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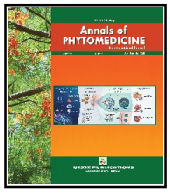

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Vegetables as edible vaccines: A next-generation approach to immunization

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Abstract

Edible vaccines are an emerging strategy for improving global immunization by harnessing genetically engineered vegetables to deliver antigenic proteins through oral consumption. This approach offers significant advantages over conventional vaccines, including low production cost, ease of distribution without cold-chain requirements and needle-free administration, making it especially suitable for mass immunization in resource-limited scenarios. Vegetables such as tomatoes, lettuce, carrots and spinach have shown promise as ideal host systems due to their short growth cycles, wide consumer acceptance and potential for raw consumption. Despite their potential, key challenges remain, including dose standardization, antigen stability, regulatory clearance and public awareness. This review explores the development, benefits and challenges of vegetable-based edible vaccines and highlights their role as a sustainable, accessible platform for future immunization programs.

1. Introduction

According to the World Health Organization (WHO, 2025), vaccines are biological preparations that stimulate the immune system to recognize and combat specific pathogenic microorganisms, thereby providing immunity against infectious diseases. Traditional vaccines are produced through labour-intensive processes involving fermentation, purification, cold storage, transportation and sterile delivery systems, which make them expensive and difficult to access for populations in developing countries (Koul, 2022). These challenges have driven the search for alternative, cost-effective and easily distributable immunization strategies.

One of the most promising approaches is the development of edible plant-based vaccines, in which antigenic genes from pathogens are introduced into the plant genome, enabling plants to produce the target antigens. Consumption of the edible parts of these plants can induce a protective immune response in humans (Athulya and Vethamoni, 2018). Unlike conventional vaccines, edible vaccines are needle-free, reducing the need for trained medical personnel and eliminating the costs associated with purification, refrigeration and complex delivery systems (Daniell *et al*., 2016).

Vegetable crops are ideal candidates for edible vaccine production, as they preserve antigen integrity (Tiwari *et al*., 2009; Concha *et al*., 2017). Commonly studied vegetable hosts include tomato, potato, carrot, lettuce, spinach, and cabbage, all of which can be genetically engineered using *Agrobacterium*-mediated transformation or chloroplast transformation techniques to express antigens at high levels in edible tissues (Ma *et al*., 2003; Saxena and Rawat, 2014). The use of vegetables not only ensures scalability and affordability but also supports localized production, reducing dependence on centralized manufacturing and cold-chain logistics.

After COVID-19, the urgency to develop rapid, affordable immunization tools accelerated plant-based vaccine research. Unlike centralized biopharmaceutical production, vegetable crops can serve as regional "biofactories", enhancing vaccine sovereignty in developing nations (Shah *et al*., 2024). Furthermore, their use in producing monoclonal antibodies and therapeutic proteins expands their role beyond prophylaxis.

2. History

Hiatt *et al*. (1989) were the first to introduce the concept of producing antibodies in plants for passive immunization. The earliest report of an edible vaccine, a *Streptococcus* surface protein expressed in tobacco was documented in a 1990 patent application. Building on this foundation, Dr. Charles Arntzen proposed the use of transgenic plants as production and delivery systems for subunit vaccines (Arntzen, 1997). During the early 1990s, several antigens, including *Streptococcus* mutans antigen A, hepatitis B surface antigen (HBsAg) and the heat-labile toxin B subunit (LT-B) of enterotoxigenic *Escherichia coli* (ETEC), were successfully expressed in tobacco and potato plants (Mason *et al*., 1992). Subsequent research demonstrated that plant-derived HBsAg could elicit mucosal immune responses upon oral consumption, with optimized antigen accumulation achieved in potato tubers (Richter *et al*., 2000).

A breakthrough in edible vaccine research was achieved with the first human clinical trials using transgenic potatoes expressing the LT-B antigen, which confirmed that orally administered, plant-derived

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vaccines are both safe and capable of inducing systemic and mucosal immune responses (Tacket *et al*., 1998). In the same year, researchers supported by the National Institute of Allergy and Infectious Diseases (NIAID) provided the first evidence that edible vaccines could safely stimulate strong immune responses in humans, highlighting their potential to reduce the prevalence of infectious diseases such as hepatitis and diarrhoea, particularly in resource-limited regions. Since then, advancements in plant biotechnology such as chloroplast transformation and the use of viral vectors have substantially increased antigen yield and stability, strengthening the promise of edible vaccines as a cost-effective and needle-free immunization approach (Daniell *et al*., 2001).

Between 2010 and 2024, new milestones included chloroplast-based expression of SARS-CoV-2 antigens in tomato and lettuce (Buriev *et al*., 2024), lyophilization for antigen stability (Rosales-Mendoza and Márquez-Escalante, 2023), and multi-antigen vaccines targeting cholera and ETEC (Kumari *et al*., 2021). These advancements demonstrated not only safety but also long-term shelf stability under ambient storage.

3. Standards for edible vaccines

In addition to their historical development, edible vaccines must meet specific standards to ensure safety, efficacy, and practicality (Table 1).

Table 1: Key standards for the development and deployment of edible vaccines

Standard	Description	References
Safety	Vaccine must be non-toxic, non-allergenic and free from contaminants such as pesticides or pathogens	Arntzen, 1997; Daniell *et al*., 2001
Immunogenicity	Plant-expressed antigens must elicit strong systemic and mucosal immune responses.	Mor and Arntzen, 1998; Tacket *et al*., 2000
Consistency and dose control	Each edible unit should contain a consistent and effective antigen dose	Daniell *et al*., 2001
Stability	Antigens must remain stable during storage, handling and processing (*e.g*., cooking or freezing)	Daniell *et al*., 2001
Genetic containment	Transgenes must be stable, with measures to prevent unintended spread to other crops or wild plants.	Arntzen, 1997
Scalability and reproducibility	Production should allow large-scale cultivation while maintaining consistent antigen expression.	Arntzen, 1997; Daniell *et al*., 2001
Regulatory compliance	Must meet guidelines from regulatory agencies (WHO, FDA and EMA) for clinical trials, biosafety and environmental release	Mor and Arntzen, 1998
Antigen bioavailability and post-harvest stability	Antigen must remain active through maturation, storage and minimal processing (*e.g*., freeze-drying). Encapsulation within cell walls or starch granules can improve oral uptake.	Rosales-Mendoza and Márquez-Escalante., 2023; Shah *et al*., 2024

4. Ideal characteristics of a host plant for edible vaccine production

- **Wide consumption and acceptability:** The plant should be commonly consumed, palatable and culturally acceptable to encourage compliance without requiring extensive processing (Koul, 2022).
- **Ease of genetic transformation:** It should be amenable to stable genetic transformation with minimal risk of transgene silencing, rearrangement or instability (Tiwari *et al*., 2009).
- **High biomass and rapid growth:** Fast-growing plants with high yield potential are preferred to ensure large-scale and cost-effective production (Daniell *et al*., 2016).
- **High antigen expression:** The host should allow accumulation of the antigen at high levels, ideally in edible tissues such as fruits, tubers or leaves, ensuring an effective immune response.
- **Antigen stability:** The expressed antigen must remain stable during storage and distribution, ideally without requiring a cold chain (Ma *et al*., 2003).
- **Tissue-specific expression:** The system should support organ or tissue-specific promoters to localize antigen production in edible parts, reducing metabolic load on the plant.
- **Stress resistance:** Tolerance to biotic (pests, diseases) and abiotic (drought, salinity and temperature) stresses is crucial for consistent field-level production (Concha *et al*., 2017).
- **Short generation time:** Rapid life cycle facilitates quick scaling up of production and generation of successive transgenic lines (Daniell *et al*., 2016).

- **Biosafety considerations:** Self-pollinating crops are preferred over cross-pollinating ones to minimize transgene escape and ensure gene containment (Daniell *et al*., 2016).
- **Safety for consumption:** The host plant must be non-toxic, non-allergenic, and meet regulatory and biosafety guidelines for genetically modified crops (Saxena and Rawat, 2014).

5. Methods of edible vaccine production

Edible vaccines, similar to conventional subunit vaccines, contain antigenic proteins but lack pathogenic genes, ensuring their safety for human consumption. However, they may not completely prevent disease transmission and may pose risks to immunocompromised individuals (Koul, 2022; Sahai *et al*., 2013). The development of these vaccines through genetic engineering involves isolating the gene encoding the antigenic protein from the pathogen, incorporating it into a safe gene vector and integrating it into the plant genome to enable expression of the desired antigen (Concha *et al*., 2017; Esmael and Hirpa, 2015). This process demands meticulous design of the gene construct, including the selection of an appropriate promoter, transit peptide, coding region and selectable marker along with insertion sequences. Additional considerations include codon optimization, adjustment of GC content, elimination of cryptic splicing and premature transcription termination sites, removal of mRNA instability sequences and incorporation of 5' and 3' regulatory elements to ensure efficient gene expression (Glick and Patten, 2022 and Ma *et al*., 2003).

Several transformation techniques, such as the biolistic (gene gun) method, chimeric virus-mediated transformation, electroporation, and *Agrobacterium tumefaciens*-mediated transformation, have been effectively employed to develop edible vaccines (Saxena and Rawat, 2014) (Figure 1).

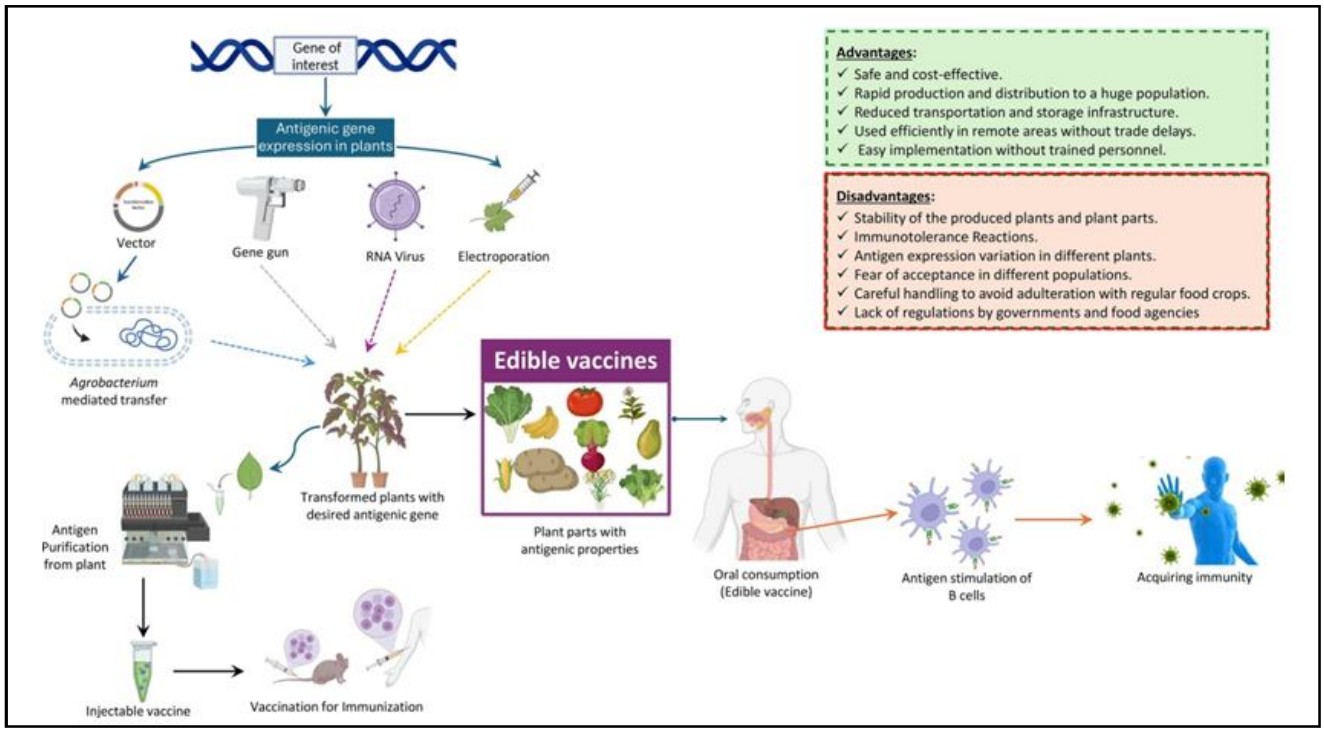

Figure 1: Concept of an edible vaccine (Pudhuvai *et al*., 2025).

5.1 *Agrobacterium*-mediated nuclear transformation

A. mediated nuclear transformation has been widely employed for developing edible vaccines in various vegetable crops, owing to its high efficiency in integrating foreign genes into the plant nuclear genome and producing stable, heritable transgenic lines. Among the first vegetable crops to be transformed was potato (*Solanum tuberosum*). Arakawa *et al*. (1997) successfully expressed the *E. coli* heat-labile toxin B subunit (LTB) in transgenic potatoes, demonstrating its immunogenicity in mice following oral administration. This strategy was further validated in a landmark human clinical trial, where volunteers consumed transgenic potato tubers expressing the Norwalk virus capsid protein (NVCP), resulting in significant serum IgG and mucosal IgA immune responses (Tacket *et al*., 2000)

Tomato (*Solanum lycopersicum*) has been utilized as a host plant for expressing the Norwalk virus capsid protein (NVCP), where oral administration of transgenic fruits successfully induced both systemic and mucosal immune responses in animal models (Huang *et al*., 2005). Similarly, cucumber (*Cucumis sativus*) has been genetically engineered through *A.* mediated nuclear transformation to express the hepatitis B surface antigen (HBsAg) in its fruits and leaves, providing a cost-effective platform for large-scale oral vaccine production (Soria-Guerra *et al*., 2011). Root crops such as carrot (*Dacus carota*) have also been transformed to express HBsAg, with antigen accumulation in taproots confirmed by ELISA, demonstrating their potential use in oral immunization (Rosales-Mendoza *et al.,* 2008). Moreover, leafy vegetables like lettuce (*Lactuca sativa*) have been engineered to produce Measles virus hemagglutinin (MV-H) and feeding fresh transgenic leaves to mice resulted in the production of neutralizing antibodies, underscoring their promise as efficient plant-based vaccine

delivery systems. Collectively, these studies highlight the versatility of *A*. mediated nuclear transformation across diverse vegetable crops and its immense potential for developing affordable, orally deliverable vaccines.

5.2 Biolistic transformation

Biolistic transformation, commonly known as the gene gun method, is a direct DNA-delivery technique in which DNA-coated microscopic particles (typically gold or tungsten) are physically propelled into plant cells. Unlike *A*. mediated transformation, this approach bypasses the need for bacterial vectors and is particularly useful for species that are recalcitrant to Agrobacterium infection. This technique has been successfully applied to develop several edible vaccine candidates. For instance, Kapusta *et al*. (1999) reported the expression of hepatitis B surface antigen (HBsAg) in carrot (*D. carota*), while Levengood *et al*. (2024) highlighted its application in producing experimental vaccines against Lyme disease, anthrax, tetanus, plague, rotavirus, cholera and canine parvovirus.

Mason *et al*. (1998) demonstrated that potato (*Solanum tuberosum*) transformed with the *E. coli* heat-labile enterotoxin B subunit (LT-B) gene *via* biolistic transformation produced immunogenic LT-B, which successfully induced both mucosal and systemic immune responses in mice following oral administration. Similarly, Yan *et al*. (2009) reported the transformation of carrot with the human papillomavirus (HPV) E7 antigen, which triggered a cytotoxic T-cell response in animal models. Moreover, leafy vegetables such as spinach (*Spinacia oleracea*) and lettuce (*L. sativa*) have been explored for biolistic expression of HBsAg, achieving promising levels of antigen accumulation (Muthamilselvan *et al*., 2016). Despite these successes, the method still faces challenges, including low transformation efficiency, random DNA integration and variable expression levels across transformants.

5.3 Chloroplast transformation

Chloroplast transformation is an advanced genetic engineering strategy in which foreign genes are integrated into the plastid genome rather than the nuclear genome. This approach offers several unique advantages over conventional nuclear transformation techniques, including exceptionally high transgene expression levels (up to 40% of total soluble protein), maternal inheritance that minimizes the risk of transgene escape through pollen and the ability to stack multiple genes through polycistronic expression (Daniell *et al*., 2016). These features make chloroplast transformation an attractive platform for the production of edible vaccines in plants.

One of the earliest and most notable examples is the expression of the cholera toxin B subunit (CTB) in transplastomic lettuce (*L. sativa*), which resulted in high antigen accumulation and induced strong mucosal and systemic immune responses in animal models (Daniell *et al*., 2001; Ruhlman *et al*., 2007). Similarly, lettuce has been used to express the *E. coli* heat-labile enterotoxin B subunit (LT-B) in chloroplasts, with the antigen shown to remain stable and immunogenic following oral delivery (Davoodi-Semiromi *et al*., 2010). It has also been used to express hepatitis B surface antigen (HBsAg) and malaria antigens in leafy vegetables, achieving encouraging expression levels and positioning these crops as promising candidates for cost-effective, orally delivered vaccine systems (Daniell *et al*., 2009). Overall, chloroplast genetic engineering represents a powerful and scalable technology for developing next-generation edible vaccines.

6. Gene transfer in the environment and containment strategies for edible vaccines

The release of genetically modified (GM) crops, including those developed as edible vaccines, raises concerns regarding the unintended flow of transgenes into the broader environment. Gene escape can occur through pollen dispersal, seed contamination or horizontal gene transfer, potentially affecting wild relatives, non-target crops, or ecosystems. To mitigate these risks, several containment strategies have been developed, which broadly fall into two categories: physical isolation and genetic containment.

6.1 Physical isolation

Physical isolation involves spatial, temporal, and agronomic measures to minimize cross-pollination and transgene escape. GM crops are cultivated in isolated areas, often away from sexually compatible wild relatives or conventional crops, and both small- and large-scale field trials are conducted under controlled environments (James, 2013). Greenhouse cultivation and contained growth facilities can further restrict gene flow. Additional measures include leaving surrounding fields fallow after GM crop cultivation to prevent volunteer plants from establishing in subsequent cycles. While effective, physical isolation is resource-intensive and requires consistent management at every stage of production to ensure biosafety (Lu and Snow. 2005; James, 2013).

6.2 Genetic containment

Genetic containment strategies aim to reduce the biological potential of GM crops to spread their transgenes. Various technological approaches include:

- **Male sterility or incompatibility systems:** Utilize natural or engineered infertility to limit pollen-mediated gene flow (Arntzen, 2005).
- **Genetic use restriction technologies (GURTs):** Control fertility or seed development to prevent transgene propagation.
- **Chloroplast transformation:** Targeting foreign genes to the chloroplast genome ensures maternal inheritance, as chloroplast DNA is typically not transmitted *via* pollen, effectively reducing the risk of transgene escape.
- **Use of non-food or contained crops:** Edible vaccine production in non-food crops like tobacco reduces the likelihood of accidental entry into the food chain, and recombinant biopharmaceutical crops are often required to meet GRAS (generally recognized as safe) status.

6.3 Integration of containment measures

A combination of physical and genetic containment approaches is recommended to achieve maximal biosafety. Proper agronomic practices, including site selection, crop rotation, and monitoring, are crucial in preventing environmental gene transfer. Chloroplast transformation, in particular, has emerged as a promising method for producing edible vaccines with minimal ecological risk.

Table 2: Edible vaccines developed in vegetables: Antigen targets and applications

S.No.	Vegetable	Antigen/vaccine-target	Disease	Description	References
1	Tomato	Hepatitis B surface antigen (*HBsAg*)	Hepatitis B	The *HBsAg* gene was isolated, cloned, and introduced into tomato (*S. lycopersicum*) plants *via A.* mediated transformation. This study represents the first effort in this region to develop *S. lycopersicum* as a potential edible vaccine platform against the Hepatitis B virus.	Inam *et al*., 2022
2	Tomato (TOMAVAC)	S1 protein of SARS-CoV-2	COVID-19	Transgenic tomato expressing~0.77 µg/g SI antigen. In humans, feeding ~38.5 µg/day of antigen for 3 days resulted in a weekly increase in serum Nabs (~1.2-fold per week) with no severe side effects.	Buriev *et al*., 2024
3	Tomato	CTB	Cholera	Antigen expression level was 0.3% of the total soluble protein.	Jiang *et al*., 2007
4	Tomato	Rabies nucleoprotein (RNP)	Rabies	Antigen expression level was 0.2% of the total soluble protein.	Perea Arango *et al*., 2008
5	Tomato	Human β-amyloid (Aβ)	Alzheimer's	-	Youm *et al*., 2008
6	Tomato	RSVF protein	Serious respiratory tract disease	Antigen expression level was 0.3% of the total soluble protein.	Sandhu *et al*., 2000
7	Potato	HBsAg	Hepatitis B	Transgenic potato tubers expressing approximately ~8.5 µg/g *HBsAg* induced an elevated anti-*HBsAg* antibody response in about 50-60% of the volunteers who consumed them.	Thanavala *et al*., 2005
8	Potato	Major capsid protein VP6	Viral diarrhea	Antigen expression levels in transformed potatoes were 0.1% of the total soluble protein.	Matsumura *et al*., 2002
9	Lettuce	HBsAg	Hepatitis B	Lettuce plants transformed *via A.* mediated expression of the hepatitis B surface antigen (HBsAg) showed confirmed antigen presence in seedlings, demonstrating the potential of lettuce as a viable vehicle for HBsAg delivery.	Marcondes and Hansen 2008
10	Lettuce	CTB/CTB fusion (*e.g.*, CTB-COE	Cholera/porcine epidemic diarrhoeavirus epitope	Transgenic lettuce expressing the CTB-COE fusion protein successfully produced correctly folded, pentameric antigens with GM1-binding activity, confirming biological functionality. This system shows promise as an edible vaccine platform against porcine epidemic diarrhoeavirus, pending immunogenicity testing in animal models.	Huy *et al*., 2011
11	Lettuce	CT-B Protein	SARS-CoV-2	Antigen expression level was 0.01% of the total soluble protein	Singh *et al*., 2023
12	Lettuce	Norwalk virus capsid protein (NVCP)	Viral gastroenteritis	Transgenic lettuce induced mucosal *IgA* response in preclinical trials.	Kim *et al*., 2023
13	Pea	Emogglutinin protein (H)		-	Satyavathi *et al*., 2003
14	Spinach	Cholera toxin B subunit (CTB) fused with COE epitope (sCTB-Scoe)	Porcine epidemic diarrhoea (PED)	Spinach was used as a plant-based expression system for sCTB-sCOE fusion protein. Oral administration induced strong systemic and mucosal immune responses in mice.	Chung *et al*., 2016
15	Spinach	*Bacillus anthracis* protective antigen (PA)	Anthrax	Chloroplast-transformed spinach expressing the PA antigen successfully induced protective immunity in mice following oral immunization	Koya *et al*., 2005
16	Carrot	Hepatitis B surface antigen (HBsAg)	Hepatitis B	Transgenic carrot root cultures expressing HBsAg elicited the production of HBsAg-specific antibodies upon oral immunization.	Rosales-Mendoza *et al*., 2008
17	Carrot	*E. coli* heat-labile toxin B subunit (LTB)	Traveller's diarrhoea	Transgenic carrot suspension cultures expressed functional LTB with GM1-ganglioside binding activity; oral delivery induced an immune response.	Tiwari *et al*., 2009
18	Carrot	MV-H	Measles virus	-	Marquet-Blouin *et al*., 2003
19	Cucumber	Hepatitis B surface antigen (HBsAg)	Hepatitis B	Transgenic cucumber fruits and leaves expressed HBsAg, offering a low-cost platform for oral immunization.	Soria-Guerra *et al*., 2011

7. Current status and examples of edible vaccines in vegetable crops

Research on edible vaccines in vegetable crops is progressing rapidly, with several successful examples at laboratory and early clinical trial stages. The table below summarizes key examples (Table 2).

8. Mode of action

Edible vaccines are genetically engineered plant-derived antigens that stimulate an immune response upon oral consumption. Unlike conventional vaccines, which are administered by injection, edible vaccines are delivered *via* edible plant tissues, such as fruits and leaves, which serve as both carriers and protectants for the antigenic proteins. The primary mechanism of action involves interaction with the gut-associated lymphoid tissue (GALT), initiating both mucosal and systemic immunity (Arntzen, 2005; Tacket, 2004).

After ingestion, the plant cell wall safeguards the antigen from degradation in the stomach's acidic environment, enabling it to reach the small intestine essentially intact. In the intestine, specialized epithelial microfold (M) cells facilitate the transport of the antigen to underlying antigen-presenting cells (APCs), such as dendritic cells and macrophages. These APCs process the antigen and display it on major histocompatibility complex (MHC) molecules to T helper cells, which in turn stimulate B lymphocytes to differentiate into plasma cells. The resulting plasma cells secrete antigen-specific immunoglobulin A (IgA) into the mucosal lining, conferring localized immunity and immunoglobulin G (IgG) into the bloodstream, ensuring systemic protection (Ruhlman *et al*., 2010).

A critical advantage of edible vaccines is their ability to induce immunological memory, enabling the host to mount a rapid, robust response upon subsequent exposure to the pathogen. Moreover, oral delivery mimics the natural route of infection for many pathogens, thereby enhancing the effectiveness of the mucosal immune response. Edible vaccines are considered safe, cost-effective and suitable for mass immunization, particularly in resource-limited regions, since they do not require needles or cold chain storage (Daniell *et al*., 2001; Arntzen, 2005).

Recent studies show that edible vaccines can fine-tune Th1/Th2 balance, promoting mucosal tolerance while reducing allergenicity. Co-expression of mucosal adjuvants, such as CTB or LTB, enhances antigen uptake and IgA secretion, thereby strengthening both mucosal and systemic immunity (Daniell *et al*., 2023).

9. Advantages of edible vaccines

Edible vaccines offer multiple advantages over conventional vaccines, combining biological efficacy with economic and logistical benefits.

- **Efficient immunization:** Plant-derived vaccines elicit both systemic and mucosal immune responses without requiring adjuvants as the antigens expressed in plant tissues are naturally taken up by gut-associated lymphoid tissue (Daniell *et al*., 2023).
- **Mucosal and systemic protection:** Oral administration induces secretory IgA antibodies at mucosal sites, providing a first line of defence against pathogens entering *via* the gastrointestinal or respiratory tracts.
- **Cost-effective and cold-chain-free:** Edible vaccines are thermally stable and do not require refrigeration, sterile injections or trained personnel, reducing production and distribution costs in developing regions.
- **Long shelf life and stability:** Seeds, tubers or dried plant tissues with low moisture content allow long term antigen preservation even under ambient conditions.
- **Simple and scalable production:** Vaccine antigens can be produced through normal agricultural practices without fermenters or bioreactors, enabling large-scale and low-cost cultivation.
- **Safe and widely acceptable:** These vaccines do not involve live or attenuated pathogens, eliminating reversion risk and contamination concerns. Oral delivery increases compliance, especially among children.
- **Multivalent and next-generation potential:** Transgenic plants can express multiple antigens or molecular adjuvants simultaneously enabling multivalent and second generation vaccines.
- **Rapid scalability:** Established transgenic lines can be quickly propagated through seed multiplication or breeding ensuring fast vaccine production during outbreaks (Daniell *et al*., 2023).

10. Limitations of edible vaccines

- **Dosage standardization issues:** Variation in antigen expression between plants or plant parts makes precise dose delivery difficult (Khan, 2023).
- **Antigen degradation:** Heat-labile antigens may lose activity during cooking or processing (Tiwari *et al*., 2009).
- **Regulatory and biosafety concerns:** Approval of genetically modified (GM) crops is time-consuming and faces public resistance (Saxena and Rawat, 2014).
- **Risk for immunocompromised individuals:** May not be suitable for people with compromised immune systems or dietary restrictions (Sahai *et al*., 2013).
- **Gene containment challenges:** Potential risk of transgene escape through pollen flow to non-GM crops (Daniell *et al*., 2016).
- **Limited clinical validation:** Few human clinical trials have been conducted, and long-term efficacy and safety need further evaluation (Khan, 2023).
- **Public acceptance and ethical issues**: Consumer hesitation toward GM foods continues to limit commercialization. Transparent labelling, biosafety communication, and participatory policy frameworks are needed to increase public confidence (Koul, 2022; Rosales-Mendoza *et al*., 2023).

11. Regulatory and ethical considerations

Edible vaccines face dual oversight as both food and pharmaceutical products. Global regulatory agencies (FDA, EMA and GEAC) require assessment of allergenicity, gene flow and pharmacokinetics before approval (WHO, 2025). Ethical issues include equitable access, intellectual-property management and avoiding monopolization of genetic resources. Harmonized global regulations and public-sector initiatives are essential to ensure safe and affordable deployment.

12. Future prospects

With advances in molecular biology, genome editing, and plant biotechnology, edible vaccines are likely to become more precise, safe and widely accepted. Research is ongoing to enhance antigen expression levels, improve dosage control and develop multi-antigen vaccines targeting multiple diseases. Integration with nanotechnology and controlled-release systems may further improve their effectiveness. If these challenges are addressed, vegetables as edible vaccines could revolutionize global immunization programs, making vaccination more accessible, affordable and acceptable.

13. Conclusion

Vegetables as edible vaccines represent a revolutionary approach to global immunization efforts, especially in resource-limited regions. By providing a low-cost, needle-free, and easily distributable vaccine option, they have the potential to bridge the global vaccination coverage gap. Although challenges such as dosage consistency, biosafety and regulatory approvals must be addressed, rapid advancements in biotechnology offer hope that edible vaccines will soon become a mainstream immunization strategy. If combined with supportive policies and transparent communication, vegetable-based edible vaccines can emerge as transformative tools for equitable global health, bridging immunization gaps where conventional vaccines remain inaccessible.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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