

**A REVIEW ON PATCH VACCINATION AS A MODERN FORM OF DRUG DELIVERY**

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\*Corresponding author e-mail: [patilanagha189@gmail.com](mailto:patilanagha189@gmail.com)**ABSTRACT**

Nanopatch is a modern technique which designed to target the network of immunologic antigen presenting cells in the dermis and epidermis layers under the skin to enhance the efficacy of vaccination. Nano patch contains the micro sized needles that are painlessly penetrating and the nano-formulated medicines, drugs and vaccines directly go to the immune system. The comparative studies outline that there is increased stability, conventional route, easy to use and also the wide range of vaccines can be used. Nano patch one day will be self-administered or given by a non-medical person, which reduces the administration cost and also relieve from burden on health care professionals. Receiving vaccines from doctor's office or health clinic may soon be outdated.

**KEYWORDS:** Vaccines, Nano patch , Microneedle.**INTRODUCTION**

Vaccines are pharmacological formulations that incorporate the disease-causing antigen which could innocuously induce an immune response when administered into a healthy human being, without causing the disease itself. [1] Numerous studies noted that the measured efficacy of vaccines is highly affected by the route of administration. Researchers investigated that the skin layer that lies beneath the stratum corneum is supported by a densely connected network of immune-response modulating antigen presenting cells (APCs), most significantly represented by the Langerhans cells and dermal dendritic cells in the epidermis and dermis of skin. [2] Firstly, the strategic targeting of the epidermis and dermis, without disrupting the underlying subcutaneous tissue, is a manually difficult technique that requires the hand of professionally trained healthcare personnel. As a potential solution to these drawbacks, microneedles have been proposed as an alternative delivery route that could replace hypodermic syringes. [3]

"Nano-patch is defined as an adhesive patch containing micro sized needles that painlessly

penetrate the skin to deliver nano-formulated drugs and vaccines".

Microneedles are a medium for delivery of vaccines that avoids the pain associated with ordinary hypodermic needles. They are a merely seven tenths of a millimeter in length, and the volume of vaccine is minuscule. The Nanopatch consists of thousands of vaccine coated microprojections that perforate into the outer layers of the skin when applied with an applicator device. The tips of Nanopatch's microprojections are coated with a vaccine material and release this material directly to the large numbers of key immune cells immediately below the skin surface. A new patch vaccine-delivery based on hundreds of microscopic needles that dissolve into the skin could allow persons without medical training to painlessly administer vaccines while providing improved immunization against diseases. Instead of a liquid containing whole killed or attenuated virus, this vaccine uses dry virus-like particles (VLPs) which simply coat the needles in the presence of a simple stabilizing agent, reducing the need for refrigeration a potential boon for use in developing countries. The lower dose required when using microneedles, also reduces the potential side effects. (As shown in figure 1 and figure 2)

This method can induce higher levels of antibodies as well as rapid recall immune responses following lethal challenge infection. Our previous study showed that microneedle vaccination induced higher levels of antibody-secreting cells in spleen and bone marrow compared to intramuscular vaccination.

**APPLICATION METHODS:** Drug delivery through Nano-Patch is done in following ways:

- i) Sand paper aided delivery
- ii) Iontophoresis enabled delivery
- iii) Projectile Delivery

**i) Sand paper aided delivery:** The micro-projections containing drug/vaccine delivers the drug/vaccine into the epidermis by creating a puncture on the skin surface. The epidermis is rich of Langerhans cells which are members of our Immune system. These cells move to the nearest Lymph node and display the antigen to the T-cells. T-cells specifically recognizes one type of antigen and creates a corresponding antibody. (As shown in figure 3)

Once this recognition procedure is completed the antibodies will provide immediate protection and these cells will protect from getting the same disease twice. Thereby providing life time protection.

**ii) Iontophoresis enabled delivery:**

**Jet Pressured Needle free Injection:** Devised in the year 2001 by The Medical House and Bioject. This device has a specialized nozzle through which the drug is delivered. A three component system comprising an injection device, especially designed nozzle and air cartridge is present. (As shown in figure 4.1 and figure 4.2)

Instead of creating a puncture on the skin surface, this device forces the drug through skin pores by the help of air pressure, thereby effectively delivering the drug without the help of needle.

**Advantages of jet injectors:**

1. They eliminate the risk of cross contamination.
2. Different settings allow adjustment for different skin types.
3. They are portable.
4. They are less expensive than syringes, since they have to be bought once.
5. They provide greater precision.
6. There is no syringe waste with jet injectors, reducing medical waste.
7. The absence of a needle helps those who are afraid of needles.

**Disadvantages of jet injectors:**

1. They are larger than syringes and are thus harder to carry around while out.

**iii) Projectile Delivery:**

Epidermal powder immunization (EPI) and particle-mediated epidermal delivery (PMED) utilize helium gas to deliver powdered proteins, polysaccharides, inactivated pathogens, or DNA-coated particles into the epidermis at supersonic speeds. Conventional protein antigens must be specially formulated for delivery by EPI, and are spray dried into powders of suitable density and size (20–70  $\mu\text{m}$ ). In PMED, gold beads 1–3  $\mu\text{m}$  in diameter are coated with vaccine and delivered by needle-free jet injection into the epidermis. This approach may be particularly suited to DNA vaccines, as deposition of coated particles into the stratum corneum and epidermis may encourage DNA uptake and expression by resident antigen-presenting cells. (As shown in figure 5) [4, 5, 6, 7]

**Advantages of patch vaccination: [8]**

1. Delivery of nano-sized particles directly to the immune system
2. Delivery of molecules that normally cannot penetrate the skin
3. Lower dosages and less side effects
4. Easy to use, no needle-stick injury, low risk of infection, pain-free
5. Can be self-administered, or given by a non-medical person
6. Smaller, lighter, lower transport cost
7. Mass production therefore cost benefits
8. Suitable for public health programs e.g. air-drop into disaster zones
9. Suitable for veterinary purposes
10. Biocompatible and biodegradable material used to make patches
11. Can achieve short- & long-term delivery

**Disadvantages of patch vaccination: [8]**

The outer layer of skin is different from person to person. It varies in thickness, humidity, age, gender and other factors. This is one of the potential problems for nanopatch vaccination.

**APPLICATIONS OF NANO-PATCH IN VACCINATION OF DISEASES:**

**1) Live-attenuated measles vaccine by patch vaccination:**

In the study, the researchers developed a technique to dry and stabilize the measles vaccine which depends on a live attenuated virus and showed that it remained effective for at least 30 days after being placed onto the microneedles. They also demonstrated that the dried vaccine was quickly released in the skin and able to prompt a potent immune response in an animal model. It promotes induction of measles-specific salivary IgA and a tendency to increased

frequency of MV-specific IFN-producing T cells. The skin is enriched in professional antigen-presenting dendritic cells (DC) including, epidermal Langerhans cells (LC), and dermal DC. Transcutaneous immunization (TCI) using a patch has recently emerged as a promising approach to target anti-infectious vaccines to DC. [9]

It has been largely discussed that alternative needle-free vaccination routes would increase vaccine coverage and boost measles eradication efforts [10]. Both wild-type measles virus (MV) and vaccine MV strains infect DC including epidermal LC [11, 12] and can induce signalling via Toll-like Receptor (TLR) [13]. Since the live-attenuated MV vaccine delivered by skin puncture using bifurcated needles appeared to be poorly immunogenic, we reasoned that it could be more efficient when administered transcutaneously. [14]

## 2) *Tetanus Vaccine Patch Development:*

Tetanus is an infectious disease of the nervous system. It causes severe, painful muscle spasms and can eventually lead to locking of the jaw and can spread to the muscles of the abdomen, upper arms and thighs. [15] Transcutaneous immunization (TCI), using a topically applied needle-free patch, allows the delivery of an antigen and/or adjuvant into the skin, providing a powerful and effective alternative to traditional immunization [16]. By taking advantage of antigen-presenting cells in the skin, TCI has been shown to induce robust immune responses to a wide variety of protein antigens, including those derived from bacterial and viral pathogens [17].

## 3) *Influenza patch vaccine:*

Seasonal influenza causes three to five million cases of severe illness and 250,000–500,000 deaths annually. [18] Microneedle patches are especially attractive for self-vaccination because they are compatible with live, inactivated and subunit vaccines, administer a consistent dose, offer thermostability and can be manufactured inexpensively. Moreover, microneedle-based influenza vaccines are expected to be well accepted by practitioners and the general public and have the potential to be more immunogenic.

Scientists have developed an influenza vaccine delivered via microneedle patch that provided 100 percent protection against a lethal influenza virus in mice more than one year after vaccination. [19]

## 4) *Transcutaneous Vaccination for the Cholera Toxin:*

The causative agent of cholera, *Vibrio cholerae*, generates acute diarrhea in infected individuals in which, without proper treatment, death is inevitable.

Transcutaneous immunization involves the application of a thin patch to skin to expose a patient to an antibody proliferating antigen. Studies conducted by Glenn et al reveal that a mixture of the dissociated subunits of the cholera toxin when administered as a vaccine produces a strong immune response in mice. The presence of the beta subunit in the skin will cause an immune response and the production of antibodies. The patch occupies very small area of overall skin surface. The system is isothermal. Blood flow at the skin-dermis interface immediately removes the antigen. [20]

## 5) *Patch Vaccination for Anthrax:*

Gram-positive bacterium *Bacillus anthracis*, the etiologic agent of anthrax, has been identified as one of the potential bioterrorist and warfare agents. [21] Transcutaneous immunization (TCI) induced long-term neutralizing antibody titers that were superior to those obtained with aluminum-adsorbed recombinant protective antigen (rPA). Forty-six weeks after completion of TCI, 100% protection was observed against lethal anthrax challenge. [22]

## CONCLUSION

Drug delivery via needles has changed little in the past 150 years, and still carries risks associated with invasive procedures for example, doctors being accidentally stuck with a used needle. Needles have to be sterilised, and vaccines kept at cool temperatures to maintain their stability. However nanopatch would mean vaccines could be distributed in rural regions with soaring temperatures without fears of stability and without risk of contamination. Within the nanopatch are thousands of projections of dry-coated vaccines, which mean the drug goes straight to the cells under the skin, not via the muscle as with traditional vaccines.

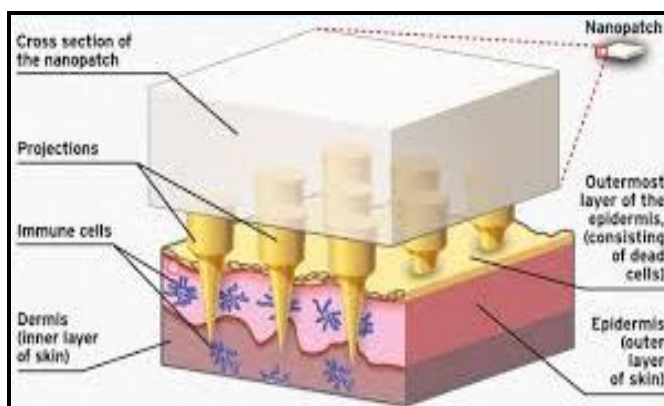
Nanopatch is needle-free device that targets a narrow layer just below the skin surface rich in antigen presenting cells for improved vaccination over the needle and syringe which gives the advantages of no needle-stick injury, low risk of infection, pain-free, easy to use. It also requires low dose than traditional vaccines hence less side effects. The nanopatch could herald a day of safe, cheap and efficient, self-administered drug delivery.

## ABBREVIATIONS:

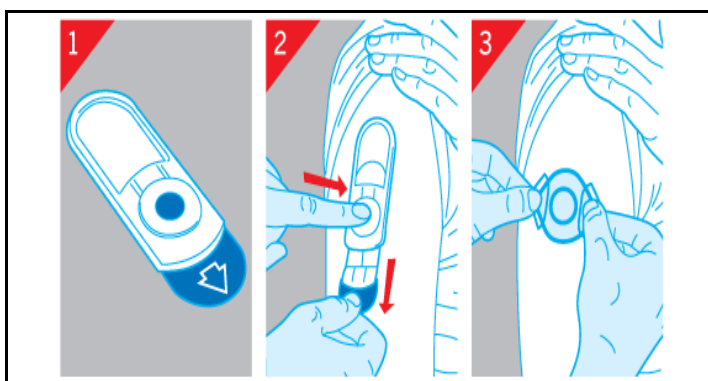
LC = Langerhans cell; TCI = Transcutaneous immunization; MV = Measles virus; DC = Dendritic cells; IFN = Interferon; TLR = Toll-like Receptor; IgA = Immunoglobulin A; DNA = Deoxyribonucleic acid; EPI = Epidermal powder immunization; PMED = Particle-mediated epidermal delivery



**Fig1: Nano patch**



**Fig2: Nano patch drug delivery through skin layers.**



**Fig3: Sand paper aided delivery**



**Fig4.1: Jet injector (Biojector 2000) used for investigational purpose.**



**Fig4.2: Jet injector applied to skin for injection**



**Fig5: Epidermal powder immunization device**

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