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Introduction to Vaccines in Brief and a Detailed View of Edible Vaccines.

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ABSTRACT: VACCINE is a biological preparation that enhances the immunity of a body to a particular disease.It contains an agent which is having a resemblance with a disease causing microorganism and is often made from killed or weakened form of microbes.In this review article we are going to study about a different form of vaccine I.e. EDIBLE VACCINE. Edible vaccines includes the introduction of selected desired genes into plants and then these altered plants are induced to manufacture altered protein. We will understand the concept behind edible vaccine and it's mechanism of action.we will also discuss how the edible vaccines are used in the treatment of many diseases such as cholera, hepatitis B,measles,etc.Also we will study some downside of edible vaccines.

I. INTRODUCTION:

A vaccine is a biological preparation that provides active acquired immunity to a body from a particular infectious disease. A vaccine contains an agent that resembles the disease causing microorganism and is typically made from weakened or killed form of microbes. This agent trigger the immune system of a body to acknowledge the agent as a threat, demolish it, and to further acknowledge and demolish any of the microorganism linked with that agent that it may come across in future. The word vaccine is derived from a Latin word 'vacca' for cow. This vaccine is developed for use in cowpox. Edward Jenner in 1796 used this vaccine in human beings resulting in protection of human beings from smallpox. Jenner's work was continued by Louis Pasteur. Vaccines can be Prophylactic (e.g. to prevent the effects of a future infections by any natural or wild pathogen) and Therapeutic(e.g. vaccine against cancer).

CONCEPT OF EDIBLE VACCINES:

The phrase Edible vaccine was first used by Charles Arntzen in 1990 and refers to any food ,typically plants that produces vitamins, proteins and other nourishment which act as a vaccine against certain disease. Edible vaccines are subunit vaccine that involves the introduction of gene of interest into the plants and the transgenic plant is then induced to manufacture altered protein. Transgenic plants are used as a vaccine production system for edible vaccine. The genes encoding antigens of bacterial and viral pathogens can be expressed in plants in such a way that they retain native immunogenic properties. Edible vaccines originally thought to be useful only for preventing infectious diseases but, now it has also found application in preventing autoimmune disease, birth control , cancer ,etc. Edible vaccines are currently boosted to develop a vaccine for a number of human and animal diseases.

PRODUCTION OF EDIBLE VACCINE:

Edible vaccine can be produced by incorporation of a transgene in a selected plant cell. This process is known as Transformation and it leads to a transgenic plant. Incorporation of transgene can be done by two methods,

- Direct delivery method :In this method ,the incorporation of transgene is done without combining with vector.
- Indirect delivery method: In this ,the incorporation is done by combining with a vector . It is subclassified on the basis of use

1)plant bacteria
2)plant virus

Direct gene delivery method:

It is a simple and a vector independent method which leads to a stable transformation of a plant. In this method ,RNA/DNA (epitope sequence) is directly introduced into the plant cell. The most commonly used method for this is BOLISTIC METHOD.

Biolistic method :

This method is also known as gene gun method or micro projectile bombardment method. In this method the RNA/DNA is kept in the microcarrier which is made up of gold or tungstent. Then this microcarrier is kept inside the gene gun under high pressure of helium gas. Due to pressure the entire microcarrier along with the DNA/RNA

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is directly inserted into the plant cell. This method is expensive. Biolistic method is differentiated on the basis of where the antigen gene is expressed,also known as Antigen Expression Method,

1) Chloroplast transformation: Antigen gene is directly introduced in the chloroplast such that it increases the protein. It is most commonly used.
2) Nuclear transformation: Antigen gene is directly introduced in the nucleus of the plant cell and with the help of non homologous recombination the transformation will take place.

Indirect gene delivery method:

It is a vector mediated method. In this thedesired plant cells are infected with plant bacteria plant virus to produce the desired protein. TheRNA/DNA(antigenic sequence) is incorporated in the plant bacteria or plant virus which act as a vector . This vector is used to infect the plants. Depending on the vectors ,this method is classified into two,

1) Agrobacterium mediated gene transfer:

Agrobacterium is a gram negative bacteria. It infects the plant cell and transfers their gene to plant nucleus.Commonly used species are A.tumefaciens andA.rhizogenes. This method is used to yield stable integration of gene into plant genome. This is a slow process and yield is low but simple and cost effective.

2) Genetically engineered plant virus:

The method involves modification of plant virus to produce viral coat protein chimeric gene. The antigen gene and viral coat protein gene is combined and inserted in the virus. This combination is known as viral coat chimeric gene. This virus will further infect the plant. As the viral genome replicates the antigen gene will also replicate and accumulate in the plant cell. In plant, this techniques leads to transient antigen expression.

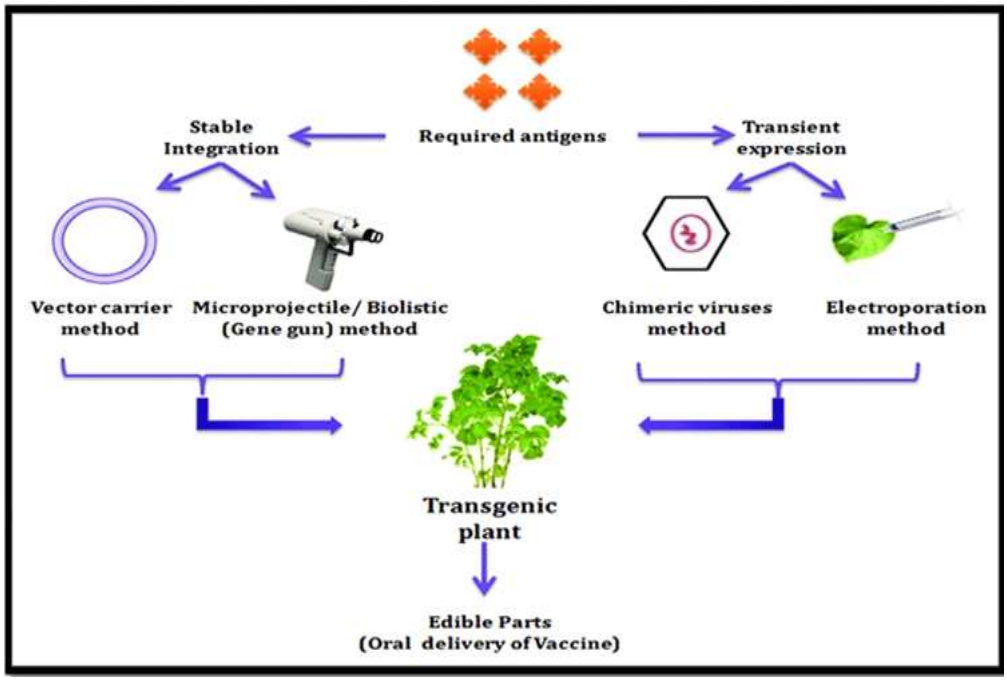

Fig 1: schematic representation of various method of producing Edible vaccines.

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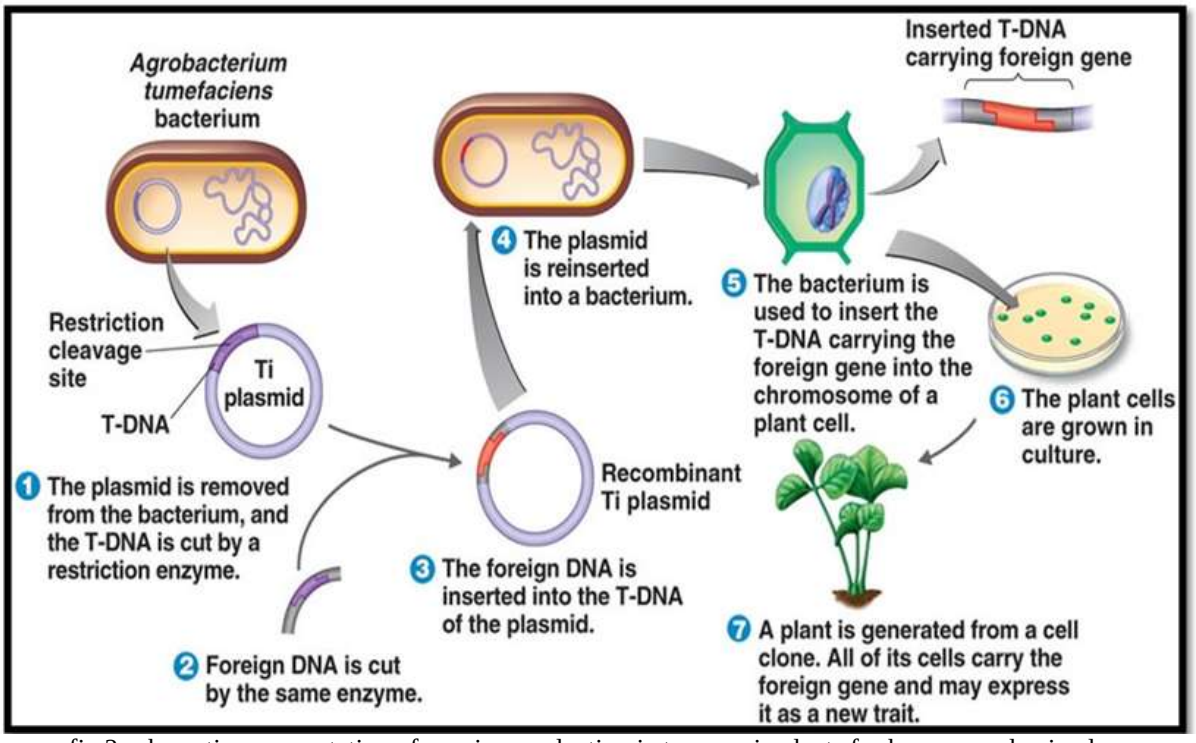

fig 2:schematic representation of vaccine production in transgenic plants for humans and animals.

MECHANISM OF ACTION OF EDIBLE VACCINE:

Since a pathogen invades a human body via different routes such as urogenital, gastrointestinal and respiratory tract which is having a mucosal lining that acts as a barrier. Here the mucosal immunity comes into picture which becomes the defense mechanism. In the same way edible vaccines stimulates the mucosal immunityki other traditional vaccines. The transgenic plant containing antigen when ingested it gets masticated and degraded in stomach by the action of digestive enzymes. Further when it goes to the

gastrointestinal tract,there is a presence of payer's patch on the outer side of intestine. Payer's patch is an enriched source of IgA producing plasma cells and have the potential to populate mucosal tissue and serves as mucosal immune effector site.The breakdown of edible vaccine near payer's patch, consisting of 30-40 lymphoid nodules and contain follicles on the outer surface of intestine. These follicles acts as a site for antigen to penetrate the intestinal epithelium, results in accumulation of antigen within organized lymphoid structure. The antigen then comes in contact with M cell, and M cell passes the antigen to macrophages and B cell. These B cell migrate to lymphoid malt area where the become active and known as plasma cellwhen they release a antibody. These antibody penetrates the epithelium in the lumen andneutralizes the virus inside the lumen. In this way the mucosal immunity is activated by the edible vaccine. In recent research, the goblet cells capture the antigen and directly display it in the small intestine.

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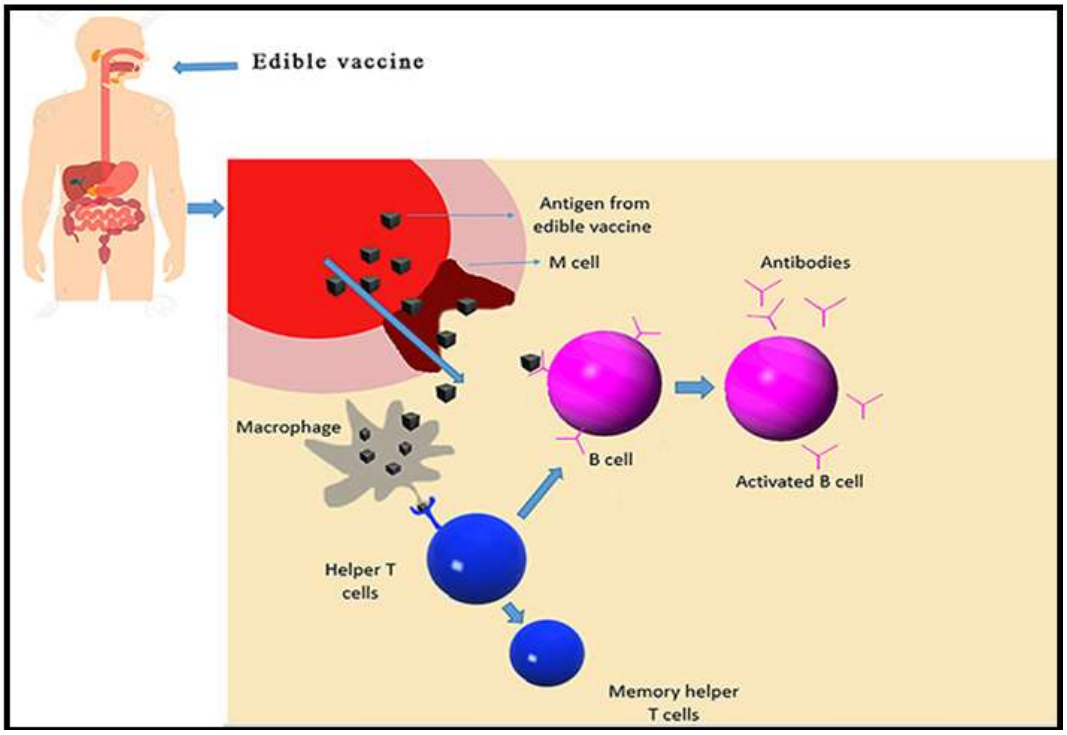

Fig 3: Mechanism of action of Edible vaccine.

APPLICATIONS OF EDIBLE VACCINE:

1) Malaria:

Malaria is a life threatening disease typically caused by the bite of an infected anopheles mosquito resulting ins increase of morbidity and mortality rate worldwide. Three antigens are currently taken in consideration for the development of a plant based vaccine for malaria. Merozoite surface protein (MSP) 4, MSP 5 from plasmodium falciparum and MSP 4/5 from P.yoelli.

2) Hepatitis B:

Hepatitis B (HBV) is the viral infection of liver which is estimated to infect 400 million people around the world The Hepatitis B surface antigen (HbsAg) is used against Hepatitis B as a vaccine. For hepatitis B parental VLPs could invoke specific antibodies in mice. First human trial of a potato based vaccine against Hepatitis B have reported encouraging result. The quantity of HBsAg needed for one dose could be achieved in a single potato. When cloned into CaMv, plasmid HBsAg subtype showed higher expression in roots as compared to leaf tissue of transgenic potato.

3) Measles:

It is a viral infection, spreads through the air droplets produced from coughing or sneezing. It is serious for small children's, but is easily preventable by a vaccine. Edmonstan strain antigen ,consist measles virus hemagglutinin ,which was selected for the manufacturing of edible vaccine, which can be transformed into tobacco plant by plasmid /vector.MV-H edible vaccines does not cause atypical measles, which may occasionally seen with other current vaccines. Transgenic rice , lettuce, baby food against measles are also being developed.

4) Cancer therapy:

Several transgenic plants are studied to generate monoclonal antibodies, that are identified as an effective cancer therapy agent. Example is doxorubicin is responsible for breast cancer, lung tumour,ovarian cancer and colon cancer , is attacked by the monoclonal body of soya bean.It is fount to be efficient.

5) Autoimmunization:

In past few years,analyst have found several cell protein that can attain autoimmunity in people incline to type l diabetes mellitus. Potato was the first plant used for the development of edible vaccine for diabetes. This developed transgenic potato when fed to non obese diabetic mice , resluts in increased level of IgGin blood.IgG is an antibody that suppress the harmful immune response. It is found that protein is proven

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successful in suppressing the immune attack and delayed the time of high blood sugar level.

ADVANTAGES:

1) It is effective as delivery vehicles because it doesn't require adjuvants.
2) They are subunit vaccines and attenuated pathogens are not used as edible vaccine uses antigen gene and produces protein and this protein will never revert back to its infectious form to cause disease. Hence edible vaccines improves the safety of individual.
3) They elicit mucosal immunity unlike traditional vaccine.
4) They are cost effective in availability,storage, preparation, production and transportation.It can be store at room temperature and does not require cold chain supply in transportation.
5) Seeds of transgenic plant can be dried and further used to produce the same edible vaccine.
6) It can be produced easily at mass level because the production is in plant it can be easily produced in mass.
7) It is orally administered and is self operated ,no health care professionals are required. It reduces the risk of contamination.
8) It can be multicomponent vaccine. Hence they are called as second generation vaccine.

DISADVANTAGES:

1) It can develop immunotolerance. Since , edible vaccines are produce in plants, an individual can develop immunotolerance against a peptide or a protein.
2) Consistency of dosage and protein content vary from plant to plant and generation to generation. These factors can not be controlled as plants are biomanufacturers, so their will be difference in vaccines in terms of consistency.
3) Ripeness of fruit also affect the proteins that are present in the form of antigen.
4) Stability of vaccines differ from plant to plant.
5) Some food can't be eaten raw so ,cooking is required which leads to denaturation of antigen or it can weaken the protein which is present.
6) Distinguishing the real fruit /vegetable and the vaccine fruit/vegetable is a major drawback.

II. CONCLUSION:

From this review article ,we understood the concept of edible vaccines. Edible vaccines are a great discovery in the field of biotechnology, which provides economical vaccines that is particularly useful in immunizing people in emergent nations, where the transportation, high cost of vaccine and supply of cold storage environment are obstructing the efficacious vaccination. Edible vaccine have overcome all the obstacles that have been in the oath of rising vaccine technology. In future, edible plant derive vaccines show a greater probability of safer and a powerful immunization. Edible vaccines provides a brighter and better future, when the treatment of diseases is not painful but fruitful one. An individual ca be protected from diseases by just eating fruit/Vegetables. Edible vaccines provides a greater opportunity for the people to get vaccinated and for the developers as well.

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