The Journal of Phytopharmacology 2025; 14(2):127-129
Online at: www.phytopharmajournal.com

Mini Review

ISSN 2320-480X
JPHYTO 2025; 14(2): 127-129
March- April
Received: 26-03-2025
Accepted: 12-04-2025
Published: 15-05-2025

doi: 10.31254/phyto.2025.14208

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Transgenic plants as bioreactors for the production of edible vaccines

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ABSTRACT

With the advent of transgenic approach, plants are being looked upon as potential bioreactors or bio-factories for the production of immunotherapeutic molecules. Transgenic technology is that technology in which a gene is transferred from any source to any sink by the tools and techniques of biotechnology. This technology can be utilised for the production of edible vaccines or green vaccines in plants. The low cost of production and possibility of increasing production by micro-propagation via tissue culture makes plant vaccines an attractive product. The present article discusses edible vaccines, their advantages, concerns and future prospects.

Keywords: Transgenic Plants, Edible Vaccines, Green Vaccines.

INTRODUCTION

Commercial production of oral vaccines requires stringent purification protocol & is quite expensive. The cost and production of vaccines are very high. Generation of antigens and antibodies in plants against pathogens for inducing active and passive immunity is possible through transgenic approach. Plants can be a useful system for producing vaccines because large amounts of antigen could be produced at a relatively low-cost using agriculture instead of sophisticated and expensive cell culture-based expression system [1].

Transgenic technology is being utilised for the benefit of mankind for the production of pest and insect tolerant plants, abiotic stress tolerant plants which can tolerate drought, salt, cold etc, enhancing nutritional quality of plants. Through this technology, genes can be transferred in plants from unrelated sources. Pest resistant *Bt* cotton, Golden rice for enhancing Vitamin A content, Flavr Savr tomato for delayed ripening are some of the well-known examples of transgenic plants [2,3].

Transgenic plants can be generated for the production of antigens and antibodies. The antigens and antibodies produced in the edible parts of the plant can be consumed raw and this serves the purpose of edible vaccine [1,4,5]. The edible parts of transgenic plants, when consumed, elicits the immune response in body and protects against disease. Edible vaccines developed for the production of antigen serves the purpose of active immunity. When they produce antibody, they serve the purpose of passive immunity [1]. The mechanism of action of edible vaccine is that they induce the activation of mucosal immune response system of the body.

Transgenic approach for edible vaccines

Transgenic plants for the production of edible vaccines can be made by various genetic transformation techniques like *Agrobacterium* mediated transformation. Gene expressing antigen or antibody are transferred to Ti plasmid of bacterium *Agrobacterium* and then transferred to plants. Other methods of gene transfer include micro projectile bombardment and electroporation [1,4,5].

Advantage of edible vaccine

Major advantage of transgenic plants that expresses antigens in their edible tissues is that they can be used as an inexpensive oral vaccine production and delivery system. Through edible vaccines, immunization is possible simply through consumption of the edible part. Antigens or antibodies expressed in plants can be administered orally or as any edible part of the plant. To prevent possible denaturation during cooking, the edible part of the plant to be used as vaccine is fed raw to experimental animals. It avoids cumbersome purification protocol as edible vaccines can be consumed directly. These genes for antigens or antibodies can be expressed in high quantities within edible parts with the help of strong organ specific promoters. Transgenic material, in the form of seed or fruit can be easily stored and transported from one place to another without fear of its degradation or damage.

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Refrigeration of these edible vaccines is not required which is a mandatory requirement of vaccines produced through conventional methods [1,4,5].

Plants of choice for making edible vaccines

For the production of edible vaccines or antibodies, it is desirable to select a plant whose products are consumed raw to avoid degradation during cooking. Thus, plants like tomato, banana and cucumbers are generally the plants of choice for developing edible vaccines.

Initially tobacco plants were generally utilised for the production of edible vaccines. But because of high levels of toxic alkaloids in leaves, studies on animal feeding on tobacco are not practised without substantial purification of tobacco derived antigens. Potato has also been a choice in several studies [1,4,5].

Some Examples of edible vaccines

The first report of edible vaccine came in 1997 by Arntzon et al. [6] who expressed hepatitis B surface antigen (*HBsAg*) in tobacco by genetic engineering. Some other examples of antigens produced in transgenic plants are Cholera toxin B subunit in tobacco [7], Rabies virus glycoprotein in tomato [8]. Edible plant vaccines against diarrhoea, expressed in potato and antibody against dental caries, expressed in tobacco [1,4,5]. Transgenic potatoes with CT-B gene of *Vibrio cholera* was reported to be effective in mice [7]. Transgenic tobacco producing measles virus H protein (MV-H) when fed to mice elicited antibody production to a high level [9]. Examples of some edible vaccines are shown in Table 1.

Table 1: Some examples of edible vaccines developed [4]

Disease for which the edible vaccine developed	Gene	Transgenic Plant	Clinical Trial	Results
Cholera	*CT-B* gene of *Vibrio cholerae*	Transgenic potato	Done on mice	Enhanced immunity
Measles	*MV-H*	Tobacco	Done on mice	Enhanced antibody production
Diarrhoea	*LT-B*	Tobacco & Potato	Done on mice	Enhanced antibody production
Rotavirus	*Rota virus VP7*	Potato	Done on mice	Enhanced immunity

Concerns regarding edible vaccines

The concept of edible vaccines is very promising but its execution is a challenging task. The plant-based vaccines vary according the size of the fruit, seed etc. produced. This variation in size of the edible parts require meticulous prescription of doses according to size or weight of the edible part [1,4-5]. The risk of under dose or overdose due to size & weight variation of plant parts needs to be standardised. The dose of vaccine, its efficacy, safety, quality needs to be standardised for plant-based vaccines. Public apprehension regarding the new concept of edible vaccines needs attention. Allergy to plant vaccines has been expressed and needs to be addressed suitably taking case by case studies.

Future Prospects

Concept of edible vaccines is an innovative idea to combat many diseases like Malaria, Hepatitis Measels, Rabies, Cancer, Autoimmune diseases etc. Further research and development and approval from WHO after meeting quality standards and their efficacy is needed. This technology holds a bright sustainable, eco-friendly, inexpensive method of oral vaccination.

CONCLUSION

Transgenic plants are being looked upon as a source for producing large scale antigens and antibodies which can serve the purpose of active and passive immunization by oral consumption. The low cost of production and possibility of increasing production by micro-propagation *via* tissue culture makes plant vaccines an attractive product.

Conflict of interest

The authors declared no conflict of interest.

Financial Support

None declared.

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HOW TO CITE THIS ARTICLE
Mishra RR. Transgenic plants as bioreactors for the production of edible vaccines. J Phytopharmacol 2025; 14(2):127-129. doi: 10.31254/phyto.2025.14208