Indian J.L.Sci. 6 (1) : 113-116 , 2017 Review Article ISSN : 2277-1743 (Print)
ISSN : 2278-7879 (Online)

EDIBLE VACCINES : A NEW APPROACH IN IMMUNIZATION

DUSHYANT KUMAR SHARMA[1]

Department of Zoology, Govt. Model Science College, Gwalior, Madhya Pradesh, India

ABSTRACT

Edible vaccine i.e. a vaccine that can be eaten (plant derived vaccines) is a new approach in the field of vaccination. Several plant-derived vaccine antigens have been found to be safe and induce sufficiently high immune response. In comparison to traditional vaccines, these vaccines have some significant advantages. Edible plant parts can be excellent alternatives for the production of vaccines. Edible vaccine is a concept which is a cost-effective, easy-to-administer, easy-to-store, safe and socio-culturally acceptable vaccine. They also have applications in birth control, malaria and cancer therapy.

KEYWORDS : Edible Vaccines, Immunization

One of the greatest achievements in science is the development of vaccines. Vaccines have been revolutionary for the prevention of infectious diseases. They have prevented a large number of deaths caused, every year, by dreadful diseases like smallpox, polio, hepatitis etc. Diseases like smallpox and polio have been successfully eradicated by vaccination. The word 'vaccine' has been derived from Latin word vaccīn-us, from vacca, cow. It was Edward Jenner who, for the first time, in 1748, deliberately inoculated people with cowpox virus, in order to protect them from smallpox.

Types of Vaccines

On the basis of type of pathogen, used in the preparation of the vaccine, there are various types of vaccines. Some of these are in current use while there are some which are under experiments as given in table 1.

Edible Vaccines

The worldwide need to produce safe and affordable vaccines with a minimum requirement of manufacture and processing, together with the advancements achieved in biotechnology, have promoted the development of efficient alternatives to traditional ones(Gomez et. al, 2009). Traditional vaccines are not entirely safe. Plant-derived vaccines comprise a new area in the field of vaccines. Plants offer general advantages for large-scale economic production, product safety and ease of storage and distribution (Holásková et al., 2015). Edible vaccines hold great promise as a cost-effective, easy-to-administer, easy-to-store, fail-safe and socio-culturally readily acceptable vaccine delivery system, especially for the poor developing countries (Lal et.al, 2007, Jain et. al, 2013, Barzegari et.al,2014). Several plant-derived vaccine antigens have been found to be safe and induce sufficiently high immune response. Edible plant parts can be excellent alternatives for the production of vaccines.

Production of Edible Vaccine

Edible vaccines involves introduction of selected desired genes into plants and then inducing these altered plants to manufacture the encoded proteins. The process is called transformation and such plants are called transgenic plants. Plants like banana, potato, tomato, lettuce and rice are under study to be used as edible vaccines. The genes, encoding orally active antigenic proteins, are isolated from the microbe and integrated into the genome of the selected plant. The foreign DNA can be introduced in the plant either by gene gun method or through Agrobacterium tumefaciens, a naturally occurring soil bacterium which has the ability to get into plants through some kind of wound. A circular plasmid -Ti plasmid (tumor inducing) is present in the bacteria which enables it to infect plant cells and integrate into their genome. Once the genes are integrated into the genome of the selected plant, the plant produces the specific proteins in its parts or products (Fig.1). Production of transgenic plants is species dependent and takes 3 to 9 months. The part or product is fed raw to the human /animals to bring out immunization. Multi-component vaccines can be obtained by crossing two plant lines harboring different antigens.

Mode of action of Edible vaccine

The antigens in transgenic plants break up in the intestines. The antigens are released, taken up by M cells in the intestinal lining that overlie peyer's patches and gut-associated lymphoid tissue (GALT). It is passed on to macrophages, other antigen-presenting cells; and local

[1]**Corresponding author**

Types of Pathogen/Antigen	Vaccine
Vaccines in current use ***Whole Organism*** Natural intact organism Attenuated Inactivated (killed) ***Subunit (Subcellular fragments)*** Capsular polysaccharide Surface antigen Toxoid	Vaccinia, Cowpox virus Sabin polio, measles, mumps, Hepatitis A, Influenza, Cholera *Streptococcus pneumonia, Nesseria meningitides* Hepatitis B Tetanus, Diphtheria
Vaccines under experiments Anti-idiotype DNA vaccine Synthetic peptide vaccine **Edible vaccine**	

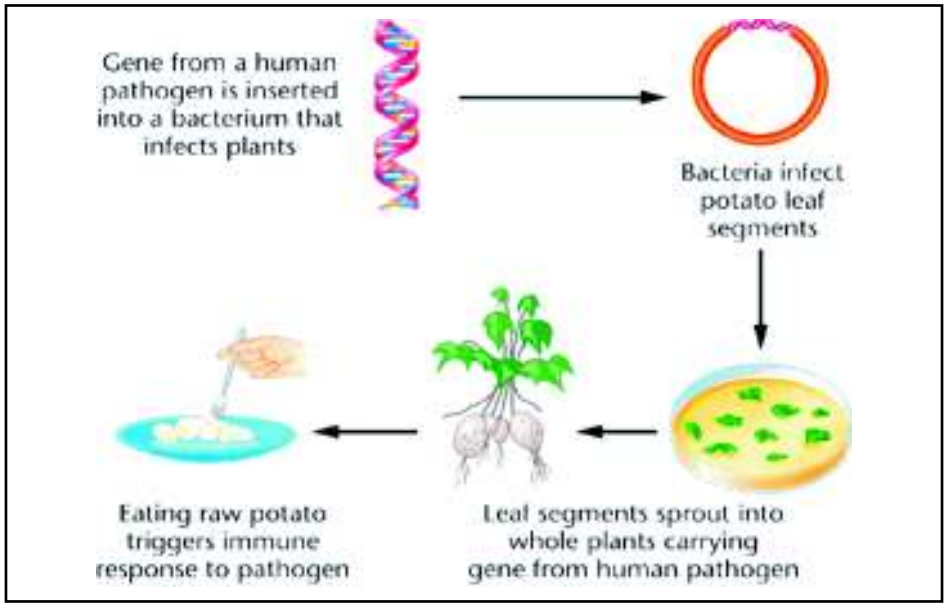

Figure 1 : Production of Edible Vaccine (www.lookfordiagnosis.com)

lymphocyte populations, generating serum IgG, IgE responses, local IgA response and memory cells, which would promptly neutralize the attack by the real infectious agent (Figure, 2) (de Aizpura et. al., 1988; William and Langridge, 2000).

Advantages of Edible Vaccine over Conventional Vaccines

Edible vaccines have a bright future. In comparison with traditional vaccines, these vaccines have some significant advantages such as low cost, greater safety, and greater effectiveness. The major advantage of the oral vaccination system is the stimulation of both mucosal and systemic immunity (Davoodi-Semiromi et al., 2010). As they consist of antigenic proteins and do not involve any pathogenic gene, edible vaccines are safe and do not have side effects. Their production is highly efficient i.e. plants can be grown in a small area with high yield. They can be grown locally using standard methods and do not require large intensive pharmaceutical manufacturing facilities. Vaccines exhibit good genetic stability. They are heat-stable

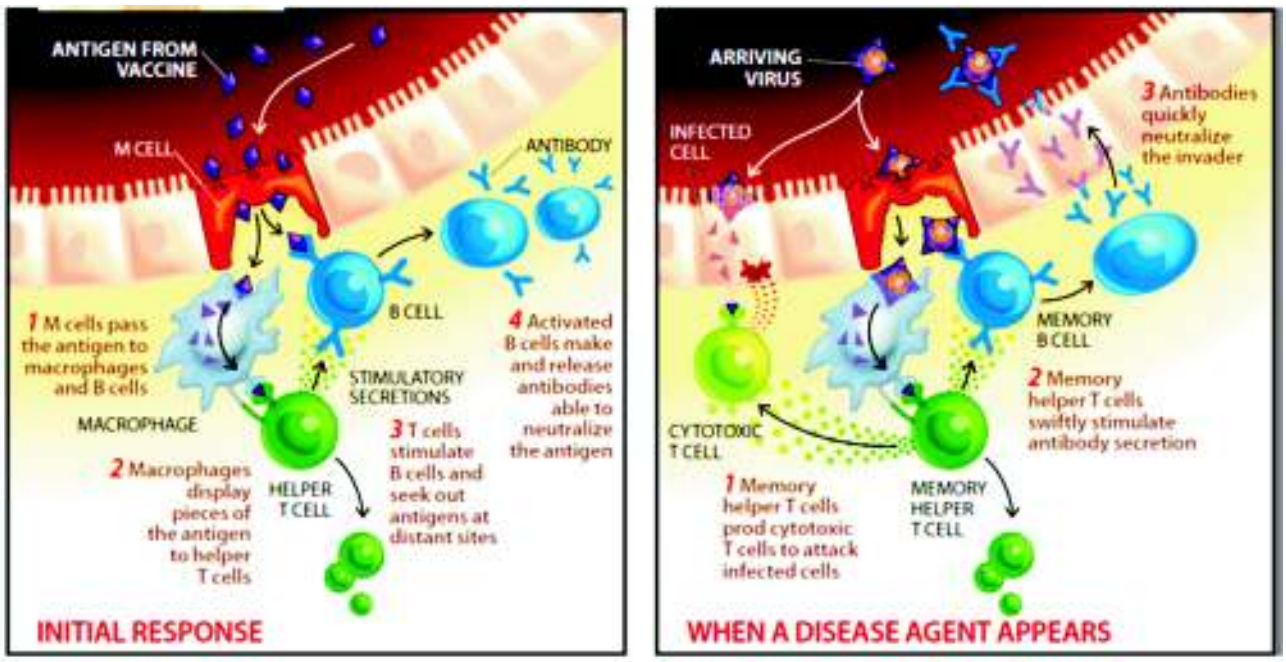

Figure 2 : Mode of Action of Edible Vaccines(by William H. R. Langridge, 2000)

and do not require cold-chain maintenance. Vaccines can be stored near the site of use and eliminate long-distance transportation. As these vaccines do not require syringes and needles, chances of infection are very less. There is no need for skilled medical personnel. Edible vaccines also have applications in birth control, malaria and cancer therapy.

Limitations

The concept of edible vaccine seems to be a very revolutionary one. But there are many questions which need to be answered. The first problem is that the antigenic protein may be rapidly degraded in the digestive tract. The determination of the right dosage is a major problem in edible vaccines. The dose may vary according to a person's weight, age and sex. The dose may also depend on fruit/plant's size, ripeness and protein content. The amount to be eaten is very critical because too low a dose would fail to induce antibodies and too high a dose would, instead, cause tolerance. Orally administered antigen often tolerize rather than immunize.

Current Status

Although the plant-made vaccine field started three decades ago with the promise of developing low-cost vaccines to prevent infectious disease outbreaks and epidemics around the globe, this goal has not yet been achieved completely(Chan and Daniell 2015.). Currently, the edible vaccines are being developed and focused for a number of human and animal diseases, including measles, cholera, foot and mouth disease and hepatitis B, C and E. In 1996, Prakash reported that tomato plants, expressing rabies antigens, could induce antibodies in mice.

In the case of hepatitis B, both stable and transient expression systems have been developed in various plants, including potato, lettuce, tobacco, tomato and carrot (Young et al., 2016) Successful expression of antigen in plant has been demonstrated in various animals. The vaccines have also been checked for their efficacy in humans.

Juárez-Montiel et al.,2015 reported that mice orally immunized with common corn smut(huitlacoche)-derived B subunit of the cholera toxin showed significant humoral responses that were well-correlated with protection against challenge with the cholera toxin . Their

findings demonstrate the feasibility of using edible corn smut as a safe, effective, and low-cost platform for production and delivery of a subunit oral vaccine.

Tavizi et al., (2015) reported that strawberry is a suitable bioreactor for production of recombinant proteins especially edible vaccines. They reported that mass production of human pro-insulin could be possible in roots and shoots of strawberry. Improved understanding of plant molecular biology and consequent refinement in the genetic engineering techniques can lead in designing of new vaccines which can induce very specific and sufficiently high immune response.

CONCLUSION

Edible vaccine seems to be a better solution to get rid of various diseases as it has more advantages compared to traditional vaccine. It would overcome the problems associated with traditional vaccine of cost, production, distribution and delivery. Edible vaccines might be especially beneficial and profitable to populations of developing world. But there are many problems associated with them. Before becoming a reality, all such issues need to be overcome.

REFERENCES

Barzegari A1, Saeedi N., Zarredar H., Barar J., Omidi Y., 2014. The search for a promising cell factory system for production of edible vaccine. Hum Vaccin Immunother. **10**(8):2497-502.

Chan H. T. and Daniell H., 2015. Plant-made oral vaccines against human infectious diseases-Are we there yet? Plant Biotechnol J. **13**(8):1056-70.

Davoodi-Semiromi A., Schreiber M., Nalapalli S., Verma D., Singh N.D., Banks R.K., Chakrabarti D., Daniell H., 2010. Chloroplast-derived vaccine antigens confer dual immunity against cholera and malaria by oral or injectable delivery. Plant Biotechnol J. **8**:223-242.

de Aizpura H. J., Russell-Jones G. J., 1988. Oral vaccination. Identification of classes of proteins that provoke an immune response upon oral feeding. J Exp Med **167**:440- 51.

Gómez E.1., Zoth S.C., Berinstein A., 2009. Plant-based vaccines for potential human application: a review. Hum Vaccin. **5**(11):738-44.

Holásková E., Galuszka P., Frébort I., Öz M.T., 2015 Antimicrobial peptide production and plant-based expression systems for medical and agricultural biotechnology. Biotechnol Adv., **03** : 007

Huang Z., Dry I., Webster D., Strugnell R., Wesselingh S., 2001. Plant derived measles virus hemagglutinin protein induces neutralizing antibodies in mice. Vaccine **19**:2163-71.

Jain A.1., Saini V., Kohli D.V., 2013. Edible transgenic plant vaccines for different diseases. Curr Pharm Biotechnol. **14**(6):594-614.

Juárez-Montiel M., Romero-Maldonado A., Monreal-Escalante E., Becerra-Flora A., Korban S.S., Rosales-Mendoza S., Jiménez-Bremont J.F., 2015. The Corn Smut ('Huitlacoche') as a New Platform for Oral Vaccines. PLoS One. **10**(7):e0133535.

Lal P., Ramachandran V. G., Goyal R., Sharma R., 2007. Edible vaccines: current status and future. Indian J Med Microbiol. **25**(2):93-102.

Prakash C. S., 1996. Edible vaccines and antibody producing plants. Biotechnol Develop Monitor 27:10-3.

Sharma D. K. and Sharma T., 2015. Immunology. New India Publishing Agency, New Delhi.

Tavizi A., Javaran M. J., Moieni A., Mohammadi-Dehcheshmeh M., Mohebodini M., Ebrahimie E., 2015. Root and shoot parts of strawberry: factories for production of functional human pro-insulin. Mol Biol Rep. **42**(5):1013-23.

William H. R. Langridge, 2000. Edible vaccines. Scientific American ,September : 66-71.

Young H. J., Se H. P., Ki-Beom Moon, Jae-Heung Jeon, Hye-Sun Cho and Hyun-Soon Kim, 2016. The Last Ten Years of Advancements in Plant-Derived Recombinant Vaccines against Hepatitis B. Int. J. Mol. Sci. 17: 1715.