PLANT BASED ORAL VACCINES FOR HUMAN AND ANIMAL PATHOGENS – A NEW ERA OF PROPHYLAXIS: CURRENT AND FUTURE PERSPECTIVES

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ABSTRACT

Vaccination remains a high priority for animal disease prevention and control especially on account of rising antimicrobial resistant strains of pathogens and frightening increase in new emerging and reemerging pathogens. Traditional vaccines have limitation like residual virulence, need of extensive safety precautions, production difficulty and huge initial investments. Additionally, they are inefficient in producing a protective response at mucosal surfaces such as of lungs and intestinal tract, the actual sites where disease agents enter the body. Recent advances in plant molecular farming has resulted in genetic manipulations in plants to make them bioreactors for production of various recombinant proteins, by using infectious vectors or stable transgenic systems, which formulate the edible/oral vaccines. Such plant-based oral/edible vaccines have several advantages like they are functionally similar to conventional vaccines, demonstrate extended storage period in food grains;

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are heat-stable and does not require cold storage, eliminate need for expensive purification steps, are free from contaminating pathogens, can be produced in large scale in a time bound fashion and their delivery is easier with practical feasibility for large masses application. Additionally, these are also ideal for vaccination of animals and birds living in the wild areas thereby preventing many zoonoses. However, at this moment there are many practical challenges like degradation of vaccine antigen by enzymes of upper digestive tract, dosage regime, oral tolerance and the issues concerned to the use of genetically modified plant. In the near future the biomedical applications of these vaccines could become a common alternative to conventional vaccines, for which there is a great need to strengthen research and development activities in this promising area for protecting health of animals as well as of humans.

1. Introduction

Rising antimicrobial resistant strains, food safety issues of antibiotic residual toxicity effects in animal food and animal products (meat, egg and milk) and a frightening increase in emerging and re-emerging animal and human pathogens has demanded the need for safe and effective vaccines to combat various infectious diseases for safeguarding health issues of humans as well as of their companion animals including the livestock and pets (Swayne, 2003; Lal et al., 2007; Verma et al., 2007; Dhama et al., 2008a,b; Kumar et al., 2011; Kumar et al., 2012a,b; Deb et al., 2012). Induction of mucosal immunity is the key mechanism for providing protection to the host from infectious diseases. Conventional vaccines, administered generally through parenteral route, stimulate a robust and specific immune response, but are incompetent to produce fully defensive mucosal immunity as required during respiratory and intestinal tract infections, the sites at where disease causative agents actually enters the host’s body. Besides, conventional vaccines have several other limitations like residual virulence, extensive safety precautions regarding personal and environmental contamination, difficulty in production, sometimes requirement of specific growth conditions and cell associated nature (Movahed and Hampson, 2008).

For induction of mucosal immune responses the vaccine need to be delivered through appropriate inoculation route with suitable adjuvant(s). Advances in biotechnology and molecular biology have paved new ways like DNA vaccination, cell based vaccination and use of chitosan and nanoparticles for the delivery of vaccines antigens (Dhama et al., 2008a,c; Dzung et al., 2011). Other methods include plant molecular farming in which genetic manipulations in plants are carried out so as to make them bioreactors and producers of a range of recombinant proteins thereby to be used as edible/oral vaccine components (Ryblicki, 2010; Buonaguro et al., 2010; Lossl and Waheed, 2011; Yoshimatsu et al., 2012; Kumar et al., 2012; Mikschofsky and Broer, 2012). Transgenic plants and non-pathogenic commensal or food starter bacterial strains can be used for oral delivery of vaccine antigens. Curtis and Cardineau was the first to express *Streptococcus mutants* surface protein A antigen in tobacco which was the mark of new vaccine era (Gómez et al., 2009). The concept of edible vaccine got further impetus after hepatitis B surface antigen was expressed in tobacco plants by Arntzen and co-workers (Mason et al., 1992). Vaccine antigens expressed in transmissible vectors or stable transgenic systems thus formulate these novel vaccines which offer convenient and safe advances for oral vaccination, considered to be a useful and practicable alternative to conventional injectable vaccines. These plant based oral vaccines deliver antigens directly to the first line of defense at the mucosal surfaces of gut, induce both local and systemic immune responses (Dus Santos and Wigradovitz, 2005; Streitfeld, 2006; Daniell et al., 2009; Santi, 2009; Rybicki, 2010; Salyaev et al., 2010; Obembe et al., 2011; Wani et al., 2011).

2. Mechanism of Action

Plant-based edible vaccines are recombinant protein vaccines, in which choice of plant species is used to produce the selected antigen(s) which are capable of inducing protective immunity against the particular animal pathogens on their oral delivery in the form of an edible vaccine (Lossl and Waheed, 2011). The genetically modified plant or the plant part expressing the candidate vaccine antigen when taken orally undergoes mastication process and the majority of the plant cell degradation occurs in the intestine by the action of digestive or bacterial enzymes on thereby releasing the vaccine antigens. Peyer’s patches (PP) are an enriched source of secretory immunoglobulin (IgA) producing plasma cells and have potential to populate mucosal tissue and serves as mucosal immune effector sites (Streitfeld, 2006; Hefferon, 2010; Takahashi et al., 2010). The breakdown of edible vaccine near PP, consisting of lymphoid nodules on the outer surface of the intestine and contain follicles, which on antigenic stimulation develops the germinal center. Through these follicles antigen penetrates into epithelium of intestine and accumulates antigen within organized lymphoid tissues. The vaccine antigen then comes in contact with M- cells or with the deep invaginations or pockets in the basolateral plasma membrane of the intestinal luminal cells. The component of immune system like B-cell, T-cells and macrophages are accumulated in these pockets. M-cells expressing class II MHC molecules and antigens transported across the mucous membrane by M-cells can activate B-cells within these lymphoid follicles (Hefferon, 2010; Takahashi et al. 2010). The activated B-cells leave the lymphoid follicles and migrate to diffuse mucosal associated lymphoid tissue (MALT) where they differentiate into plasma
cells that secrete the IgA class of antibodies. These IgA antibodies are transported across the epithelial cells into secretions of the lumen where they can interact with the antigen present in the lumen (Rudzik et al., 1975; Yuki and Kiono, 2003). Gene encoding antigen from pathogenic organisms, virus, bacteria or parasites, have been characterized and for which antibodies are available, can be handled in by inserting the entire structural gene into a plant or animal transformation vector between 5’ and 3’ regulatory elements and subsequent introduction of the vector having the foreign gene into plant or animal species. This leads to the development of transgenic plant or animal species. This is followed by subsequent immunogenicity test and ultimately administration is done by eating (Dus Santos and Wigdorovitz, 2005; Daniell et al., 2009; Santi, 2009; Buonaguro et al., 2010; Rybicki, 2010). Schematic representation of the mechanism of action of plant based edible vaccines is depicted in Figure 1 and its construction/formulation, production, testing and applications are depicted in Figure 2.

Figure 1: Immunological mechanisms of action of plant based edible vaccines.

Figure 2: Pictorial diagram depicting construction/formulation, production, testing and applications
3. Which part of plant is used for producing edible/oral vaccines?

Edible parts of different plant species like the grains or fruits are utilized for the expression of desired antigen of interest. Cereals like rice and maize, fruits like banana, leaves of many plants (tobacco, alfalfa, peanut leaves), tubers like potatoes, tomatoes, soybean seeds, cowpea, pea, carrot, peanut and lettuce have been extensively used for high levels of antigenic protein expression (Walmsley and Arntzen, 2000; Dus Santos and Wigdorovitz, 2005; Daniell et al., 2009; Buonaguro et al., 2010; Rybicki, 2010; Rukavtsova et al., 2011; Yang et al., 2011; Wani et al., 2011; Hayden et al., 2012; Yoshimatsu et al., 2012; Huy et al., 2012; Wang et al., 2012; Loza-Rubio et al., 2012; Ahmad et al., 2012).

The higher expression of exogenous protein(s) is stress inducing factor for the plant cells. Various modern applications like selective promoters have been used to achieve higher levels of candidate antigens in the desirable plant parts. Several things have to be kept in mind when selecting an expression host like gene of interest to be expressed in leaves (Mason et al., 1996), germinating seedlings (Rodriguez, 1999), chloroplast (Dauvillee et al., 2010; Lossi and Waheed, 2011) or in dry tissues like cereals (Streatfield et al., 2001) based on the final part to be used for the vaccination purpose. The advantages of using grains as an expression host are many like it can store proteins for years, is cost effective, large volumes of desired products can be produced in short span of time, and can be easily harvested and processed. The most common plant used for expression of protein is tobacco because of its transforming ability. The ultimate goal of using transgenic plants as production systems for animal and human vaccine antigens is to facilitate easier delivery of immunizing antigen so that mass immunization programmes against various infectious diseases can be achieved in a time bound fashion (Dus Santos and Wigdorovitz, 2005; Streatfield, 2006; Daniell et al., 2009; Santi, 2009; Rybicki, 2010; Salyaev et al., 2010; Obembe et al., 2011; Wani et al., 2011; Ahmad et al., 2012).

4. Plant based edible/oral vaccines in livestock, poultry and human diseases

Most of the respiratory diseases in humans and livestock, diarrheas in newborn and venereal diseases are potential targets for oral vaccines. Various edible vaccines are being developed for countering different diseases of humans and animals all over the world and many of them are under clinical and experimental trials. Plant based oral vaccines have been found to elicit protective immunity against various diseases of livestock/domestic animals including poultry as well as for humans (Azhar et al., 2002; Dus Santos and Wigdorovitz, 2005; Streatfield, 2006; Karaman et al., 2006; Mishra et al., 2008; Daniell et al., 2009; Santi, 2009; Rybicki, 2010; Buonaguro et al., 2010; Lugade et al., 2010; Rybicki, 2010; Salyaev et al., 2010; Obembe et al., 2011; Shoji et al., 2012; Huy et al., 2012; Wang et al., 2012; Loza-Rubio et al., 2012). Various antigens / proteins of the disease causative agent used in plant based edible vaccines have been reported to be eliciting immunity against various diseases of animals, which are enlisted as below.

4.1 Livestock/domestic animals

Anthrax (Protective antigen domain IV, PA (diV); Escherichia coli (Intimin O157:H7; Heat labile toxin, B subunit), Escherichia coli enterotoxigenic (F4 fimbrial adhesion; FaeG), Rabies (G and N epitopes/antigens), Brucellosis (U-Omp19), Bovine Rotavirus (BRV) (Capsid protein VP4 fused to b-glucuronidase; VP6; Co-expression of VP2, VP6 & VP7 as VLP), Foot and mouth disease (FMD) (VP1, VP4 epitope and proteins 2C & 3D), Rinderpest (RP) (HN protein, Peste des Petits Ruminants (PPR) (HN protein), Bovine pneumoniae pasteurellosis (Shipping fever) (GS60 outer membrane lipoprotein), Porcine epidemic diarrhea (Spike protein), Papilloma virus (L1 protein), Transmissible gastroenteritis coronavirus (Spike –S glycoprotein), Porcine reproductive and respiratory syndrome (GP5), Classical swine fever virus (E2 glycoprotein as fusion with ubiquitin fragment), Actinobacillus pleuro-pneumoniae (ApxIIA exotoxin), Canine parvovirus (VP2 epitope as fusion with GUS), Fasciola hepatica (Cysteine protease fusion with ubiquitin fragment) and Ascaris suum (14-kDa protective surface antigen of L3 larvae) along with recent efforts to develop edible vaccine against Taenia solium as well (Azhar et al., 2002; Yusibev et al., 2002; Karaman et al., 2006; Mishra et al., 2008; Longjam et al., 2010; Wani et al., 2011; Deb et al., 2012; Huy et al., 2012; Wang et al., 2012; Loza-Rubio et al., 2012).

4.2 Poultry

Newcastle disease (ND) (F and HN surface glycoproteins), Avian infectious bronchitis (IB) (SI glycoprotein), Infectious bursal disease (IBD) (VP2 protein), Avian reovirus (ARV) manifestations (σC minor coat protein), and avian influenza virus (AIV) (HA proteins) (Lamphear et al., 2004; Widorovitz et al., 2004; Dus Santos and Wigdorovitz, 2005; Daniell et al., 2009; Davoodi-Semiromi et al., 2009; Santi, 2009; Rybicki, 2010; Wani et al., 2011; Shoji et al., 2012). Rice with VP2 protein of IBD virus was effective against virulent IBD infection (Wu et al., 2007).

4.3 Humans

Points to shine in mind while choosing the vehicle for vaccine:

- Plant should be hardy
- It should be palatable and well relished
- It should be indigenous and easily available
- Transformation can be done easily

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In humans also plant based edible vaccines have been found protective for Cholera (subunit B, CTB), Human respiratory syncytial virus (F protein), Hepatitis B (HBsAg) (Hayden et al., 2012), Measles (H protein), Japanese encephalitis virus (JEV) (envelope protein E), Norwalk viral gastroenteritis (virus capsid protein), Malaria (MLC chimeric recombinant protein) (Kumar et al., 2012), Helicobacter pylori (UreB antigen), Anthrax (protective antigen domain IV, PA(dIV)), E. coli (intimin of O157:H7, synthetic genetic (eit) comprising of Intimin, Tir, and EspA peptides of O157:H7; Heat labile toxin, B subunit), human papilloma viruses (HPV) (HPV 16 E7 protein, HPV major capsid protein L1), Tetanus (for both human and animals) (antigen TetC), Rabies (Farmed and wild animals, humans) (Glycoprotein and nucleoprotein epitopes), Crimean-Congo hemorrhagic fever (glycoprotein), Alzheimer's disease (amyloid β-peptide), Borreliosis (outer surface protein) (Mishra et al., 2008; Daniell et al., 2009; Buonaguro et al., 2010; Lagade et al., 2010; Rybicki, 2010; Wani et al., 2011; Nojima et al., 2011; Rukavtsova et al., 2011; Ghiasi et al., 2011; Soria-Guerra et al., 2011; Meirelles-Richer et al., 2011; Yoshida et al., 2011). Also for other diseases like Human immunodeficiency virus (HIV), Influenza, Cervical cancer, Measles, and Allergic, asthmatic and autoimmune diseases Type 1 diabetes and Alzheimer's disease these novel vaccines are being explored.

Recently utilizing transient plant based expression system engineered influenza virus HA proteins were produced in Nicotiana benthamiana, which when used as antigens for immunization in mice provided considerable level of immune protection against these virus infections, and paving the way for rapid production of influenza vaccine antigens (Shoji et al., 2012). These examples open the way for the development of an edible vaccine against other pathogen infection in livestock. Efficacy of edible/oral vaccines in some of the diseases having public health significance like Anthrax, Brucellosis, Rabies, Influenza etc. indicates their practical potentials for combating zoonoses. The above examples of plant based vaccines in animals and humans open the way for the development and applicability against other pathogens too.

5. Commonly used plants and base of its use are enlisted below

5.1 Fruits and tubers

An interesting fact about fruits is that some of them have been used as vehicle for edible vaccines. The first prototype plant-derived vaccines were developed in tobacco because of the ease of transformation and regeneration of this plant. Fruit-derived E. coli vaccine has also been developed based on the highly immunogenic heat-labile enterotoxin (LT) of E. coli and it is the first fruit derived anti-diarrheal edible vaccine (Giddings et al., 2000). Tomato is a well documented vehicle for vaccine and has been structured for carrying antigens of rabies virus glycoprotein G (McGarvey et al., 1995), respiratory syncytial virus F glycoprotein (Sandhu et al., 2000), hepatitis E virus surface protein (Ma et al., 2003), Yersinia pestis F1-V antigen (Alvarez et al., 2006), synthetic HBV / HIV antigen (Shchelkunov et al., 2006), Norwalk virus capsid antigen (Zhang et al., 2006), hepatitis B virus surface antigen (HBsAg) (Lou et al., 2007) and synthetic polypeptide containing epitopes of the diphertheria, pertussis and tetanus (DPT) exotoxins (Soria-Guerra et al., 2007). Tomatoes have also been used for the production of edible malaria vaccine wherein it has been found that oral immunization of mice with recombinant merozoite surface protein (MSP) 4, MSP 4/5 and MSP1, co-administered with choler toxin Nsubunit B CTB) as a mucosal adjuvant, induce antibody responses effective against blood-stage parasite (Ruf et al., 2001; Mason et al., 2002).

Potato has the potential benefit of carrying E coli heat-labile enterotoxin (LT-B) (Haq et al., 1995), Norwalk virus coat protein (Mason et al., 1996), rabbit haemorrhagic disease virus (RHDV) VP60 (Castanon et al., 1999), HBsAg (Richert et al., 2000), a combination cholera / E. coli / rotavirus vaccine (Yu and Langridge, 2001), human papillomavirus E7 and L1 proteins (Franconi et al., 2002; Biemelt et al., 2003; Warzecha et al., 2003), and Newcastle disease virus envelope proteins (Berinstein et al., 2005). Potato has also been engineered to express cholera toxin B subunit (CT-B), analogous to the closely related LTB, induced both serum, and intestinal anti-CT-B antibodies (Arakawa et al., 1998).

5.2 Leafy plants

Edible leaves from the transgenic plants that have also been tried for the preparation of edible vaccine include alfalfa, spinach, lupins and lettuce. Alfalfa carrying VP1 of FMDV (Wigдоровitz et al., 1999) and spinach for rabies virus (Modelski et al., 1998) were used . Transgenic yellow lupins leaves were tried for the expression of surface antigen of hepatitis B virus (S-HBsAg) (Pniewski et al., 2006). The DNA fragment encoding hepatitis B virus surface antigen was introduced into Agrobacterium tumefaciens LBA4404 and is used to obtain transgenic lupin (Lupinus luteus L.) and lettuce (Lactuca sativa L.). Mice that are fed the transgenic lupin tissue developed significant levels of hepatitis B virus-specific antibodies (Waghulkar, 2010).

5.3 Seeds as a vehicle for edible vaccine

Maize or corn seed has been used as a carrier for E. coli LT-B toxin subunit (Chikwamba et al., 2002; Woodard et al., 2003). Antigen expressed in transgenic corn are stable, and the product of the cloned gene can be highly concentrated and homogeneous in corn germ. Maize seed with transmissible gastroenteritis virus (TGEV) subunit vaccine can save pigs from the disease (Lamphear et al., 2002; Horn et al., 2003; Streetfield et al., 2003). Rice has also been tried as a carrier for vaccines like that of FMD structural protein (Wang et al., 2012). Fusion protein of E. coli LT-B and an epitope of porcine epidemic diarrhoea virus has been designed which was reported to be an effective vaccine (Oszvald et al., 2007). Antigens against Ascaris suum fused with cholera toxin have
been developed (Matsumoto et al., 2009). The edible vaccine Aβ rice has been proved effective in Alzheimer's disease (AD) (Nojima et al., 2011).

There are several such examples, among which, immunogenic effect of transgenic potato tubers and tobacco leaves carrying a Norwalk virus capsid protein (NVCP) in mice has been studied (Mason et al., 1996), successful expression of antigen in plants came into light for rabies virus G protein in tomato (McGarvey et al., 1995) and expression of rotavirus VP7 in transgenic potatoes and subsequent oral immunization of the transgenic tubers to the mice for eliciting serum IgG and mucosal IgA specific for VP7 (Wu et al., 2003) are quiet noteworthy. Other remarkable plant virus vaccines production involves expression of ORF2 partial gene of hepatitis E virus in tomatoes (Ma et al., 2003), development of edible transgenic potato vaccine was made to express synthetic LT- B gene into potato plants that protects mice against E. coli heat-labile enterotoxin (LT) (Mason et al., 1998), gene of protective antigen (PA) of anthrax expressed in plant system was possible to develop edible anthrax vaccine (Azhar et al., 2002) and delivery of tetanus antigen Tet C in plants (Tregoning et al., 2004) has been explored. Engineered influenza virus HA proteins have been produced in Nicotiana benthamiana, which provided considerable level of immune protection in mice, paving the way for rapid production of influenza vaccine antigens (Shoji et al., 2012).

Experimental Animals

For experimental trials, animal models include mice, pigs, guinea pig and rabbit, and also sometimes the natural animal host (Cattle, sheep, pig, chicken) and humans (Wani et al., 2011).

6. Administration

Plant based oral vaccines are given via foods comprising of edible parts of the transgenic plant. They have the added advantage especially in poultry where stress associated with handling or disturbing birds during individual vaccination is avoided, and also sometimes due to the water deprivation there are chances of ineffective vaccine delivery through drinking water. These food-based vaccines should be considered for the commercial poultry industry for safeguarding from various other infectious diseases (Wani et al., 2011).

7. Advantages of plant-based vaccines

Plant based edible/oral vaccines possess a number of potential beneficial features - cheap, safe, produced rapidly, easy to store, distribute and deliver, no cold chain management and remove injection nervousness (Streatfield et al., 2001; Tiwari et al., 2009; Hefferon, 2010; Loza-Rubio and Rojas-Anaya, 2010; Wani et al., 2011). The additional advantage of stimulating both mucosal and systemic immunity help prevent strongly various diseases of respiratory and gastrointestinal systems. Some of the salient advantages of plant-based vaccines and comparative benefits over conventional vaccines have been summarized as below and also showed in table 1 and figure 3.

- Similar to conventional vaccines, plant based antigens can induce effective neutralizing antibodies in hosts.
- Can be stored for extended periods in food grains.
- Heat-stable recombinant proteins can be generated.
- Production is cost-effective.
- Expensive fermentation and purification procedures are not required.
- Need of refrigerated storage transportation under cold-chain maintenance and sterile delivery systems are eliminated.
- Large scale production can be achieved in time bound fashion.
- Free from conventional vaccine contaminants - bacterial or viral pathogens.
- Needle-free delivery vaccine delivery is painless, time and labor-saving and also reduces the cost of syringes and needles.
- Administration is safe and without stress: no muscle damage as compared to needle based vaccine injections or local abscess formation in meat animals.
- Herd immunity can be easily achieved due to mass immunization potential.
- Mucosal adjuvants can be incorporated to augment induction of immunity and protection level.
- Plants can be grown easily and locally, so have wide applicability probabilities especially in developing countries also.

Many a limitations of conventional vaccines are alleviated viz., residual virulence, requirement of extensive safety precautions, production difficulty and larger cost.
### Table 1: Conventional vaccines vis-à-vis plant based edible vaccines.

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<thead>
<tr>
<th>Conventional/Traditional Vaccines</th>
<th>Plant Based Edible vaccines</th>
<th>References</th>
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<tr>
<td>Comprised of weakened, live attenuated or killed pathogen</td>
<td>Comprises of plasmid / vector carrier system or metal particles containing small segment of target DNA sequence.</td>
<td>Mercenier et al., 2001; Taylor and Fauquet, 2002</td>
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<tr>
<td>Injected intramuscularly or subcutaneously</td>
<td>Given orally</td>
<td>Mishra et al., 2008</td>
</tr>
<tr>
<td>Inefficient in producing a protective response at mucosal surfaces</td>
<td>Efficient in producing a protective response at mucosal surface.</td>
<td>Yuki and Kiono, 2003; Streatfield, 2006</td>
</tr>
<tr>
<td>Possess residual virulence</td>
<td>No residual virulence</td>
<td>Streatfield, 2006; Lal et al., 2007; Mishra et al., 2008</td>
</tr>
<tr>
<td>Need extensive safety precaution</td>
<td>Have a wide margin of safety.</td>
<td>Daniell et al., 2001</td>
</tr>
<tr>
<td>Production difficulty and larger cost</td>
<td>Relative ease of production and cost effective</td>
<td>Nochi et al., 2007</td>
</tr>
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### Conclusion and Future Perspectives

Transforming plants to carry vaccines is a new frontier medical technology that can prove to be very effective, if rightly implemented, in providing accessibility to developing and underdeveloped countries where rates of viral diseases are especially high. Moreover, edible vaccines hold great potential, especially in countries where transportation cost, poor refrigeration, and needle use complicate vaccine administration. Due to these reasons, the vaccines may be ideal for facing bio-weapons and veterinary use. Protein antigen expressed in plant tissue like seeds, tubers, and leaves makes delivery of the vaccine antigen easier and practically feasible application to large masses. These are also ideal for the vaccination of animals and birds living in the wild areas and also preventing the zoonotic diseases. However, a major hurdle is how to move the vaccine through the rumen/stomach without damaging or inactivating it, and evaluation of dosage requirements. This biomedical applications of plants in the form of plant based oral/edible vaccines could become a
common alternative to conventional vaccines in the near future, for which there is a great need for research over the next decade in this promising area for safeguarding health of animals including poultry and humans too.

Further, edible vaccines may prove to be a solution that will enable the positive effects of vaccines for reaching and to decrease some potential hazards associated with parenteral vaccines viz., allergic reactions, presence of some toxic substances, and risk of reversion of attenuated strains to pathogenic one. It is interesting to note that various modern applications have been used to achieve higher levels of candidate antigens in the desirable parts. Plant based oral vaccines are given via foods comprising of edible parts of the transgenic plant with the desired vaccine. They have the added advantage especially in poultry where stress associated with handling or disturbing birds for individual vaccination is avoided, and also the water deprivation for vaccine delivery through drinking water. Third world countries can benefit from edible vaccines because the methods in production are reasonably affordable and the vaccine products would be more openly accessible to the population. With further advances in biotechnology and molecular biology, the techniques of production will be likely conquered to make plant derived vaccines more efficient and dependable. In spite of various clinical trials, till date no commercial plant based edible vaccines are available. However, many researchers project that some plant based edible vaccines will be available commercially in the near future.

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