

Microneedles for painless immunization

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NEW(S)

American scientists have successfully developed a new technology using ‘microneedles’ to deliver painless immunization. People might get immunized in future through a ‘stick-on’ skin patch containing tiny microneedles. Sullivan and other experts from Emory University and Georgia Institute of Technology conducted the study. The microneedles are small enough that they do not draw blood or cause pain, but dissolve into the skin.^[1]

(RE)VIEW

Injection is probably the most feared among the routes of drug administration. Rather than the needle pain, the fear factor (needle phobia) is the one that mostly worries the patients. The most convenient and commonly used route is oral, but has its own limitations like, uncertainty of absorption, unsuitability for certain drugs (insulin, many vaccines, etc) and so on. A device that overcomes these disadvantages may be ‘microneedles’. Microneedles are extremely small needles (micron-scale needles with a length of a few 10s to a few 100s of microns) intended for painless drug administration (less intense than a mosquito bite).^[2] Jet injection, though needleless, is costlier, might cause bruising and has no great response from patients as expected.

In an effort to overcome the earlier mentioned limitations, drug delivery research has focused on the transdermal delivery route. Transdermal drug delivery has been severely limited by the inability of most drugs to enter the skin at therapeutically useful rates. The superficial layer of skin, stratum corneum, is a formidable barrier to transdermal drug delivery. In the last 10 years, usage of microneedles were proposed as a tool to pierce stratum corneum, in order to create minute drug delivery channels without stimulating

underlying pain receptors. Even macromolecules can be administered through this method.^[3]

Microneedles have been fabricated with a range of sizes, shapes and materials. Most drug delivery studies have emphasized solid microneedles, which have been shown to increase skin permeability to a broad range of molecules. Needle arrays (akin to the head of a tooth brush, the microneedles are fixed in many rows, as groups, each containing 10 or more needles) have been used to pierce holes into skin to increase transport by diffusion or as drug carriers that release drug into the skin from a microneedle surface coating. Hollow microneedles have also been developed and shown to inject insulin to diabetic rats.^[4]

The microneedle has been designed to mimic a mosquito's proboscis in dimensions with an external diameter of 60 μm , as opposed to 900 μm for conventional needles. Initially they were fabricated using silicon dioxide and later using titanium, which are capable of penetrating about 3 mm under the skin to administer drugs or extract blood. They were brittle, hence liable to break on impact with skin.^[5] Roger Narayan *et al.* of the University of North Carolina used two-photon polymerization of organically modified ceramic (Ormocer[®]) hybrid materials to create microneedles resistant to breakage.^[6]

The two tested methods of microneedle drug delivery^[7] are as follows:

Poke and soak (wordings slightly modified from the original reference)

Microneedles can be poked into the skin creating microholes (transient aqueous transport pathways of micron dimensions to increase drug permeability, including hydrophilic macromolecules), followed by drug application in the form of a patch.

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Coat and poke

In this method, the drug is coated onto the microneedles and inserted into the skin.

EXPERIMENTAL EVIDENCE

Dissolving microneedle patch

In a study in mice, microneedles of 650 microns in length and about the width of a few strands of human hair were assembled into an array of 100 needles to penetrate the outer layers of skin. They were made from a polymer, poly-vinyl pyrrolidone that has been shown to be safe. The freeze-dried influenza vaccine was mixed with the vinyl-pyrrolidone monomer before being placed into microneedle molds and polymerized at room temperature using ultraviolet light. The dissolving microneedles appear to provide improved immunity compared with hypodermic needle vaccination. Furthermore, they may be self administered. Mass production of microneedle patches are expected to cost similar to the conventional needle-and-syringe and should be useful for other immunizations.^[8,9]

Antimicrobial-coated microneedle

Possibility of infection has been an obstacle to the widespread use of microneedles. Modifying the microneedle surface with an antimicrobial (coating with a thin film of silver) prevented microbial growth. Another approach incorporated an antimicrobial into the microneedle material itself.^[10]

Degradable microneedle

This type dissolves in the skin surface and releases the antimicrobial, guarding against infection. They can be used for single-use drug delivery, such as vaccines.^[10]

CLINICAL EVIDENCE

Drug delivery through microneedle skin punch

Transdermal drug delivery has been successful in varied conditions, like pain management, congestive heart failure, hormone replacement, etc. Large molecule protein and polypeptide drugs can neither be delivered with traditional passive transdermal patches nor by mouth because they are deactivated in the gut. By painlessly punching a series of microscopic holes in the outer layer of skin, microneedles have the potential to expand the range of drugs and vaccines that can be delivered transdermally.

Naltrexone, used to treat opiate addiction, is a skin-impermeable molecule. In healthy humans, the skin was prepared by pressing and removing a thumb-sized patch (containing 50 stainless steel microneedles each 620 microns in length) on each subject's arm followed by application of naltrexone gel and a protective dressing to the prepared area. Controls were

treated similarly, but without the microneedle preparation prior to naltrexone gel. Effective blood levels of naltrexone were obtained for at least 48 hours in the test subjects. No detectable drug levels were seen in controls. Furthermore, unlike oral route, drug given by microneedle bypasses the liver, with consequent marked reduction in harmful drug metabolites like naltrexol. Such administration also reduced the drug dose by 1/5th (10–12 mg in the gel vs 50 mg tablet). Photographs of a microscopic needle transdermal patch and punctured skin site can be seen in this website.^[11]

Using solid polymer microneedles arrays is a promising method for transdermal delivery of insulin, incretin mimetics and other protein-based pharmacologic agents for treatment of diabetes mellitus. Microneedle-based insulin delivery (inserted 1 mm into the intradermal space) effectively reduced postprandial glucose levels with reported minimal pain and preference over subcutaneous catheter delivery in diabetic patients. Such delivery may also have faster onset of action.^[12,13]

It has been shown that traditional hypodermic syringe was less safe and up to five-times more painful than microneedles. Damage to skin blood vessels and nerve endings are minimal and so also pain and risk of needle stick injuries. It has also been shown that the microneedle punctured site healed quicker compared with the traditional counterpart.^[14]

Future

Microneedles may be integrated with micropumps and biosensors to provide autonomous sampling of blood, analysis and drug-delivery capabilities for treatment of chronic disease. For example, one needle, pump and sensor unit would assay glucose in interstitial fluid, whereas another unit would deliver insulin in a continuous or programmed manner.^[15]

To conclude, the microneedle is a new technology to administer drugs by self without pain but with much improved compliance. This technique encompasses the concepts of transdermal drug delivery with patches and microhypodermic injections. Microstructured drug delivery devices have tremendous potential in a wide range of instances, from single use vaccine administration to daily insulin administration and so forth. Presently, there is very little scientific literature describing the use of microneedle-drug-delivery on humans. It may be apt to add a universal statement (well known to experimental/clinical researchers, especially involving a new drug/device), 'However, more clinical studies have to be done to assure safety and effectiveness of drug delivery involving microneedles.'

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