Popular Article
TRENDS IN AGRICULTURE SCIENCE
Vol.2 Issue 10 October 2023, Page: 821-825

Edible Vaccines: Promises and Challenges

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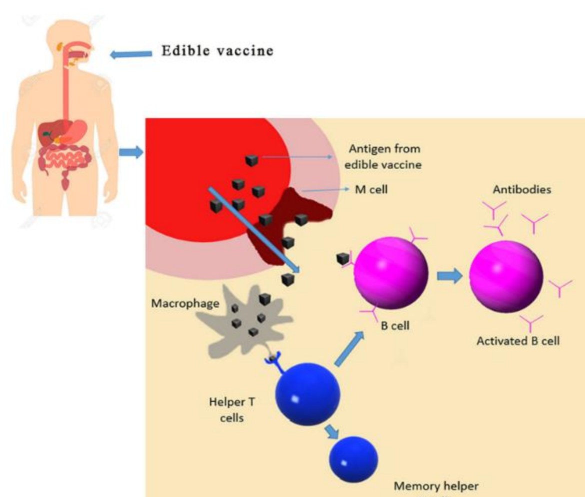
https://doi.org/10.5281/zenodo.10055474

Edible vaccines, a concept introduced by Charles Arentzen in 1990, are a form of oral vaccination that utilize transgenic plants or animals to stimulate the immune system. These vaccines have the potential to greatly impact global vaccine programs, particularly in developing countries. In 1998, the National Institute of Allergy and Infectious Diseases approved the use of edible vaccines due to their impressive ability to elicit an immune response. Edible vaccines offer several advantages, including cost-effectiveness, non-invasiveness, convenience, safety, and ease of administration. They are predominantly targeted against viruses and bacteria that cause harmful illnesses in humans, animals, and poultry. However, no edible vaccine has been approved by the United States Food and Drug Administration (USFDA) as they fall under the category of genetically modified crops.

Mechanism of Action

Edible vaccines are able to stimulate both humoral and mucosal immunity. Mucosal immunity includes both innate and adaptive components, such as T and B cells, which together make up the Mucosa Associated Lymphoid Tissues (MALT). Immunoglobulin IgA also plays an important role in providing immunity.



Production of Edible Vaccine

Edible vaccines are created by inserting specific genes into plants, resulting in the production of necessary proteins. This can be achieved by the process known as "Transformation," and plants known as "Transgenic plants." These genetically modified

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Published: 30 Oct 2023

crops are designed to provide additional immunity against various diseases, including measles, cholera, pneumonia, foot and mouth disease, and hepatitis B, C. Edible vaccines contain immunogenic proteins but not the genes or infectious agents themselves. The selection of the antigenic epitope region and highly efficient plants are crucial factors in producing high levels of these vaccines. There is no evidence showing that edible vaccines cause illness in the host system.

Types of Transformation in Plants

1. The direct gene delivery method is a simple and vector-independent approach to introducing DNA or RNA into plant cells. One common method used is the biolistic method, also known as the gene gun or micro-projectile bombardment method. In this method, the desired DNA or RNA is coated on tiny gold or tungsten beads, which act as carriers. These coated beads are placed in a gene gun and exposed to high-pressure helium gas. The pressure causes the beads to move and penetrate the targeted plant cell. However, this method has some drawbacks. It can be quite expensive to implement, and there is a risk of harming the plant cells during the delivery process. Despite these challenges, the direct gene delivery method has been successfully used to produce vaccines for various diseases. Some examples of vaccines that have been produced using this method include those for cholera, Lyme disease, anthrax, tetanus, plague, rotavirus, and canine parvovirus.
2. Indirect gene delivery is a method used to introduce desired genes into plant cells. In this method, plant bacteria or viruses are used as vectors to infect the plant cells and produce the desired protein within them. The most commonly used indirect gene delivery method is Agrobacterium Mediated Gene Transfer, which involves the use of bacteria such as *A. tumefaciens* and *A. rhizogenes*. Although this method is slow and has low yield, it is cost effective. Examples of vaccines produced using this method include those for tuberculosis, dengue, avian flu virus, and Ebola.

Types of Edible Vaccines

1. Plant based edible vaccines
2. Algae based edible vaccines
3. Whole-cell based edible vaccines
4. Probiotic based edible vaccines
5. Insect based edible vaccines

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Plant-based Edible Vaccines

Multiple plant species, including Apple, Arabidopsis, Banana, Beans, Canola, Carrot, Clover, Lettuce, Maize, Papaya, Potato, Peanut, Rice, Spinach, Tobacco, and Tomato, have been identified as suitable candidates for the production of edible vaccines. Among these species, banana is considered the most promising candidate for supplementing edible vaccines for humans. In 1986, the first transgenic tobacco was introduced, which was able to express human growth hormone. In animals, the first edible vaccine was developed for TGEV (Transmissible Gastroenteritis Virus) in pigs.

Plant species	Vaccine model
Potato	Tetanus, diphtheria, hepatitis B, Norwalk virus, mink enteritis virus, rabbit haemorrhagic virus
Rice	*E. coli*, Hepatitis B
Banana	Hepatitis B
Tomato	SARS, Norwalk virus, *Vibrio cholera*, Alzheimer's disease, Pneumonia, , Bubonic plague
Lettuce	Enteric diseases, Classical Swine Fever, Hepatitis B
Tobacco	Chicken Infectious Anaemia, Hepatitis B, Coccidiosis, Newcastle Disease virus, Influenza virus
Alfalfa	*Echinococcus granulosus*, Foot and-Mouth Disease
Carrots	*E. coli*, *Helicobacter pylori*
Corn	*E. coli,* rabies, transmissible gastroenteritis coronavirus
Spinach	Rabies virus
Safflower	Insulin
Apple	Human Respiratory Syncytial Virus
Peas	Norwalk virus
Papaya	*Taenia solium*

Algae-based Edible Vaccines

Algal edible vaccines are similar to plant edible vaccines. Unicellular green algae have similar positive traits to plant frameworks and some unique advantages as vaccine candidates. One advantage is that algal biomass can accumulate very quickly, and the entire biomass can be utilized for vaccine

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production. However, there are only a few strains of algae that are considered edible for humans and can be genetically engineered to deliver antigens against various diseases.

Algae species	Disease
Chlamdomonas reinhardtii	Malaria, Foot and mouth disease, Classical swine flu, White spot syndrome, *Staphylococcus aureus*, Human papilloma virus
Dunaliella salina, *Phaeodactylum tricornutum*	Hepatitis B

Whole-cell based Edible Vaccines

Whole cell	Disease
Saccharomyces cerevisiae	Influenza, *Actinobacillus pleuropneumoniae*

Probiotics based Edible Vaccines

Genetically modified bacteria can be used as edible vaccines. Lactic acid bacteria such as *Lactobacillus* spp have been found to serve as potential candidates for preparation of edible vaccines.

Genetically modified bacteria	Disease
Lactobacillus casei	Anthrax
Streptococcus gordonii	HIV
Bacillus subtilis	Helicobacter infection
Listeria monocytogenes	Influenza, HIV

Insect based Edible Vaccines

The Baculovirus expression vector system (BEVS) and insect cell culture have become popular choices for producing recombinant proteins due to their advancements and improvements. Insect cells are particularly beneficial as they can produce large quantities of proteins and also perform modifications such as glycosylation, phosphorylation, and protein folding. *Bombyx mori* larvae or pupae are commonly used for mass production of recombinant proteins and as a sustainable method for delivering vaccines, particularly through the use of edible vaccines with silkworms. Baculoviruses

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are considered safe, non-infectious, and non-pathogenic, making them a suitable choice for an edible vaccine system.

Advantages of Edible Vaccines

1. In comparison to traditional vaccines, edible vaccines do not require a complex framework for purification, sterilization, packaging, or distribution, resulting in decreased long-term expenses.
2. Vaccine distribution, management and storage are less difficult than with conventional vaccines.
3. Easy administration through oral route.
4. Sterilization is not required for edible vaccine.
5. For producing edible vaccine, machines and equipment's are not required, can grow easily in cell culture compare to economical method.

Disadvantages of Edible Vaccines

1. Development of immune tolerance
2. Dosage varies from plant to plant, generation to generation, and fruit to fruit.
3. Difficult in selection of suitable plant.
4. Palatability and stability of vaccine in fruit is also a major issue.
5. Not suited for children under the age of one year.
6. People may develop an allergy to the fruit or vegetable expressing the foreign antigen.

Conclusions

Edible vaccines have emerged as a breakthrough in biotechnology, providing a safer and more effective way to prevent life-threatening diseases. Unlike conventional vaccines, edible vaccines are cost-effective, do not require refrigeration, and can be administered orally. They have the potential to offer protection against diseases such as HIV, TB, Corona, Malaria, Heart disease, Diabetics, Dengue, and respiratory diseases. Fruit-derived edible vaccines not only serve as a means of immunization but also provide nutritional benefits. This makes them particularly suitable for use in developing countries where malnutrition is a major concern. By incorporating the vaccine into fruits, individuals can receive both immune protection and essential nutrients.

However, the widespread acceptance and attention for edible vaccines pose a challenge. Some people have concerns about genetically modified products and their potential impacts on society and the environment. Despite these concerns, the benefits of edible vaccines far outweigh their potential side effects. Further research and development in this area are needed to dispel any doubts and usher in an era of better control over infectious

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