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Edible Vaccine Concept Preparation and Application

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Abstract: *Vaccines are one of the most effective tools for controlling human and animal diseases, yet their widespread use is limited in developing countries due to high production costs, cold chain requirements, and the need for trained personnel for administration. Edible vaccines, produced in transgenic plants, offer a promising alternative by combining biotechnology with immunology. Such vaccines eliminate the need for refrigeration, enable oral delivery, reduce costs, and allow large-scale production in locally grown crops. Various plants including bananas, rice, maize, potatoes, tomatoes, soybeans, and tobacco have been successfully engineered to express antigens against diseases like measles, cholera, hepatitis B, malaria, HIV, and even cancer and diabetes. These plant-based vaccines leverage natural bio-encapsulation for gastrointestinal stability and mucosal immunity, making them a viable strategy for both human and veterinary applications. Despite challenges such as low antigen expression and stability, advances in plant transformation techniques and molecular farming continue to strengthen the feasibility of edible vaccines. This innovative approach holds great potential for global health, particularly in resource-limited regions, by providing a safe, effective, and affordable method of immunization.*

Keywords: Antigen, Edible vaccine, Biotechnology, Immunity, Immunology

I. INTRODUCTION

Vaccines are regarded as the main instruments for human and animal health intervention. If the cost of producing vaccines can be decreased and they can be stored without refrigeration, then their usage can be expanded, particularly in developing nations. Certain restrictions, such as the cost of vaccines, the requirement for "cold chains" from the vaccine's manufacturer to the site of use, and the reliance on injection, are obstacles to accessing health care services in developing nations. Vaccines made from plants are not subject to these restrictions. The goal of ongoing research is to overcome these constraints by figuring out how to use transgenic plants to make oral (edible) vaccinations. Increased safety, low-cost mass vaccination programs, and a broader use of immunization for veterinary purposes are all proposed by plant-derived vaccines.[1].

New methods for producing vaccinations were created in the 1980s with the introduction of contemporary molecular biology technology. Proteins from harmful bacteria, viruses, or parasites make up these vaccines; often, proteins are not made by the pathogens themselves, but rather by the expression of the gene encoding the protein in a "surrogate organism." [2].

The primary drawback of vaccinations is their reliance on cold chain systems, which are utilized to deliver and store them under carefully monitored circumstances.[3].

Additional restrictions include the possibility of negative reactions, such as those brought on by improper procedures or reactions that are a natural part of the inoculation.[4].

Similar to subunit preparation, edible vaccines are designed to contain antigen but lack the genes necessary for the formation of the entire pathogen.[5].

Many human and animal diseases, such as cholera, measles, foot and mouse disease, and hepatitis B and C, are currently being treated with edible vaccinations.[6].

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Recently, plant-based edible vaccines have been used to produce vaccines. The conversion and synthesis of antigens into plants, as well as the oral administration of such vaccines to elicit antigen-specific immune responses, are the primary objectives of plant-based edible vaccines. The expression and purification of vaccines, recombinant proteins, enzymes, and numerous biopharmaceuticals in a range of plant species, such as potatoes, corn, tomatoes, carrots, lettuce, and spinach, have recently made extensive use of plant-based expression system platforms and advanced pre-clinical and clinical evaluation stages. Because of its ease of use and safety, low production costs that enable local production and minimal processing of plant materials, natural bio-encapsulation, which promotes stability in the gastrointestinal (GI) tract, and protective immunogenicity at the GI mucosa, oral administration of edible vaccines is the preferred method of vaccination.[7,8].

II. METHOD OF PREPARATION

2.1. Selection of the Desired Gene and Plant

The main prerequisite for creating edible vaccines is introducing the desired genes into plants and then causing these modified plants to produce the encoded proteins. Transgenic plants are modified plants that have undergone this process, which is known as transformation. One of the main elements influencing the success of possible edible vaccines is the selection of the pathogen of interest's essential epitope area or regions. Low levels of foreign protein expression in transgenic plants have been a hurdle to the development of edible vaccines. Total soluble protein (TSP) expression rates range from 0.01% to 2%, which may reduce the immunogenicity of consumable vaccine proteins.[9].

2.2 Plant Transformation

2.2.1. Antigenic Gene Transformation through a Suitable Vector

Since tobacco was transformed, a lot of work has gone into creating effective techniques for genetic transformation and maximizing the expression of foreign genes in plants.Serum albumin, human a-interferon, human erythroprotein, and murine IgG and IgA immunoglobulins are among the foreign proteins that have been effectively expressed in plants.

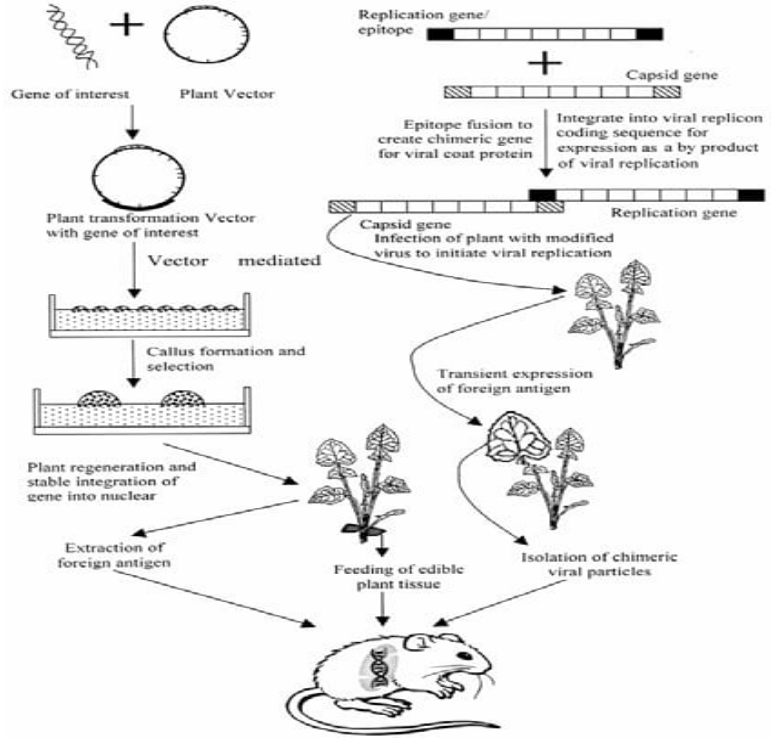

Fig 1.1 Strategies for the production of edible vaccine. PV (plasmid Vector)

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Numerous attempts to create different antigens and antibodies in plants have been made in recent years. After being isolated and purified from the plant tissue, antigens or antibodies produced in plants can be given parenterally (for example, by intramuscular or intravenous injection) or orally as any edible portion of the plant.[10].

Although Agrobacterium-mediated transformation is still the preferred technique for dicots, a general technique for transforming plants, including monocots, known as the biolistics method, has emerged. The use of potent and organ-specific plant promoters, the incorporation of ER-targeting and ER-retention signals to target the protein into the endoplasmic reticulum (ER), the development of an optimal translation start site context, and the modification of codons to accommodate the expression of prokaryotic genes in plants are additional methods for expressing foreign genes in plants. To prevent deterioration while cooking, it is preferable to choose a plant whose components can be eaten raw when producing edible vaccines or antibodies. Therefore, the preferred plants are typically those like tomatoes, bananas, and cucumbers. Certain virus-based vectors can be employed to express the gene temporarily in order to produce the products quickly, even though gene expression into the genome permits the material to be maintained in the form of seeds (Fig. 1.1). This could also have the benefit of enabling very high levels of product expression, which aren't usually possible in transgenic systems.[11].

III. CHOICE OF HOST PLANT FOR EDIBAL VACCINE

3.1. Banana

Bananas can be grown in tropical climates. This climate is present in the majority of third-world nations. Consequently, the majority of research is favoring the use of bananas as a vehicle for consumable vaccinations.[12]. One must ensure that the transgenically modified plant is appropriate for growth in the nations that most need this technology when contemplating an expression system for a possible vaccine. In 2005, Kumar and associates presented the first report on antigen expression in bananas. The s gene, which codes for the hepatitis B surface antigen (HBsAg), was converted into an em bryonic cell of the banana cultivar (cv).

Fig.3.1.Banana for vaccine

Bananas are the most commonly employed plant species in the production of edible vaccines. It doesn't need to be prepared. The proteins did not break down even after cooking. It's cheap in comparison to other plants. Plants that produce bananas produce HBsAg. The leaf contains antigen.[14]

3.2. Rice

A cholera vaccine that is edible and made from genetically modified rice. There is a cholera vaccine, but it only offers temporary protection and needs to be refrigerated.[15]. In an experiment to assess the protective efficacy against Chlamydophila psittaci by oral immunization, based on transgenic rice expressing Major Outer Membrane Protein (MOMP), mice were given rice as the expression system to create an edible vaccine. Immunoglobulin G (IgG) and IgA against Myoprotein were produced in comparable amounts by the mice fed the transgenic rice and the mice fed the MOMP protein directly together with E. coli heat-labile enterotoxin, B component (LTB).[16].

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Fig 3.2 Rice for Vaccine

Other plant species that have been used to create edible vaccines include rice. Having a high level of antigen expression and being often utilized in baby food were advantages over other plants.[17].

3.3 Maize

Fig 3.3.Edible vaccine using maize

A protein from maize plants is utilized to generate the vaccine against the Hepatitis B virus. It doesn't require refrigeration and is less expensive. After being specifically identified, the cells that expressed the glycoprotein were employed in immunonization tests. Six groups of sheep were selected to receive the vaccination; each group was given 40 g of non-transformed maize kernels, 0.5 mg, 1 mg, 1.5 mg, and 2 mg of protein, and inactivated rabies vaccine, respectively.[18].

3.4. Potato

A vaccine made of potatoes to fight the Norwalk virus, also known as the stomach virus, which is contracted by tainted food and drink. The infection causes diarrhea and excruciating stomach ache.[19]. Another study demonstrated an immunological response to the Hepatitis B virus utilizing potatoes as the expression system. Significant morbidity and mortality are caused by the Hepatitis B virus (HBV), despite the availability of safe and effective injectable vaccinations.[20].

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Fig 3.4. Edibal vaccine using potato

The main benefit of creating edible vaccines from potatoes is how easily they can be modified and distributed. One major drawback is that warmth denatures antigens, therefore refrigerators are not necessary for storage.[21].

3.5. Tomato

Tomatoes can be used as a vector to create vaccinations against HIV/AIDS, rabies, and anthrax.[22]. Researchers have successfully produced a transgenic tomato that can be used as an edible vaccine to prevent diphtheria, pertussis, and tetanus (DPT), a multicomponent illness. The tomato known as "flavr savr" was the first genetically modified product to be sold commercially. The amount of DPT present in the total soluble fruit protein was estimated using ELISA plate analysis. A mixture of DPT toxoids, which are found in tomatoes, was administered orally to one set of mice, whereas wild-type tomato material was given to the negative control.[23].

Fig 3.5. Edible vaccine using Tomato

Vaccines against the bubonic plague, pneumonia, and septicemia were developed using tomatoes. It may be grown in a variety of conditions and grows quickly.Vitamin A, which is abundant in tomatoes, may strengthen your immune system. However, it deteriorates swiftly.[24].

3.6 Soyabean

In this study, the endoplasmic reticulum (ER) of soybeans (Glycine max) produced the B-subunit of thermolabile toxin from E. coli bacteria, producing a total antigen level of up to 2.4 percent of the total soybean seed protein without any issues after drying for additional processing.[25].

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Fig 3.6. Edible vaccine using soyabean

3.7 Tobacco

After Arntzen and colleagues discovered HBsAg in tobacco, the idea of an edible vaccination gained momentum. In 1990, tobacco was used to create the first edible vaccine, and it was discovered that 0.02 percent of the total soluble leaf proteins contained recombinant protein, a surface protein from Streptococcus.[26].

Fig 3.7. Edibal Vaccine Using Tobacco

Transgenic tobacco expresses the VP1 protein to shield hens from infectious anemia. A polypeptide linked to hepatitis B can be produced by tobacco. Additionally, a vaccine against coccidiosis is being developed using it.[27].

IV. ADVANTAGES

4.1 Vaccines that are edible can be consumed like fruits and vegetables.
4.2 Producing in bulk on-site, transporting, and storing it without refrigeration is simple and inexpensive.
4.3 Without refrigeration, they can be kept as seeds, oils, and dehydrated tissue.
4.4 No need for an injection or a qualified medical professional. [28-30].

V. APPLICATION

5.1. Measles

For those who are older than 18 months at the time of vaccination, the currently available vaccine results in 95% seroconversion. [31,32]. Additionally, research has looked into the possibility of using transgenic carrot plants to transport viral antigens in order to create a vaccine against measles.[33]. In addition to exhibiting secretory IgA in their feces, mice given tobacco that expressed MV-H (measles virus haemagglutinin from Edmonston strain) were able to achieve antibody titers five times the level thought to be protective for people.[34]. Mice given tobacco that generated

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MV-H (Edmonston strain measles virus haemagglutinin) developed secretory IgA in their feces and antibody titers five times more than what is thought to be efficacious and preventive for humans.[35].

5.2. Malaria

With 300 to 500 million new cases of infection and 1.5 to 2.7 million fatalities per year, malaria continues to rank among the leading causes of morbidity and mortality in the globe. Three antigens—merozoite surface protein (MSP) 4 and 5 from Plasmodium falciparum and MSP 4/5 from P. yoelli—are presently being studied for the creation of a plant-based malaria vaccine.[36].

5.3. Hepatitis B

Mice were used to assess the generation of antibodies after HBs Ag was produced in transgenic potato plants.[37]. A crucial consideration in the development and administration of vaccines, as well as when introducing new raw animals given HBsAg potatoes elicited a primary immune response; after a few weeks, booster vaccination administered by the parent route resulted in a quick recall response that lasted for at least 150 days.[38]. By administering a single sub-immunogenic parenteral dosage of yeast-derived recombinant HBsAg to mice and then oral transgenic potatoes, the prime boost technique produced antibodies that peaked at >1,000 mIU/mL right away and remained at >200 mIU/mL for five months.[39].

5.4 Cancer

To target doxorubicin for lung, colon, ovarian, and breast cancers, soybeans have been genetically modified to produce monoclonal antibodies.[40]. It has been demonstrated that certain plants may effectively manufacture monoclonal antibodies, which are effective cancer treatment agents. Monoclonal body (BR-96), for instance, is a potent antidote for the medication doxorubicin, which causes lung cancer, breast cancer, ovarian cancer, and colon tumors.[41].

5.5 Diabetes

Globally, around 100 million people suffer with diabetes. Type I diabetes, sometimes referred to as juvenile-onset diabetes or insulin dependent diabetes mellitus (IDDM), typically affects children and young adults and makes up 5–10% of all diabetes diagnoses in North America. The findings were interesting: whereas 70% of mice who were not treated acquired diabetes, only 20% of pre-diabetic mice fed transgenic plants did.[42].

5.6 HIV

There has been some initial success splicing the HIV protein into CPMV.[43]. The expression of the Tat protein has recently been effectively injected into TMV from spinach. Up to 300–500 µg of Tat antigen were found in per gram of spinach leaf tissue.[44].

VI. CONCLUSION

Edible vaccines offer a safe, cost-effective, and needle-free alternative to conventional vaccines, with the potential to address global health challenges. While issues like low antigen yield and standardization remain, advances in plant biotechnology are steadily overcoming these barriers, making edible vaccines a promising tool for future immunization programs, especially in developing regions.

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