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New Approach to Transdermal Drug Delivery System: Microneedles

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ABSTRACT:

The primary obstacle that must be overcome for success is the skin's remarkable waterproof properties. By using this pathway, medication molecules can enter the systemic circulation. The administration of pharmacological molecules involves a variety of formulation strategies, such as the use of lipophilic prodrugs or analogues, permeation enhancers, saturation systems, and entrapment in vesicular systems. Additionally, the release and penetration of the medicine via the skin is influenced by the adhesive combination, the physical delivery mechanism, and the release liner. With its dual administration system, the revolutionary microneedle combines the benefits of transdermal patches with hypodermic injections. A transdermal patch of (1-2) cm2 that is made up of thousands of hollow microneedles is put to the skin to make it more permeable. The upper layers of the epidermis are penetrated by networks of microneedles, ranging in length from 100 to 1000 m, which allow micrometry.drugs to enter the body. When a micro needle injection is performed, the patients won't feel any pain because the needles are too little to trigger nerve endings. An overview of microneedles for use in medicine administration applications is given in this review. Miniaturized needles are described and introduced. The scope is established and specific specifications for microneedles designed for transdermal medication administration are discussed. a fundamental microfabrication component. The processes for producing microneedles and using microneedles to administer drugs that have been described so far are examined and criticised.

Key words: Transdermal drug delivery, Microneedles, Skin anatomy, percutaneous permeation.

Introduction

When a medicine is administered transdermally, the dermis of the skin is traversed before systemic dispersion. Therefore, properly speaking, this does not only refer to the term "patch," but also to more modern methods like microneedling, as well as the classic subcutaneous injection method of employing a hypodermic needle and syringe.

A microneedle is, by definition, a needle with representative parts (such as diameter) in the micrometric length scale. This definition, however, is very broad because it covers the majority of common hypodermic needles used in clinical practise. Although there are numerous examples of "micro needles" in the literature that range in length from millimetres to inches, the definition of a micro needle is one in which the length of the needle is less than one millimetre.We can say that micro needles are significantly smaller than usual needles, especially with respect to length.

A novel delivery technique that uses miniature needle tables to pierce the epidermal layer has come to light in recent years. The stimulation produced by the insertion of micro needles in the skin is weak and it is viewed as painless since the needles are short and do not reach the nerve-rich regions of the sections of the skin [1],[2]. Microneedles and a patch-like structure can be used to create a system that effectively works. It possesses all the positive traits of a conventional transdermal patch, such as continuous release, use, and discretion. A Microneedle patch, which is painless in contrast to a normal patch, enables the administration of nearly macromolecular drugs (including insulin and vaccine). Such a patch would not only provide a covert and user-friendly method of drug delivery, but also possibly a secure method of medication administration requiring the least amount of involvement from medical personnel. Several businesses are presently working to develop microneedle technology for transdermal medication delivery [3].

SKIN ANATOMY-

The biggest organ in the human body, the skin serves a variety of purposes. It functions as a physical barrier environment, controls fluid loss and body temperature, sends sensory information to the neurological system, and processes immunological information for the immune system. The superficial epidermis, dermis, and hypodermis are the three primary layers of skin, as seen in figure 1. The epidermis is between 50 and 150 m2 in size. Keratinocytes, which are thick and continually renewing and moving cells, make up the majority of it. In addition to these cells, the epidermis is where the majority of langerhans cells that present the antigen are found. The stratum corneum, a 10–20 m2 thick layer of 15–30 stacked, dead, and cornified cells, is the epidermis' outermost layer. These so-called corneocytes have overlapping, flat, hexagonal cells with a diameter of roughly 30 m2. Through the use of unique protein rivets, which connect the cells to one another mechanically, layers of stacked lipids and interconnected mechanical scaffolding are created [4]. The primary element of the skin's water barrier is the stratum corneum. [5] The dermis makes up the majority of the skin, and it mostly consists of

collagen and elastin fibres. This fibrous network gives the skin traction. Skin has resistance and elasticity, and it supports the neurological and vascular networks.

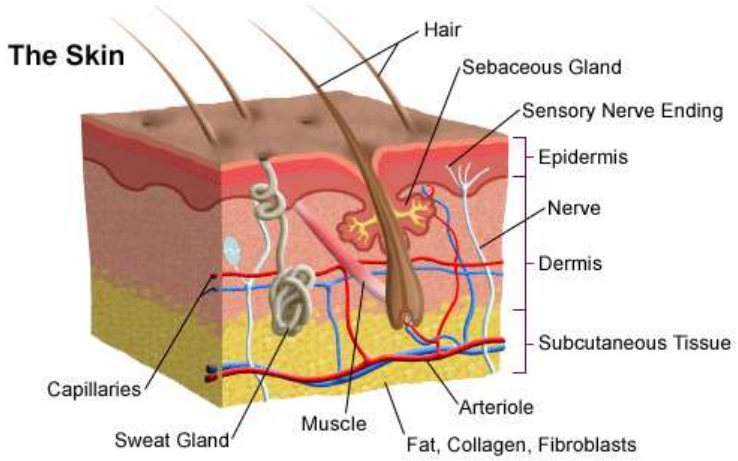

Figure 1: anatomy of skin

Collagen fibres in the upper papillary portion of the dermis are tiny and unevenly spaced. Collagen fibres that extend mostly parallel to the skin's surface and along specific axes, known as langer lines, are tightly packed and clustered in the deep reticular area. [5],[6] The hypodermis (subcutaneous), which is made up of loose, fatty connective tissue, serves as the dermis' support structure. On the surface of the body and between individuals, its thickness varies greatly [4].

Microneedles for drug delivery

The concept of a range of miniaturized needles for medicines. Delivery purposes basically date back to 1976 and a patent (filed in 1971) from gerstel and place to alza corp. [22] In this patent, a medication delivery device. Miniature projections (i.e. Micro needles) and medications the tank is claimed.

The needles are small enough to penetrate only the diaper cornea and can be solid or hollow. Delivery fromthe device can occur by diffusion or by convection by applying a force on the support of the tank. Figure 2 shows a drawing of the original. Document illustrating the device. Although not quite point, some predecessors of gerstel and place patents they exist, in particular for the delivery of vaccines.

Figure 2: the original concept of a microneedle-based transdermal patch from the patent of gerstel and place 1976 [22]

Microneedles [12], a drug reservoir [16], adhesives, and a rate-controlling membrane are all components of the device.

The administration of microneedle-based medications is most frequently carried out with needle tables in a specific location in order to achieve physiologically relevant delivery rates. Without utilising a specific insertion instrument (such as a high speed piston), a micro needle board with several needles must be inserted on the skin with the least amount of force possible. Additionally, the patch must penetrate independent of skin type, subject, or the level of humidity because its purpose is to deliver medications. All of these variables have a significant impact on the penetrating force needed. Then, given that experimental evidence by Davis et al. shows a high correlation between the interfacial area between the microneedle and skin and the penetration of microneedles into the skin, it is plausible to assume that the safety margins of 3 to 5 times may be required. Poor insertion is provided by a narrow interfacial area. Obligate. In other words, a pointed needle will penetrate tissue better than a blunt needle since the interface has a smaller surface area. It is debatable how many needles would be needed to attain therapeutic delivery rates if a network of hollow microneedles were used to give drugs

through convection. The insertion force of the needles won't need to be as strong because fewer needles can be used. essentially accurate. However, the delivery rate per needle must be higher while using fewer needles than when using numerous needles. Even though high performance can result in significant flow resistance in micrometric size needle holes 8, the fundamental drawback of fluid dynamics is that when a microneedle is put into the skin, the surrounding tissue will deform. The fabric will become extremely compressed as a result, and by partially retracting the needle after insertion, you can release the compacted tissue and simultaneously reduce fluid permeability in the tissues. From 9 to 10, the flow resistance reduces. In conclusion, delivery must be done across a large region utilising numerous needles in order to obtain therapeutic delivery rates with micro needles without leaks. In turn, a table with several microneedles needs a sharp needle with a low insertion force in order to allow manual insertion.

Microneedle Types

A division of the microneedles that are frequently utilised in literature. It depends on whether microneedles are produced inside or outside of an aircraft. The axis of the microneedles in the plane (figure 3a) are made parallel to the substrate's surface. The advantage of this setup is that the needle length may be precisely adjusted. A drawback is that two-dimensional matrices are challenging to create. On the other hand, microneedles out of plane (figure 3b) are simple to manufacture on tables and stand out from the substrate. Instead, length and high aspect ratios pose significant manufacturing difficulties for this kind of needles.Another useful point of distinction it is if the microneedles are solid or hollow. Hole needles with a needle hole, or light, allow a liquid transport through the microneedle.

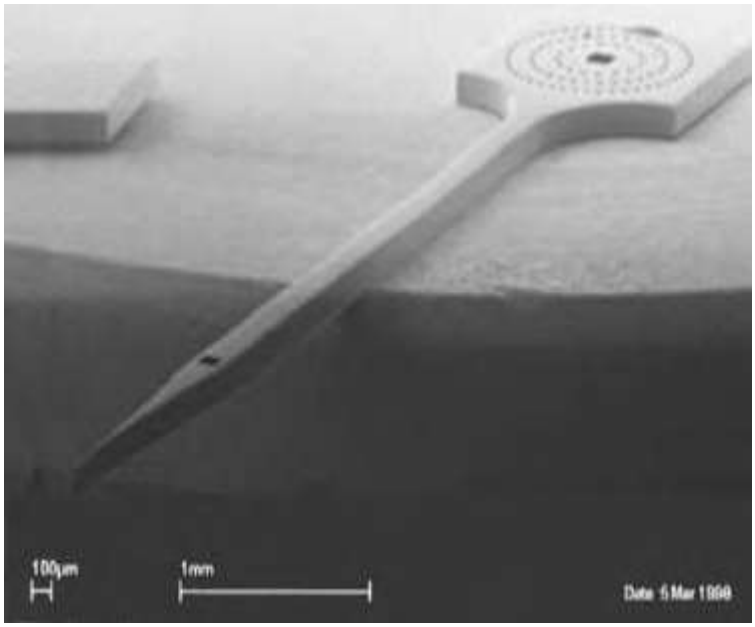

Figure 3: (a) 6 mm long, hollow, in-plane microneedle. From talbot and pisano [23].

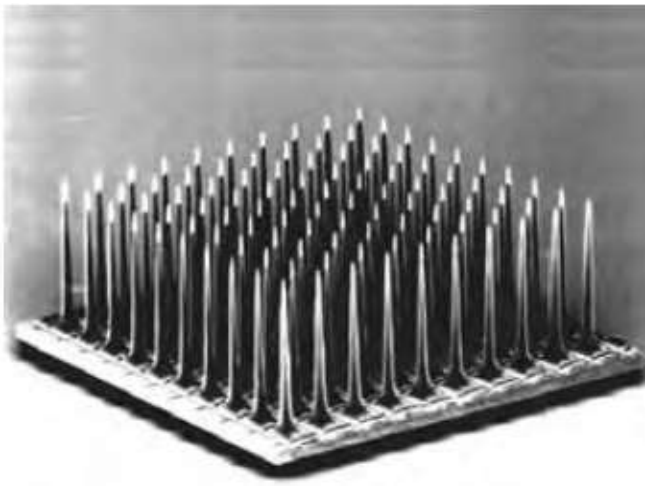

Figure 3:(b) individually addressable, 1.5 mm Long, solid, out-of-plane microneedles used as electrodes. From campbell et al. [24]

The following sections will give an overview of drug Delivery microneedles, related fabrication techniques and Design principles.

1. MEMS-

Microsystems technology (MST) or Microelectromechanical systems (MEMS) are terms used to describe devices having submillimeter characteristics. By incorporating mechanical structures into microdevices, MEMS expands production methods created in the microelectronics sector. As a result, MEMS devices can be made to control fluid flow, interact with the environment, or simply be employed as small-scale mechanical devices. commonly used MEMS devices include 4 Unicef's estimated cost for needles and syringes, which includes proper disposal, is based on extremely large volumes.

2. Solid microneedles

Although not transdermal, solid microneedle arrays were among the first microneedle networks for drug administration when they were initially proposed in 1993 by Dizon et al. [25] The net has silicon pyramidal tips. offers one of the most straightforward designs of microneedles at densities of thousands per square centimetre. Needless to say, they are etched in a potassium hydroxide (KOH) solution, and the geometry is established in monocrystalline silicon using an anisotropic engraving rate in conjunction with a controlled engraving cut mask. The needles have a sharp apex with a tip radius of less than 100 nm because of controlled engraving (with intersection of crystalline planes) [26].Before pushing the network into the cell Cultures, the matrix was utilised to transfect the cells enveloping the needles with foreign dna.

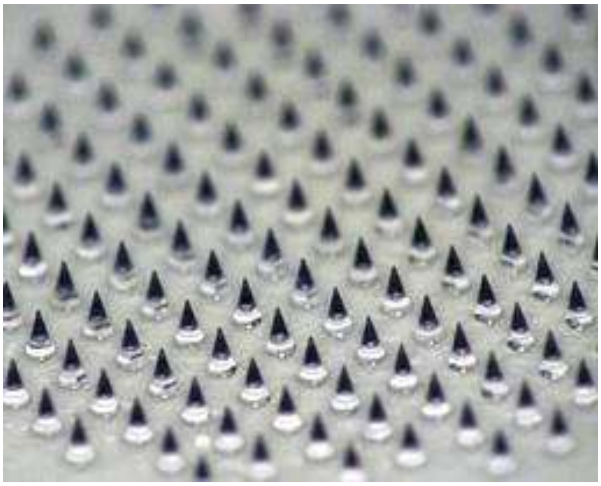

Fig 4.Solid microneedles

3. Hollow microneedle arrays

Hollow microneedles, as opposed to solid ones, allow for active medication injection into tissues. This has the apparent benefit of allowing you to deliver a certain amount of medication for a predetermined period of time, which opens up applications where rather big dosages are required to produce a therapeutic effect. Additionally, pressure delivery increases the potential for flow direction and control.

Outside the plane, the first hollow microneedles were displayed. Mcallister et al. In 1999[27]

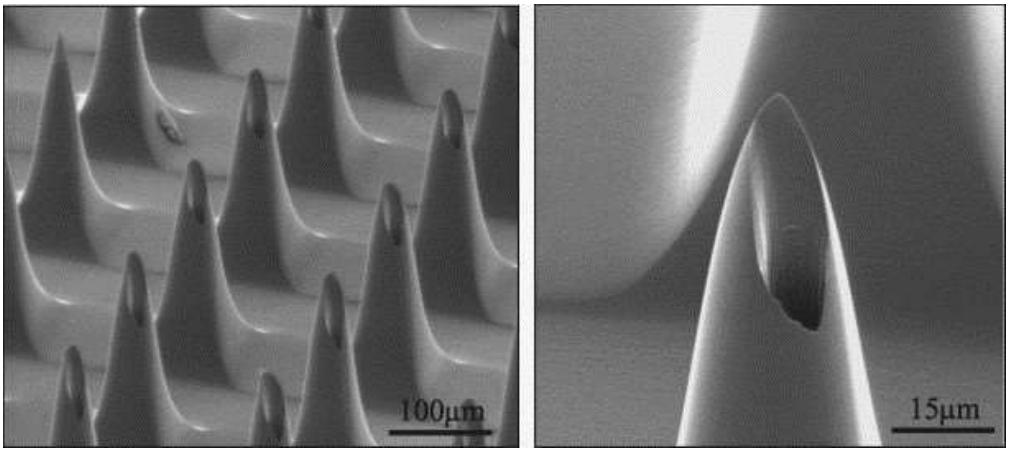

Fig 5: Hallow microneedles

APPLICATION:

Microneedles have been employed for a variety of purposes, including the delivery of genes to specific cells and neurostimulation. In most applications, the skin serves as the type of barrier that must be physically avoided in order to build a path to an object. Whether driven by the size of the objective or the benefit of drilling in a minimally invasive location, tiny needles are preferred to large-scale devices.

A network of silicon needles out of the plane with 100 needles that were each 1.5 millimetres long was one of the earliest microneedles to be written about in the literature (figure 2b)[12]. They are really frail. The purpose of the needles, which served as electric electrodes, was to stimulate the brain's visual cortex so that the user could see. In the plan, tiny needle probes were employed in connection with this application to record the activity and chemosimulation of brain tissue. [13] [14]

Solids, asymmetrical, To enable EEG (electroencephalogram) measurements for the control of anaesthesia, microneedles were employed to enter the stratum cornea [15][16]. To prevent the skin layer of electricity acting as an insulator, 200 m long needles were employed in this instance. Similary Impedance needles were used to measure skin lesions in order to detect skin cancer, although microneedle probes were also employed for diagnosis [17]. Scibase AB is the company actively promoting the technology, which is anticipated to hit the market in 2007 or 2008 [18]. Body sampling fluids comparable to the trunk of a mosquito are another application for microneedles, which Oka et al. produced in a hollow plane millimetre long, sawn blood needle microneedle. [19]

It has been shown that interstitial fluid can be sampled by capillary action using dies of 350 long, flat needles, excluding microneedles [20]. The microneedles have also been produced for microdialysis, which involves removing liquid through a hole in a needle outfitted with a semipermeable filter membrane. [21]

Despite having additional uses, drugs are the subject of the great majority of published microneedle articles. a variety of delivery methods.

VISION

View a medicine delivery system with tiny needles as having some of the same beneficial qualities as the transdermal traditional patch. Similar to the conventional patch, the system is portable and can be quickly fastened, for instance, to the upper arm. These are the benefits of such a system:

- Administration without pain.
- Easy to use: otc compatible
- Discretion
- Continuous release
- Controlled version
- Safer driving

Administration without pain: Only the skin's superficial layers, which have a low density of nerve receptors, are penetrated by microneedles that are a few hundred micrometres long. the insertion of tiny needles beneath the skin. considered to be painless.

Easy to use: A patient can essentially apply the intended system without any training since it functions similarly to a standard transdermal patch. However, using specialised insertion equipment and techniques to accomplish this is highly unfavourable. Therefore, the microneedles' insertion force must be minimal, and the insertion technique must be trustworthy and effective. It is logical to assume that the system, for some pharmaceuticals, can be offered over the counter if this is done (OTC).

Integrating a microneedle network with a flat, compact dosing system results in a patch that is a discrete device that can be utilised below clothing.

Continuous release: A discrete device can be used for longer durations, thus allowing delivery at therapeutic levels.

Controlled release: The mechanism used for drug release makes it possible to precisely measure the release pace. Integration can be used to accomplish this. Active dosing systems provide the opportunity to modify supply on time and in breadth using passive elements, such as flow restrictors or membranes, or active devices. Closed circuit systems can be used with even the most sophisticated active elements.

Safer handling: micro needles exceed a few hundred the micrometers of a surface present much less risk accidental punctures that hypodermic needles. As micro needles do not reach the blood, the risk of blood-borne pathogen transmission is also reduced.

Conclusion

Microneedles can theoretically be introduced into the skin by matrices containing hundreds of them without any assistance because they require extremely little insertion force. In vivo, it can penetrate human skin. in areas with clinical relevance. By exerting pressure or placing the seal needles in the skin tissue, it can be opened at the time of delivery and sealed tightly via thin membranes. The advantages of a transdermal patch and needles can be combined in a product that is created with a high process performance microneedle.

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