Microneedle: a Effective and Safe Tool for Drug Delivery

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Abstract: Microneedle-based vaccination with the current anthrax vaccine produced an equally effective immune response to intramuscular injection in rabbits using smaller dosage say researcher from Maryland and North Carolina. In the study researchers compared the efficacy of immunizing rabbits with the current anthrax vaccine intradermally using a microneedle and intramuscularly using a conventional needle. Results showed that intradermal delivery required less dosage to induce similar antibody levels as those seen following intramuscular injection. Rabbits that were administered the vaccine using the microneedle-based technique showed protection against inhalation anthrax at 100%, while those vaccinated using conventional methods were protected at 71%.

Keywords: anthrax vaccine, intradermal, immunizing, intramuscular

Introduction
For over 150 years, syringes and hypodermic needles have been utilized to deliver drugs into patients.1 Because of the transport barriers that exist in other delivery routes; injection is still a prominent method for drug delivery today. Currently, the smallest needles that are commercially available for injections are 30 gauges for conventional syringes and 31 gauge for pen injectors, which are utilized mainly for insulin delivery. The 30 and 31 gauge needles have outer diameters of 305 and 254 µm, respectively.6 As stated previously microneedles can be fabricated to only penetrate the 10-15 µm of the skin. This means there is no pain when taking blood samples for glucose measuring devices.

Microneedle Vaccination Technique Protects Rabbits Against Inhalation Anthrax Using Smaller Dosage:
Microneedle-based vaccination with the current anthrax vaccine produced an equally effective immune response to intramuscular injection in rabbits using smaller dosage say researcher from Maryland and North Carolina. They report their findings in the December 2006 issue of the journal Infection and Immunity (Science Daily (Dec. 13, 2006). Sivamani, Raja K et.al compared microneedle injections with topical application (TA) to investigate if microneedles enhance in vivo drug delivery past the stratum corneum under the tile of work “Clinical microneedle injection of methyl nicotinate: stratum corneum penetration”. John A. Mikszta, et. al from BD Technologies, Research Triangle Park, North Carolina 27709,5 U.S. Army Medical Research Institute of Infectious Diseases, Frederick, Maryland had shown under the title “Microneedle-Based Intradermal Delivery of the Anthrax Recombinant Protective Antigen Vaccine” that the recombinant protective antigen (rPA) of Bacillus anthracis is a promising anthrax vaccine. They compared serum immunoglobulin G levels and toxin-neutralizing antibody titers in rabbits following delivery of various doses of vaccine by microneedle-based intradermal (i.d.) delivery or intramuscular (i.m.) injection using conventional needles. Intradermal delivery required fewer antigens to induce levels of antibody similar to those produced via i.m. injection during the first 2 weeks following primary and booster inoculation. This dose-sparing effect was less evident at the later stages of the immune response. Rabbit’s immunized i.d. with 10 µg of rPA displayed 100% protection from aerosol spore challenge, while i.m. injection of the same dose provided slightly lower protection (71%). Groups immunized with lower antigen doses were partially protected (13 to 29%) regardless of the mode of administration. Overall, our results suggest rPA formulated with aluminum adjuvant and administered to the skin by a microneedle-based device is as efficacious as i.m. vaccination6,7.

Applications of Microneedles
1 Blood Glucose Measurements
As stated previously microneedles can be fabricated to only penetrate the 10-15 µm of the skin. This means there is no pain when taking blood samples for glucose measuring devices. There is a huge market in glucose testers due to diabetic patients and hospitals. Kumetrixs
is an example of a company that fabricates such a device. The micro-needle is penetrating to the skin and draws a very small volume of blood (less than 100 nanoliters) into the disposable. Chemical reagents in the disposable react with the glucose in the blood to produce a color. The blood-glucose concentration will be measured either electrochemically or optically, and the resultant value displayed on the monitor.

2 Transdermal Drug Delivery
The conventional transdermal drug delivery limits the applicability to small drug molecules because the stratum corneum does not have any nerves. Since microneedles that are long enough and robust enough to penetrate across this layer, but short enough to not stimulate the nerves in the deeper tissue, have the potential to make transdermal delivery a painless and much more viable option. With the use of hollow microneedles it allows the delivery of medicines, insulin, proteins, or nanoparticles that would encapsulate a drug or demonstrate the ability to deliver a virus for vaccinations. An array of needles ranging from 300-400 needles can be designed to puncture the skin and deliver the drug.

3 Molecular and Cell Biology
Microneedles have been applied for the delivery of membrane impermeable molecules into cells. For application in molecular cell biology, methods for the delivery of peptides, proteins, oligonucleotides, DNA and other probes that alter or assay cell function is desired. Arrays of microneedles were fabricated and utilized to deliver DNA into plant and mammalian cells, as a method for transforming cells.

4 Target Drug Delivery
Additionally, microneedles have been utilized to target drug delivery to a specific region or tissue in the body, thus avoiding detrimental effects that can result from administering certain drugs systemically. This targeting can reduce side effects, minimize the dose of an expensive drug, and/or provide a means of delivery to a location that is difficult to treat. For instance, a multichannel silicon microneedle has been microfabricated to deliver bioactive compounds into neural tissue while simultaneously monitoring and stimulating the neurons in vivo. In addition, microneedles have been used to penetrate vessel walls of normal and atherosclerotic rabbit arteries in vitro demonstrating potential use for targeted delivery of antirestenosis drugs.

Electrically Conductive Microneedle Roller: An electrically conductive microneedle roller includes stacked discs, each of which includes a plurality of radial grooves, a plurality of microneedles that are received in the radial grooves of the disc, an electrically conductive bracket that supports the stacked discs, and a handle that supports the bracket. Electric current flows to the skin via the microneedles and provides electric stimulation. The discs are assembled using UV bond thereby reducing the assembly time. The roller has enhanced service life since the microneedles do not fall off from the roller since radial grooves holding the microneedles have tapered shape.

Others Applications
Prausnitz and his colleagues have been working since the mid 1990s to develop microneedle technology for painless drug and vaccine delivery through the skin. Much smaller than conventional hypodermic needles, the microneedles in the arrays are made of titanium, stainless steel or various polymers – The Georgia Tech team has also developed manufacturing processes for microneedle patches and tested the ability of the needles to deliver proteins, vaccines, nanoparticles, and small and large molecules through the skin. "We expect microneedles to be less painful than conventional hypodermic needles because they are too small to significantly stimulate nerve endings," Prausnitz explained. "The NIH grants will allow us to move forward with perfecting the manufacturing process, refining the techniques for optimally inserting the microneedles into the skin and ensuring that vaccine delivered this way produces the necessary immune response.

Future Applications
Microneedle Skin Therapy
Microneedle skin therapy is still in testing development, but it seems to show much promise. Microneedle therapy is a way to rejuvenate the skin without destroying the epidermis. It is similar to laser treatments but with less damage. Companies like the Clinical Resolution Lab utilize treatments using microrollers. Microneedles penetrate the epidermis and break away old collagen strands. The only disadvantage of this method is that it causes blood oozing, which laser treatments do not. It does The collagen strands that are destroyed create more collagen under the epidermis. This leads to youthful looking skin. However have advantages such as: increased collagen, non sun-sensitivity upon treatment, no breaking of the epidermis, lower cost, and ease of application.

Microneedles: Flu Vaccine in Painless Skin Patches under Development:

a) Injection needle-free
b) Virus Vaccine Testing

Influenza Vaccination

D) Medicine & Health / Other
An array of microneedles in a patch could be used to administer the flu vaccine through the skin. Image shows a prototype patch of stainless steel needles. Flu vaccine delivered through painless microneedles in patches applied to the skin could soon be an alternative to delivery through hypodermic needles, according to researchers at Emory University and the Georgia Institute of Technology in Atlanta. Using new grants from the National Institutes of Health (NIH) totaling approximately $11.5 million over five years, researchers from the two institutions plan to develop a new vaccine product using the microscopic needles.
Marketed products:
Dermaroller 0.5mm for Home Use, Wrinkles, Scars, Age Spots
Current Bid: $49.98

New Metal Derma Roller with Vitamin Cosmetic
Current Bid: $229.00

Cellulite, acne scar stretch marks dermaroller skin 1.5
Current Bid: $20.50

Dermaroller 0.5mm for Home Use, Wrinkles, Scars, Age Spots
Current Bid: $49.98

NEW 3 LINE, DERMA ROLLER, 2.0mm, WRINKLES, DERMAROLLER
Current Bid: $79.95

Different Structured Microneedles available in the Markets:
Conclusion
Many people, particularly children, are ‘needle-phobes’. In addition, there are several patients, such as diabetics who are dependant on multiple injections on a daily basis. Many other disease conditions also require the delivery of therapeutic agents to the skin, while the outbreak of a pandemic would necessitate mass vaccinations. A solution to the problems posed by needle-based injections is the development of microneedles. This technology will help realize the development of new and improved devices, which will be smaller, cheaper, pain-free and more convenient with a wide range of biomedical and other applications.

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References

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