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Edible Vaccines: A Revolutionary Approach to Immunization

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Abstract

Edible vaccines represent an innovative method in immunization, using genetically engineered plants to produce antigenic proteins that act as vaccines when consumed. This process involves inserting specific genes encoding vaccine antigens into plants, which then synthesize these proteins in their edible parts, such as fruits or vegetables, making them suitable for oral administration. These vaccines offer the benefit of inducing both mucosal and systemic immunity by interacting with the mucosa of the digestive tract. Here, antigens are absorbed by specialized cells within the gut-associated lymphoid tissue. The use of transmucosal carriers improves the efficiency of antigen delivery, and bioencapsulation within plant cells protects antigens from degradation in the digestive system. This ensures their stability and effectiveness even after extended storage at room temperature. Edible vaccines have the potential to offer a needle-free, cost-effective, and accessible alternative to traditional vaccines, overcoming challenges such as the need for cold storage and limited shelf life.

Key words: Edible Vaccines, Gene Transformation, Immunization, Genetically engineered plants

Introduction:

Edible vaccines are a type of medication consumed as food by humans and animals to enhance their immune system (Mor et al., 1998). Essentially, these vaccines are derived from transgenic plants and animals that produce agents capable of triggering an immune response. Various plants have been identified and studied for their potential as edible vaccines, with some being genetically modified to express antigens for diseases such as rotavirus, gastroenteritis, cholera, autoimmune disorders, and rabies. Although potatoes have been frequently used in these experiments, they may not be the best option for edible vaccines, as cooking methods like frying or boiling can degrade some antigenic proteins. Foods like bananas, tomatoes, carrots, peanuts, corn, and tobacco show more promise as edible vaccines since they can be eaten raw and are widely available. Additionally, these plants are well-suited for genetic engineering (Sahoo et al., 2020). The vaccine components in these foods work by activating the body's immune system to recognize, destroy, or prevent attacks from pathogens like viruses, bacteria, fungi, or other foreign invaders (Rajangamet al., 2018). Vaccines play a vital role in preventing both infectious and non-infectious diseases.

Production of edible vaccines:

Edible vaccines can be produced by introducing a transgene into the chosen plant cells.The integration of the transgene can be done without combining with vector by direct gene delivery method or by combining with the vector by indirect gene delivery method. The transgene can be expressed in the plants by two transformation system depending on the site where antigen should be merged with the cells stable transformation and transient transformation system. (Chen and lai; 2015).

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Vector mediated gene transfer:

It includes agro bacterium mediated gene transformation and genetically engineered plant viruses.

Agro bacterium mediated gene transformation

DNA is introduced into the T-region of a disarmed Ti-plasmid of Agrobacterium tumefaciens (a plant pathogen), which is then co-cultured with the plant cells and/or tissue targeted for transformation. The integration of exogenous genes and the infection of the plant tissue with the modified Agrobacterium T-DNA has been has been essential forstudying stable gene incorporation into the plant genome, as well as in the production of transgenic proteins (Jan et al., 2016). Although this technique is relatively slow and yields can be low, it was initially applied to tobacco plants and a few other species. Over time, its use has expanded to include most vegetable species, including those in the Leguminosae and Gramineae families (Sahoo et al., 2020).

Chimeric virus method

Plant viruses are genetically engineered to carry specific genes and are then used to infect their natural hosts, such as edible plants, where these cloned genes are expressed to varying extents in different edible parts of the plant. Some viruses can be modified to display fragments of antigenic proteins on their surfaces, including cowpea mosaic virus, alfalfa mosaic virus, tobacco mosaic virus, cauliflower mosaic virus (CaMV), potato virus, and tomato bushy stunt virus (Hafiz and Eyob, 2015).

Direct Gene Delivery Method

Direct gene delivery is the simple method. In this the selected DNA or RNA is directly introduced in to the plant cell.

Direct gene delivery method

The most widely used direct gene delivery method is the biolistic method, also known as the gene gun or micro-projectile bombardment method. This technique is vector-independent and is typically employed when gene transfer via Agrobacterium-mediated transformation is not feasible. In this process, DNA or RNA is coated with gold or tungsten, which serves as a micro-carrier. The coated DNA is then loaded into a gene gun and subjected to high-pressure helium gas. The resulting pressure propels the coated DNA, allowing it to penetrate the targeted plant cells. Although effective, this method is costly and can cause damage to the plant. Biolistic methods can be used for both nuclear and chloroplast transformation. Nuclear transformation involves incorporating the desired gene into the plant cell's nucleus through non-homologous recombination, while chloroplast transformation involves injecting the gene into the chloroplast to enhance protein expression. Among these, chloroplast transformation is the most commonly adopted method for producing edible vaccines (Kurup et al., 2020). Examples of vaccines produced using biolistic methods include those for cholera, Lyme disease, anthrax, tetanus, plague, rotavirus, and canine parvovirus (Wu et al., 2003).

Electroporation method

DNA is introduced into cells by briefly exposing them to a high-voltage electrical pulse, which is believed to create temporary pores in the plasmalemma (a thin layer of tissue covering the cell surface). Since the cell wall acts as an effective barrier to DNA, it must first be weakened by enzymatic treatment to allow the DNA to enter the cell (Hafiz and Eyob, 2015).

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Mechanism of edible vaccine:

The primary drawback of oral vaccination is the digestion of macromolecule antigenic proteins in the stomach due to its highly acidic pH. However, edible parts of plants can be consumed directly, as the robust outer wall of plant cells protects the antigens from being degraded by stomach enzymes and secretions. This protective mechanism is known as bioencapsulation (Hirlekar and Bhairy, 2017). The plant cell membrane breaks down in the intestine, releasing the antigens (Lössl and Waheed, 2011).

These antigens are then taken up by M cells, specialized epithelial cells in the gastrointestinal tract with a high capacity for transcytosis of various microbes and macromolecules. M cells are located over Peyer's patches (PPs), which are clusters of lymphatic nodules, also known as aggregated lymphatic follicles. PPs are rich sources of secretory immunoglobulin A (IgA), which generates plasma cells capable of populating mucosal tissues and serving as mucosal immune effector sites. The breakdown of edible vaccines (EVs) near PPs leads to antigenic stimulation of the follicles and the development of the germinal center. The antigen penetrates these follicles into the intestinal epithelium and accumulates within organized lymphoid tissues (Aggani, 2013).

The immune system, composed of B cells, T cells, and macrophages, is concentrated in these lymphoid follicles. M cells, which express class II major histocompatibility complex molecules, transport antigens across the mucous membrane, thereby activating B cells within the lymphoid follicles. Once activated, B cells leave the follicles, migrate to diffuse mucosa-associated lymphoid tissues, and differentiate into plasma cells that secrete serum IgG, IgE, local IgA, and generate memory cells. These memory cells can neutralize subsequent attacks by the original infectious agent in the body. Additionally, administering EVs to mothers could potentially immunize the foetus in utero through transplacental transport of maternal antibodies, or the infant through breast milk (Takahashi et al., 2010; Streatfield, 2006; De Aizpurua and Russell-Jones, 1988).

Applications:

Edible vaccines are being developed for the prevention of various diseases, including malaria, measles, hepatitis B, cholera, E. coli infections, HIV, and anthrax, making them a versatile tool in public health. They utilize oral immunization, which is more accessible and less intimidating than traditional methods, and benefit from the protective nature of plant cell walls that allow vaccine proteins to survive stomach acidity and reach the intestine. Transgenic plants, such as genetically modified potatoes and tobacco, have been shown to effectively express vaccine proteins, with studies indicating that cooking does not significantly inactivate these proteins, ensuring their stability. Ongoing clinical trials are crucial for assessing the safety and efficacy of these vaccines, paving the way for their practical application in immunization programs, particularly in developing countries (Hirlekar andBhairy, 2017).

Conclusion:

Edible vaccines (EVs) are a promising advancement in immunization, particularly for developing countries, due to their low cost and ease of production. They can be cultivated locally, enhancing accessibility and reducing the need for cold storage, which is a significant barrier for traditional vaccines. The successful implementation of EVs depends on addressing socio-cultural acceptance, environmental safety, and the stability of genetically modified plants. Overall, EVs have the potential to improve public health outcomes by providing safer and

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more effective vaccination strategies in regions that need them most.

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