Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2014, Volume 2, Issue 4
ISSN:2321–3647(online)

A Review on Novel Trends in Vaccine Delivery Systems

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ABSTRACT

Vaccines are the most preferred way to protect human health as they offer protection against a variety of infectious diseases. They play a vital role as they protect not only the individuals but also the entire community. But painful hypodermic needles have limited their usage as they sometimes cause injuries and are relatively unsafe. This has paved way for the scientists to search for alternative means of vaccine delivery. In this article, we summarize some of these novel technologies like use of microneedles, needle-free injections, nasal delivery of vaccines, edible vaccines and melt in mouth strips. These drug delivery techniques have grown significantly in response to above mentioned challenges. All these approaches provide improved safety, better compliance and are non-invasive means of vaccine delivery. Absence of hypodermic needles also significantly reduces the chances of disease transmission. These techniques are used for delivery of vaccines, DNA, proteins, insulin and other macromolecules. The future of vaccine delivery is assured to be significantly influenced by many such promising technologies.

Keywords: Microneedles, needle free injections, edible vaccines, melt in mouth strips

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Received 24 March 2014, Accepted 31 March 2014

Please cite this article in press as: Subramanyam PV *et al.*, A Review on Novel Trends in Vaccine Delivery Systems. . American Journal of Pharmacy & Health Research 2014.

INTRODUCTION

The introduction of vaccines into medical practice at the beginning of the twentieth century has had an extraordinary impact on human health, and represents an unparalleled success story[1].The use of immunizing agents to control and prevent disease is an established component of public health practice throughout the world[2].Most industrialized countries strongly value immunization as a cost-effective means to prevent disease and save on treatment costs, and as a means to preserve economic development. Immunization is also valued by some industrialized countries as an asset against bioterrorism[3].The success of vaccines has been profound; numerous diseases have been brought under control, particularly in developed nations. The best vaccination efforts have been able to either eradicate (wipe out worldwide) or eliminate (eradicate within national or regional boundaries) a given disease[4].

Unsafe injections, needle injuries, accidental needle sticks, needle phobia and possible side effects due to high plasma concentration are the major drawbacks of conventional vaccine delivery[5]. The continued efforts of researchers within biopharmaceutical companies and across the ecosystem, who are persuing new techniques and strategies in vaccine development, create tremendous opportunities to protect against many more life-threatening diseases in the future[6].As the market grows, innovative approaches to development and production will be needed to accelerate delivery of novel products[7].Some of these approaches include:

Microneedles

Microneedle consists of an array of micro structured projections coated with a drug or vaccine[8]. They are generally one micron in diameter and range from 1-100 microns in length[9]. When applied to skin in a manner similar to transdermal patches, they create pores, allowing the passage of hydrophilic drugs, mimicking the action of hypodermic needles[10].They mechanically penetrate the skin and inject drug just under the stratum corneum where it is rapidly absorbed by capillary bed into bloodstream[11]. Microneedles have been fabricated with various materials such as: metals, silicon, silicon dioxide, titanium, polymers, glass and other materials[12]. Microneedles have been used to deliver small molecules, peptides, proteins, oligonucleotides, DNA, vaccines and other compounds[13]. Microneedles are further categorized as (Figure.1.):

1. Solid microneedles

An array of solid microneedles is pierced into the skin followed by application of drug patch at the treated site. The process of drug transport across skin may occur by diffusion or by iontophoresis if an electric field is applied[14].

2. Drug coated microneedles

Here the entire drug to be delivered is coated on the needle and is inserted into the skin for drug release by dissolution[15].

3. Dissolving microneedles

Here microneedles are prepared using dissolving or degrading polymers that encapsulate drug, which then release drug into skin with predetermined kinetics[16].They offer additional benefits like small storage and disposal size, inexpensive fabrication and ease of use to enable self-administration[17].

4. Hollow microneedles

Hollow microneedles facilitate active fluid flow through the needle bore and into the skin, which can lead to much faster rates of delivery which can be modulated over time[18].They have also been used to remove fluid from the body for analysis such as blood glucose measurements and to continuously carry drugs into the body using simple diffusion or pump system[19].

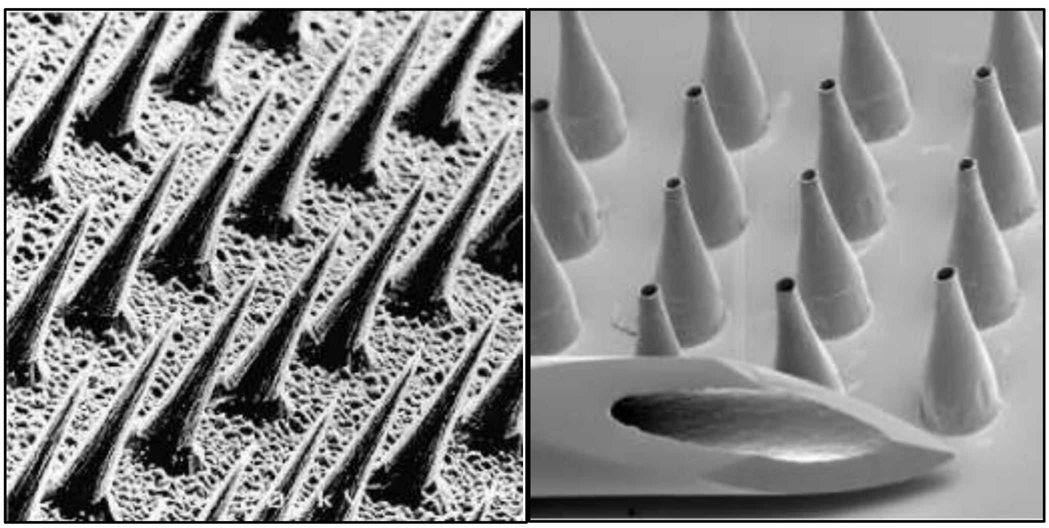

Figure.1:a. Solid microneedles and b. hollow microneedles.

Fabrication of microneedles

Solid microneedles are fabricated using silicon, polycarbonate, polymethyl methacrylate, poly-lactic-co-glycolic acid (PLGA), polyglycolic acid (PGA), polylactic acid (PLA), maltose, stainless steel, titanium, nickel and ceramics[20].

NEEDLE FREE TECHNOLOGY

Needle-free vaccine delivery is supported by many prominent public health organizations involved in vaccine delivery as it shows improved safety, better compliance, decreased pain associated with injection and faster vaccine delivery at reduced costs[21].

This technology uses force generated by a compressed gas (typically air, CO_2 or nitrogen) to propel the vaccine at high velocity through a tiny orifice, delivering the vaccine in a fraction of second to the skin, subcutaneous tissues, and underlying shallow muscle[22].Components of needleless injection include (Figure.2.) a nozzle which acts both as the passage for drug and as the surface which contacts the skin, a drug reservoir which holds injection fluid and a pressure source that provides necessary driving energy to the drug for injection[23]. The devices available in the market either use mechanical or stored pressure as energy storage elements[24].

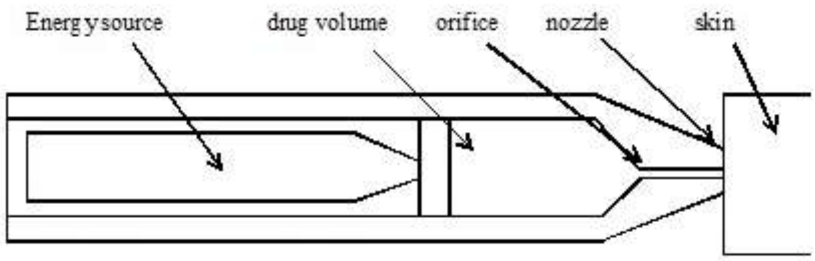

Figure. 2: Components of a needle-free injection.

Needle free technologies can be broadly divided into 3 types:

1. Powder injections

The principle involved is that the energy generated by a transient gas jet is used to accelerate a premeasured dose of particulate drug formulation. Here the particles pierce only the stratum corneum, which is the outermost barrier of the skin[25].The particles must be sufficiently robust to survive the highly energetic gas jet within the device as well as ballistic impact with the skin[26].

2. Liquid injections

The basic principle of this injection is, if a high enough pressure is generated by a fluid, the liquid will punch a hole into the skin and will be delivered into the tissues in and under the skin[27].

3. Depot or projectile injections

They are given in the muscle to create a store of the drug which is continuously released over a specified time period[28].

NASAL DELIVERY

Intranasal delivery of vaccines is needle free, non-invasive, does not require sterile preparation and the large surface area of nasal mucosa along with the highly vascularized epithelium serves as rapid onset for therapeutic effect[29].Formulation strategies employed include two major types; particulate antigen delivery systems where antigenic material is entrapped or presented on surface of the particle and solution systems where the antigen is dissolved or suspended within a simple solution vehicle[30].Mucosal application of vaccines with an appropriate adjuvant can induce immune responses at both systemic and mucosal sites and as a consequence, may prevent not only infectious diseases but also colonization at mucosal surfaces[31].

EDIBLE VACCINES

Edible vaccines are the antigenic proteins that are genetically engineered into a consumable crop[32]. They contain DNA fragments from the original pathogen which code for a protein that is usually a surface protein of the pathogen. This is responsible for eliciting the body's immune response[33].They are delivered through bio-encapsulation which protects them from gastric secretions and they finally breakup in the intestine to be taken up by M cells in the intestinal lining[34].Multicomponent vaccines can be obtained by crossing two plant lines having different antigens[35].

For production of edible vaccines, it is desirable to select a plant whose products are consumed raw to avoid degradation during cooking like bananas, cucumbers, potatoes and tomatoes[36].Other foods under study include lettuce, wheat, soybeans and corn[37].These plant vaccines serve as an inexpensive means of processing and expressing proteins, avoid contamination with animal pathogens, improve the stability of heat liable vaccine components and ensure oral delivery[38].

Disadvantages

But the major concern with whole fruit or vegetable vaccine is the consistency of dosage from fruit to fruit, plant to plant and generation to generation[39].Other drawback includes contamination of crops through cross pollination and of the vaccine itself in plant debris spreading as dust and as pollutants in surface and groundwater[40]. Precautionary methods should be taken as the chances of these drugs to accumulate in non-target organisms is more[41].

To overcome some of these drawbacks, the research into plant-based vaccines has recently shifted from food crops to genetically modified plants which are not generally eaten. Here, vaccine components produced in the leaves are freeze-dried, ground up and placed in gelatin capsules[42].

MELT IN MOUTH STRIPS

These strips contain immunogens which are meant to be dissolved in child's mouth. The strip sticks to the tongue and dissolves in less than a minute. This innovative drug-delivery system was developed by Johns Hopkins undergraduate biomedical engineering students[43].

CONCLUSION

The interests of scientists and the scientific advances in immunology have lead to the development of novel trends of vaccination. Microneedles prove to be a useful method for patients by enabling them to self-administer drugs eliminating the hazards of painful hypodermic needles. Needle-free injections are mainly advantageous in mass immunization programs as they are available at reduced costs and also eliminate the need for sterilization of needles. Edible vaccines offer enormous potential as production platforms for vaccines as they are an easier way to immunize people especially in case of developing countries where storing and administering of vaccines is difficult. Apart from the different techniques discussed here, there is a lot of scope for developing new methods in vaccination. A wide range of possible novel vaccine delivery technologies are still in early research and development phases and they require a thorough analysis before being introduced into the market. The major obstacles being faced to develop these innovative techniques include developing an appropriate vaccine formulation which is compatible with the delivery technology, complexity of the available devices, level of investment required to support such alternative technologies. But these novel technologies need to overcome all these challenges to provide vaccines to the developing world. Hence time has come for these innovative techniques to make their mark.

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