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REVIEW ARTICLE

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A Path for Horizing Your Innovative Work

A REVIEW ON EDIBLE VACCINES

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Abstract: Vaccines and antibodies play a key role in healthcare. However, the cost of production and maintaining a chain for vaccine distribution has so far hampered realizing their full potential. Expression of antigens as vaccines and of antibodies against antigens of pathogens in transgenic plants is a convenient and inexpensive source for these immunotherapeutic molecules. Edible plant vaccine against diarrhea, expressed in potato, HIV/AID'S, expressed in tomato, is already in preclinical human trials. Attempts are being made to express many proteins of immunotherapeutic use at high levels in plants and to use them as bio-reactors of the modern era. Research underway is dedicated to solving these limitations by finding ways to produce oral (Edible) vaccines in transgenic plants.

Keywords: Edible vaccine, Transgenic plants, Human papilloma virus.

INTRODUCTION

Edible vaccines are the antigenic proteins that are genetically engineered into a consumable crop. The crop food product contains the proteins which are derived from some disease causing pathogen. People eat the crop, the food is digested, and some of the protein makes its way into the blood stream. This immune response would now neutralize the pathogen should the person ever encounter it in the future[1].

The first report of production of edible vaccine (a surface protein from streptococcus) in tobacco, at 0.02% of total leaf protein level, appeared in 1990 in the form of patent[2].

The selected desired genes into plants and then inducing these altered plants to manufacture the encoded proteins. This is a concept about decade ago, it has become reality today. Nowadays it prevents autoimmune disease, birth control, cancer therapy. Edible vaccines are composed of antigenic proteins and do not contain pathogenic genes. Thus they have no way of establishing infection and safety is assured. Worldwide 20% infants are still left un-immunized; and responsible for approximately two millions unnecessary deaths every year this is because of the constraints on vaccine production, distribution and delivery[3]. In contrast, plant-based vaccines rely on the measles virus gene for the H protein being genetically cloned into the plant. The genetically engineered tobacco plant made to produce interleukin 10 will be tested to treat Crohn's disease, an intestinal disorder[1].

Advantages[1]

- Edible plants are very effective as a delivery vehicle for inducing oral immunization.
- Adjuvant for immune response is not necessary.
- Feasibility the oral administration compared to injection
- Separation and purification of vaccine is easy from plant material
- Effective maintenance of vaccine activity by controlling the temperature in plant cultivation
- Easy for mass production system by breeding compared to an animal system
- Reduce need for medical personnel and sterile injection conditions
- Antigen protection through bio encapsulation

- Heat stable, eliminating the need for refrigeration

Disadvantages[1]

- Dosage of vaccines would be variable
- Not convenient for infants.

Side effects[8]

Research by the national institute of allergy and infectious diseases (NIAID) and the University of Meryland School of medicine showed no serious side effects in a small study using genetically-engineered potatoes to make toxin of the E coli, a diarrhea causing bacterium. The edible vaccine carries only part of the allergens compared to injection methods that reduce anaphylactic shock.

Mechanism of action[3]

The antigens in transgenic plants are delivered through bio encapsulation, i.e. the tough outer wall of plant cells which protect them from gastric secretions and finally break up in the intestine. The antigens are released, taken up by mast cells in the intestinal lining that overlie peyer's patches and gut-associated lymphoid tissue (GALT), passed on to macrophages, other antigen presenting cells; and local lymphocyte populations, generating serum IgG, IgE responses, local IgA response and mammary cells, which would promptly neutralize the attack by the real infectious agent.

Types of Edible vaccines

Edible vaccine using Banana[1]

Vaccines or subunit vaccinations, Banana is desire vector, Research is leaning towards the use of bananas as the vector since most third-world countries, who would benefit most from edible vaccines, are in tropical climates that are suitable for growing bananas.

Figure 1 Banana for vaccine[1]

Advantages

It grows in tropical climates

It can be eaten raw as compare to potato or rice that need to cooked.

Edible vaccine using genetically modified rice[4]

Edible vaccine using genetically modified rice used in cholera. The cholera causes by vibrio cholera travels from host to host in water, it cause the gut and bloody the stool of victims. A vaccine is existing but provides short lived protection; some require refrigeration. But now Japanese researchers have created a strain of rice that can act as a vaccine and last for more than a year and half at room temperature. Vaccine based rice deliver to digestive tract for the initiation of antigen-specific mucosal and systemic immune responses.

Figure 2 Edible vaccine using genetically modified rice[4]

Advantages

- It does not require needles, purification or refrigeration.
- It pusses less risk of contaminating normal crops and have broader utility.

Edible vaccine using maize[5]

Maize plants that produce the protein known as HbsAg, maize plants to produce a protein used to make the Hepatitis B virus vaccine.

Figure 3 Edible vaccine using maize[5]

Advantages

- It is cheaper and not need to be refrigerated.
- Not require skilled person and needles to deliver the vaccine

Edible vaccine using Potato[6]

A potato-based vaccine to combat the Norwalk virus (stomach virus), which is spread by contaminated food and water. The virus causes severe abdominal pain and diarrhea. The Norwalk virus and closely related members of the same virus family account for more than 90% of non-bacterial gastroenteritis, and cause of infant mortality. Eating of potato was effective way to develop immunity to the E. coli toxin.

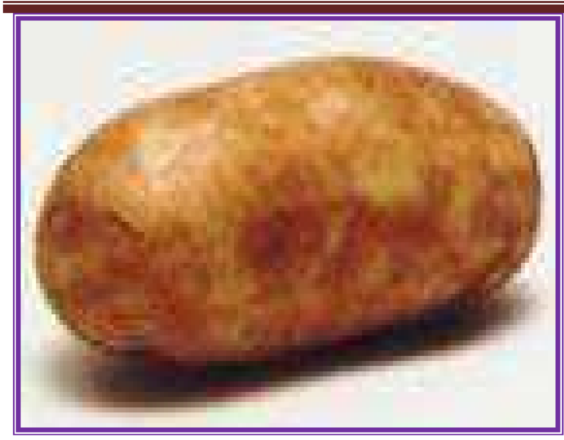

Figure 4 Potato vaccine[6]

Advantages

- It is safe and stimulates antibodies
- Ease, affordable and effective.

Edible vaccine using tobacco[7]

Human papilloma viruses are the causative agent for cervical cancer, being also involved in skin, head, and neck tumors. More than 150 different types of Human papilloma virus (HPV) are known. The most commonly found HPVs in cervical carcinomas are HPV 16 and 18. Virus proteins E6 and E7 are known as onco-proteins, these are promising target for the development of HPV-associate tumors. The HPV16 E7 protein in the cytoplasm of tobacco (nicotiana benthamiana) plants. The E7 production level was fivefold higher (15 microgram of protein per gram of fresh leaf)

Figure 5 Edible vaccine using tobacco[7].

Advantages

- It is palatable oral delivery system
- Purification is not required so it is inexpensive

Vaccines on a plate [5]

Generally antibodies are sensitive to temperature, and so the material would have to be eaten raw. Dr Julian Marr (one of the leading scientists in this field) produces his vaccine against oral bacteria in a potato- one that must not be cooked! However, this crunchy vegetable is not the only option; there are potential vaccine candidates in bananas, maize, tomato and tobacco plants.

Another problem is ensuring the vaccine survives the digestive processes of the gut. One possible method would be to use attenuated (i.e. rendered harmless) strains of gut bacteria such as Salmonella. However, as with any attenuated organism, this could carry some risk. An alternative method would be to encapsulate the antibodies so that they are protected from the digestive chemicals in the gut. One option would be to naturally encapsulate the antibody within seeds- which are slowly digested.

One aspect that biotechnology companies would also need to consider would be how effective these vaccines actually are. Currently, most experimental vaccines do not provide adequate protection with just one dose, and biotech companies are looking at ways to boost this immune response. The immune response could be increased by adding an adjuvant (i.e. another chemical which boost the immune response).

Preparation of edible vaccines[3]

Introduction of foreign DNA into plants genome can either be done by bombarding embryonic suspension cell cultures using gene-gun or more commonly through Agrobacterium tumefactions, a naturally occurring soil bacterium, which has the ability to get into plants through some kid of wound (scratch). It pusses a circular "Ti plasmid" (tumor inducing), which enables it to infect plant cells, integrate into their genome and produce hollow tumor (crown gall tumor), where it can live. This ability can be exploited to insert foreign DNA into plant genome. But prior to this, the plasmid needs to be disarmed by deleting the genes for auxin and cytokinin synthesis, so that it does not produce tumor. Genes for antibiotic resistance are used to select out the transformed cells and whole plants, which contains the foreign gene; and for expressing the desired product, which can then be regenerated from them.

50-100 plants are transformed together at a time. Production of plant is species dependent and takes 3-9 months. Some antigens, like viral capsid proteins, have to self-assemble into VLPs (virus like particles). VLPs mimic the virus without carrying DNA or RNA and therefore are not infectious. Each single antigen expressed in plants must be tested for its proper assembly and can be verified by animal studies, Western blot; and quantified by enzyme-linked immunosorbentassay (ELISA).

Figure 6 Preparation of Edible Vaccines[3]

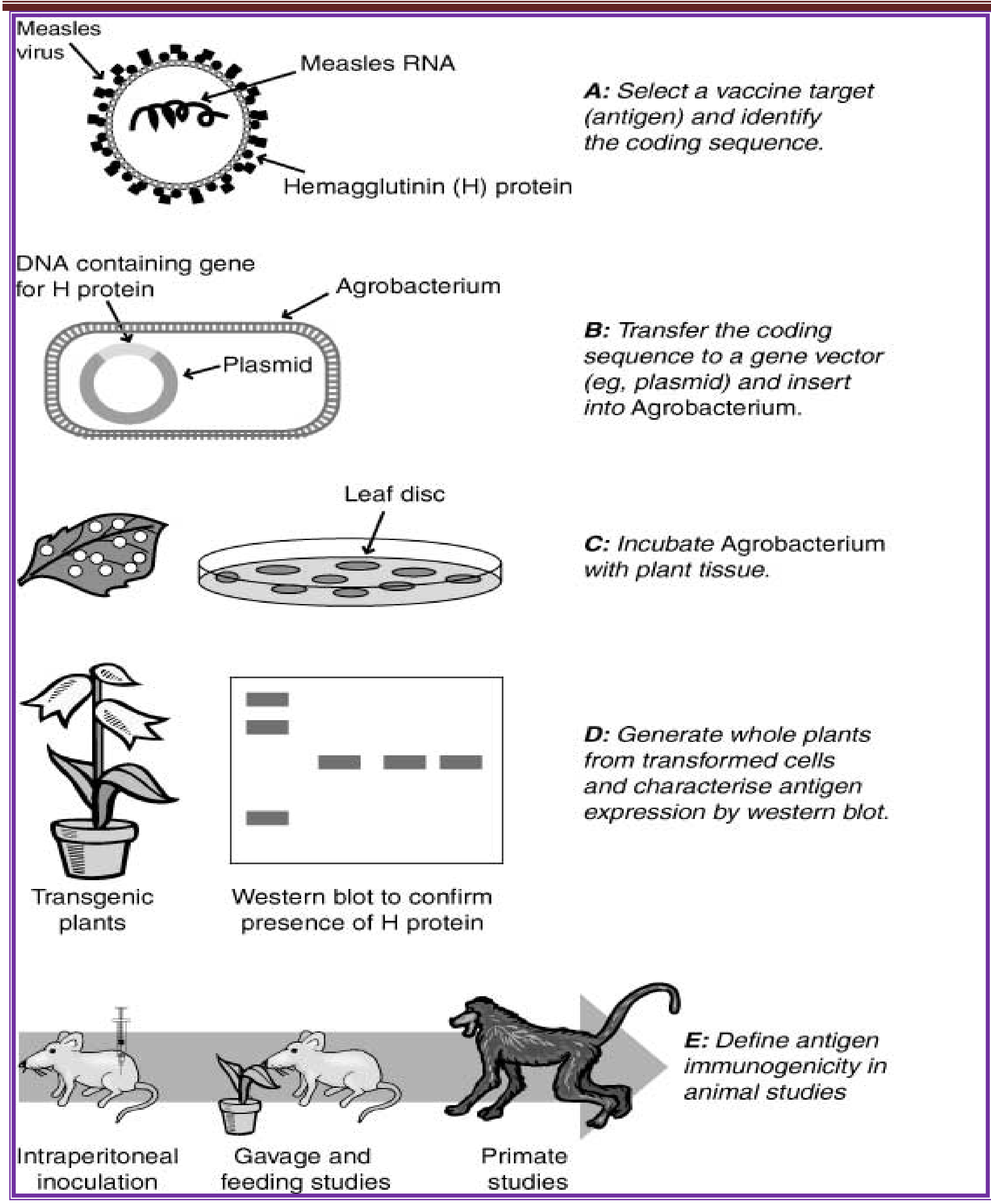

Figure 7 Strategy for the development of plant edible vaccine[8].

Table 1

Proteins with application for humans or animal vaccines and expressed by transgenic plants[1]

Disease target(source of the protein)	Target species for the vaccine plant expression system	Protective capacity of vaccine
Enterotoxigenic E. coli (humans)	Tobacco	Immunogenic when administered orally
Enterotoxigenic E. coli (humans)	Potato	Immunogenic and protective when administered orally
Enterotoxigenic E. coli (humans)	Maize	Immunogenic and protective when administered orally
Vibrio cholera (humans)	Potato	Immunogenic and protective when administered orally
Hepatitis B virus (humans)	Tobacco	Extracted proteins is Immunogenic when administered by injection
Hepatitis B virus (humans)	Potato	Immunogenic when administered orally
Hepatitis B virus (humans)	Lupin	Immunogenic when administered orally
Hepatitis B virus (humans)	Lettuce	Immunogenic when administered orally
Norwalk virus(humans)	Tobacco	Immunogenic when administered orally
Norwalk virus(humans)	Potato	Virus like particles form and Immunogenic when administered orally
Rabies virus (humans)	Tomato	Intact glycoproteins
Human cytomegalic virus	Tobacco	Immunogenically related protein

Rabies hemorrhagic disease (rabbits)	Potato	Immunogenic and protective when administered by injection
Foot and mouth disease (agricultural domestic animals)	Arabidopsis	Immunogenic and protective when administered orally
Foot and mouth disease (agricultural domestic animals)	Alfalfa	Immunogenic and protective when administered by injection or orally
Transmissible gastroenteritis corona virus (pigs)	Arabidopsis	Immunogenic when administered by injection
Transmissible gastroenteritis corona virus (pigs)	Tobacco	Intact protein and Immunogenic when administered orally
Transmissible gastroenteritis corona virus (pigs)	Maize	Protective when administered orally

CONCLUSION

This review gives complete information about the importance, different types of edible vaccines produced by transgenic plants. It provides all information from basics to protocol of production, newly developed edible vaccines specifically on HBV, measles along with success stories. Transgenic plants vaccines are cost-effective, easily reproduced, and cannot be contaminated by mammalian pathogens. Plant tissues can be directly fed to patients as “edible vaccines”, which eliminates the need for purification and refrigeration, takes advantage of “bio encapsulation”, and could stimulate mucosal immunity. Local agricultural production and processing facilities could be utilized.

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