

Fruit Derived Edible Vaccines: Natural Way For The Vaccination

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Abstract: Vaccine is a biological preparation which is used to establish or improve immunity to a particular disease. The usual traditional vaccines are generally microsomal preparations which can be harmful & cannot be tolerated by small babies to be vaccinated. To overcome such problems .Fruit Drug Delivery System is introduced, where the vaccination is done by means of fruit which synthesize the antigenic material that provides immunization to vaccinated patient. This system has vast advantages over traditional one as the fruits are tasty, natural way of vaccination. These are also called as subunit vaccines. Normally to make a subunit vaccine, the gene for one of the protein for one of the infectious agents, such as bacteria & viruses, is produced in another system. The plant thus shows synthesis of that protein in fruit. The proteins targeted for use in subunit vaccine are antigens, which may be thought of as the molecular structure of pathogen. In viruses, antigens are usually proteins which appear on the surface of virus & are well recognized by immune system. If humans are exposed to the antigens, they recognize it as a foreign molecule & develop an immune response against it, if exposed to real bacteria or virus; their system can mount an effective & protective effect. The edible fruits are very effective as a delivery vehicle for inducing oral immunization, adjuvant for immune response is not necessary, excellent safety and economic feasibility of oral administration compared to injection are some potent advantages over traditional vaccines.

Keywords: Fruit, Vaccination, Transgenic plant, Edible vaccines, Antigen expression.

1. Introduction:

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters. Vaccination is the administration of antigenic material (the vaccine) to produce immunity to a disease. Vaccines can prevent or ameliorate the effects of infection by a pathogen.

One of the most promising new strategies for production and oral delivery of vaccine antigens is by transgenic edible plants using the methods of molecular biology, plant geneticists can readily

introduce genes of interest into plants where they are stably expressed in the plant tissues, including the edible parts. These genes encode putatively protective vaccine antigens from viral, bacterial, and parasitic pathogens that cause disease in humans and animals. The vaccine can be delivered by ingestion of the edible part of the transgenic plant, or the high-yield production of purified protein for oral.

Use transgenic plant can be used as a bioreactor for large-scale, high-yield production of purified protein for oral.

In biology, on the other hand, a fruit is a part of a flowering plant that derives from specific tissues of the flower, mainly a single ovary. Transgenic plants present a novel system for both production and oral delivery of vaccine antigens. Production of protein antigen in food plants is substantially cheaper than production in bacterial, fungal, insect cell, or

mammalian cell culture. Edible plants themselves can also serve as the oral vaccine delivery system. In broad terms, a fruit is a structure of a plant that contains its seeds¹.

2. Advantages fruit derived vaccine:

1. Ease of administration.
2. Eliminate the concern about transmission of human and animal pathogens by vaccines.
3. Reduce the need for trained medical personnel to administer the vaccine.
4. Remove the need for needles and syringes.
5. Convenience and safety in storing and transporting vaccines.
6. Delivery of multiple antigens.
7. Possible production of vaccines with low costs.
8. Adjuvant for immune response is not necessary.
9. Excellent safety and economic feasibility of oral administration compared to injection.

10. Easy for separation and purification of vaccines from plant materials.

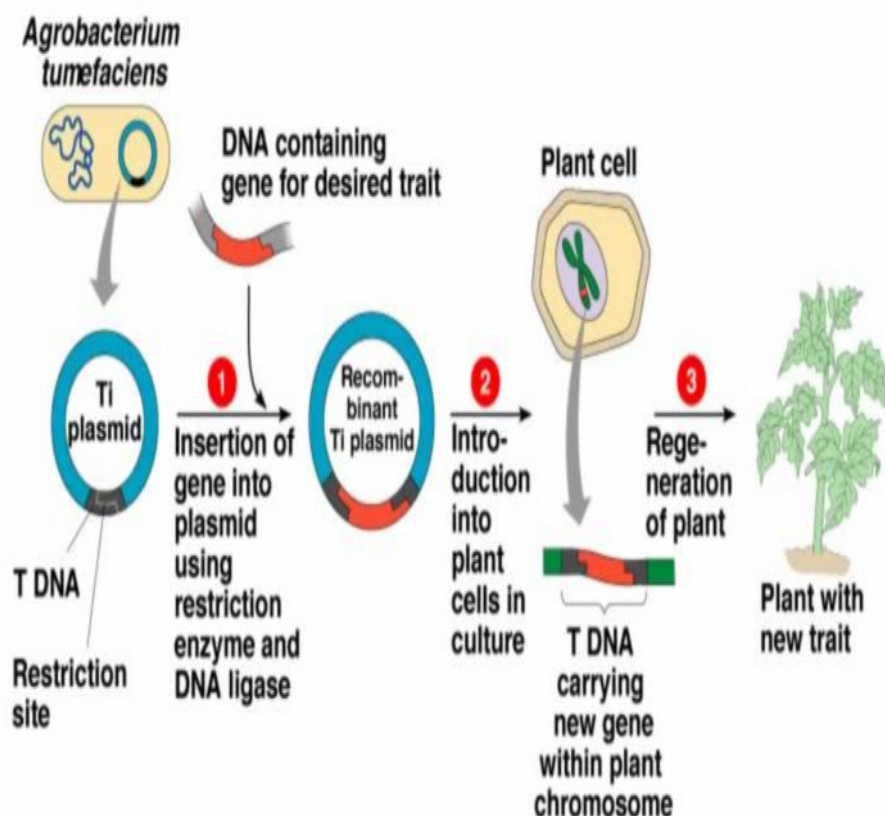
11. Enhanced compliance. (Especially in children)

12. Heat stable, eliminating the need for refrigeration².

3. Procedure for development of fruit derived vaccine:

The foreign DNA can be transiently expressed by infection of susceptible plants with the recombinant virus encoding foreign DNA. The foreign genes can be stably expressed by integrating the foreign DNA into the plant nuclear genome or into the circular chloroplast genome present in multiple copies. Chloroplast can process eukaryotic proteins, with the correct folding and formation of disulfide bridges. The molecular techniques used to construct plant-derived vaccines³.

Figure – 01 : Showing the Procedure for the development of fruit derived vaccine.



4. Examples of fruit derived vaccine:

1. The first prototype plant-derived vaccines were developed in tobacco because of the ease of transformation and regeneration of this plant.

2. *A transgenic potato vaccine*

It is engineered to express cholera toxin B subunit (CT-B), analogous to the closely related LT-B, induced both serum, and intestinal anti-CT-B antibodies after being fed to mice in four doses. These antibodies neutralized the cytopathic effect of CT on Vero cells. When challenged with intra-ileal injection of CT, the immunized mice had a 60% decrease in diarrhea fluid accumulation compared to mice fed control potatoes⁴.

3. *Typhoid fever vaccine from fruit polysaccharide*

4. *Plant-derived edible vaccine against hepatitis B virus.*

The infectious hepatitis B virus represents 42 nm spherical double-shelled particles. However, analysis of blood from hepatitis B virus carriers revealed the presence of smaller 22 nm particles consisting of a viral envelope surface protein. These particles are highly immunogenic and have been used in the design of hepatitis B virus vaccine produced in yeast. Upon expression in yeast, these produced in yeast. Upon expression in yeast, these proteins form virus-like particles that are used for parenteral immunization. Therefore, the DNA fragment encoding hepatitis B virus surface antigen was introduced into *Agrobacterium tumefaciens* LBA4404 and used to obtain transgenic lupin (*Lupinus luteus* L.) and lettuce (*Lactuca sativa* L.) cv. Burpee Bibb expressing envelope surface protein. Mice that were fed the transgenic lupin tissue developed significant levels of hepatitis B virus-specific antibodies. Human volunteers, fed with transgenic lettuce plants expressing hepatitis B virus surface antigen, developed specific serum-IgG response to plant produced protein.

5. *Plant-derived vaccines against diarrheal diseases.*

5.1. *ETEC.*

The first plant-derived ETEC vaccine was based on the highly immunogenic heat-labile enterotoxin (LT) of *E. coli*. This toxin consists of an enzymatically active-A subunit with ADP ribosyl transferase activity associated with five immunogenic binding subunits, designated LT-B. LT-B binds to the GM1 ganglioside present on the epithelial cell surface. Antibody to LT-B induced by vaccine could interfere with binding of the toxin to its target thereby protecting against diarrhea, and in fact, immune responses to LT-B offer short-term protection against infection with LT-producing *E. coli*⁵.

5.2 *Transgenic potatoes expressing LT-B*

Haq et al. transferred the gene encoding LT-B via *A. tumefaciens* into tobacco and potato plants and fed these tobacco leaves and potatoes to mice. The plant-derived LT-B assembled into pentameric structures and bound to ganglioside, like bacteria-derived LT-B. Mice that consumed multiple 5 g-doses of these potatoes developed serum IgG and mucosal IgA anti-LT-B, responses similar to those of animals immunized with 20 µg doses of purified LT-B expressed in bacteria. In a subsequent study, mice fed three weekly doses of 5 g of tuber tissue containing either 20 or 50 µg of LT-B, had higher levels of serum and mucosal anti-LT-B than those gavaged with 5 µg of bacterial LT-B []. Vaccinated mice were challenged with 25 µg of fully toxinogenic LT to assess vaccine efficacy. Although none of the vaccinated mice was completely protected, the potato-derived vaccine provided a significant reduction in intestinal secretion. Control mice fed non-transformed potatoes, developed no antibodies, and no reduction in secretion in the patent mouse assay⁶.

5.3. *Transgenic corn expressing LT-B*

Transgenic corn is inexpensive to produce and can be scaled up rapidly, with corn generation time of 3–4 months. Corn-derived proteins can be expressed at high levels up to 10 mg/g of corn germ, and the expressed protein is very similar to native source protein. Antigens expressed in transgenic corn are stable, and the product of the cloned gene can be highly concentrated and homogeneous in corn germ. Streatfield et al. developed a prototype transgenic corn containing the gene encoding LT-B.

The transgenic corn vaccine was formulated as defatted corn germ meal, prepared by standard commercial processing techniques, with uniform particle size and a homogeneous mixture of LT-B in the vaccine. In preclinical studies in mice, the transgenic corn germ meal stimulated serum IgG responses and fecal IgA responses. Mice fed LT-B corn, but not control corn, were protected from LT-induced intestinal secretion. The protection elicited by the LT-B corn was similar to that elicited by an equivalent amount of purified bacterial LT-B⁷⁻⁸.

6. *Edible malaria vaccines that bear fruit*

In the case of malaria, Wang et al. have demonstrated that oral immunization of mice with recombinant merozoite surface protein (MSP) 4, MSP 4/5 and MSP1, co-administered with cholera toxin B subunit (CTB) as a mucosal adjuvant, induce antibody responses effective against blood-stage parasite. For those studies, however, proteins were expressed in *E. coli* and protection was only evident when high dose antigen was administered. Whether oral delivery of a

plant-derived malaria vaccine would induce significant immune responses in humans is uncertain. It has been suggested that antigen expression levels in plants are so low that an unrealistic quantity of plant material would have to be consumed to achieve meaningful immunity⁹⁻¹⁰.

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5.Conclusion :

Manipulating ordinary food plants into useful pharmaceutical products is a distant extension of traditional medicinal chemistry. Preclinical and preliminary clinical studies of prototype plant-derived vaccines have proved the principle that antigens delivered in transgenic plants can stimulate immune responses in healthy adults without use of buffers or mucosal adjuvants.

heat-labile Enterotoxin (LT): Potatoes expressing a synthetic LT-B gene.

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