EMERGING ERA OF MICRONEEDLE TECHNOLOGY FOR TRANSDERMAL DRUG DELIVERY SYSTEM

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INTRODUCTION:

The skin is an important organ that protects the body from harmful effects including massive water damage and synthetic chemical attacks. The primary skin barrier, the stratum corneum, which is a component of the epidermis, is made up of 15-20 corneocyte layers.3-5 Transdermal medication delivery offers an important alternative to oral and hypodermic injections.

There are three layers to human skin: the hypodermis, dermis, and epidermis. It might solve the problem of drug degradation and liver or gastrointestinal absorption. It is non-invasive, painless, and self-administered.

Microarray patch technology was developed to deliver high molecular-weight drugs without the use of injections. In order to increase patient compliance, it can give delayed drug release. The surface structure of microneedles (MNs) allowed for the delivery of the medicine in the form of a bandage. MNs are composed of numerous unique micro projections that vary in size, shape, and support from a base. Their heights range from 25 to 2,000 mm. As per a 1976 patent, ALZA was the first business to create MNs. As seen in Figure 1, MNs allow for non-invasive access to the patient's dermis and allow for the direct absorption of medications into the systemic circulation. This study will concentrate on MN technologies that have lately made considerable strides towards breaking through the subcutaneous barrier and enabling enhanced transdermal medication delivery. We'll focus on the latest recent developments in MN design.

It will highlight When MN inventions go from academic research to commercial applications, challenges to effective MN encroachment and some crucial safety considerations will be taken into account. The industry has begun to see the entry of some commercial MN products that aid in the transdermal delivery of medications and vaccines. The novel coronavirus disease COVID-19 (Coronavirus disease 2019) illness has been classified as a global pandemic by the World Health Organisation (WHO). For the treatment of this condition, researchers recently produced the recombinant coronavirus vaccine (PittCoVacc).

Researchers have looked at microneedles (MNs) for transdermal medication administration and for overcoming the drawbacks of the existing methods. A micron-sized needle is used in a microneedle device. The problems with transdermal patches and hypodermic needles prompted the creation of the microneedle drug delivery system, which is seen as a hybrid of the two.

The fundamental problem with transdermal technology is that many drugs cannot exert their therapeutic effects because they cannot penetrate the skin quickly enough. The stratum corneum can be penetrated by hydrophilic, high-molecular-weight compounds thanks to the advanced method known as microneedles. More drug molecules can permeate the skin when drugs are administered using a microneedle device because the drug molecules can pass through the stratum corneum layer.

The distinguishing features of this approach include its speedier onset of action, improved patient compliance, self-administration, enhanced permeability, and efficacy. additionally, to If microneedle tips are left inside the skin, problems may arise since they are much smaller and thinner than the thickness of human hair and can shatter. These limitations are rather infrequent and can be overcome by carefully choosing the microneedle material. The main objective of this technology is to disrupt the stratum corneum by generating larger transport pathways of micron size, which are larger than molecular dimensions and smaller than holes made by hypodermic needles, allowing large molecules to pass through and increasing permeability. Traditional methods include chemical and lipid procedures, as well as electric ones like iontophoresis and electroporation.

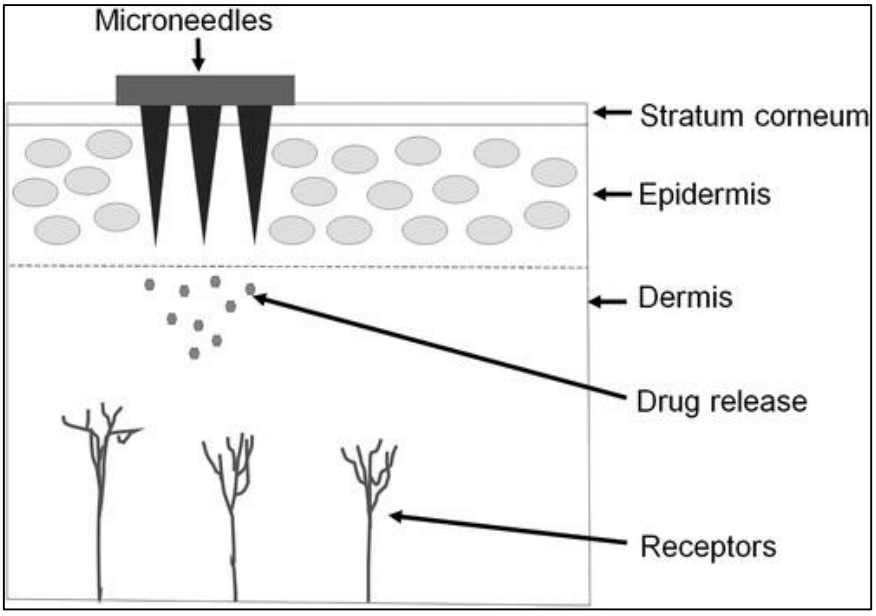


Figure 1: Microneedle

Table-I: Comparison between topical cream, transdermal patch, hypodermic needle, and microneedle drug delivery systems

	Topical cream	Transdermal patch	Hypodermic needle	Microneedle
Description	Emulsion/ emulgel/ cream/ ointments	Adhesive patch to be placed on the skin	Fine, hollow tube having a sharp tip with small opening at the end	Micron size needles are aligned on the surface of a small patch
Onset of action	Slow	Slow	Faster	Faster
Pain	Painless	Painless	Painful	Painless
Bioavailability	Poor	Insufficient	Sufficient	Sufficient
Patient compliance	Less	Better	Less	Better
Self-administration	Possible	Possible	Not possible	Possible
Mechanism of drug delivery	Permeation through skin pores.	Drug has to cross stratum corneum barrier, thus poor diffusion of large molecules	Drug placed directly in the dermis	Bypass stratum corneum and drug placed directly into epidermis or dermis hence enhanced permeability

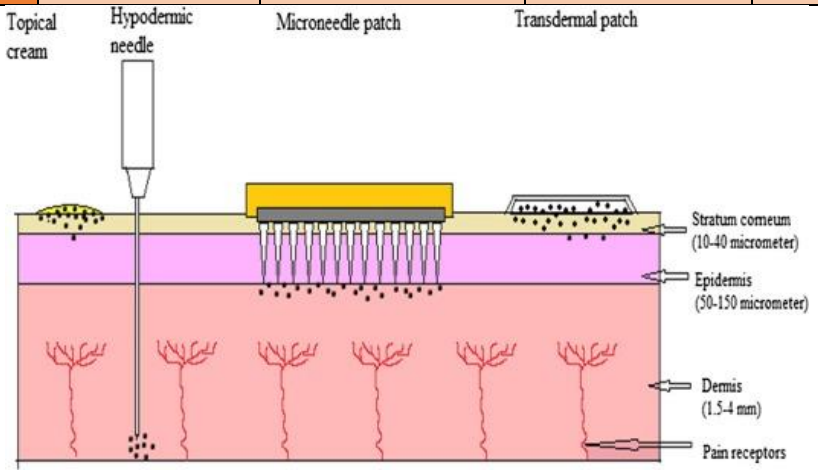


Figure 2: Comparison of topical cream, hypodermic needle, microneedle patch and transdermal patch

MECHANISM OF DELIVERY

The diffusion mechanism is used to administer the medicine via the topical route. The skin is momentarily damaged during the medication delivery process using microneedles. In order to administer enough medicine to produce the necessary therapeutic response, a microneedle device is created by arranging hundreds of microneedles in arrays on a tiny patch (similar to that of a typical transdermal patch available on the market). By cutting through the stratum corneum, it avoids the barrier layer. The medicine is immediately injected into the epidermis or upper dermis layer, where it enters the systemic circulation and, upon reaching the site of action, produces a therapeutic reaction. In Fig. No. 02 [2], the mechanism of drug administration using microneedles is shown.

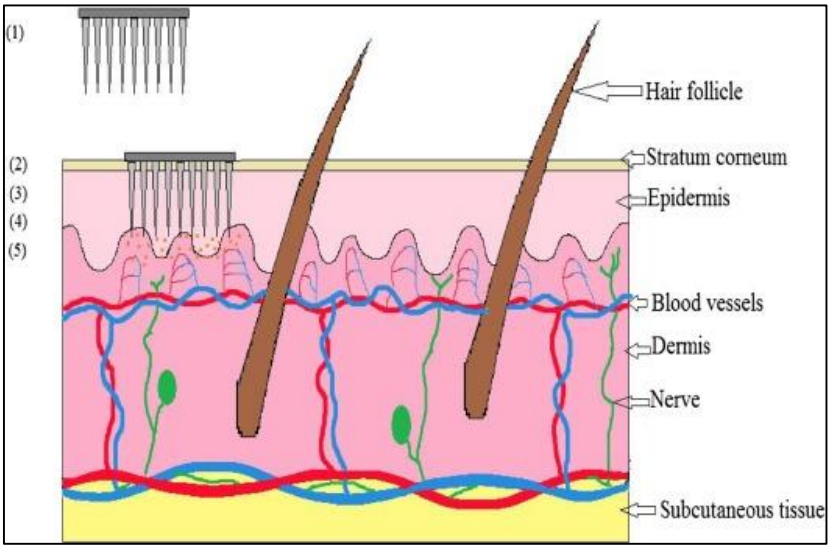


Figure 3: Mechanism of drug delivery by microneedle device: (1) Microneedle device with drug solution; (2) Device inserted into the skin; (3) Temporary mechanical disruption of the skin; (4) Releasing the drug in the epidermis; (5) Transport of drug to the site of action

METHODOLOGY FOR TRANSDERMAL DRUG DELIVERY:

A variety of methods employed for transdermal drug delivery through hollow or solid MNs are poke and patch system in

Poke and Patch

When a patch is applied on the top of these MNs, needles form micropores into the skin upon removal of it.

Coat and Poke

The MNs perforate the skin, and afterward, the drug containing coating is released through hydration.

Dip and Scrape

The MNs or microblade are first dipped in a drug solution and then scraped over the skin leaving behind the drug within the microprojections generated by the MNs.

Poke and Flow

This approach is used for hollow MNs. The MNs are made up of polymers in which the drug is encapsulated. The incorporated drug is released for a more extended period[1]

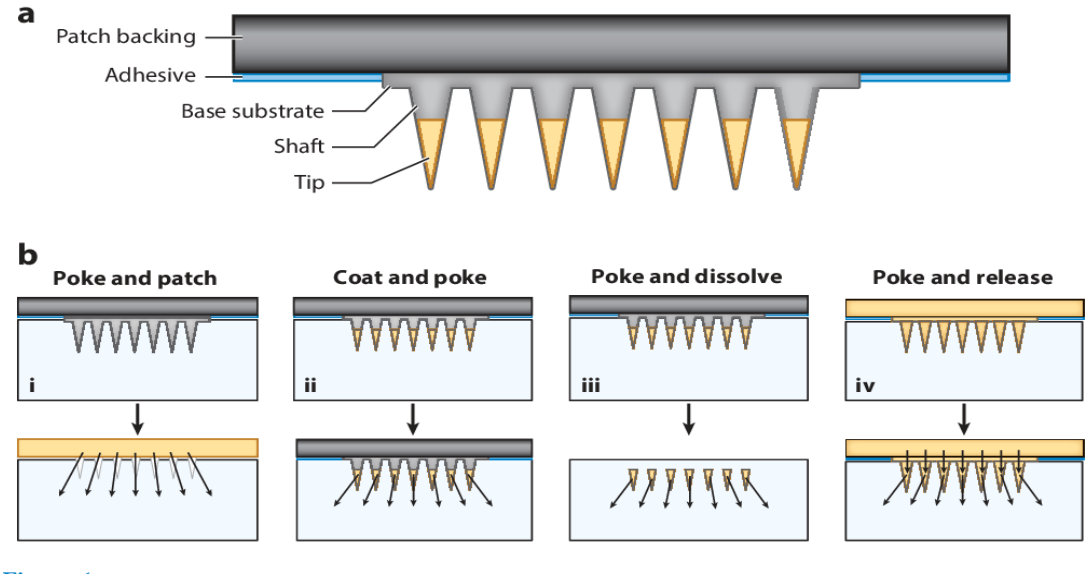


Figure 4: Microneedle patch (MNP) designs and operations. (a) Microneedles comprise a shaft and tip that often encapsulates or is coated with drug. The microneedle array is mounted on a base substrate that is attached to a patch backing to facilitate handling and skin adhesion. (b) Drug delivery approaches for MNP use. MNPs can (i) be used as a pretreatment, after which a drug formulation is placed on the skin surface for slow drug release through residual pores in the skin (poke and patch); (ii) be coated with drug in a water-soluble matrix that is released in the skin (coat and poke); (iii) encapsulate drug in water-soluble microneedles that dissolve in the skin (poke and dissolve); or (iv) encapsulate drug in the patch backing and, in some cases, the microneedles that slowly release drug through the non-water-soluble microneedle matrix (poke and release).

Types of microneedles:

Most patches share a few similar characteristics, even though the microneedle design varies depending on the distribution mechanism, kind of microneedle, and action of the medications to be delivered. A typical microneedle has a tapered sharp tip and measures 150–1500 mm in

length, 50–250 mm in breadth, and 1–25 mm in tip thickness. Standard materials for microneedles include metal, silicon, polymer, glass, and ceramic. The medication is often injected into or applied to the microneedle tip, which is attached to the substrate base below to create an array. For convenience, the patch backing—which includes a skin adhesive to enhance contact with the skin—is bonded to the microneedle array. There are normally four varieties of microneedles. Metal and silicon, which offer powerful mechanical qualities and don't contain any pharmaceuticals, are the main materials used to make solid microneedles. Thus, it is vital to continue applying the medication to the area after putting the microneedles. In contrast, the medicine is administered concurrently with the application when coated microneedles are used on the skin's surface. The medicine may be included into the biodegradable matrix when dissolving microneedles, in which case there will not be any sharp debris left over following microneedle application. Because the medication is contained in all locations, including the microneedle's tip and the backing of the patch, hydrogel microneedles provide gradual drug delivery. Since the properties of microneedles vary depending on the kind, a design that is appropriate for the microneedles should be chosen based on the medication dose, time until the drug starts to take effect, length of time it takes to deliver, efficiency of distribution, packing, and sharp waste.

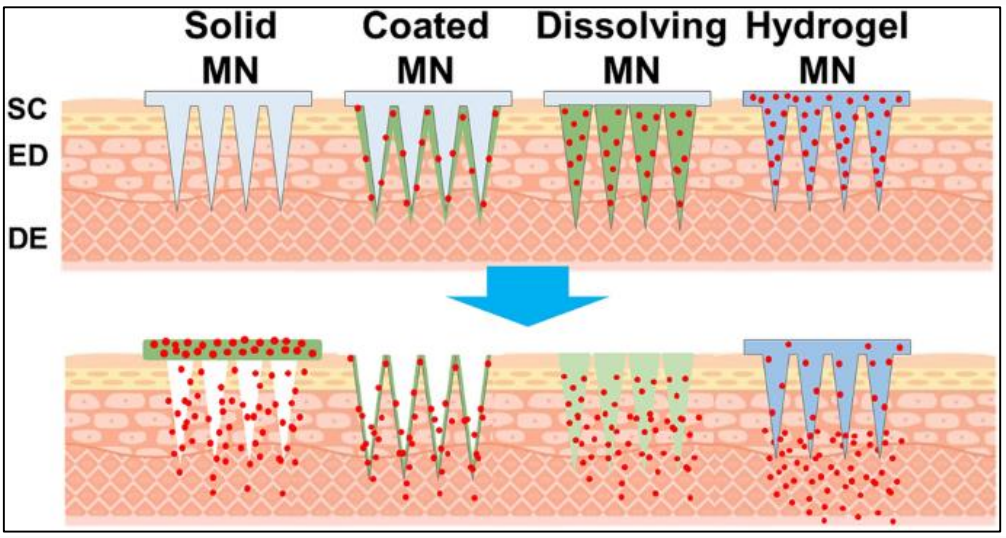


Figure 5: Schematic illustration of the types of microneedles and their drug delivery methods.

SOLID MICRONEEDLE

Hydrogel microneedles administer drugs gradually because the drug is present everywhere, including the tip of the microneedle and the backing of the patch. A design that is suitable for

the microneedles should be chosen based on the medication dose, time until the drug begins to take effect, length of time it takes to deliver, efficiency of distribution, packing, and sharp waste since the qualities of microneedles vary depending on the type. Drugs can be delivered over and extended time by including reagents that keep the pores open for a longer duration.[4]

COATED MICRONEEDLES

With coated microneedles, a water-soluble matrix is applied to the surface of a solid microneedle so that the medicine dissolves quickly into the skin after microneedle insertion (Fig.4b). The coating formulation should create a film on the microneedle's surface and retain adherence throughout storage and skin insertion. The coating recipe needs to have enough viscosity to accomplish this. It is important to think about where the coating formulation will be applied. It is usually more cost-effective to just administer the medications at the microneedle's tip, where the skin is really penetrated. By adjusting how deeply the microneedle is dipped into the coating formulation in the case of dip coating, the drug-coated area can be managed. By adjusting the coating formulation's surface tension, one can regulate how widely the microneedle spreads, hence determining the drug-coated area. The medication's speedy skin dissolution in coated microneedles causes a rapid commencement of pharmacological action. Repeating the formulation coating process results in a thicker coating, however due to dose restrictions, this method is not suited for drug delivery.[4]

DISSOLVING MIRCONEEDLES

The actual microneedles can be constructed from materials that are water-soluble or biodegradable, contain the medicines, and have the necessary mechanical strength to pierce the skin (Fig. 4c). A dissolving microneedle can be inserted into the skin without producing sharps waste because it quickly dissolves or disintegrates when it comes into touch with skin fluid. The main method for producing dissolving microneedles is solvent casting with a water-soluble biodegradable polymer. Commonly used cellulose-based biodegradable polymers include carboxymethyl cellulose (CMC) and methyl cellulose.The microneedles also contain saccharides, such as trehalose and sucrose, which help the formulation dissolve and stabilise biomolecules. The drug-containing tip's formulation should be compatible with the medication, have mechanical strength, and have a viscosity that is sufficiently low to fill the microscale mould space thoroughly and bubble-free. The base substrate, which doesn't contain any drugs,

might be more viscous than the tip, have weak mechanical properties, or be made of something that isn't water soluble. Recent research have looked at ways to reduce the amount of time that microneedle patches need to be worn by fast removing the tips from the base substrate without requiring the tips to fully dissolve in the skin. A microneedle patch that may rapidly separate after skin insertion by applying shearing force was described by Li et al. By capturing a droplet on the microneedle, the mechanical strength of the device may be adjusted. Also, the base substrate, which was made of a foam able substance, was removed from the microneedle tip within 2 minutes.created insertion-responsive microneedles enabling instant microneedle separation following application to the skin. On the side of the microneedle base, a tiny single wall was constructed; this allowed for a quick mechanical separation of the tip and base. Studies are being done to increase the quantity of medicine that can be integrated in these microneedles because, like dissolving and coated microneedles, this technique is not ideal for administering high amounts. [4]

HYDROGEL MICRONEEDLES

The medicine is contained in all sections of the hydrogel microneedle tip, base substrate, and patch backing and released slowly while the patch is worn against the skin (Fig. 4d). Since the microneedle patches are mostly made of hydrogel, they are hydrated but not dissolved when they come into contact with skin fluids. Diffusion allows a significant amount of the medication in the hydrogel to reach the skin. This technique can provide huge doses of medication since the drug can be distributed across the entire microneedle patch; nevertheless, the patch-wearing period is lengthy due to the slow drug delivery rate. [4]

MICRONEEDLE FABRICATION MATERIAL AND ITS PROPERTIES

Silicon

In the 1990s, silicon was used to create the first microneedle. Silicon has a crystalline structure and is anisotropic in nature. Its characteristics depend on how the crystal lattice is aligned, which exhibits a range of elastic moduli (50 to 180 GPa). Because to its flexibility, a variety of sizes and forms of needles can be produced. It is a versatile material thanks to its appealing physical characteristics. Silicon substrates are capable of batch production and can be made precisely. The use of silicon in microneedles is constrained by its high cost and labour-intensive complex fabrication method. In addition, there are some biocompatibility issues, as silicon is brittle, some part may break and remain in the skin thus causing some health issues.[1]

Metal

Titanium and stainless steel are the two major metals used. Alloys made of palladium, nickel, and palladium-cobalt are also employed. They are biocompatible and have good mechanical qualities. Metals are more ideal for making microneedles than silicon because they are robust enough to prevent shattering. Stainless steel was the first metal utilised in the creation of microneedles. A good substitute for stainless steel is titanium. [1]

Ceramic

Alumina (Al_2O_3) is mainly used because of its chemical resistance. It forms a stable oxide because of the highly energetic ionic and covalent bonds between Al and O atoms. Other types of ceramics used are calcium sulphate dihydrate [Gypsum ($CaSO_4$ $0.2H_2O$)] and calcium phosphate dihydrate [Brushite ($CaHPO_4.2H_2O$). In recent years an organically modified ceramic called Ormocer® has been used. It is a three-dimensionally cross-linked copolymer. A polymer with different properties can be produced by using different organic units during polymerization. Mainly they are produced using a micro-molding technique. Ceramic slurry is cast into a micro-mold. Micro-moulding techniques are cheaper processes, and also have the potential for scale-up.[1]

Silica glass

On a tiny scale, glass can be used to create a variety of forms. Although biologically inert, silica glass is brittle by nature. More elastic is borosilicate glass, which is composed of silica and boron trioxide. They are less time efficient because they are typically made manually. Glass MNs are solely utilised for research presently, not for commercial application. [1]

Carbohydrate

One of the most often used sugars is maltose. You can also employ polysaccharides like galactose, mannitol, trehalose, sucrose, and xylitol in addition to other sugars. Moulds made of silicon or metal are used to shape carbohydrate slurries. To create the microneedles, the drug-loaded carbohydrate mixture is cast into the moulds. The release of drugs into the skin is controlled by the time-dependent breakdown of carbohydrates. Although inexpensive and safe for human health, carbohydrates degrade at high temperatures, making the production process challenging.[1]

Polymer

A wide variety of polymers including poly (methyl methacrylate) (PMMA), polylactic acid (PLA), poly (lactic-co-glycolic acid) (PLGA) , polyglycolic acid (PGA), poly (carbonate), cyclic-olefin copolymer, poly (vinylpyrrolidone) (PVP), poly (vinyl alcohol)

(PVA), polystyrene (PS), poly (methyl vinyl ether-co-maleic anhydride), SU-8 photoresist are reported for microneedles preparation. These polymers are typically used to create microneedle arrays that dissolve or degrade and form hydrogels. These polymers can be used to create microneedles that are stronger than glass and ceramics but less strong than other materials. [1]

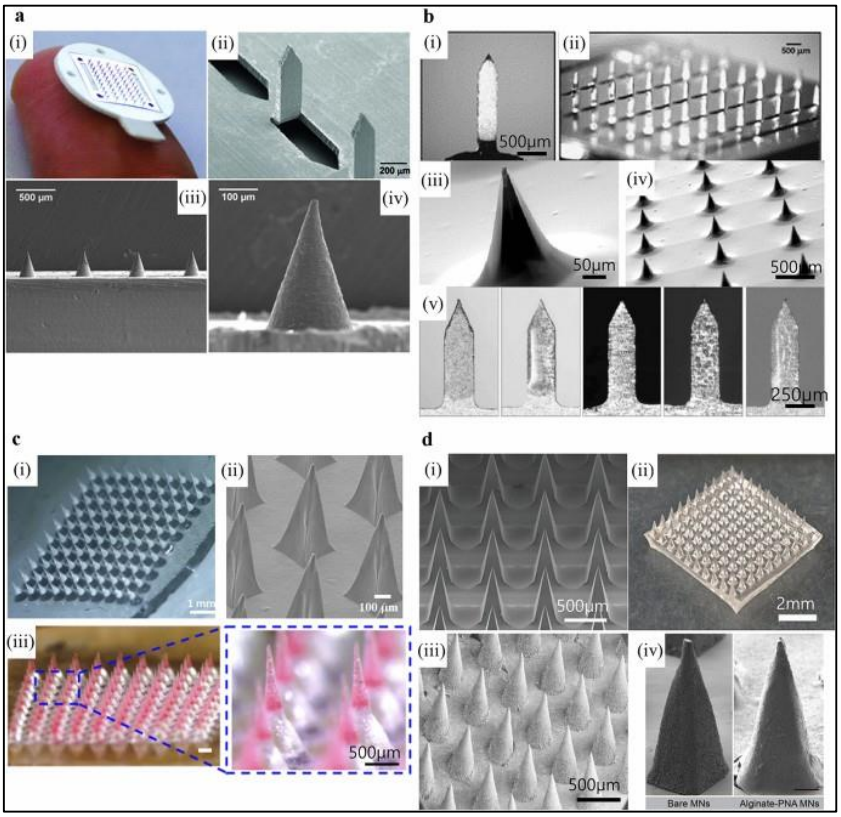


Figure 6: a. Solid microneedles composed of stainless steel (i and ii) and titanium (iii and iv). **b**. Coated microneedles composed of stainless steel (i and ii) , silicon (iii and iv), and titanium (v). **c** Dissolving microneedles composed of CMC (i), HPMC (ii), and PLGA (iii) .**d** Hydrogel microneedles composed of HA (i and ii) , PVA (iii) , and alginate (iv).

Fabrication Methods:

Different materials are used to produce MNs. The method of the fabrication depends upon the types of material used.

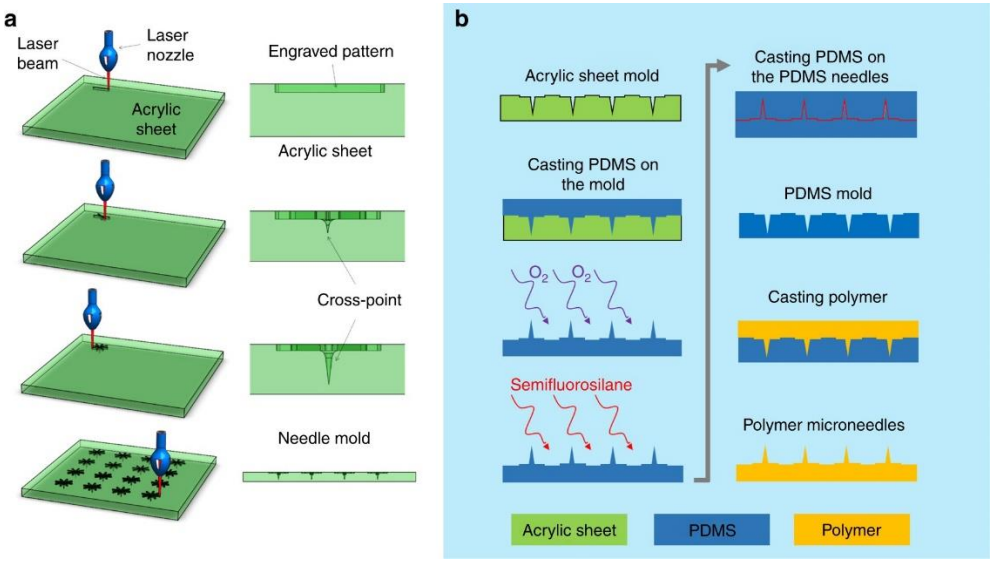
Etching

It is one of the used methods for the fabrication of MNs. It involves the reaction between substrate and etchant. This method is divided into dry etching and wet etching based on the etchant used. Wet etching involves using a liquid etchant to etch the substrate in order to give it the desired shape. Wet etching is still widely employed in fabrication despite its low selectivity and accessibility of materials. On the other hand, gas is utilised as an etchant in dry etching. Dry etching produces images with great resolution and a deeper etching depth, but it

is expensive and labour-intensive. The MNs used in this approach have mainly been silicon and metal. 28,73 Using the reactive ion etching approach, silicon hollow MNs for transdermal hemodynamic dysfunction therapy were created. [1]

Laser cutting

It is a productive technique for creating uniform MNs. MNs are shaped using cutting equipment. Due to the cutting machine's subpar accuracy, this procedure is only effective on materials that are a particular degree of toughness or hardness. Most metal and silicon MNs use this technique. Molds and laser cutters were used to make the polydimethylsiloxane (PDMS) MNs. [1]



Fabrication of microneedle mold. (a) CO2 laser cutter was used to fabricate microneedle acrylic mold using the proposed cross-over lines (COL) technique, (b) the acrylic mold was used to fabricate polydimethylsiloxane (PDMS) microneedles mold, which can be used to fabricate a variety of polymer-based microneedles.

Photolithography

This technique involves transferring a design pattern from a photomask to a substrate coated with photosensitive material using radiation sources like X rays or visible ultraviolet (UV) lamps. As a result, a 3D structure is created on the substrate. Other methods, such as using a free or switchable laser source and varying the UV intensity, are used to create the 3D structure. The creation of polymeric hollow MNs using photolithography processes benefits from this methodology. Micromolding. In this technique, MNs are created using micro- or nanoscale moulds. Materials that are liquid or molten are cast into the shapes. The MNs are separated from the shells after solidification. It is more cost-effective than other technologies and a simple, time-saving method for mass production. For sugar and polymeric MNs, this approach

is more practical. The polymeric MN array was made by the researchers using a micromolding method. summarises the typically used materials and their fabrication methods.

Table 2: Materials and methods used for Microneedle fabrication

Material	Technique
Silicon	Wet etching, dry etching, 3D Laser Cutting
Metal	Laser Cutting, Laser ablation, micromolding, metal electropolating
Ceramic	Ceramic micromolding and sintering lithography
Carbohydrates	Micromolding
Polymers	Micromolding, Drawing Lithography, Photolithography

EVALUATION OF MNS:

Techniques of Visual Characterization the insertion or penetration behaviour of the MNs may be impacted by their geometry. Using optical or electrical microscopy, as well as ocular inspection, geometry and the measurement of tip radius, height, and length were assessed. Confocal laser microscope and scanning electron microscopy (SEM) were utilised to obtain 3D pictures, which assists in quality control. SEM offers information on surface topography and composition. With the aid of fluorescently-labeled molecules, 78 compounds included in the MNs were identified and viewed using visual inspection, fluorescent microscopy, and confocal laser scanning microscopy. [1]

Mechanical Properties

MNs must be sufficiently tough, hard, and mechanically strong to penetrate the skin without fracturing it. Electrical measurements, force/displacement tests, dye marks, and other mechanical tests are used to measure insertion forces. Histological staining, cryosectioning, optical microscopy, and confocal microscopy are all used to gauge insertion depth. 80 Research on in vitro permeation The Franz diffusion cell device can be used to determine the rate at which medicines enter the skin. Pig ear skin is frequently employed in the test by being mounted between the donor and receptor compartments. For skin treated with MN and skin that was not treated, the drug penetration profiles were plotted for the cumulative amount of drug release as a function of time. [1]

In Vivo Studies

On the basis of hairless rat animal models, numerous rebuilt skin models are employed for in vivo experiments. One of the characteristics monitored by the Delfin VapoMeter is trans epidermal water loss. [1]

In Vitro/In Vivo Correlation Studies

In the in vitro in vivo correlation investigation, hairless pig skin was mounted on a Franz diffusion cell. The pH and temperature of the dissolving media were kept at a level that replicated in vivo conditions, and the in vitro experiment looked at the drug penetration profile. Hence, all in vitro study variables and conditions were associated with those in vivo. [1]

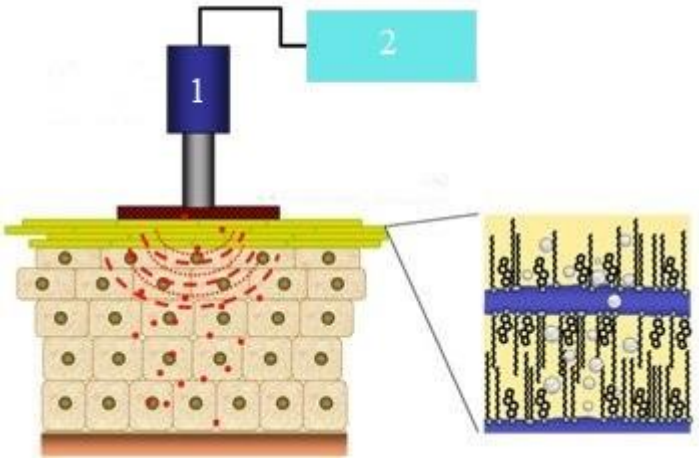
Skin Irritation Studies

The application location may experience mild to severe erythema as a side effect of transdermal administration. The Draize method was employed to gauge the intensity of skin irritability. At the location of action, the dermatological changes were seen both before and after the patch was applied. [1]

RECENT ADVANCEMENTS OF MN-BASED TECHNIQUES FOR DRUG AND VACCINE DELIVERY

The applications of MNs, in conjunction with physical methods, were studied to improve drug distribution and better regulate drug delivery through the skin.

Sonophoresis in Combination with MNs -



1. Ultrasonic Transducer
2. Power Supply

Figure 7: Sonophoresis

Sonophoresis is the term used to describe the process of using ultrasound to deliver medicinal chemicals via the skin. By changing the lipid composition of the top layer of skin and creating cavitation, this approach uses ultrasound (3 W/cm2; 20 kHz to 10 MHz) to increase medication

permeability (formation and oscillation of gas bubbles). The ultrasonic frequency can be adjusted to control the penetration of medicines through skin. Gene delivery and transcutaneous immunisation exploit this physical enhancer. 85 Bovine serum albumin is a high-molecular-weight substance that is delivered by both ultrasound and MNs. The combined 1.5 mm of MN patch and 15 W ultrasonic frequency resulted in an increase in permeability to 1 mm/s, which is nearly 10 times more than the permeability indicated by passive diffusion. [1]

Iontophoresis in Combination with MNs -

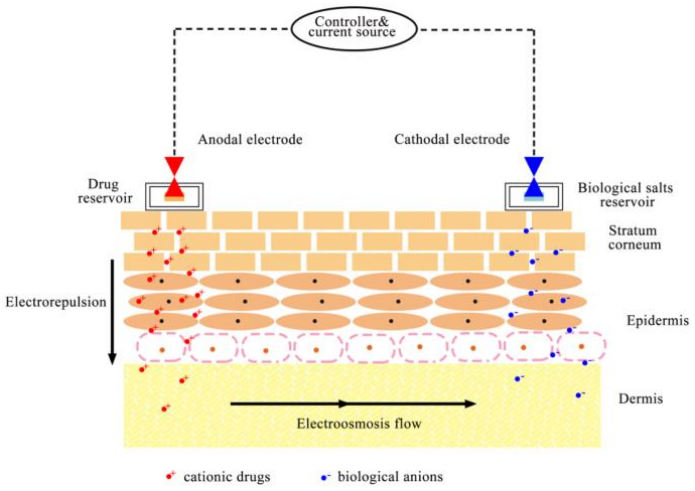


Figure 8: Iontophoresis

Improved skin permeation and rate of release of different medications with low absorption capacity are produced by facilitating the passage of ions through a membrane when an external modest electrical potential difference is supplied (0.5 mA/cm2 or less). Combining iontophoresis with MN is useful since it regulates drug delivery by regulating current. Electronic methods can help increase patient compliance by allowing patients to adjust their dose as necessary. In a study, high molecular weight compounds D2O and fluorescein isothiocyanate (FITC)-dextrans were delivered using a combination of MN and iontophoresis. The molecules' skin permeability increased as a result, according to the findings. [1]

Electroporation in Combination with MNs -

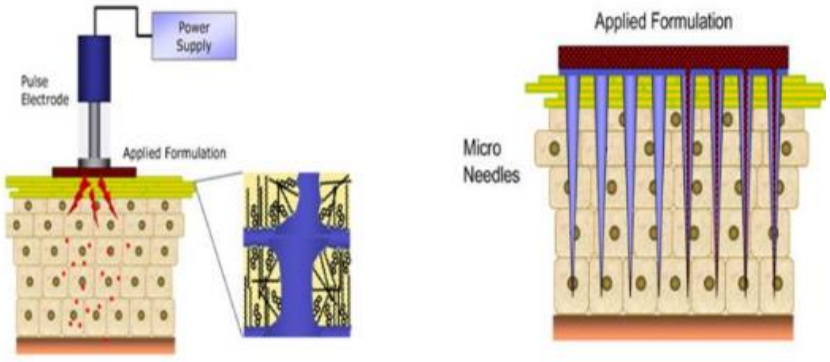
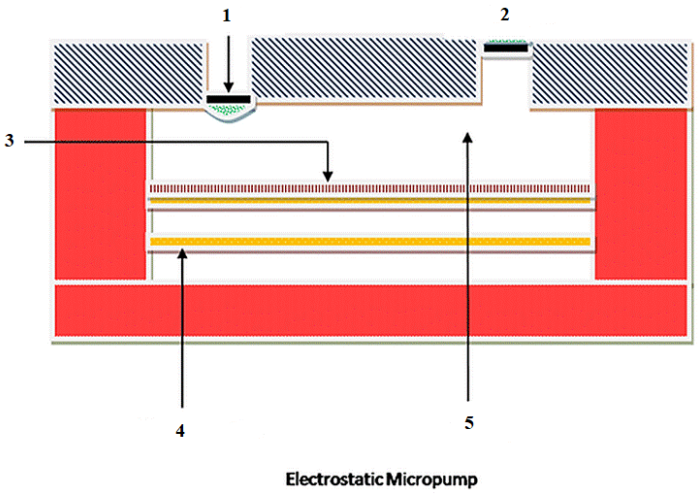


Figure 9: Electroporation

By creating tiny aqueous pores in the lipid bilayer of the skin with high voltage current for a brief period of time, electroporation causes localised disruption. Drugs with a range of lipophilicity and molecular weights, including those with a molecular weight greater than 7 kDa, can have their molecular permeability accelerated using this method. By combining it with chemotherapy, the electroporation technology can be used to treat malignancies more effectively. The macromolecular medication FITC/dextran was delivered via an MN electrode array. According to the findings, electroporation and MNs improved the distribution of macromolecular medicines. [1]

Micropumps in Combination with MNs-



1. Inlet Liquid
2. Outlet Liquid
3. SeparatingMembrane
4. Working Electrode
5. Pumping Compartment

Figure10: Micropumps

The combination of MNs with micropumps offers efficient medication delivery. Pumps keep an eye on the flow rate of concentrated medicinal solution in accordance with delivery criteria. These pumps have the ability to regulate fluid removal based on the amount of metabolites.

For continuous fluid distribution, researchers demonstrated MN integration with an on-chip microelectromechanical system displacement micropump. Longer duration continuous pumping has been accomplished. [1]

Pocketed and Grooved MNs-

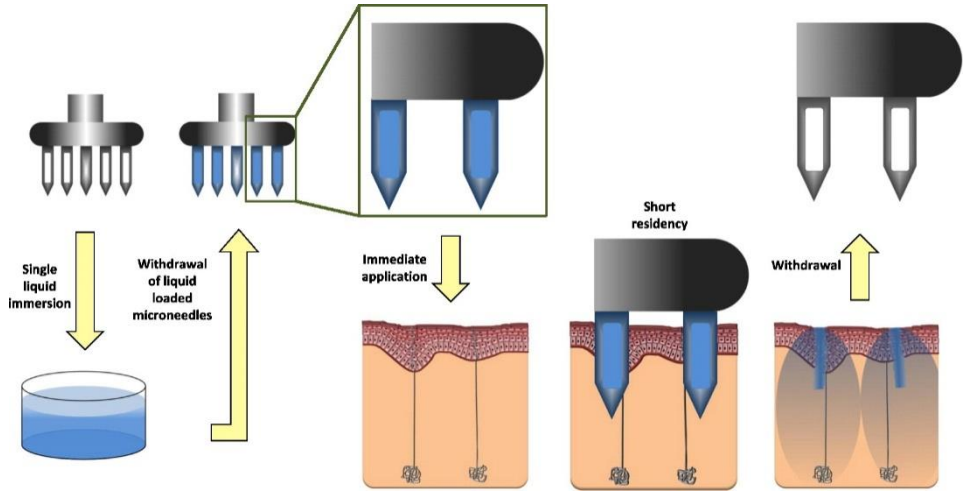


Figure11: Graphical Abstract of Pocketed and Grooved Microneedles

When changing surfaces, MNs can descend to a certain depth and pick up more drug loads. We build polymeric MNs with a broad base, sharp tips, and embedded shafts with grooves to assess their ability to carry drugs. When compared to smooth MNs, MNs with greater antigen-loading capacity showed a significantly stronger reaction to antibody. 91 A modified groove-embedded MN array was created by the scientist to deliver ovalbumin through skin. Due to the loading of more antigens in the grooves, MNs with more and deeper grooves produced a stronger antibody response.MNs made with grooves therefore offer a better instrument for intradermal vaccination.[1]

MNs Combination of Vibratory Actuation

The injection force, which should not be greater than the fracture force, must be carefully controlled in order for MNs to penetrate the skin. Vibration weakens the insertion force by causing thermal damage owing to frictional engagement and tissue injury through fluid cavitation. This conjunction encourages the fabrication of MNs with low Young's moduli utilising metals or polymers. 8 In a study, the vibration frequency and applied force were used to explain the mosquito's probing behaviour. The imposed stresses increased stability and allowed for higher compressive strengths. The outcome demonstrated consistent vibration-assisted MN delivery. [1]

Applications of microneedle drug delivery:

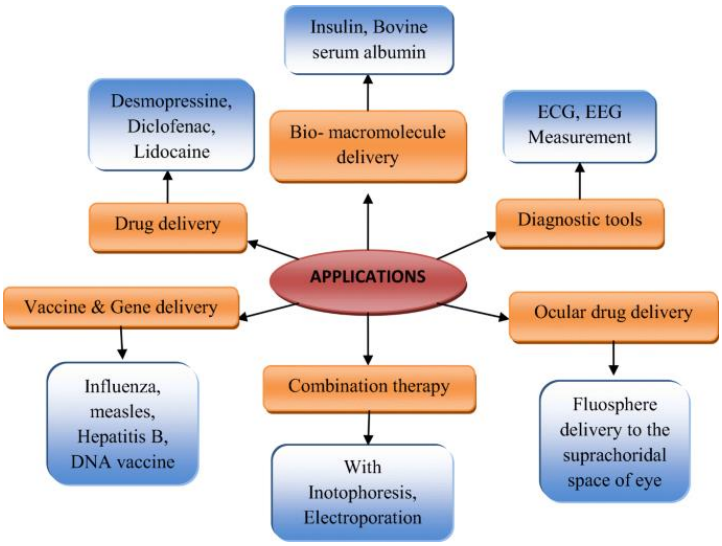


Figure12: Microneedle Applications

1. The capacity of a molecule to permeate the skin determines the efficacy of a transdermal application. Due to their large molecular weight, many compounds, primarily peptides and vaccines, have encountered difficulties during production and application.
2. MNs have demonstrated successful intradermal administration of such compounds, and in some situations, they have been found to be more efficient at delivering smaller dosages for the same therapeutic benefit than the existing conventional delivery systems. For instance, when using MN instead of a conventional intramuscular injection, a similar change in hemagglutinin inhibitory antibody titer was observed with less than half the drug quantity.
3. The success of the MN systems was evident from the approval from many regulatory agencies for seasonal influenza vaccine delivered by MN. MN have been studied to address several skin conditions such as viral warts,dermatitis, and psoriasis.
4. MN have also shown their efficacy in treatment of skin cancer.
5. MN have not only been studied in intradermal delivery, but they also find application in ocular drug delivery.
6. MN have shown to effectively treat ocular diseases like glaucoma, maculardegeneration, Uveitis and retinal vascular occlusion . Currently, most microneedles that are available on the market are indicated for cosmetic purposes. Dermaroller helps to improve health of skin, while dissolving microneedles are used to treat acne.[3]

Merits and Demerits of MNs

Merits :

1. The administration of large molecules is possible.
2. Non-invasive and painless application.
3. Avoid the first-pass metabolism.
4. Enhanced drug efficacy results in dose reduction.
5. Ease of administration.
6. Controlled drug delivery.
7. Faster healing at the injection site achieved.
8. Good tolerability without irritation.
9. The cost of production and distribution reduced.
10. Targeted drug delivery achieved at a specific area of skin.

Demerits:

1. Dosage accuracy may be less.
2. Administration of only a small dose of a drug ispossible.
3. Possibility of skin irritation.
4. Upon removal of the patch, the needle may break and
5. remain intact in the skin.
6. External environment may affect delivery, for example,
7. hydration of the skin.
8. Compressed dermal tissues can block hollow MNs

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