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Potential of plant-derived edible vaccines: a vial or a potato?

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Abstract: Since time immemorial, various defense mechanisms have been employed to combat several infectious diseases, in animals as well as in humans; however, from the commencement of the nineteenth century, vaccines were created and utilized majorly. The utilization of vaccines derived from plants is an evolving biotechnological tool that promises limitless potential in fighting viral, bacterial, and fungal diseases. The development of transgenic plants involves the incorporation of a desired antigen of pathogens into the selected host plant by a chosen genetic transformation method.Potatoesare a cardinal candidate to vehicle green factory vaccines; as they can be stored easily for longer period, they are grown widely – are people's fourth food choice globally, with impeccable nutritional benefits: rich in vitamin C and Zinc, hence they have significantly higher potential to be impactful in disease control,in mostlow resource settings of Sub-Saharan Africa, due to their ease mode of culturing. Potatoes have monoclonal propagation, and they form a pentameric doughnut-like structure with the non-toxic part of subunit proteins, reducing the chances of horizontal gene transfer to wild types.This review article stipulates the notable benefits of plant-derived edible vaccines against the conventional oral vaccines.

Keywords: Edible vaccines; Transgenic plants; Potato; Subunit proteins; Vaccine antigens

Introduction

A vaccine is a synthetic compound employed to come up with antigenic properties to ameliorate immunity against one or more diseases, and the act thereof of administering it, is known as vaccination.Edible vaccines are easily manageable and near user-site mode of vaccination, via the oral route; they are synthesized genetically from fruits and/or vegetable

plants. Plant-based edible vaccines fail-safe as they contain not the pathogenesis genes, hence bringing about disease-free immune response in the body(Yuki *et al.,* 2013). Not only that, edible vaccines hold limitless potential over conventional vaccines as they beat the need for refrigeration or cold storage chain, because most plant models such as potatoes have a low spoilage rate, they also curb the medical personnel to patient demand ratio as in the case of traditional oral vaccines that need qualified medical personnel to administer the vial(Streatfield *et al.,* 2001). Production cost and even distribution issues especially in remote areas are equally a challenge that can potentially be overcome by immunizing people with green manufactured vaccines. Little to no shortages can be recorded with the use of a potato over a vial as vaccine carrierbecause higher yield is assured using crops thus, more than 70% coverage of the target population would be immunized(Xu *et al.,* 2011). Consequently, this will promote the agricultural sector and in turn, bring about food security,especially in low resource settings. In addition, potato is the world's fourth staple food after rice, wheat, andmaize(Rashid *et al.,* 2024);hence what better way than to use a people's first choice non-cerealcrop to be their medicine(Smith, 2004) and provide food security to humankind.Most edible vaccines from diverse plant candidates can deliver both mucosal and complete immunity.

Concept of plant-based edible vaccines

Edward Jenner is believed to be the father of vaccinology in the West, following his inoculation of a boy aged 13 with vaccinia virus against Smallpox in 1796; a couple of years later the debut of Smallpox vaccine was initiated(Willis, 1997). And today, Smallpox has been eradicated and was declared nonexistent in the world by WHO.Two centuries that followed, Dr. Charles J. Arntzen, invented the concept of plant-based vaccinesthat were genetically transformed, to develop and deliver subunit vaccines. This inventory was followed by a series of immunogenicity tests for efficiency inlaboratory rats as the animal model and it was found effective, hence the National Institute of Allergy and Infectious Diseases declared it approved at product stage development level(Tripurani *et al.,* 2003).The notion of engineering plants to obtain healthier ones is an ancient concept(Mason *et al.,* 1998); over a hundred years now, food crops are being modified by means of selective breeding, until the arrival of modern biotechnology, where genetic engineering techniques such as de novo cultivation are employed to breed crops on a large scale, so as to carter for the world, via the utilization of selected elite foundation materials from wild plants, then introduce rapid traits genetically to return desired features and alas, create new crops.

Brief history of edible vaccines derived from plants

Severally, scientists have attempted to produce vaccines from plants, where essential proteins were developed in diverse plants, some examples are as follows:a transgenic leaf tissue of *Arabidopsis thaliana* produced the essential protein, secretory antigens of the heat-labile enterotoxin B subunit in early targets to fight against Diarrhea and Tuberculosis(Rigano *et al.,* 2004).Kapusta *et al.,* 1999 developed an edible vaccine derived from lettuce to combat inflammation of the liver using the Hepatitis B surface antigenic protein; embryogenic clones of papaya were transformed to attack *Taenia solium,* a causative agent of Cysticercosis(Hernández *et al.,* 2007). Peanut seeds were genetically transformed using seed specific legumin promoter and developed the CTB-Rabies glycoprotein to control cholera and rabies(Tiwari *et al.,* 2009).

Considerations in developing a plant-produced edible vaccine

- Risk assessment of the selected antigen is cardinal, to ensure that the vaccine isharmless and secure(Svennerholm *et al.,* 1989). Hence the antigen must be screened in its entirety for non-pathogenicity(Barlow *et al.,* 2002) as well as determine whether

it is amenable to maximal expression in the plant candidate of choice, in turn its ability to induce protective responses to the body's immune system.

- The plant to be employed needs to undergo total evaluation(Betz *et al.,* 2000), as the carrier of the transgene is a pivotal point to note beforehand(Walker, 2005). Responding to questions like; can the plant be consumed without cooking? Is it grown widely in the target area without adverse effects on the wild type? Can it be stored with ease without a rapid spoilage rate? How amenable is the plant of choiceto genetic transformation and regeneration?
- Quantify the number of doses that would suffice for full immunization(Bredehorst & David, 2001) and determine the appropriate mode of delivery, to do away with issues of vaccineunderuse or overuse(Strobel & Mowat, 1998). Equally sort out the process of securing a genuine license and a certified board to manage and control the vaccine accessibility, production, and distribution.
- Overall, reception of genetically developed plant bio-product by the public, can't be overlooked; there is need to clearly explain the pros and cons to everyone in the society(Cockburn, 2002), to have positive attitude towards the genetically modified crops and therefore, a warm welcome of the vaccine.

Developing edible vaccines

The genetic transformation of plants for vaccine production occurs by incorporating the selected gene into the candidate plant to produce the encoded protein. For the transformation to be successful, there is need to use a non-pathogenic coat protein, specific to a virus or bacteria or parasite(Shchelkunov *et al.,* 2004). Diverse protective epitopes can be chosen to develop a plant-based edible vaccine, this selection can eventually be leveled-up to carter for as much people as the target population requires. The gene of interest must be selected from non-pathogenic microbes that are encoded in specific antigen; this can be handled in the following ways:

***Agrobacterium* gene mediated transfer**

Agrobacterium tumefaciens is a soil gram positive bacterium with circular Ti (tumor inducing) plasmid of about 200kb; alternatively, referred to as the 'natural genetic engineer' because it possesses genetic materials that are capable of synthesizing phytohormones together with cytokinin and auxins(Nyaboga *et al.,* 2014). Thus, it is widely used as a plant transformation vector, because upon infection, the plant genome incorporates the plasmid's T-DNA(De Block, 1988).Therefore, creating a swollen wound on the plant tissue, therein forms a bunch cells, also known as gall (Fig. 1), implying that the T-region of the dismantled plasmid inducing tumor has randomly incorporated the recombinant DNA into the agrobacterium(Pratiwi & Surya, 2020). This disarmament of the plasmid involves the removal of the genes for cytokinin and auxins synthesis, to get rid of possible formation of any tumor (gall) upon transformation(Ishida *et al.,* 1989). Although this method of developing an edible vaccine from plants is quite lengthy with low to medium yield, it has however, shown satisfactory potential in flowering plants like potato(Bánfalvi *et al.,* 2020). Numerous experiments that have been carried out by biotechnologists have proven effective with use of *Agrobacterium tumefaciens* approach – researchers reported that the traits of interest were expressed by the targeted genes.

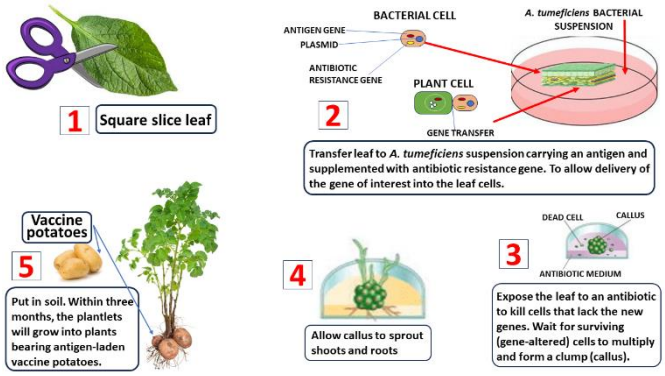

Fig. 1: Potato-based edible vaccine transformed using *Agrobacterium*method

Gene-gun

The gene gun method alternatively known as the biolistic approach employs the gun to fire metallic shots made from gold or tungsten and covered in DNA coding for the target gene, towards the inside of the candidate plant cells(Leissing *et al.*, 2022). Consequently, the successfully transformed cells are grown into plantlets and eventually multiplied to have sufficient copies of plants carrying the same genetic makeup(Ismagul *et al.*, 2018). Despite being a sophisticated approach, the biolistic method is highly attractive because of its non-dependability on the ability to regenerate the species, due to the un-deviated entry of DNA inside the plant cells. Albeit, the device particle gun is very costly, hence majorly setting back the wide use of this approach.

Electroporation

This method involves the production of transient pores within the plasma lemma, this is achieved by exposing the cells inserted with DNA to an electrical pulse of very high voltage(Darmawan *et al.*, 2020). The plant cell wall is comprised of polysaccharide extracellular matrices of pectin and cellulose that makes it rigid, hence serving as a stable blockage to hinder DNA from penetrating into the cytoplasm(Ozyigit, 2020). For this cause, it is imperativeto make the cell wall flexible by treating it to moderate enzyme degradation, to make it porous and selectively permeable for easier entry of the DNA into the nucleus of the plant cell.

Chimeric viruses

Modern biological tools of entire protein production and limited expression of non-indigenous protein are the two main biotechniques utilized in chimeric viruses(Lei *et al.*, 2020).Desired genes are produced by genetically engineered plants (Fig. 2), furthermore, the cloned genes contained in the various edible parts of the natural hosts are infected with the antigenic protein, expressing at distinct gradients(Barker *et al.*, 1992). Plant viruses such as but not limited to: Potato Virus Y, Cauliflower Mosaic Virus, Tomato Bushy Stunt Virus, Alfa Mosaic Virus; can be designed anew for maximal expression of the essential segments of surface antigens(Debernardi *et al.*, 2020).

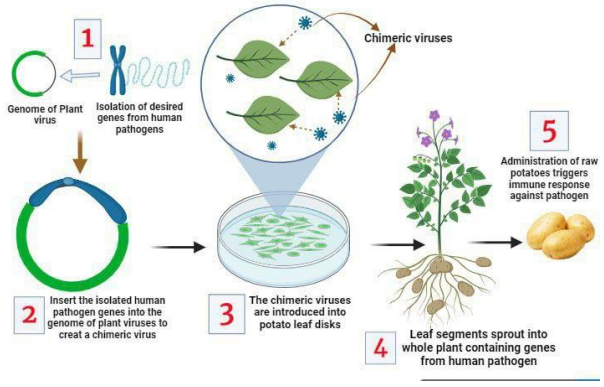

Fig. 2: Development of edible vaccine from potato using Chimeric virus method

Mode of defense of edible vaccines produced from plants

Mucosal immunity refers to the immune response regarding the mucous membrane acted upon by the immunoglobulin A (IgA). Over 80% of pathogens attack the human body via mucosal surfaces, often entering through the gastrointestinal, urogenital as well as the respiratory pathways(Yu & Langridge, 2000). This makes mucosal immunity the excellent choice of the defense mechanism, with the oral route potentially being the prime efficient path of mucosal immunization, due to the ability to produce mucosal immunity and cell mediated immune response by edible vaccines(Singhal & Mishra, 2023).

However, with oral vaccination such as the use of a vial, the macromolecule antigenic protein within the stomach walls is digested by the acidic nature of the stomach lining. Whereas the use edible vaccines produced from plants, beats this challenge, reason being – the plant tissue can be consumed with insulation from the rigid cell wall rendering protection to the antigenic proteins against enzyme degradation and acidic secretions by internal organs while in the stomach(Roychoudhury, 2020).

A specialized cascade of epithelial cells found in the GIT (Gastro-Intestinal Tract) called Microfold cells (M-cells), are a form of transcellular cells that transport macromolecules, antigens in this case, across the interior of a cell (Fig. 3). Thereafter, the released antigens are captured in vesicles on one side of the intestinal lining that covers the Gut-associated Lymphoid Tissue (GALT) alongside the Peyer's Patches (PP)(Hirlekar & Bhairy, 2017). The PPs make up an ensemble of lymphoid follicles, with an abundance of secretory IgA, whose function is to produce potent plasma cells capable of occupying mucosal tissue, in turn playing the role of mucosal immune effector sites(Awale *et al.,* 2012). The ingested edible vaccine is digested close to the PPs, this is followed by the stimulation of antigenic follicles, which eventually penetrate the intestinal epithelium – accumulating therein the lymphoid tissues, and results in the establishment of a germinal center within the aggregated of lymphatic follicles(Buriev *et al.,* 2024).

The developed germinal center is what is also known as the immune system, it is made up of a group of lymphatic tissues, namely: macrophages, T-cells, and B-cells.The M-cells express molecules of the complex second class Muco-Histo-Compatibility side by side with the antigens released in the transcellular mucosal surface enclosed with lymphoid follicles and they activate the B-cells(Tacket *et al.,* 2004).After activation, the B-cells transit towards the Mucosal-associated Lymphoid Tissue (MALT), where the secretion of serum immunoglobulins: G, E and local A takes place, including the production of plasma cells and the generation of memory cells to countercheck infectious invasion present in the body, brought by original causative agent(Youm *et al.,* 2007).

That being so, administering plant-based edible vaccines to pregnant women, is potentially a fail-safe fetus-in-utero immunization because the maternal antibodies would be transported, within the placenta, it is also a potential efficient mode of immunization for infants via breast milk from lactating mothers fed on the plant-based edible vaccine(Sahoo *et al.,* 2020).

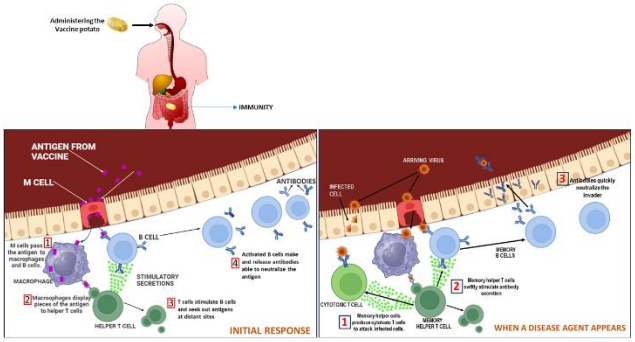

Fig.3: Mechanism of action of a transgenic potato-derived edible vaccine

Potato as candidate of choice for production of edible vaccines

Potato tubers were utilized to vehicle diabetes related proteins as well as anti-*E. coli* vaccines. However, it was reported that too much boiling could breakdown essential proteins present in the transgenic potato(Mason *et al.*, 1998). Despite this, potato is still a cardinal edible vaccine choice plant as it holds numerous advantages,such as: long shelf-life as it does not spoil easily, equally eliminates the need for cold chain storage due to its high tolerance to heat, it has specific promoters for clonal propagation,it can be grown without much difficulties in any favorable climate and producemedium to high yield with up to only three months of maturity period(Millam, 2004).Not only is it a fourthcash crop in the world but it also has nutritional benefits: rich in vitamin C,Zinc, and carbohydrates, overall it has proven to be efficient in several diseases, hence its predominant use in clinical trials related to edible vaccines(Bajaj, 1987).

Table 2: Potato-derived edible pharmaceutical proteins, bio-manufactured for medical reference and clinical trials

Plant candidate	Infection	Bio-product	Result
Potato	Biovine group A rotavirus (GAR)	Major capsid protein Virus protein (VP6)	Anti-VP6 response was seen in sera of adult Bagg albino(BALB/c) mice via Western Blot assay, suggesting usefulness of reagents for diagnostic purposes (Matsumura *et al.*, 2002)
Potato tuber and leaf	Cholera and Diabetes	CTB-INS (Insulin)	Insulin synthesized from the plant was joined to the subunit of CTB at the C-terminus extremity, therefore, delivering it directly into the GALT of the immunized animal models (Arakawa *et al.*, 1998a)
Potato tuber	Transmissible gastroenteritis (TGE)	Glycoprotein S	A spike protein from the TGE coronavirus showing oral immunogenicity after administration of tuber extracts containing N.gs to the mice, the gs protein specific antibodies were seen in the serum(Gomez *etal.*, 2000)
Leaf and tuber of potato	Foot and mouth disease (FMD)	Structural virus protein (VP1)	The immunization process showed no notable variations between the use of a single or double CaMV 35S promoter in the potato system, as the animals treated presented similar FMDV VP1 specific antibody response(Carrillo *et al.*, 2001)
Potatotuber	Rabbit hemorrhagic syndrome	Structured virus protein (VP60)	Rabbits were orally immunized with transgenic potato tubers to curb the lethal infection of intravascular coagulation and

			produce the capsid virus protein(Martín-Alonso *et al.*, 2003)
Potatotuber	Gastroenteritis	Capsid of rotavirus glycoprotein VP7	RT-PCR and Western blot detected stable transcription of the VP7 gene and expression in potato cells, showed successful induction of both humoral and mucosal responses in BALB/c mice fed with the fiftieth-generation transgenic tuber tissue from potato (Li *et al.*, 2006).
Potato leaf	Diarrhea	Neutralizing epitope of Porcine Epidemic Diarrhea Virus (PEDV)	Genomic PCR was employed to ascertain the positive regenerants from transgenic potato plants of PEDV epitope gene; while about 0.1% of the summed up soluble tuber protein was established using ELISA(Kim *et al.*, 2005).

Clinical applications

Numerous studies have shown the success of potato tuber and potato leaf derived products in vaccine development to control and manage certain infectious diseases, affecting animals as well as humans(Tiwari *et al.*, 2009). Stipulated below are some approaches to develop green factories for vaccine production:

Cholera

Cholera is caused by the bacterium*Vibrio cholerae*, which triggers intestinal acute diarrheal infection after consumption of unclean food or water(López-Gigosos *et al.*, 2011).Potatoes were genetically engineered to develop an affinity for G_{M1}-ganglioside to the CTB five ring structure(Kim & Langridge, 2003). Mice were immunized orally with serum as well as intestinal CTB-specific antibodies, neutralizing its toxicity on Vero cells(Kim *et al.*, 2017). About 60% less of the diarrheal fluid was recorded from the small intestine of the transgenic plant immunized mice, due to the blockage of bond formation between enterotoxin and cell-surface receptor G_{M1}-ganglioside. Results showed the potential of potato-based edible vaccine in protective immunity, against cholera (Arakawa *et al.*, 1998b).

Periodontal disease

Porphyromonas gingivalis is the oral anaerobic, gram-negative bacterium that brings about periodontal disease, it attaches the fimbrial protein to linings covered with saliva(Lee *et al.*, 1992). Complementary DNA fragments of *fim*A were amplified and located in the genomic DNA of transgenic potato leaf using PCR.Furthermore, after the transgenic potato tuber was boiled, a new protein of band size~6.5kDa was seen via immunofluorescence after acrylamide gel electrophoresis was run. Immunoblot analysis portrayed the likelihood of developing an endogenous Fim A protein in plant-derived edible vaccines for protection against periodontal disease (Shin *et al.*, 2009).

Enterotoxigenic *Escherichia coli* (ETEC)

Besides livestock, humans are also majorly affected by enteric infections, chiefly caused by enteroxigenic *Escherichia coli* (ETEC) strains. The bacteria use short attachment pili to colonize the intestinal lumen of enterocytes(Roy *et al.*, 2010). A manufactured gene particular to the plant of choice coding for *Escherichia coli* heat-labile enterotoxin B subunit (LT-B) against ETEC was genetically transformed into a potato plant. One group of mice was fed on

raw transgenic potato tubers and another group was gavage with bacterial LT-B, bi-weekly. Following the third dose, the first group of mice presented more serum and mucosal levels as compared to the second group that was injected with bacterial LT-B. This illustrates the potential plant-derived edible vaccines have over conventional vaccines(Rosales-Mendoza *et al.,* 2009).

Hepatitis B

Hepatitis B virus attacks the liver cells and causes inflammation therein, it is transmitted through blood and bodily fluids related to blood, in instances such as: sharing sharp objectives like needles and razor blades, unprotected sexual intercourse or via unsafe blood transfusion procedures. Richter *et al.,* 2000, presented data on the production of a transgenic potato using tuber specific *patatin*, expressing Hepatitis B surface antigen (HBsAg) prior to clinical trials. An upsurge in HBsAg-specific serum antibodies was seen in mice orally immunized with the tuber extracts, though intraperitoneal delivery could potentially boost the immune response(Youm *et al.,* 2007). Thus, the following steps were incorporated to achieve this; the protein target within the plant cell alongside the extremities 5' and 3' closely analyzed for accumulation of the antigen, this resulted in polyadenylation signals aiding in the amelioration of integration of the HBsAg into the endoplasmic reticulum of the plant cell.

Alzheimer's Disease

Accumulation of plaques made of peptides that are not soluble ß-amyloid in the brain causes Alzheimer's disease. Kim *et al.,* 2003, transformed shoots of Irish potato (*Solanum tuberosum* L.) by inserting a gene encoding ß-amyloid; Northern Blot analysis was employed to ascertain the presence of the plant genome, while antibodies were developed to observe the expression of recombinant ß-amyloid using ELISA. It was shown that the transgenic plants had five-fold more specific-antigens than the non-transgenic ones (Morgan *et al.,* 2000).

Cervical Cancer

Various risky sexually transmitted genotypes of Human Papillomavirus (HPV) cause cervical cancer (Bosch *et al.,* 2002). HPV-like particles were expressed in potato, a first trial in human subjects was conducted parenterally and results showed the safety and tolerable immunogenicity of the plant-derived edible vaccine (Evans *et al.,* 2001). Efficiency test was proven potent in the second phase study, whereKoutsky *et al.*, 2002 concluded that the potato-derived HPV-like particles are essential for HPV prophylaxis.

Edible plant vaccines versus traditional vaccines

Both plant produced and conventional vaccines can be integrated with other vaccine approaches as they are being administered(Sahoo *et al.,* 2020). Additionally, they both render intra-placenta sero-conversion of antibodies from immunized expectant mother to the unborn fetus(Patel *et al.,* 2022). Most of all, vaccines in general are not usually warmly welcomed by the public, could be due to lack of ample understanding, coupled with stringent laws and debates regarding intellectual property rights. Plant-based edible vaccines and conventional vaccines have several contrasts, some of which are tabulated below:

Plant-based edible vaccines	**Conventional Vaccines**
Uniquely oral route of administration	Oral or intravenous mode of administration
Do not need qualified medical personnel to administer	Need qualified medical personnel to administer
Eliminates the need forrefrigeration	Require cold chain storage
Pharmafood is a desirable vaccine carrier with nutritional benefits	Vial or injection are not as desirable and come with minimal adverse effects
Can be produced and stored near user-site, making them easily and readily accessible	Manufactured from licensed countries only and transported to other parts of the globe
Assures a more even and inclusive distribution within the target population	Distribution hardly reaches the remote areas of the world

Enhanced compliance to all age groups, especially children	Usually not admissible to persons below 2 years old and above 65 years old
Relatively inexpensive cost of production	Generally costly to develop
Stimulates both mucosal and humoral immune systems	Stimulates only the humoral immune system
Improved safety and immune response due to unattenuated pathogens of subunit vaccines	Requires subsidiary elements (adjuvants) to stimulate immune response
Antigens from plants randomly organize in particles resembling viruses making them efficient vectors for vaccine production, as plant viruses can't impact animals or humans	Conventional vaccines are developed from cultured mammalian cells, that could potentially contaminate animal or human viruses
Some plants can't be eaten raw, and cooking may denature essential proteins	Do not need cooking to be administered, hence essential proteins are left intact

Current updates on plant-based edible vaccines

There is a limited database on plant-based edible vaccines, and even with the few developed so far, none of them have been licensed for commercial use in humans to date. This could be due to stringent regulatory requirements in the industry.Albeit tobacco cells in suspension culture were employed by Dow Agrosciences to produce a vaccine against Newcastle Disease, a viral infection common in poultry. In 2006, the United States Department of Agriculture licensed the commodity, and it was scored as the premier vaccine produced from plants to be commercialized(Vermij & Waltz, 2006).

Health Canada, 2022, approved a Corona Virus Disease-2019 vaccine derived from plants with particles like virus; manufactured by Medicago Inc. Two doses were to be administered 21 days apart to persons of age 18 and above, via the intramuscular route. However, the sponsor cancelled their authorization on March 31st, 2023,(Health Canada, 2022).Scientists at the University of Tokyo in Japan, ground dry uncooked rice seeds into fine powder carrying a vaccine against cholera and traveler's diarrhea, this was for the premier attempt in humans. Prior to consumption, the MucoRice-CTB was to be dissolved in cold or warm water and be taken right away(Yuki *et al.*, 2013). This study pointed towards the role of gut microbiome in vaccine effectiveness, by stimulating immunity via the intestinal mucosal membranes(Yuki *et al.*, 2022).

Prospectson plant-derived edible vaccines

Vaccines made from plants and plant products prove to be a reliable monetized option for immunization in the 21st century. They umbrella specific imposed on niches, such as cost of production, distribution, and administration of vaccines, especially in low resource settings. With the immergence of Artificial Intelligence (AI), it is highly probable that it can be used as a pivotal engine to source out much stable and efficient antigens as well as epitopes for subunit vaccine production. Additionally, to have maximal yield of protein, it will be imperative to ameliorate the biotechnological tools to bring about transient expression, thus in the coming years, the plant-produced platform of vaccines couldexpand exponentially, with fail-safe experiments in clinical applications.Prior to actualizing the potential of green factories in the development of vaccines, it is imperative to get control of the technological hiccups faced by researchers in the past – such as the complexity in producing reliable, affordable, and effective vaccines to combat cholera, diabetes, or HIV. Everyone is still at risk if there is a deficit of vaccines in the world, hence a fruit or plant derived vaccine promises to curb these gaps and render protective immunity in the quest of preventing infectious diseases.

Conclusion and Perspectives

Edible vaccines produced from fruits and/or plants are a great highlight of modern biotechnology and bio-product development. They ease immunization, via oral administration that has overcome challenges of safe and reliable vaccination systems,coupled with the inexpensive mode of manufacturing them, more so in the developing countries where infectious diseases are endemic. Deeper exploration into this emerging inventory could potentially secure safer and effective immunization approaches, especially if the plants or fruits of choice are fully and massively grown in the target population.

Indeed, the conventional vaccines are available and accessible to combat various diseases and in turn, reduce the case fatality rate. On the other hand, they are overshadowed by their inadequacy in maximal delivery, and they fall short in achieving the desired therapeutic responses principally in the furthest locations from the manufacturing site, due insufficient vaccines and even the few available have no cold storage chain to preserve them for longer periods. Conventional vaccines are without doubt safe and effective drug delivery systems – nonetheless, infectious diseases are still claiming millions of lives due to unavailability of full dosages following huge financial costs in the production and distribution processes. Causing great concern especially in affected areas, where health care services are not readily available.

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Conflicts of interest

The authors declare that there is no conflict of interest.

Abbreviations

WHO – World Health Organization; **CTB** – Cholera Toxin B subunit;**LT-B** – Heat-labile Toxin B subunit;**DNA** – Deoxyribonucleic acid; **Kb** – Kilobase pairs;**kDa** – Kilodalton;**CaMV** – Cauliflower Mosaic Virus; **PCR** – Polymerase Chain Reaction; **ELISA**– Enzyme-Linked Immunosorbent Assay; **Ig**– Immunoglobulin

Author contributions

Beenzu Siamalube: Writing – original draft, Formal analysis, Methodology. **Emmanuel Ehinmitan**: Data curation, Software, Writing – original draft. **Justus Onguso**: Conceptualization, Project administration, Supervision. **Steven Runo**: Investigation, Resources, Supervision. **Maina Ngotho**: Validation, Writing – review and editing, Supervision.

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