

Plant Made Edible Vaccines-Paving the Future

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Abstract: Vaccine is a substance that stimulates the production of specific antibody for protection against a specific disease. They would be more widely used especially in case of developing countries if their cost of production could be reduced and if they could be distributed without refrigeration. Edible vaccines hold great promise as a cost-effective, easy-to-administer, easy-to-store, fail-safe and socioculturally readily acceptable vaccine delivery system, especially for the poor developing birth control, cancer therapy, etc. Edible vaccines are currently being developed for a number of human and animal diseases. It involves introduction of selected desired genes into plants and then inducing these altered plants to manufacture the encoded proteins. Introduced as a concept about a decade ago, it has become a reality today. A variety of delivery systems have been developed. Initially thought to be useful only for preventing infectious diseases, it has also found application in prevention of autoimmune diseases.

Keywords: Edible vaccines, plants, transgenic, human pathogen

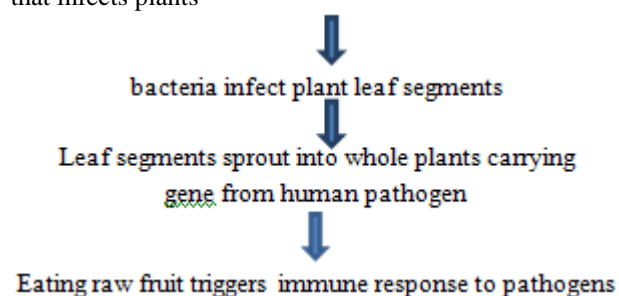
1. Introduction

Transgenic plants have become attractive as bioreactors to produce heterologous proteins that can be used as vaccines. Various types of antigens that are successfully expressed in different plants are E.coli, heat labile enterotoxin B subunit (LT-B) in tobacco and potato, Rabies virus G protein in tomato, Hepatitis B virus surface antigen in tobacco and potato, Norwalk virus capsid protein in tobacco and potato, H5N1 influenza HA VLP and H1N1 influenza HA1 in *Arabidopsis* and *Nicotianabenthamiana*, Protective antigen (PA) in tobacco etc.[1] Cereal crops have also been used as experimental model as they have ample amount of soluble proteins in endosperms enhancing the antigen concentration and reducing oral dose. Vaccines derived from transgenic plants have been investigated in preventing infectious diseases in animals with some vaccines gone into early phase target animal trials.

Present abstract describes the expression of vaccine antigens in transgenic plants to produce edible vaccines. The vaccines produced from transgenic plants have high efficiency in passive immunization against bacterial or viral diseases and through this strategy production vaccine can be done on a large scale to assess the possibilities of oral immunization in the near future. [2]

2. Method

Gene from a human pathogen is inserted into a bacterium that infects plants



Advantages of Edible Vaccines

- 1) Much lower costs of production
- 2) Safety - no animal-related contaminants, no syringes and needles used
- 3) Higher stability (e.g. proteins in seeds can be preserved for years even at room temp.)
- 4) Easier compliance, especially for multi-dose vaccinations --- Vaccines can be kept and administered orally at home
- 5) Cost-effective and easier administration of vaccines for animals (livestock, pets etc.)
- 6) Especially suitable for less developed countries or regions.

Early developments in plant-derived vaccines

The first demonstration of expression of a vaccinogen in plants occurred in 1990 when Curtiss and Cardineau [P1] expressed the *Streptococcus mutans* surface protein antigen A (SpaA) in tobacco. After incorporation of the transgenic tobacco tissue into the diet of mice, a mucosal immuneresponse was induced to the SpaA protein. Although the mice were not challenged with the pathogen, the induced antibodies were demonstrated biologically active when they reacted with intact *S. mutans*. Reports have since followed of expression of a hepatitis antigen in tobacco and lettuce [3,], a rabies antigen in tomato [5], a cholera antigen in tobacco and potatoes [6, 7] and a human cytomegalovirus antigen in tobacco [8]. Animal trials demonstrating antigenicity of plant-derived vaccinogens include tobacco- and lettuce-derived hepatitis B surface antigen [9, 10], a tobacco- and potato-derived bacterial diarrhoea antigen [11], a potato-derived Norwalk virus antigen, and an *Arabidopsis*-derived foot-and-mouth disease antigen [11]. To date, the data obtained do not allow determination of protective immunity either because the animal model is not susceptible to the disease-causing agent, or because of strict containment issues with the pathogen (as in foot-and-mouth disease).

Recent developments in plant-derived vaccines

Recent research has concentrated on meeting the prerequisites for application of plant-derived vaccines to the human and animal health industries. Information on dosage, best delivery method and response type, strength and length has been acquired for pathogens including *Vibrio cholerae*, HIV, *Pseudomonas aeruginosa* [9], murine hepatitis virus, and foot-and-mouth disease virus [12]. Further investigation

has examined the use of synthetic genes, targeting of vaccinogen expression to specific plant tissues, investigation of the induced immune response and progression to human clinical trials.

3. Conclusion

Edible vaccines hold great promise as a cost-effective, easy-to-administer, easy-to-store, fail-safe and socioculturally readily acceptable vaccine delivery system, especially for the poor developing countries. It involves introduction of selected desired genes into plants and then inducing these altered plants to manufacture the encoded proteins.

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