can lead to oral vaccines that may be convenient and easily deployable.

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