INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Review Article

MICRONEEDLE: AS A FUTURE PROSPECTIVE TOOL

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Article Received on: 18/11/11 Revised on: 06/12/11 Approved for publication: 14/01/12

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ABSTRACT
Optimization of drug delivery through human skin is important in modern therapy. With the limitations of oral drug delivery and the pain and needle phobias associated with traditional injections, drug delivery research has focused on the transdermal delivery route. 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 micro needles. Evolving micro needle 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. Using the tools of the microelectronics industry, microneedles have been fabricated with a range of sizes, shapes and materials. To address practical applications of microneedles, the ratio of microneedle fracture force to skin insertion force (i.e. margin of safety) was found to be optimal for needles with small tip radius and large wall thickness. Microneedles inserted into the skin of human subjects were reported as painless. Together, these results suggest that microneedles represent a promising technology to deliver therapeutic compounds into the skin for a range of possible applications.
KEYWORDS microneedle, microelectronics, genome mapping, skin insertion force

INTRODUCTION

Most drugs are administered in the form of pills or injections, but these methods of delivery are not always optimal. Medication taken orally must not only be absorbed successfully out of the intestine into the bloodstream, but also survive the harsh and enzyme-rich environments of the gastrointestinal tract and first pass through the liver. Drugs that cannot be taken as pills are usually administered by injection, which introduces the problems of pain, possible infection, and expertise required to carry out an injection. Both routes of delivery have added limitations as bolus delivery methods, where the full dose of drug is introduced into the body at once. An approach that is more appealing to patients and offers the possibility of controlled release over time using transdermal drug delivery .The initial challenge to the development of such transdermal patches for the administration of a wide spectrum of drugs was the size of the molecules. These patches are scientifically known as Transdermal Drug Delivery Patches. They deliver drugs to the body through the skin. Since the skin acts like a natural barrier, these patches are limited to the delivery of drugs of small molecular sizes such as nicotine and progesterone. Â Since most drugs are macromolecules in nature, the skin prevents their entry through its surface. However, the past two years have witnessed spectacular breakthroughs in the field of painless drug delivery. The revolutionary work done in this field promises a novel, safer and more efficient means of administering drugs. However, this problem has been overcome by the development of Micro needles. A micro-needles are extremely minute, only a few microns in dimension, they pierce through the skin in such a way that they traverse the outer barrier layer, the Stratum corneum, but they do not pierce the nerve endings or cause any bleeding. Hence it is a bloodless and painless means of treatment. They can be fabricated out of metal, silicon dioxide, glass, fibre glass and so many other materials. They can also be solid or hollow. Solid microneedles are often coated with the drug that needs to be delivered to the body like Vitamin B and the hollow ones are used to deliver drugs Hollow microneedles can also be used to remove fluids from the body, e.g.,. Glucose for analysis[1].

Advantage And Disadvantage 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. 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. Hollow like hypodermic needle; solid—increase permeability by poking holes in skin, rub drug over area, or coat needles with drug. 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. 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. The greatest advantage of these needles is the fact that they are painless. In fact, in a particular clinical trial conducted on 12 subjects, using these microneedles, all reported that the sensation of the microneedles piercing the skin was comparable to pressing the skin against a hard surface. The actual piercing could not be felt unlike when a hypodermic needle is inserted in the skin. This is a very important advancement in the field of medicine, especially in pediatrics where children are usually afraid of needles and refuse to take their medicines. Another important advantage is that it allows accurate doses of medicine to be delivered. This is of utmost importance in

the case of diabetic patients, who take regular shots of insulin everyday and any mistake in the measurement could cause an insulin overdose. Recently, HP along with Crospon, a medical device manufacturer, has developed a transdermal skin patch. It incorporates the patented HP inkjet technology. Its specialty is that it includes around 150 microneedles and a microchip which automatically regulates the dosage and timing of the drug delivery. It also has around 400 cylindrical reservoirs, so that more than one drug can be delivered at a time, thus being advantageous to patients on multi-drug regime, which is difficult to remember and follow. Another advantage of the micro-needle drug delivery system is the ease of use and safety. Often young diabetics, especially children, go through the trauma of having to inject themselves twice a day. The micro-needle transdermal drug delivery patch eliminates this hurdle and also prevents accidents such as, breaking needles, air pockets in the syringes, etc. It is also extremely safe because the abrasions made by these needles are much smaller than traditional hypodermic syringes and other skin abrasions such as, scratches or cuts. Since it doesn't bleed it reduces the risk of infection. The ultimate breakthrough, though, in this field has come very recently. Mark Prausnitz, a chemical and biological engineer at Georgia Institute of Technology, has published a paper in the journal Nature Medicine, which talks about transdermal drug delivery patches with dissolvable microneedles for the delivery of vaccines. This idea has taken the world of biomedical engineering by storm as it talks of a safer and possibly more efficient means of vaccination. These needles are made of biocompatible and biodegradable polymers, which when inserted into the skin deliver the medicine and dissolve it into the body. A laboratory test using these needles was done, to deliver the flu vaccine to a group of mice as opposed to the traditional needles that were used for the other group. At the end of a 30 day test period, both the groups of mice showed the same level of resistance gained. To top it all, the mice that were injected using the microneedles showed a lower level of virus in their lungs than the other, proving that this method was probably more effective. Therefore this device sees an optimistic future in vaccination drives around the world, for various viruses, as they are more effective and much more hygienic and safe, as compared to traditional needles, were there have been cases of use and reuse in certain countries with lax medical standards. Thus, the transdermal micro-needle drug delivery patches are an innovative invention in today's world. Its advantages of being painless, safe, and hygienic and user friendly are very promising for its commercial growth. But some scientists and organizations are also voicing certain possible disadvantages. Firstly, these microneedles might cause skin irritation and allergy. Secondly, the dissolvable needles raise concerns because the polymers used to manufacture them may become slightly toxic when in the blood stream. And finally, the cost of these patches are little too high for everyone to afford. But these issues are easy to tackle. Allergies can be prevented by using a suitable skin cream or anti-allergenic. The dissolvable needles can be developed using cellulose-based polymers, which are safe to human body. The costs too can be reduced, when they are mass produced. A large number of companies are already in the planning stage to invest in this technology. This would make the product easily accessible and affordable[2,3].

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.

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 millimetres 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.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.

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[4].

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).

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.

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[5].

Microneedles: A Novel Approach To Transdermal Drug Delivery

A microstructured transdermal system also called microneedle consists of an array of microstructured projections coated with a drug or vaccine that is applied to the skin to provide intradermal delivery of active agents, which otherwise would not cross the stratum corneum. The mechanism for delivery, however, is not based on diffusion as it is in other trandsermal drug delivery products. Instead, it is based on the temporary mechanical disruption of the skin and the placement of the drug or vaccine within the epidermis, where it can more readily reach its site of action; 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. It is smaller the hypodermic needle, the less it hurts when it pierces skin and offer several advantages when compared to conventional needle technologies. 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. 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.

Current Research In Microneedles Technology

The first microneedle arrays reported in the literature were etched into a silicon wafer and developed for intracellular delivery in vitro by Hashmi et a. These needles were inserted into cells and nematodes to increase molecular uptake and gene transfection. Henry et al.[6] conducted the first study to determine if microneedles could be used to increase transdermal drug delivery. An array of solid Microneedles was embedded in cadaver skin, which caused skin permeability to a small model compound. In a follow-up study, McAllister et al. studied permeability of cadaver skin to a range of different compounds and found that insulin, bovine serum albumin, and latex nanoparticles as large as 100 nm in diameter could cross the skin after treatment with microneedles. Mathematical modelling of the data indicated that transport of these compounds was by simple diffusion. Extending in vitro findings to the in vivo environment, Lin et al[7] used microneedles either alone or in combination with iontophoresis to deliver 20-mer phosphorothioated oligodeoxynucleotides across the skin of hairless guinea pigs. A related study further demonstrated microneedle- enhanced delivery of desmopressin and human growth hormone using a similar approach . Using solid microneedles of a different design, Martanto et al. delivered insulin to diabetic hairless rats in vivo. Microneedle arrays were inserted into the skin using a high-velocity injector and shown by microscopy to embed fully within the skin. Matriano et al. examined the use of Microneedles to deliver ovalbumin as a model protein antigen coated onto the needle surface. Microneedles were prepared with a dry-film coating of antigen and then inserted into the skin of hairless guinea pigs in vivo using a high-velocity injector. Mikszta et al. studied delivery of naked plasmid DNA into skin using microneedles. The arrays were dipped into a solution of DNA and scraped multiple times across the skin of mice in vivo to create microabrasions. Recently Lee et al (2008) has studied on dissolving microneedles for transdermal drug delivery. This study presents a design that encapsulates molecules within microneedles that dissolve within the skin for bolus or sustained delivery and leave behind no biohazardous sharp medical waste[8-10].

CONCLUSION

Transdermal micro-needle drug delivery patches promise to revolutionize the field of medicine, vaccination and disease treatment. It can effectively attempt to phase out oral medication and thus reduce the time required for a treatment. This device is also another triumph of engineering solutions in the medical world, proving how simple technology can be used to solve intractable problems and doing so, it contributes in uniting scientists from various disciplines as well. Thus, the micro-needle transdermal drug delivery patch has the potential to be among one of the most important scientific inventions of modern times.

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