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## Review Article

# Edible Vaccines: A Comprehensive Review of Biotechnology, Production and Potential in Disease Prevention

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## ABSTRACT

Edible vaccines represent an innovative and promising development in biotechnology, employing genetically altered plants to generate antigenic proteins that can trigger immunity against infectious diseases. This method involves inserting genes that encode specific antigens into consumable plants like potatoes, bananas, tomatoes, rice, maize, lettuce, and soybeans. These genetically modified plants produce vaccine proteins that, when ingested, activate both mucosal and systemic immune responses. Edible vaccines have demonstrated potential in combating diseases such as hepatitis B, cholera, measles, diarrhea, malaria, HIV, anthrax, and infections caused by enterotoxigenic *Escherichia coli*. Compared to traditional vaccines, they offer numerous benefits, including lower production costs, needle-free delivery, ease of storage and transport, enhanced patient compliance, and decreased reliance on cold-chain logistics, making them particularly advantageous for developing nations. Additionally, plant-based vaccine production reduces contamination risks linked to animal-derived products and facilitates large-scale production through agricultural methods. Recent progress in genetic engineering, molecular biology, and transgenic plant technology has greatly enhanced the expression of antigens, their stability, and the effectiveness of vaccines. Despite these advancements, issues such as variable dosage, low antigen production, environmental impacts, public acceptance of genetically modified crops, and regulatory hurdles still restrict their commercial use. Presently, research is directed towards enhancing vaccine delivery, stability, and mass production through cutting-edge biotechnological and nanotechnology-based methods. In summary, edible vaccines offer a safe, cost-effective, and efficient alternative to conventional vaccination techniques and have considerable potential to improve global healthcare and disease.

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## INTRODUCTION

Edible vaccines represent a cutting-edge use of biotechnology, where genetically altered plants are employed to generate antigenic proteins that trigger immune responses against infectious diseases. Vaccination remains one of the most efficient strategies for managing infectious diseases and decreasing global mortality rates. Traditional vaccines are typically derived from attenuated or inactivated pathogens, purified antigens, or recombinant products, and are commonly delivered via injections. Despite their high efficacy, conventional vaccines face several drawbacks, including significant production expenses, reliance on refrigeration and cold-chain logistics, transportation challenges, contamination risks, issues related to needles, and restricted availability in developing nations. To address these issues, researchers have created edible vaccines by utilizing transgenic plants as biological production units. This approach involves inserting specific genes that code for desired antigens into consumable plants like potatoes, bananas, tomatoes, rice, maize, lettuce, soybeans, tobacco, and other crops. These genetically engineered plants produce antigenic proteins that, when ingested, activate both mucosal and systemic immune responses. Edible vaccines are deemed safer than many live vaccines because they express only specific antigenic proteins rather than the entire pathogen. Significant strides in molecular biology, plant tissue culture, genomics, proteomics, and genetic engineering have greatly advanced the creation of edible vaccines. These plant-derived vaccines have demonstrated encouraging outcomes against illnesses like hepatitis B, cholera, measles, HIV, malaria, diarrhea, anthrax, and infections caused by enterotoxigenic *Escherichia coli*. The benefits of edible vaccines include low production costs, needlefree administration, simple oral delivery,

the ability to store them long-term without refrigeration, a decreased risk of contamination, and their suitability for large-scale immunization efforts, particularly in remote and economically disadvantaged areas. Despite these advantages, challenges such as low antigen expression, inconsistent dosages, environmental issues, regulatory hurdles, and public acceptance of genetically modified crops persist. Nonetheless, edible vaccines offer a safe, cost-effective, and promising alternative to traditional vaccination methods, with significant potential to enhance global healthcare and disease prevention in the future.

## History of Edible Vaccines

Edible vaccines are vaccines produced in genetically modified plants where antigenic proteins are expressed in edible parts such as fruits, leaves, or tubers. The concept emerged to overcome limitations of conventional vaccines, including high cost, need for refrigeration, injections, and trained healthcare workers. These vaccines stimulate mucosal immunity through oral administration and are especially useful in developing countries. The first major breakthrough occurred in 1990 when researchers successfully expressed *Streptococcus mutans* surface antigen (SpaA) in transgenic tobacco plants, demonstrating antibody responses in experimental animals. Later, scientists developed transgenic plants expressing hepatitis B surface antigen (HBsAg) and heat-labile toxin B subunit (LT-B) of *Escherichia coli*. In 1998, the first human trial using genetically engineered potatoes carrying *E. coli* toxin antigen showed enhanced intestinal antibody production without major side effects, proving that edible vaccines could induce immune responses in humans. Researchers expanded edible vaccine technology using several plant species such as tobacco, potato, banana, tomato, rice,



lettuce, papaya, peanuts, and algae. Vaccines were developed against diseases including hepatitis B, cholera, diarrhea, rabies, tuberculosis, cysticercosis, measles, and rotavirus. Plant-based vaccines provided advantages such as low production cost, easy storage, needle-free administration, and improved accessibility. Several studies highlighted the importance of selecting safe antigens, optimizing expression levels in plants, evaluating storage stability, and determining proper dosage for complete immunization. Scientists also emphasized regulatory approval, public acceptance of genetically modified crops, and biosafety evaluation before large-scale use. Although still developing, edible vaccines are considered a promising biotechnology for global immunization programs. They offer a potential solution for improving vaccine availability and reducing infectious diseases, particularly in low-resource regions where traditional vaccination systems face logistical challenges.

### **Concept of Edible Vaccines**

Edible vaccines are produced by introducing selected antigen-encoding genes into plants through genetic engineering. These genetically modified or transgenic plants synthesize specific antigenic proteins that stimulate an immune response when consumed. Unlike conventional vaccines, edible vaccines do not contain pathogenic genes and therefore cannot cause infection. The vaccine antigen is usually expressed in the edible parts of plants such as banana, potato, tomato, rice, lettuce, and tobacco. The concept of edible vaccines was developed mainly by Charles Arntzen during the 1990s. The process involves transformation, where desired genes from viruses, bacteria, or parasites are inserted into plant cells. The plants then produce antigenic proteins, which act similarly to subunit vaccines. When the plant

material is eaten, these proteins activate both mucosal and systemic immunity by stimulating T-cells and B-cells in the digestive tract. This provides first-line defense against pathogens entering through mucosal surfaces. Edible vaccines offer several advantages over traditional injectable vaccines. They are cost-effective, easy to produce, and suitable for large-scale production. Since they are administered orally, they eliminate the need for needles, syringes, trained medical personnel, and reduce the risk of needle-associated infections. They also possess good genetic stability and heat stability, reducing dependence on cold-chain storage and transportation. Plant-based systems minimize contamination risks from animal pathogens because plant viruses do not infect humans. These vaccines are being investigated for protection against diseases such as cholera, hepatitis B, hepatitis C, hepatitis E, measles, rabies, foot-and-mouth disease, tuberculosis, diarrhea, HIV, respiratory infections, and dental caries. They may also help immunize infants through maternal antibody transfer during pregnancy or breastfeeding. Due to their safety, affordability, and ease of administration, edible vaccines have great potential for mass immunization programs, especially in developing countries. Although still under research and development, edible vaccines represent an innovative approach combining biotechnology, agriculture, and immunology for future disease prevention.

### **TYPES OF VACCINE**

Mainly types of vaccine

- A. Live attenuated (LAV): Tuberculosis, Oral polio vaccine, Measles, Rota virus, Yellow Fever
- B. Inactivated (killed antigen): Whole cell pertussis, inactivated polio virus, Hepatitis A



C. Subunit (purified antigen): Acellular pertussis (aP), Haemophilus influenzae type B (Hib), Pneumococcal (PCV-7, PCV-10, PCV-13), Hepatitis B (hepb)

D. Toxoid (inactivated toxins): Tetanus toxoid (TT), Diphtheria toxoidE. Viral vector vaccine: Zaire ebolaviruse

### **Advantages and Disadvantages of Edible Vaccines**

#### **ADVANTAGES:**

- 1) In comparison to traditional vaccines, edible vaccines do not require a complex framework for purification, sterilization, packaging, or distribution, resulting in lower long-term expenses.
- 2) Vaccine distribution and management are less difficult than with conventional vaccines.
- 3) Conception of a raw material is another advantage of plant-based vaccine.
- 4) In terms of animal immunization, edible vaccines appear to be more promising.
- 5) Don't need to Cook.
- 6) Not much storage conditions are required as compared to normal vaccine.
- 7) Children's compliance is improved.
- 8) Low-cost vaccine manufacture is a possibility.
- 9) Reduction in the necessity for surgery and sterile injection situations.
- 10) Easy to accessible.
- 11) Ease of administration.

12) Process of sterilization is not necessary for edible vaccine.

13) It is high demand as administration through oral route.

14) Efficient mode of action for immunization.

15) For producing edible vaccine, machines and equipments are not required if easily grow in cell culture compare to economical method.

#### **DISADVANTAGES:**

- 1) Development of immune tolerance particular in protein and peptides.
- 2) Dosage form consistency varies from plant to plant, generation to generation, and fruit to fruit.
- 3) Stability of vaccine in fruit is unknown.
- 4) Dose ratio will be differed because of several factors like plant, protein content and ripeness of fruits.
- 5) Difficult in selection of suitable plant.
- 6) Main element which we required it should not be Cook.
- 7) Palatability is also a major issue.
- 8) Not suited for children under the age of one.
- 9) There is a need to make a distinction between vaccine fruits and regular fruits.
- 10) People may develop an allergy to the fruit or vegetable expressing the foreign antigen.
- 11) Consistency of same quality vaccine production might not be guaranteed.

#### **Mechanism of Action of Edible Vaccines**



Edible vaccines are oral vaccines produced in transgenic plants that stimulate both mucosal and systemic immunity. After consumption, the tough plant cell wall protects the antigen from degradation in the acidic environment of the stomach, a process known as bio-encapsulation. In the intestine, digestive enzymes break down the plant cells and release the antigen. The released antigen is taken up by specialized Microfold (M) cells present over Peyer's patches and gut-associated lymphoid tissue (GALT). These antigens are then transferred to antigen-presenting cells such as macrophages and dendritic cells, which activate helper T-cells and B-cells. Activated B-cells differentiate into plasma cells and produce antibodies such as IgA, IgG, and IgE, along with memory cells. Secretory IgA provides protection at mucosal surfaces by neutralizing pathogens during future exposure. Edible vaccines therefore induce both humoral and cellular immune responses and provide long-lasting immunity with minimal side effects. This oral immunization approach is particularly useful because it is needle-free, easy to administer, and suitable for large-scale vaccination programs, especially in developing countries.

### Limitations

- Development of immunotolerance to vaccine peptide or protein.
- Consistency of dosage form from fruit to fruit, plant to plant, and generation to generation is not similar.
- Stability of vaccine in fruit is not known.
- Evaluating dosage requirement is tedious.
- Selection of the best plant is difficult.

- Certain foods like potato are not eaten raw, and cooking the food might weaken the medicine present in it.

## CHOICE OF HOST PLANT EDIBLE VACCINE

### 1. TOBACCO

Tobacco was one of the first plants used for edible vaccine production. Researchers successfully expressed hepatitis B surface antigen (HBsAg) and other vaccine proteins in tobacco leaves and seeds. Tobacco-based vaccines have been explored for diseases such as hepatitis B, rabies, dental caries, cholera, and human papillomavirus (HPV). Seed-based production gives high protein yield and easier storage. However, tobacco is not edible directly and requires purification before use.

### 2. POTATO

Genetically modified potatoes are widely studied as edible vaccines. Transgenic potatoes were developed to express antigens against diseases like E. coli diarrhea, cholera, Norwalk virus, hepatitis B, tetanus, and diphtheria. Human and animal studies showed increased antibody production after consuming engineered potatoes. Potatoes are easy to cultivate and distribute, but cooking may destroy vaccine proteins because heat denatures antigens.

### 3. TOMATO

Tomatoes are suitable for edible vaccines because they grow quickly, are easy to genetically modify, and can be eaten raw. Transgenic tomatoes have been studied for vaccines against malaria, rabies, HIV, and Alzheimer's disease. They maintain vaccine proteins without cooking and are easy to process into paste or puree for delivery. Their attractive appearance also helps acceptance among consumers.



#### 4. BANANA

Bananas are considered ideal edible vaccine carriers because they are eaten raw, especially by children, and grow in tropical regions where vaccination is needed most. Banana-based vaccines have been explored for hepatitis B and other infectious diseases. They are inexpensive and easy to consume. However, bananas require a long cultivation period (around 12 months), which slows production.

#### 5. MAIZE

Maize is widely used for both human and animal edible vaccines. Genetically modified maize has been developed for hepatitis B, Newcastle disease virus (NDV), rabies, HIV, and pig diseases. Corn-based vaccines can be consumed as corn flakes, chips, or tortillas. Maize offers large-scale production and good antigen stability. It is especially useful for veterinary vaccines.

#### 6. RICE

Rice is an important edible vaccine crop because it is widely consumed worldwide and does not require refrigeration. Transgenic rice has been developed for cholera and allergy-related immunotherapy. Rice-based vaccines remain stable for long periods and resist stomach acid degradation. Studies showed reduced allergic responses and protection against diarrhea-causing bacteria.

#### 7. SPINACH

Spinach has been investigated as a carrier for edible vaccines against anthrax and HIV. Scientists inserted protective antigens into spinach plants, and studies showed strong immune responses in animals. Spinach is useful because it can be eaten fresh and grows rapidly. However, research is still mainly experimental.

#### 8. LETTUCE

Lettuce is another promising edible vaccine plant because it can be consumed raw. Researchers produced vaccine antigens against *E. coli*, swine fever virus, and SARS-CoV-2 in lettuce plants. Lettuce-based vaccines may work as oral booster vaccines and help increase immunity. It is considered a versatile and easily consumable vaccine platform.

#### 9. SOYABEAN

Soybeans contain high protein levels, making them suitable for producing therapeutic proteins and vaccine antigens. Genetically modified soybeans expressing *E. coli* antigens showed strong antibody responses in animal studies. Seed storage proteins help accumulate large amounts of vaccine protein. Soybean-based vaccines are still under research but show promising immunogenicity.

#### Features of Different Plant Host Systems

##### TOBACCO

Tobacco Facile and efficient transformation system Toxic alkaloids incompatible with oral delivery; abundant material for protein characterization potential for outcrossing in field.

##### BANANA

Banana Cultivated widely in developing countries where Inefficient transformation system; little data vaccines are needed; eaten raw by infants and available on gene expression, especially for fruit adults; clonally propagated; low potential for specific promoters; high cultivation space outcrossing in field; once established, plentiful requirement; very expensive in greenhouse and inexpensive fruits are available on a 10-12 month cycle.



## POTATO

Potato Facile and efficient transformation system; tuber Relatively low tuber protein content; unpalatable is edible raw though not palatable; tuber-specific in raw form; cooking might cause denaturation promoters available; microtuber production for and poor immunogenicity of vaccine quick assay; clonally propagated, low potential for outcrossing in field; Industrial tuberprocessing well established.

## TOMATO

Tomato Relatively efficient transformation system; fruit is Relatively low fruit protein content; acidic fruit edible raw; fruit specific promoters available; may be incompatible with some antigens or for crossing possible to stack antigen genes: delivery to infants; no in vitro system to test fruit industrial greenhouse culture and industrial fruit expression processing well established.

## LEGUMES

Legumes Production technology widely established; high Inefficient transformation systems; heating or protein content in seeds; stable protein in stored cooking for human use might cause denaturation seeds; well suited for animal vaccines; industrial and poor immunogenicity of vaccine; potential seed processing well established for outcrossing in field for some species.

## ALFALFA

Alfalfa Relatively efficient transformation system; high Potential for outcrossing in field; deep root protein content in leaves; leaves edible uncooked

## Production of Edible Vaccines

### Introduction

Edible vaccines are produced using genetic engineering techniques in which selected antigen genes from pathogens are introduced into plants. These genetically modified plants are called transgenic plants. The plants express antigenic proteins that stimulate immune responses when consumed. Unlike conventional vaccines, edible vaccines contain antigenic proteins without pathogenic genes, making them safer, especially for immunocompromised individuals.

### General Production Process

The gene coding for the desired antigen is first isolated from the pathogen. This gene is inserted into a suitable gene vehicle or vector. The vector is introduced into the plant genome where the foreign gene expresses the corresponding antigen. The edible parts of the plant are then used for immunization in humans or animals.

### Stable Genomic Integration

Stable genomic integration is the most common method used in edible vaccine production. In this method, the foreign gene becomes permanently integrated into the plant genome. The transformed plants can reproduce through seeds or vegetative propagation. Stable expression allows long-term antigen production and the introduction of multiple genes for multicomponent vaccines.

### Advantages:

- Stable and long-term expression
- Suitable for large-scale production
- Organ and tissue specific expression possible
- Multiple genes can be introduced

### Disadvantages:

- Slow process

- Low transformation efficiency
- Time-consuming plant regeneration

### **Agrobacterium tumefaciens Mediated Gene Transfer**

Agrobacterium tumefaciens is a soil bacterium capable of naturally transferring DNA into plant cells through the Ti plasmid. The desired vaccine gene is inserted into the plasmid and transferred into plant cells. The transformed cells are selected using marker genes and regenerated into transgenic plants. Procedure: 1. Isolation of desired antigen gene 2. Insertion into Ti plasmid 3. Infection of plant cells using Agrobacterium 4. Integration of T-DNA into plant genome 5. Selection of transformed cells 6. Plant regeneration

#### **Advantages:**

- High gene transfer efficiency
- Stable integration
- Widely used and reliable

#### **Disadvantages:**

- Slow process
- Limited host range
- Low yield in some plants

### **Biolistic or Gene Gun Method**

The biolistic method uses high-speed DNA-coated metal particles such as gold or tungsten. These particles are shot into plant tissues using a gene gun. The DNA enters the cells and integrates into the genome.

#### **Procedure:**

1. DNA coated onto microprojectiles.

2. Acceleration using high pressure.
3. Penetration into plant tissue.
4. Integration into genome.

#### **Advantages:**

- Useful for plants resistant to Agrobacterium.
- Can transform chloroplasts and mitochondria.
- Rapid method.

#### **Disadvantages:**

- Expensive equipment
- Possible tissue damage
- Random integration may occur

### **Transient Expression Using Viral Vectors**

In transient expression, modified plant viruses are used as vectors to deliver vaccine genes into plant cells. The virus replicates inside the plant and produces high amounts of antigen for a short duration.

#### **Advantages:**

- Rapid antigen production
- High expression levels
- Useful for emergency vaccine production

#### **Disadvantages:**

- Temporary expression only
- Difficult inoculation procedure
- Not suitable for stable inheritance

### **Electroporation Method**

Electroporation introduces DNA into cells using electrical pulses. High-voltage pulses create temporary pores in the plasma membrane allowing DNA entry into the cytoplasm.

#### **Advantages:**

- Simple technique.
- Effective for protoplast transformation.
- Quick DNA delivery.

#### **Disadvantages:**

- Cell wall acts as barrier.
- Cell damage may occur.
- Requires specialized equipment

#### **Chloroplast Transformation**

Chloroplast transformation involves insertion of foreign genes into chloroplast DNA instead of nuclear DNA. DNA-coated nanoparticles are introduced using a gene gun or PEG-mediated methods. Homologous recombination inserts genes precisely into chloroplast genomes.

#### **Advantages:**

- Very high protein expression
- Low production cost
- Prevents gene silencing
- Maternal inheritance reduces gene escape
- High accumulation of recombinant proteins.

#### **Disadvantages:**

- Technically complex
- Limited plant species applicability

- Difficult regeneration process

#### **Overall Advantages of Edible Vaccines**

- Needle-free administration
- Easy oral delivery
- Reduced production cost
- Easy storage and transport
- Suitable for mass immunization
- Reduced contamination risk
- Better patient compliance

#### **Overall Limitations**

- Dose inconsistency
- Stability problems during storage
- Public concerns regarding genetically modified plants
- Regulatory and ethical issues
- Possible allergic reactions
- Difficulty in maintaining antigen concentration

#### **Conclusion**

Edible vaccines represent an innovative and cost-effective approach to immunization. Different transformation methods such as Agrobacterium-mediated transfer, biolistic methods, viral vectors, electroporation, and chloroplast transformation are used for antigen production in plants. Although several limitations still exist, edible vaccines have significant potential for future human and veterinary healthcare applications.

#### **Applications of Edible Vaccines**

## **ANTHRAX**

Anthrax is caused by *Bacillus anthracis*. Traditional vaccines require multiple doses and may produce adverse effects. Researchers developed edible vaccines using tobacco, tomato, spinach, and potato plants carrying anthrax antigens. Plant-based vaccines stimulated mucosal immunity and showed promise as safer and more convenient alternatives for anthrax protection.

## **HEPATITIS B**

Hepatitis B is a major viral infection affecting millions globally and can cause liver cirrhosis and liver cancer. Researchers developed edible vaccines using genetically modified tobacco and potato plants expressing HBsAg antigen. Potatoes became a preferred platform for oral vaccine delivery because of lower alkaloid content. Although antigen expression levels remain low, studies are exploring promoters and regulatory factors to improve vaccine production.

## **CHOLERA**

Cholera is a diarrheal disease caused by toxins produced by *Vibrio cholerae*. Transgenic potatoes and rice expressing cholera toxin B subunit genes showed effective immune responses in mice. Oral administration generated serum and secretory antibodies that protected against bacterial toxins. Agricultural seeds and edible plants are considered promising carriers for cholera edible vaccines.

## **DIABETES**

Researchers investigated edible vaccines for autoimmune diabetes using genetically modified potato and tobacco plants carrying GAD67 antigen. Studies in diabetic mice showed a lower incidence of diabetes after consuming transgenic plants. Increased IgG1 antibody levels helped suppress harmful immune responses. This research

demonstrated the potential of edible vaccines in treating autoimmune diseases.

## **HIV**

HIV attacks CD4 immune cells and eventually leads to AIDS if untreated. Scientists introduced HIV proteins into cowpea mosaic virus and spinach plants to produce edible vaccines. Transgenic plants successfully expressed HIV antigens and stimulated higher antibody production in experimental animals. These findings support the feasibility of plant-based HIV vaccines.

## **MALARIA**

Malaria is caused by *Plasmodium vivax* and *P. falciparum* transmitted through infected female *Anopheles* mosquitoes. Researchers developed transgenic tomato plants producing antimalarial edible vaccines using MSP4 and MSP5 antigens. Oral administration with cholera toxin B stimulated strong antibody responses against blood-stage parasites. This approach may reduce the cost and logistical problems of conventional malaria vaccination.

## **MEASLES**

Measles is a highly contagious viral respiratory disease mainly affecting young children. Scientists engineered tobacco and carrot plants to express measles virus hemagglutinin proteins. Experimental studies showed increased antibody production and protective immune responses. Genetically modified food plants such as rice, cabbage, and carrots are being explored as edible measles vaccines.

## **RABIES**

Rabies is caused by the Lyssavirus, a single-stranded RNA virus. Transgenic tomato plants

expressing rabies virus glycoprotein genes were used to induce immunity in animals. Studies demonstrated that modified plants stimulated anti-rabies antibody production and provided protective immunity. Tobacco Mosaic Virus (TMV) systems were also used for vaccine development.

#### Applications of Edible Vaccines

1. Rabies virus – Tobacco, Spinach – Rabies.
2. Hepatitis B – Potato, Tobacco, Banana – Hepatitis B.
3. HIV – Tomato – AIDS.
4. *Vibrio cholerae* – Potato – Cholera.
5. Cancer antigens – Wheat, Rice – Cancer.
6. Norwalk virus – Tobacco, Potato – Gastroenteritis.
7. Rabbit hemorrhagic disease virus – Potato – Hemorrhagic disease.
8. Coronavirus (gastroenteritis) – Tobacco – Gastroenteritis.
9. Alzheimer's disease antigen – Tomato – Alzheimer's disease.
10. Colon cancer antigen – Tobacco, Potato – Colon cancer.
11. Paramyxovirus – Banana, Rice, Lettuce – Measles.
12. *Plasmodium falciparum* – Tobacco – Malaria.
13. Type-I diabetes antigen – Potato – Type-I diabetes.
14. Cysticercosis antigen – Arabidopsis – Cysticercosis

## CONCLUSION

Edible vaccines are a promising advancement in biotechnology and vaccine delivery. They provide a cost-effective, needle-free, and easy-to-administer alternative to conventional vaccines, especially useful in developing countries where refrigeration and medical infrastructure are limited. Plant-based vaccines can stimulate both mucosal and systemic immunity while reducing transportation and storage costs. Research has shown their potential against several infectious diseases in humans and animals. Edible vaccines may also improve global immunization coverage and help reduce mortality from vaccine-preventable diseases. Advances in plant biotechnology, gene expression systems, and vaccine stabilization techniques have further strengthened their future prospects. However, several challenges still remain. These include low antigen expression, dosage inconsistency, protein degradation during cooking or digestion, public concerns regarding genetically modified plants, environmental safety, commercialization difficulties, and regulatory approval issues. More clinical trials and long-term safety studies are required before widespread use. Despite these limitations, edible vaccines hold immense future potential as safer, affordable, and accessible vaccines. Continued research and technological improvements may make them an important tool for preventing infectious diseases worldwide and improving public health in the future.

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