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Microneedles: Progress in Developing New Technology for Painless Drug Delivery

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Abstract: Advances in the processing of materials on a micro-scale have led to the development and introduction of devices that employ very small needles. That has 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. 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. To overcome the problems of oral route skin has been extensively studied as an alternative route of drug delivery. Skin is a large and easily accessible organ that can be readily used to administer drugs into the blood capillaries lying just tens of microns beneath the skin's surface. Despite the advantages offered by skin for drug delivery, clinical drug delivery through the skin is severely limited by the presence of the top most layers of dead cells called the stratum corneum. This layer is just 10-20 μm in depth, but is the rate-limiting barrier and only allows low molecular weight molecules with moderate oil and water solubility to diffuse through. This in turn restricts the drugs that can be delivered via the skin into a very narrow range. As a result, presently only thirteen active molecules are approved for delivery through the skin by the Food and Drug Administration.

Keywords: Microneedles, stratum corneum, hypodermic needles, microelectromechanical pump.

Introduction

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[1, 2, 3, and 4]. Microneedles are expected to be less painful than conventional hypodermic needles because they are too small to significantly stimulate nerve endings. Before microneedles find widespread use, the researchers must perfect the techniques for optimally inserting them into the skin, and complete the integration of microneedles into a full drug delivery system. The need to minimize variability in needle insertion is being addressed in part by development of an applicator device that would be part of the delivery system. A painless "microneedle" that mimics the way a female mosquito sucks blood has been built by engineers in India and Japan.

Design and Mechanism of Working: The needle could be used to draw blood, inject drugs, and as a glucose-level monitor for diabetics. A female mosquito sucks blood by flexing and relaxing certain muscles in its proboscis. This creates suction (or negative pressure) that draws blood into its mouthparts.

The new biocompatible microneedle, designed by Suman Chakraborty of the Indian Institute of Technology in Kharagpur and Kazuyoshi Tsuchiya of Tokai University in Kanagawa is based on the same principle.
In this case, the sucking action is provided by a microelectromechanical pump, which works using a piezoelectric actuator attached to the needle.
Contrary to popular belief, a mosquito bite does not hurt. It is the anticoagulant saliva that the creature injects to stop your blood clotting that causes inflammation and

pain[5, 6].

Snap safe: The new needle has an inner diameter of around 25 microns and an external diameter of 60 microns, which is about the same size as a mosquito's mouthpart. Its size and the fact that it works by suction, makes it painless. To compare, a conventional syringe needle has an outer diameter of around 900 microns.

In contrast to previous microneedles, which were made of silicon dioxide, the new device is robust because it is made of stronger titanium and related alloys, which dramatically reduces the risk of it snapping during injections.

The needle is also strong enough to penetrate as far as 3 millimeters into skin and reach capillary blood vessels.

Its size compared to earlier models also means that surface tension effects are exploited further, and the same capillary flow that draws water up into trees helps draw blood into the microneedle[7, 8].

The researchers have calculated that their needle can extract 5 microlitres of blood per second. This volume is sufficient for measuring blood-sugar levels in diabetics using a glucose sensor that can be attached to the needle in a "wristwatch" design.

"The working principle of this device follows on from our discovery that in a well-designed microneedle, surface tension forces may overcome resistance from friction and draw up blood with unprecedented efficiency,"

New Microneedle Inspired by Mosquito: Joint collaboration between the Indian Institute of Technology Kharagpur and Tokai University of Japan has resulted in a new hypodermic microneedle, which does not come with an iota of pain. This is due to the fact that it was designed after a mosquito's unique micro-electro-mechanical based suction system. This new design has a diameter of 60 microns, which is way smaller than a conventional needle that currently stands at 900 microns, and is hoped to be developed further for use in glucose monitoring, blood draws, insulin pumps and other drug delivery devices[10, 11, 12].

Proboscis-Mimicking Microneedle for Drug Delivery: Precise control over the fluidic transport and the ability to scale down the analysis to very small volumes of liquid are among the most attractive capabilities of these novel health care approaches.

Such concepts provide excellent promises in revolutionizing health care protocols for the future, with the possibilities of developing substantially improved and patient-friendly health monitoring systems."

The needle has been designed to mimic a mosquito's proboscis in dimensions, the manner that suction is created and rate of flow.

As it has an external diameter of only 60µm, as opposed to 900µm for conventional syringes, the microneedle is said to be painless.

Microneedles with similar dimensions have been created previously but have primarily been fabricated from silicon dioxide that rendered them brittle making them liable to snap, which could potentially cause a blood clot.

This latest model in the needle's development is crafted from titanium and related alloys, giving it the strength needed to administer therapeutics without the risk of snapping.

It is capable of penetrating 3mm under the skin to administer therapeutics into the capillaries or extract blood[11, 12, and 13].

Among the potential applications are: Arrays of hollow needles could be used to continuously carry drugs into the body using simple diffusion or a pump system;

Hollow microneedles could be used to remove fluid from the body for analysis – such as blood glucose measurements – and to then supply micro liter volumes of insulin or other drug as required;

Microneedles may prove useful for immunization programs in developing countries, or for the mass vaccination or administration of antidotes in bioterrorism incidents because they could be applied by persons with minimal medical training. Very small microneedles could provide highly targeted drug administration to individual cells.

Advantages of Microneedles: 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 cornea, but short enough not to puncture nerve endings. Thus reduces the chances of pain, infection, or injury.

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[5].

Hollow like hypodermic needle; solid—increase permeability by poking holes in skin, rub drug over area, or coat needles with drug[6].

Arrays of hollow needles could be used to continuously carry drugs into the body using simple diffusion or a pump system[7].

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Immunization programs in developing countries, or mass vaccination or administration of antidotes in bioterrorism incidents, could be applied with minimal medical training.

Very small microneedles could provide highly targeted drug administration to individual cells.

These are capable of very accurate dosing, complex release patterns[8].

Different types of microneedles:

Hollow Metal Microneedles for Insulin Delivery to

Diabetic Rats: The goal of this study was to design, fabricate, and test arrays of hollow microneedles for minimally invasive and continuous delivery of insulin in vivo.

Electrically Conductive Micro needle Roller: An electrically conductive micro needle roller includes stacked discs, each of which includes a plurality of radial grooves, a plurality of micro needles 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 micro needles and provides electric stimulation. The discs are assembled using UV bond thereby reducing the assembly time. The roller has enhanced service life since the micro needles do not fall off from the roller since radial grooves holding the micro needles have tapered shape.

Collagen Induction Therapy with the Micro needle Derma roller: The Micro needle Derma roller is a small plastic roller studded with about 200 extremely fine needles of medical grade stainless steel. The skin reacts to these pricks like it reacts to any other wound with the formation of the various growth factors. This process of stimulating collagen tissue production is a normal physiological reaction and is known as **Collagen Induction Therapy (CIT)**.

A Selection of Micro needle Resources

Micro needle Therapy System: MTS-Roller: The Micro needle Therapy System (MTS) is a breakthrough device, simple in concept but yielding magnificent results for the human skin. The MTS consists of a series of devices, which have both cosmetic and medical applications. Their mechanism of action is through the painless piercing of the stratum.

The Derma roller: The Derma roller is the most effective device for deep transdermal Delivery of active substances through the epidermal barrier (stratum corneum).

Skin Care Review: Derma roller: Skin care and rejuvenation information and reviews based on published research and other independent sources. Skin Care Review: Derma roller.

The Derma roller: The Collagen-Induction-Therapy with the CIT-DERMAROLLER is a perfect alternative to achieve the same goal: a new collagen-layer on the dermis. **Derma Roller.**

The Leaf and Rusher Derma Roller is a unique rolling device that significantly enhances the action of the Leaf and Rusher Treatment System.

FAQs: The studies of the University of Marburg have proven beyond any doubt the enhancement capabilities of the Derma roller.

MTS Micro needle Derma roller: Micro channel formation enhances product penetration and stimulates collagen production for rejuvenation and treatments of acne scars and stretch marks.

CIT-findings: The Collagen-Induction-Therapy (CIT) with the needling device called DERMA ROLLER%u2122 is a fairly new procedure for the stimulation of new collagen fibers

Scar-Treatment: Derma roller-Types · Scar-Treatment · Collagen-Induction-Therapy · Hair loss · Home· the Dermaroller%u2122 · Derma roller-Models · Scar-Therapies...

Dermacare Dermaroller, Roll back the years.

Microneedles: The Option for Painless Delivery: Transdermal drug delivery is limited by the extraordinary barrier properties of the stratum corneum, the outer 10-15 mm of skin. Conventional needles inserted across this barrier and into deeper tissue effectively deliver drug, but can lead to infection and cause pain, thereby reducing patient compliance**.**

The biomedical industry seeks to replace stainless steel hypodermic injection needles with needles that have smaller diameter and sharper tips, to minimize pain and tissue damage. Since the dawn of microelectronic processing, electronic devices have been fabricated to smaller and smaller scales on a silicon substrate. As technology improves and smaller devices are created with more robust processes, the complexity of these devices will increase. In the meantime, non-implantable devices, such as the microneedles, are proving to be useful and worthwhile.

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 um, respectively.[14] Micro fabrication has been utilized to create micro needles, which are orders of magnitude smaller in diameter, capable of localized and painless delivery of drugs into cells or tissues. Research into the application of micro needles for gene and drug delivery has been divided into three broad areas: cellular delivery, local delivery and systemic delivery.[15]

Until very recently, the only drugs that could permeate transdermally were those possessing a very narrow and specific combination of physicochemical properties. However, rapid advances in bioengineering have led to the emergence of various new "active" enhancement technologies designed to transiently circumvent the barrier function of the stratum corneum. These novel systems, using iontophoresis, sonophoresis, electroporation, or microneedles arrays, will greatly expand the range of drugs that can be delivered transdermally. Crucially, the delivery of macromolecules will become possible and the transdermal flux of other molecules could be enhanced by several orders of magnitude.[16]

Micro needles 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. Micro needles have been fabricated with various materials such as: metals, silicon, silicon dioxide, polymers, glass and other materials. An example of micro needles, which was fabricated by creating micron-sized holes on a silicon substrate and by using a KOH solution to create the needle shape**.** Various types of needles have been fabricated as well, for example: straight, bent, filtered, and hollow[17, 18].

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 micro needles. 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. The future of drug delivery is assured to be significantly influenced by micro fabrication technologies. These micro fabricated 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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