

## EDIBLE VACCINES

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### ABSTRACT

A new approach for delivering vaccine antigens is the use of inexpensive, oral vaccines. Edible oral vaccines offer exciting possibilities for significantly reducing the burden of diseases like hepatitis and diarrhea particularly in the developing world where storing and administering vaccines are often major problems. Even though they have some disadvantages like control of the "dosage" of the antigen that is present

in the recombinant fruit or vegetable, they have many advantages as they trigger the immunity at the mucosal surfaces which is the body's first line of defense. To overcome the disadvantage of adequate dosage, stable plant lines that produce fruits and vegetables with relatively constant amounts of the antigen need to be developed. The hope is that edible vaccines could be grown in many of the developing countries where their need is more.

**Key words :** Vaccines, edible, Immunity

### INTRODUCTION

In the last decade, advancements in the field of medicine and healthcare have been possible because of the development of newer, safer and highly effective vaccines; recombinant vaccines, subunit vaccines, peptide vaccines and DNA vaccines to name a few. Although these vaccines have an undue advantage over traditional conventional vaccines, there is a flip side to them. Not only are these vaccines expensive, but their storage and transportation pose a problem as many of them require refrigeration. This is a disadvantage in many of the developing countries.

So, as alternatives had to be thought of, it was envisaged that plants could be used as a cheap, safe and efficient production system for vaccines and thus the concept of edible vaccines was born.

### DEFINITION

Edible vaccines are nothing but transgenic plant and animal based production of or those that contain agents that trigger an animal's immune response. In simple terms, edible vaccines are plant or animal made pharmaceuticals. This essay highlights the importance of edible vaccines produced in plants.

### INITIAL DEVELOPMENTS IN DESIGNING THE EDIBLE VACCINES

The concept of edible vaccines was developed by Arntzen ([www.genomenetwork.org](http://www.genomenetwork.org)) in the 1990s. He currently heads the department of plant biology at the Arizona State University. He fell upon the idea after he attended a conference in New York, organized by the WHO. Although the idea seemed quite simple in the beginning, making it into a reality has required sophisticated science.

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The earliest demonstration of an edible vaccine was the expression of a surface antigen from the bacterium *Streptococcus mutans* in tobacco. As this bacterium causes dental caries, it was envisaged that the stimulation of a mucosal immune response would prevent the bacteria from colonizing the teeth and therefore protect against tooth decay.

### CURRENT STATUS

Several plant derived vaccines for human use are approaching the market but it is likely that the first commercial Plant derived vaccine will be a veterinary vaccine.

At least 30 such products have been expressed in plants, some providing protection against challenges with disease causing agents.<sup>[1]</sup>

The trial carried out by prodiGene Inc. showed for the first time that an oral vaccine produced in plants could protect live stock against virulence challenge.<sup>[2]</sup>

The first product to reach market could be a poultry vaccine developed by Dow AgroSciences<sup>[3]</sup>, has been proposed for market release sometime in 2006.

### HOW DO EDIBLE VACCINES WORK?

Edible vaccines contain DNA fragments from the original pathogen. These fragments code for a protein that is usually a surface protein of the pathogen. This is responsible for eliciting the body's immune response.

### SOME EXAMPLES OF EDIBLE VACCINES

- **Transgenic Potatoes For Diarrhea**

The first human trial for an edible vaccine took place in 1997. Volunteers ate transgenic potatoes that contained the b-subunit of the *E. coli* heat-labile toxin, which causes diarrhea. Ten of the 11 volunteers showed a 4-fold increase in serum antibodies.<sup>[4, 5]</sup>

Researchers at the Boyce Thompson Institute at Cornell University conducted another clinical trial of an edible vaccine in 1999. Potatoes containing the Norwalk

virus (which causes vomiting and diarrhea) fed to volunteers elicited an immune response in 19 out of 20 volunteers.<sup>[6]</sup>

The disadvantage of using potato-based edible vaccine is that it has to be consumed raw; when cooked the protein may get denatured or in some cases less effective. Research has shown that by partial boiling at least half the vaccine remained alive.

- **Transgenic Tomatoes Against Diarrhea**

In the US at the Cornell University, researchers have developed transgenic tomatoes against the Norwalk virus, which causes severe diarrhea. The tomatoes produced a surface protein specific to the virus. Mice that ate these tomatoes developed an immune response to the virus.<sup>[7]</sup>

Recently, banana has been explored as an alternative source because not only does it eliminate the need for cooking but also it's a locally grown plant. The expression of a protein in banana will depend on the identification of a tissue specific promoter. Other examples include rabies glycoprotein being expressed in viral vectors in spinach<sup>[8]</sup> and hepatitis B surface antigen in lettuce and potato.<sup>[9, 10]</sup>

#### ADVANTAGES OF EDIBLE VACCINES

1. They are cheap; therefore they can be mass-produced.
2. They can be ingested by eating the plant/part of the plant. So, the need to process and purify does not arise.
3. Extensive storage facilities like cold storage are not required.
4. If the local/native crop of a particular area is engineered to produce the vaccine, then the need for transportation and distribution can be eliminated.
5. Most importantly, they trigger the immunity at the mucosal surfaces such as those that line the mouth (mucosal immunity) which is the body's first line of defense.

#### DISADVANTAGES OF EDIBLE VACCINES

1. Will the antigens be able to survive the hostile, acidic conditions of the stomach and even if they did, will they be able to trigger the immune system in the right way? Although initial trials have shown promising results in human subjects, it is not clear what will happen when the person comes in contact with the actual virus.
2. How can the vaccine dose be controlled? This remains the most difficult task. There seems to be a danger that too high a dose could provoke oral tolerance of an invading bacteria or virus, instead of an immune response. Also, the dosage requirements for children and adults will be different. So, research is on its way to find a solution to these problems.
3. Plants are living organisms that change, so the continuity of the vaccine production might not be guaranteed.

4. Glycosylation patterns in plants differ from those in humans and could affect the functionality of the vaccines.
5. People may develop an allergy to the fruit or vegetable expressing the foreign antigen

#### CONCLUSION

The first trial on humans in 1997 (using the heat labile B- toxin from *E. coli*) is a milestone on the road to creating inexpensive vaccines that might be particularly useful in immunizing people in developing countries, where high cost and logistical issues, such as transportation and the need for certain vaccines to be refrigerated, can thwart effective vaccination programs.

The hope is that edible vaccines could be grown in many of the developing countries where they would actually be used.

Whatever may be the current situation, a day is not far off when we will be able to pluck a fruit from the garden, eat it and be protected from diseases...making needles needless...

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