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Archives of Applied Science Research, 2010, 2 (2): 61-64
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-508X
CODEN (USA) AASRC9

A novel approach of drug delivery: Microneedles

Raj K. Keservani*, Narendra Vyas and Sarang Jain

Rajeev Gandhi College of Pharmacy, Bhopal, India

Abstract

Microneedles are expected to be less painful than conventional hypodermic needles because they are too small to significantly stimulate nerve endings. Small-scale studies so far have confirmed that expectation, and additional pain studies are planned. The safety and effectiveness of microneedles must still be proven in humans before they can receive Food & Drug Administration approval for clinical use. The broad range of sizes, shapes and materials will permit production of microneedle arrays customized for the type and volume of drug to be delivered, the time period of use, and most importantly, minimizing pain.

Keywords: Microneedles, Hollow microneedles, Coated microneedles, Drug delivery.

INTRODUCTION

Puncturing of the human skin with a hollow needle is perhaps the most common invasive medical procedure to inject fluids into or extract fluids from the human body. Regardless of the size of the needle, unless an anesthetic is used, it is at least uncomfortable if not painful. During the past few years, considerable effort has been put into developing microneedles to replace the traditional hypodermic needle [1–4]. Microneedles are sharp hypodermic needles that are intended to be minimally invasive while accomplishing the task of penetrating the skin's outermost non-innervated layer to draw small volumes of blood or inject small quantities of therapeutic agents into the capillary-rich dermis layer, painlessly. It has been reported that a penetration up to 1.5mmcan be painless [5]. Typical sizes of thesemicroneedles are 40–100 μm in diameter with sub-micron in tip radii. For comparison, the smallest hypodermic needle typically used (30 gage) is about 320 μm in outer diameter and 160 μm in inner diameter. Some microneedles are hollow, while some are solid with the therapeutic agents coated on the surface that dissolves once the needle is in the blood stream [6].

Over 150 years, syringes and hypodermic needles have been utilized to deliver drugs into patients.[7] Advances in the processing of materials on a micro-scale have led to the development and introduction of devices that employ very small needles microneedles that have significant potential in devices for diagnostics, healthcare monitoring and drug delivery by mechanically perforating the outer skin layer and allowing for transdermal drug absorption or fluid sampling. These processing techniques incorporate one or more technologies that enable the precise machining, extrusion, casting, and/or forming of from one to an array or grid of microneedles. Several factors - include an aging patient population, biological drug therapies for chronic conditions, and an emphasis on patient self-monitoring and self-care are driving an evolution in the way that healthcare is delivered. Evolving microneedle systems will be well-positioned to address a significant segment of the large molecule biological drugs expected to emerge from the convergence of automated discovery and genome mapping. Before microneedles find widespread use, researchers must perfect the techniques for optimally inserting them into the skin, and complete the integration of microneedles into a full diagnostic, monitoring or drug delivery system.[8]

Microneedles are somewhat like traditional needles, but are fabricated on the micro scale. They are generally one micron in diameter and range from 1-100 microns in length. Microneedles have been fabricated with various materials such as: metals, silicon, silicon dioxide, polymers, glass and other materials.[9]

Advantages of Microneedles

1. The major advantage of microneedles over traditional needles is, when it is inserted into the skin it does not pass the stratum corneum, which is the outer 10-15 μm of the skin.[5] Conventional needles which do pass this layer of skin may effectively transmit the drug but may lead to infection and pain. As for microneedles they can be fabricated to be long enough to penetrate the stratum corneum, but short enough not to puncture nerve endings. Thus reduces the chances of pain, infection, or injury.
2. By fabricating these needles on a silicon substrate because of their small size, thousands of needles can be fabricated on a single wafer. This leads to high accuracy, good reproducibility, and a moderate fabrication cost.[10]
3. Hollow like hypodermic needle; solid—increase permeability by poking holes in skin, rub drug over area, or coat needles with drug.[11]
4. Arrays of hollow needles could be used to continuously carry drugs into the body using simple diffusion or a pump system.[12]
5. Hollow microneedles could be used to remove fluid from the body for analysis – such as blood glucose measurements – and to then supply microliter volumes of insulin or other drug as required.[12]
6. Immunization programs in developing countries, or mass vaccination or administration of antidotes in bioterrorism incidents, could be applied with minimal medical training.
7. Very small microneedles could provide highly targeted drug administration to individual cells.
8. These are capable of very accurate dosing, complex release patterns, local delivery and biological drug stability enhancement by storing in a micro volume that can be precisely controlled.[13]

Materials Used for the fabrication of microneedles

Needles have been made from:

- Glass
- Silicon
- Metal—stainless steel, solid or coat of gold over Ni, Pd or Pd-Co, and Pt.
- Biodegradable polymers, if a tip snaps off while inserted, it will easily biodegrade.[14]

Microneedle fabrication techniques

The needle fabrication process involved four steps. First, arrays of microneedles made of SU-8 epoxy photo resist were fabricated by patterning SU-8 onto glass substrates and defining needle shape by lithography. Then, the tips of the needles were sharpened using reactive ion etching. The next step involved laser drilling holes through the microneedles and base substrate oriented off-center, but parallel to the Microneedle axis. This created holes that serve as the micro fluidic needle bores for injection or infusion, which terminate in side-opening holes along the needle shaft below the needle tip. Finally, the needle arrays were coated with nickel by electroplating to increase their mechanical strength. [14]

Microneedle Design & Technology

Solid Microneedles
Hollow Microneedles
Coated Microneedles
Microneedle Arrays & Array Geometries
Microneedle Manufacturing
Material Selection Issues
Fabrication Techniques
Emerging Fabrication Methods

Microneedle Medical Market Overview

The Trend to Minimally Invasive Medicine
Drug Delivery & Self-Administration
Continuous & Remote Monitoring
Shifting Patient Demographics
Managed Care Initiatives
Commercial Microneedle Devices
Competitive Landscape

Application:

Applications for Microneedle Technology

Biosensing
Sampling
Drug Delivery
Tissue Enhancement

Commercial potency due to Therapeutic use

Antivirals
Cancer Therapeutics
Dermatology/Cosmetic Surgery
Diabetes
Diagnostics
Fertility
Genetic Engineering
Pain Management
Osteoporosis
Therapeutic Proteins/Peptides
Vaccines[8]

CONCLUSION

This innovative new treatment method means that vaccines, proteins, and hormones could soon be delivered into the body as effortlessly and painlessly as wearing a plaster. So could needle phobia soon be a thing of the past? "We expect that microneedles will be able to replace hypodermic needles in some scenarios, but certainly not all cases. They won't be useful for withdrawing significant quantities of blood for analysis. This technology will help realise 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. The future of drug delivery is assured to be significantly influenced by microfabrication technologies. These microfabricated drug delivery devices can enable efficient drug delivery that was unattainable with conventional drug delivery techniques, resulting in the enhancement of the therapeutic activity of a drug.

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