The Potential Impact of Plant-made Biopharmaceuticals for the Improvement of Global Health

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Plants offer an abundance of advantages as production platforms for biopharmaceuticals, including vaccines, antibodies and other therapeutic proteins. Plant-derived vaccines provide an alternative option to the use of conventionally-made vaccines through their delivery via the oral consumption of edible plant tissue. It is well established that a large number of infectious diseases utilize the mucosal membrane within the gut to enter the body; therefore vaccines which can be expressed within edible plant tissue offer a select advantage. As a result, plant cells not only act as the delivery vehicle itself, they protect the antigen as it passes through the harsh environment of the gastrointestinal tract. The fact that plants can produce recombinant antigens that undergo post-translational modifications which are largely similar to their mammalian-derived counterparts provides added value for vaccines made from plants rather than from bacterial culture systems. Furthermore, the relative cost of protein production from plants is much smaller than the cost of proteins generated from comparable mammalian cell culture systems.

Previously, biopharmaceutical proteins were generated solely in stable transgenic plants; more recently, transient expression systems have become increasingly prevalent. Transient expression systems based on agroinfiltration and/or virus expression vector modules are capable of producing high quantities of vaccine and other therapeutic proteins within a short time period (often within a week, depending on the virus/host plant system involved). Today, the selection of which plant expression platform is best to use for the production of a particular biopharmaceutical protein is determined by deciding whether the system should involve cell culture or entire plants, which plant species is the most suitable and whether stable transformation or transient expression systems would be most advantageous for the application in mind.

A principal incentive for the use of plants as production platforms for vaccine and therapeutic proteins is to supply efficacious, inexpensive and safe vaccines which have no cold chain requirements or need for trained medical personnel to the most needy, the rural poor who reside in developing countries. Biopharmaceuticals are in high demand to combat preventable infectious diseases that remain major causes of infant mortality in these regions. Transgenic potato plants expressing Hepatitis B virus surface antigen were the first ‘proof-of-concept’ that a vaccine expressed in plant tissue could be consumed and elicit a mucosal immune response. Since then, many other plant-made vaccines have been generated and the results of clinical trials have been encouraging. Recently, for example, a consortium of laboratories has worked towards generating a microbicide to HIV in the form of a plant-made broadly neutralizing monoclonal antibody known as VRC01. Similarly, the biotech companies Fraunhofer USA and Medicago, Inc have been steadily working toward the generation of a plant-made vaccine against pandemic influenza virus. Plant-derived vaccines and monoclonal antibodies directed toward other diseases considered to be significant challenges for developing countries, such as Human papillomavirus, are under development as well. The ability to easily upscale protein production, the low cost and the promising results in clinical trials make plant-derived vaccines a formidable solution to meet some of the world’s most difficult health needs.

Could plant-made vaccines make a significant impact on global health? The data supporting their efficacy, generated by human clinical trials, has been steadily accumulating and is now considerable in size. The result is a wider acceptance of this technology by the general public. The fact that the vast majority of patent applications for plant-made pharmaceuticals were generated at academic and publically funded research institutes is also encouraging. By ensuring that freedom-to-operate (FTO) is implemented through these institutes, plant-made biopharmaceutical technology is more readily accessible for use in developing countries. However, a blueprint pertaining to how these vaccines and therapeutic proteins could be produced in local, rural settings, and the policies which would govern this production still need to be established. Adhering to the routes already developed by organizations that specialize in supplying conventional vaccines to developing countries could be one way to go. Enabling poor countries to develop the technology themselves in order to provide for their own populations could be another. The future looks promising for plant-made biopharmaceuticals, and the time is at hand to determine whether they will make a real difference and improve global human health.

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