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MICRONEEDLES: REVOLUTIONIZING DRUG DELIVERY WITH EFFICIENCY AND PAINLESS PRECISION

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ABSTRACT

The transdermal delivery system offers significant advantages over traditional hypodermic needles, and microneedles have emerged as a promising innovation in this field. These micron-sized needles are minimally invasive, making them an attractive alternative for drug delivery and medical applications. This abstract explores recent advancements in microneedle technology, various fabrication methods, and the challenges hindering their widespread adoption. While microneedles hold great potential for improving drug administration, factors such as manufacturing complexities, material selection, and regulatory concerns must be addressed to fully integrate them into mainstream healthcare.

KEYWORDS: Transdermal, hypodermic needles, microneedles, non-invasive, fabrication.

1. INTRODUCTION

The human skin is regarded as the body's largest and most complicated organ that acts a barrier between the internal body and the external environment. Its principal defence mechanism protects the underlying organs from detrimental environmental factors, including dehydration, physical, chemical, and microbial stress, pathogens, harmful UV rays, toxins, and inflammatory agents. The skin is composed of the dermis, epidermis, and hypodermis. The epidermis consists of the stratum corneum (SC), lucidum layer, granular layer, stratum spinosum, and stratum basale. The stratum corneum is comprised of protein-rich dead keratinocytes, intercellular lipid matrix, and corneo desmosome, which acts as the main barrier that protects the skin from foreign substances. The skin's lipid-enriched structure can be crossed only by moderately lipophilic compounds to reach the underlying skin layers. The dermis is the thickest layer that lies beneath the epidermis layer, which is composed of collagen and elastin fibres that give the skin strength and flexibility. The upper layer is the dermis layer, which contains capillaries, lymph vessels, and sensory neurons (Fig.1). Below this layer is the reticular layer, which is rich in large blood vessels, deep pressure receptors, and sweat glands. The subcutaneous tissue (hypodermis) is the deepest layer of the skin and lies beneath the reticular layer. Composed of fat micro globules and loose connectives, it acts as an insulator and shock absorber, protecting the muscles and bones.[1,2]

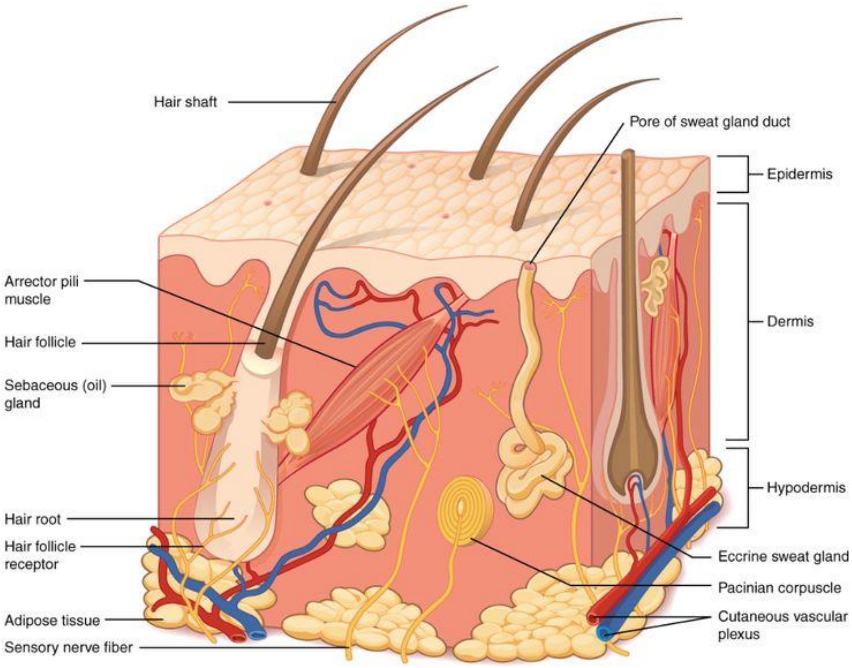

Fig. 1: Schematic representation showing different layers of skin.

The skin is an effective site for drug administration for therapeutics such as vaccines, drugs, biomolecules, and difficult-to-deliver small molecules, thus allowing for non-invasive, sustained, and controlled drug delivery systems. Transdermal drug delivery system, is a type of non-invasive and self-administered controlled drug delivery system, where the active ingredients are permeated across the skin membrane for systemic distribution. It is an adhesive drug containing device of a defined surface area to the lesion sites on the skin thereby maintaining the therapeutic concentration, reducing adverse reactions associated with systemic administration, minimizing pain and infection risk and thus ultimately increasing the patient compliance. Its main advantage over the oral administration routes is that, it avoids the gastrointestinal digestive enzyme metabolism and first pass effects. The TDDS delivers the drugs through the skin in a predetermined and controlled rate. The transdermal delivery patches are accessible, controllable and could be self-administered. Although using the skin is an attractive site for drug administration, the stratum corneum is the big barrier for transport of macromolecular drugs transdermally and thus it limits the bioavailability of therapeutics. Among the available TDDS methods, the microneedle delivery system has become a new generation of topical delivery system, which is a non-invasive delivery of medications through the skin surface, and has attracted interest of various research works in academic institutions and industrial companies.

Microneedles (MNs) are micron-sized needles that penetrate the stratum corneum for transdermal drug delivery while avoiding deeper pain receptors. First introduced by Gerstel and Place (1971) and later validated by Henry et al., MNs enhance drug permeability using MEMS technology. Their length ranges from 50–2000 μm, categorized into short, medium, and long MNs based on penetration depth. MNs offer pain-free, self-administrable drug delivery with reduced dosage requirements. They are classified as solid, coated, hollow, dissolving, or hydrogel-forming, and are made from silicon, metal, polymer, ceramic, or glass. Fabrication techniques include micro-molding, lithography, laser cutting, and 3D printing. MNs provide a minimally invasive alternative to hypodermic needles, improving patient compliance. This review explores their classification, materials, fabrication techniques, applications, and challenges.

2. TYPES OF MICRONEEDLES[3,4]

There are various types of microneedles which includes solid type, hollow type, coated type and dissolving type. Each type has its own characteristics, advantages, disadvantages and applications.

2.1 Solid Microneedle

Solid microneedles are fabricated out of different materials like metals such as stainless steel and titanium, silicon and polymers. They use poke and patch system to deliver the medicament. The medicament is delivered in two steps. The solid microneedles are first inserted in to the skin, its pointed tip penetrates into the skin creating transient microchannels. Before being removed it is replaced with drug loaded transdermal formulations (such as gel, cream, lotion etc.) or a transdermal patch, from where the drug diffuses passively into the skin layers. Solid microneedles are easy to manufacture. Also, they have superior mechanical properties and sharper tips when compared to hollow microneedles (Fig.2). It can be used as a skin pretreatment**.**

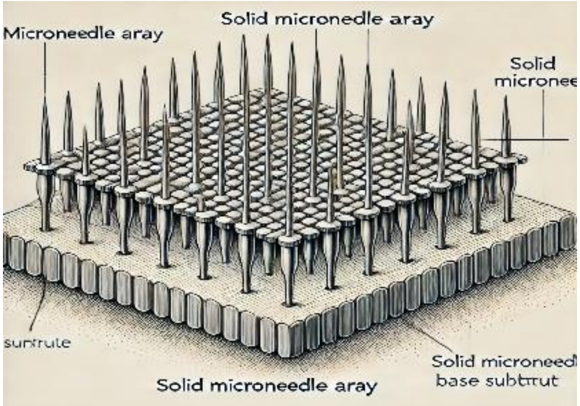

Fig. 2: Solid microneedle.

2.2 Hollow Microneedle

Hollow microneedle consists of an empty core or chamber and a bore on needle tip. The empty cavity is filled with drug fluid. They are miniature form of hypodermic needle in micron size. It follows the mechanism of poke and flow system to deliver the medicament, where the hollow microneedles when inserted into the skin forms channels of micron size and through these microchannels the drug solution diffuses passively into the skin layers. Large amount of drug solution can be administered as compared to solid microneedle. It is fabricated from various material such as silicon, ceramic, metal and glass (Fig.3). Intensive care is required in designing the needle and also during its insertion as the needle is hollow.

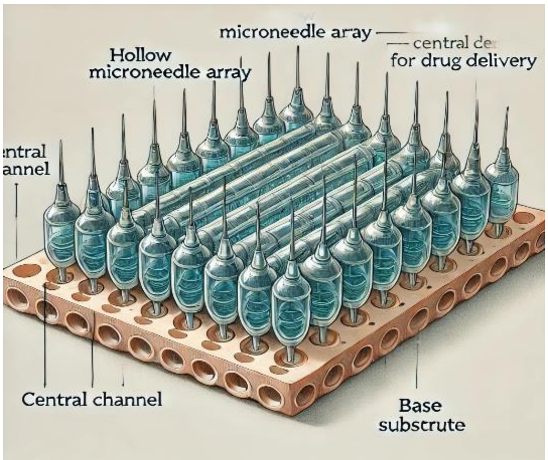

Fig. 3: Hollow Microneedle.

2.3 Coated Microneedle

Coated microneedle is a solid type of microneedle which is coated with a drug solution on the surface of the needle. It is more efficient, convenient and controlled as compared to solid MN. It uses coat and poke approach to deliver the medicament. It is a single step process where once the needle is inserted into the skin, the coated drug layer disintegrates and dissolves rapidly to release the medicament into the targeted skin layers. It is fabricated out of metal and silicon. Coated microneedle has been used to deliver protein and DNA in a minimally invasive manner (Fig.4). It carries small amount of drug as the drug carrying capability depends on the thickness of the coating layer and size of the needle.

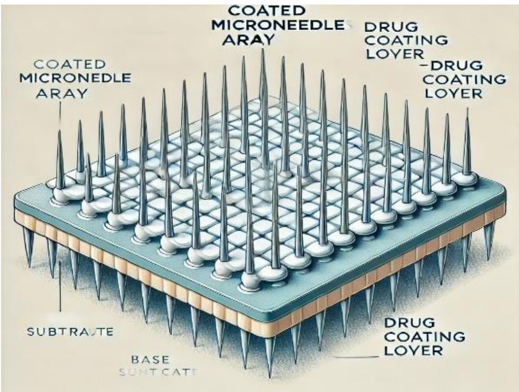

Fig. 4: Coated Microneedle.

2.4 Dissolving Microneedle

Dissolving microneedle facilitates rapid release of the medicament. It is made up of water -soluble polymers and the medicament is present inside the polymeric matrix. It allows ease of drug administration with one step application. Upon insertion into the skin, the MN dissolves to release the drug load which diffuses rapidly into the skin, leaving no needle residue behind (Fig.5). Technical expertise is required to manufacture Dissolving MN. Also dissolving of the microneedle may be time consuming.

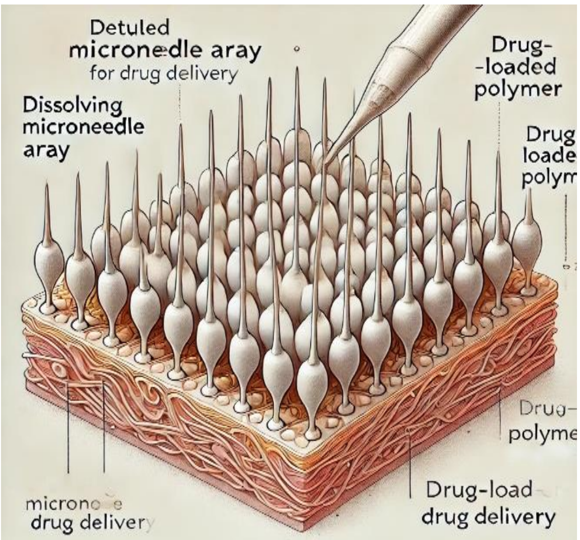

Fig. 5: Dissolving Microneedle.

3. MATERIALS FOR MICRONEEDLES[5,6]

Different types of material have been used for the fabrication of various microneedles. These materials include silicon, metal, ceramic and polymers. They have their own properties, advantages and disadvantages.

3.1 Silicon

The first microneedle was made up of silicon in 1990's. Silicon has innate flexibility so it allows easy fabrication of microneedles in terms of desirable shapes and sizes. It is used to fabricate solid, hollow and coated MN's. The use of silicon for fabrication purpose is expensive and also a time-consuming process. It may also cause fractures in the skin.

3.2 Metal

Stainless steel and Titanium are mainly used for fabrication. They have good mechanical strength and compatibility. Metals are stronger and harder to break as compared to silicon. They are used to fabricate solid and hollow microneedles. It may cause allergic reaction.

3.3 Ceramic

There are various ceramic materials such as alumina, calcium sulfate dihydrate, calcium phosphate dihydrate etc. used for fabrication. It has superior chemical properties and compression resistance. They are used to fabricate solid and hollow microneedle. Alumina has low tensile strength than other materials.

3.4 Polymers

Polymers such as PMMA (polymethyl methacrylate), polylactic acid, polycarbonate, polystyrene, SU-8 photoresist etc. are used in the production of various microneedles. Polymers have excellent biocompatibility, low toxicity and less expensive. They have less strength when compared to silicon and metal.

4. FABRICATION OF MICRONEEDLES[7]

Microneedles (MNs) are tiny (50–900 µm) devices designed for painless transdermal drug delivery. Their fabrication depends on the type—solid, coated, dissolving, hollow, or hydrogel—and utilizes techniques like micro-molding, photolithography, laser cutting, 3D printing, and injection molding. Made from materials like silicon, metals, biodegradable polymers, and hydrogels, MNs enable controlled drug release. Advances in MN technology are enhancing minimally invasive delivery of vaccines, insulin, and biologics.

4.1 Solid Microneedles

Solid microneedles (MNs) represent one of the pioneering forms of microneedle technology utilized for transdermal drug delivery. Constructed from materials such as metals, silicon or polymers, these devices operate by forming microchannels within the skin, thereby enhancing drug absorption via Passive diffusion or Iontophoresis.

4.1.1 Fabrication with Mold

a. Soft Lithography

Soft lithography is a microfabrication method for polymer and biodegradable microneedles using an elastomeric PDMS mold. A master mold, created via photolithography or laser etching, is coated with PDMS, cured, and removed as a negative template. A polymer or drug-polymer mixture fills the mold, aided by vacuum or centrifugation, then solidifies through drying or cross-linking. Extracted microneedles may undergo coating or sterilization. Cost-effective and scalable, this method enables precise, biodegradable, and hydrogel microneedles for diverse applications.

b. Micro Injection Molding

Micro-injection molding is an established method for the large-scale production of polymeric microneedles. This technique facilitates the creation of accurate, consistent, and scalable microneedle designs that exhibit excellent mechanical properties. A highly accurate master mold, typically constructed from silicon or metal, is created through techniques such as photolithography, laser etching, or micromachining. A thermoplastic polymer, such as PLGA, PLA, or PCL, is heated to its melting point. The liquefied polymer is injected into the microneedle mold under significant pressure. Once injected, the material is cooled and solidified to maintain the microneedle configuration. The resulting microneedles are removed from the mold. Subsequent surface treatments, such as drug coating or sterilization, may be performed. This technique is well-suited for high-volume production which Ensures uniformity and consistent quality in microneedle fabrication. Works with a range of biodegradable and biocompatible polymers and offers a lower production cost per unit compared to alternative methods.

c. Hot Embossing

Hot embossing is a microfabrication method employed to create polymeric microneedles with exceptional accuracy. This process entails the application of heat and pressure to a polymer material, allowing it to conform to the microneedle designs of a mold. A mold made from silicon, metal, or ceramic is crafted, featuring microneedle patterns, through techniques such as photolithography or etching. A thermoplastic polymer (such as PMMA, COC, or PLA) is positioned over the master mold. Heat and pressure are then applied to soften the polymer, enabling it to take on the microneedle configuration. The polymer is allowed to cool, solidifying the microneedle forms. The microneedles are then gently extracted from the mold. Subsequent processes may include surface treatments, coatings, or the incorporation of drugs. This Achieves highly defined microneedle structures Ideal for mass production. Works with a range of thermoplastic polymers. More economical than lithography-based techniques.

4.1.2 Fabrication without Mold

i) Lithography

a. Photolithography

Photolithography is a precise microfabrication method for silicon, SU-8 polymer, and metal microneedles. A photosensitive substrate is coated with a photoresist, exposed to UV light through a photomask, and developed to define microneedle structures. Etching (wet or dry) shapes the microneedles, followed by photoresist removal and optional surface modifications for drug loading. This technique enables uniform, high-precision microneedles, ideal for large-scale production and coated applications.

b. X-ray Lithography

X-ray lithography is a high-precision technique for creating ultra-fine microneedles, often as part of the LIGA process. A substrate coated with X-ray-sensitive photoresist is exposed to high-energy X-rays through a patterned mask. Developed structures undergo etching and can serve as molds for large-scale production via electroforming. This method produces sharp microneedles from silicon, metals, and polymers, suitable for solid and hollow designs.

ii. Machining Integrated with Chemical Etching

Machining and chemical etching is an advanced technique for fabricating high-precision microneedles from silicon, metals (e.g., stainless steel, titanium), and polymers. The process begins with mechanical shaping using laser cutting or CNC milling to establish the basic microneedle structure. This is followed by chemical etching for refinement:

- **Wet etching** uses acidic or alkaline solutions (e.g., KOH for silicon, ferric chloride for metals) to selectively dissolve material.
- **Dry etching** (plasma or reactive ion etching, RIE) employs ionized gases for precise material removal and enhanced control.

Post-processing steps, such as tip sharpening, surface coating, or sterilization, further optimize the microneedles. This method ensures sharp, smooth structures, supports large-scale manufacturing, and is suitable for both solid and hollow microneedles.

iii. Laser Engraving

Laser engraving is a high-precision, non-contact technique for fabricating microneedles from metals, silicon, and polymers. The process begins with selecting a suitable substrate based on mechanical properties and application requirements. A detailed microneedle design is created using CAD software, specifying dimensions, shape, and spacing. A concentrated laser beam is then used to engrave the microneedle pattern onto the substrate. The engraving depth, speed, and intensity are precisely controlled to achieve sharp, well-defined structures. This method effectively carves solid and hollow microneedles with minimal material stress, preserving structural integrity. Post-processing steps may include tip sharpening, polishing, surface coating for drug delivery, and sterilization to enhance biocompatibility. Laser engraving allows for intricate, customizable microneedle designs tailored for applications such as vaccine delivery and transdermal drug administration.

iv. Micro Milling

Micro milling is a high-precision machining technique used to fabricate microneedles from robust materials like metals, silicon, and ceramics. It employs small rotating tools to meticulously shape microneedles with fine tolerances, making it ideal for both solid and hollow designs used in transdermal drug delivery and medical applications. The process begins with selecting a suitable substrate, such as stainless steel, titanium, or ceramics, chosen for their strength and biocompatibility. A detailed microneedle design is created using CAD software, defining parameters like height, shape, and spacing. The substrate is then securely mounted onto a CNC milling machine, where a fine-toothed rotating cutter gradually removes material to shape the microneedles according to the CAD design. This method ensures highly controlled dimensions, producing microneedles with sharp, uniform tips. After milling, post-processing steps such as polishing, surface smoothing, coating for drug delivery, and sterilization enhance functionality and safety. Micro milling enables precise customization of microneedle geometry, accommodates various materials, and is suitable for both small-scale prototyping and large-scale manufacturing.

v. 3D Printing

Additive manufacturing, or 3D printing, is a cutting-edge method for creating microneedles, particularly for specialized uses in medication delivery, biosensing, and diagnostics. It offers a high degree of versatility and personalization by enabling the exact, layer-by-layer fabrication of microneedles from a variety of materials. This method is very helpful for quickly creating intricate, multipurpose patterns and microneedles. Several 3D printing techniques can be employed such as

a. Fused Deposition Modeling (FDM)

Fused Deposition Modeling (FDM) is a cost-effective and widely accessible 3D printing technique used for fabricating microneedles, particularly from biocompatible polymers like PLA, PCL, PLGA, and PEEK. The process starts with designing the microneedle array using CAD software, specifying parameters such as length, shape, and spacing. This design is then converted into a G-code file, which directs the 3D printer. During printing, the thermoplastic filament is heated to its extrusion temperature and deposited layer by layer onto the build platform, gradually forming the microneedles. Print settings such as nozzle temperature, layer height, and speed are optimized to achieve high-resolution structures with sharp tips. Post-processing steps include cleaning, support removal, surface smoothing, and potential drug loading or coating to enhance functionality. The microneedles may also undergo sterilization through autoclaving, gamma radiation, or ethylene oxide exposure to ensure medical safety. FDM offers affordability, ease of use, and compatibility with biodegradable materials, making it suitable for both prototyping and small-scale production. Its ability to create intricate microneedle designs enables customized solutions for transdermal drug delivery and vaccine administration.

b. Stereolithography

Stereolithography (SLA) is a high-precision 3D printing technique that uses a UV laser to cure liquid photopolymer resin, forming microneedles layer by layer with exceptional accuracy. This method enables the creation of sharp, smooth, and intricate microneedle structures, making it ideal for drug delivery, vaccine administration, and diagnostics. The process begins with CAD modeling and material selection, followed by laser-based resin curing to construct the microneedles. After printing, post-processing steps such as UV curing, surface smoothing, drug loading, and sterilization enhance functionality. SLA offers superior resolution, biocompatibility, and design flexibility but is less suitable for large-scale production due to cost and time constraints.

c. Inkjet Printing

Inkjet printing is a precise, non-contact additive manufacturing technique that deposits tiny droplets of material onto a substrate, making it ideal for fabricating microneedles, particularly hollow ones for drug delivery, biosensing, or vaccines. Using CAD-based designs, biocompatible inks such as polymers, hydrogels, or metallic inks are precisely printed layer by layer, with UV or heat curing to solidify structures. This method allows for intricate designs, controlled deposition, and easy customization. Post-processing steps like curing, surface finishing, drug loading, and sterilization ensure functionality and safety. While primarily used for prototyping, inkjet printing can be optimized for scalable production at a lower cost than micromachining techniques.

d. Two-Photon Polymerization (2PP)

Two-Photon Polymerization (2PP) is an advanced laser-driven 3D printing technique used to fabricate high-resolution microneedles with intricate geometries. It relies on the simultaneous absorption of two photons to initiate polymerization in photosensitive resins, enabling sub-micrometer precision. CAD-designed microneedles, including hollow or drug-loaded variants, are printed layer by layer using a femtosecond pulsed laser. Post-processing includes resin removal, UV or heat curing, drug loading, and sterilization. 2PP offers exceptional detail, supports complex structures, minimizes material waste, and allows for biocompatible and biodegradable resin use, making it ideal for drug delivery, biosensing, and medical diagnostics.

4.2 Hollow Microneedles

Hollow microneedles represent a specialized category of microneedles characterized by an internal channel that facilitates the direct delivery of liquids, including medications, vaccines, or biological substances, through the skin or into underlying tissues. In contrast to solid microneedles, hollow microneedles feature a cavity that allows for the delivery or extraction of substances. The hollow design permits the direct injection of drugs or fluids into the dermal or subdermal layers, effectively bypassing the skin's outer barrier. These microneedles are engineered to be minimally invasive and virtually painless, making them ideal for both medical applications and cosmetic treatments.

4.2.1 Fabrication with Mold

i. Micro-Molding (Replica Molding)

Micro-molding is a prevalent technique for manufacturing hollow microneedles. This method utilizes a pre-existing mold to replicate the microneedle design, forming both the outer contour and the internal hollow structure. The initial phase involves creating a master mold through methods such as micro-machining, photolithography, or laser etching. This master mold features cavities that outline the external form of the microneedles and their hollow interiors. The mold can be constructed from materials such as silicon, polydimethylsiloxane (PDMS), or various metals. A polymer substance (for instance, polyurethane (PU), polycaprolactone (PCL), or polymethyl methacrylate (PMMA)) is either poured or injected into the mold. After the mold is filled, the material is allowed to cure. The creation of the hollow microneedle involves precise control over the material flow to establish an internal cavity. This can be accomplished by incorporating a core template within the mold (such as a metal wire) that can be extracted once the material has hardened. Once the polymer has completely cured, the microneedles are extracted from the mold, and the core template is removed to expose the hollow channels.

Micro-molding enables the production of intricately detailed microneedles with sharp tips and precise hollow channels. This method is well-suited for the mass production of microneedles. Once the mold is established, it can be utilized multiple times, making it economical for high-volume manufacturing.

ii. Injection Molding

Injection molding is an exceptionally effective method for producing hollow microneedles, particularly when there is a demand for large-scale manufacturing. This technique entails the injection of molten polymer into a mold under pressure to shape the microneedles. The initial phase involves designing a mold for the microneedles, which is usually constructed from materials such as steel, aluminum, or silicon. The mold must feature cavities that match the desired shapes of the microneedles and include internal hollow channels. A heated polymer (such as PCL, PLGA, or PMMA) is injected into the mold at high pressure. This process allows the polymer to occupy the mold cavities, thereby forming both the external structure and the internal hollow channel of the microneedles. Following the injection, the mold undergoes a cooling process to allow the polymer to solidify. The microneedles are subsequently ejected from the mold, and the cycle is repeated. Injection molding is well-suited for the mass production of microneedles, enabling the generation of substantial quantities in a brief timeframe. This technique is capable of producing microneedles with precise geometries and sharp tips. Molds can be utilized multiple times, which helps to lower production expenses.

iii. Casting with Core – Shell Technique

The core-shell technique represents an effective approach for the fabrication of hollow microneedles. This method employs a mold and involves a two-step process to produce microneedles featuring an external shell and an internal hollow core. The initial step involves the development of a master mold, which can be achieved through methods such as micromachining or photolithography. The hollow core is established by placing a core material, such as a rod or wire, into the mold. This core serves to define the hollow channel within the microneedle. Subsequently, a second material, often a biodegradable polymer, is cast around the core. This shell material shapes the exterior of the microneedle while the core remains intact. Once the polymer has cured, the core material is extracted, resulting in a hollow channel within the microneedle. This technique allows for the creation of microneedles using various materials for both the outer shell and the core, enabling customization of properties such as biodegradability, mechanical strength, and drug delivery capabilities. The method provides precise control over the internal diameter and geometry of the hollow microneedles.

iv. Laser Drilling

In this technique, laser drilling is employed to transform solid microneedles into hollow microneedles. The process begins with the production of a solid microneedle array, which can be achieved through techniques such as micro-molding or CNC machining. A laser, such as a femtosecond laser, is utilized to create tiny holes along the length of each microneedle, resulting in hollow channels. This drilling method is highly accurate, enabling the formation of small, precise openings. After drilling, the microneedles undergo cleaning and surface treatment to enhance their smoothness and overall functionality. Laser drilling facilitates the creation of extremely small and precise holes in microneedles. This approach negates the necessity for intricate molds that would typically be needed to fabricate hollow microneedles from the ground up.

4.2.2 Fabrication without Mold

Unlike mold-based techniques, mold-free fabrication of hollow microneedles relies on direct micromachining, additive manufacturing (3D printing), or laser-based techniques to create precise microneedles with an internal hollow channel. These methods provide greater design flexibility, allowing for customized geometries, improved mechanical properties, and rapid prototyping.

i. Laser Micromachining

Laser-based techniques utilize accurate ablation or drilling to form hollow channels within microneedles. This approach is particularly effective for materials such as silicon, metals, and polymers. Initially, a solid microneedle is created through methods such as etching, deposition, or machining. A high-precision femtosecond laser or excimer laser is employed to create a hollow channel extending from the base to the tip. Techniques for surface finishing, including polishing, cleaning, and coating, are implemented to enhance functionality and biocompatibility. Exceptional precision and control over the diameter of the holes is achieved Elimination of the need for intricate molds or templates. Compatibility with a diverse array of materials, including metals, silicon, and ceramics.

ii. Micro Milling

Micro milling employs advanced CNC (Computer Numerical Control) milling machines to precisely shape microneedles from solid material blocks. A solid block of metal, polymer, or ceramic is selected as the foundational material. Then a high-speed milling machine (CNC milling) shapes the microneedles while concurrently forming a hollow channel. The finished structure undergoes polishing and treatment to ensure biocompatibility. Offers high mechanical strength, making it particularly suitable for microneedles made from stainless steel or titanium. Eliminates the need for molds, providing greater design flexibility.

iii. Chemical Etching

Chemical etching is a subtractive manufacturing method that utilizes a chemical solution to selectively eliminate material, resulting in the creation of microneedles and hollow channels. Typical materials used include silicon, stainless steel, and titanium. A protective layer is applied to the regions that need to remain unaffected. The exposed areas are treated with a chemical etchant, which dissolves the material to form the hollow channel. The resulting structure undergoes cleaning and refinement. Offers high precision for microneedles made from silicon. Compatible with biocompatible metals such as titanium.

iv. Electrochemical Etching

Electrochemical etching is a technique that utilizes an electrolyte solution along with an electric current to selectively dissolve metal, resulting in the creation of microneedles with hollow structures. Materials such as stainless steel or titanium are chosen. Then the metal is immersed in an electrolyte solution while an electric current is applied to facilitate material removal. Careful control of the etching parameters guarantees the development of uniform hollow microneedles. Subsequent steps include polishing and sterilization. They are Well-suited for producing robust metallic microneedles. Yields smooth and precisely defined hollow channels.

5. ADVANTAGES OF MICRONEEDLES[8-10]

Microneedles (MNs) represent a cutting-edge approach to drug delivery that significantly improves transdermal administration by addressing the shortcomings of traditional patches and hypodermic injections. They enable the effective transport of medications through the skin's stratum corneum with minimal invasiveness. The following outlines the primary benefits of microneedles in transdermal drug delivery:

- **Improved Skin Permeability**

The stratum corneum serves as a significant barrier to drug absorption. Microneedles create tiny channels in the skin, facilitating enhanced drug diffusion through the epidermis and dermis. This process increases the bioavailability of drugs that typically exhibit low permeability.

- **Painless and Minimally Invasive**

Microneedles are engineered to penetrate only the outer skin layers, avoiding pain receptors and blood vessels. This design reduces discomfort compared to traditional injections, thereby improving patient compliance, particularly among those with a fear of needles.

- **Avoidance of First-Pass Metabolism**

By delivering drugs directly into the systemic circulation via the skin, microneedles circumvent first-pass hepatic metabolism. This is particularly advantageous for medications with low oral bioavailability due to significant liver processing.

- **Enhanced Patient Compliance**

Conventional injections can be uncomfortable and often necessitate professional administration. Microneedles enable self-administration with minimal training, thereby increasing patient convenience and adherence to treatment regimens.

- **Potential for Controlled and Sustained Release**

Microneedles can be engineered for controlled drug release using biodegradable or hydrogel-based formulations. This capability reduces the frequency of dosing and ensures a consistent therapeutic effect.

- **Versatility in Drug Delivery**

Microneedles are effective for administering both hydrophilic and hydrophobic drugs, as well as large biomolecules such as peptides, proteins, vaccines, and genetic materials like DNA and RNA.

- **Decreased Infection and Contamination Risks**

In contrast to conventional injections, microneedles do not penetrate deeply into the skin, thereby minimizing the likelihood of infections. Their administration does not necessitate sterile conditions, making them ideal for mass vaccination campaigns and self-administration.

- **Minimized Systemic Side Effects**

By delivering medications locally or in a controlled fashion, microneedles help to reduce the systemic side effects commonly associated with oral and injectable routes. They are particularly beneficial for targeted drug delivery in cases such as dermatological conditions or localized pain relief.

- **Versatility with Various Drug Formulations**

Microneedles can accommodate a range of formulations, including:

I. Coated Microneedles: Solid microneedles coated with drugs for quick release.

II. Dissolving Microneedles: Biodegradable polymer microneedles that dissolve upon contact with skin.

III. Hydrogel Microneedles: Microneedles that swell in response to interstitial fluids, allowing for sustained drug release.

- **Potential for Vaccine Administration**

Microneedles have been investigated for transdermal vaccination, including for diseases like influenza, COVID-19, and hepatitis B. They enhance immune responses by targeting antigen-presenting cells located in the skin and can eliminate the need for cold-chain storage, thereby improving vaccine accessibility in remote regions.

- **Economical and Scalable Manufacturing**

Microneedle patches can be produced at a lower cost compared to traditional injections, utilizing biocompatible materials such as polymers, silicon, or metals. This makes them a cost-effective solution for drug and vaccine delivery, particularly in resource-constrained environments.

- **Single-Use Design to Mitigate Cross-Contamination**

Many microneedle patches are designed for single use and are biodegradable, which helps prevent needle reuse and reduces the risk of contamination and disease transmission.

6. CHALLENGES OF MICRONEEDLES

Microneedles (MNs) present notable benefits for transdermal drug delivery; however, their production involves various challenges. Key issues include material selection, structural integrity, scalability of manufacturing, and drug-loading efficiency. The following outlines the primary limitations and challenges:

- **nMaterial Selection and Biocompatibility**

Selecting appropriate materials (such as polymers, metals, silicon, or ceramics) is crucial to ensure biocompatibility and non-toxicity. Certain materials may lead to skin irritation, immune responses, or inadequate mechanical strength.

- **Mechanical Strength and Structural Integrity**

Brittle materials (like silicon) risk breaking during insertion, raising safety concerns wheras soft materials (such as biodegradable polymers) may not possess the necessary mechanical strength for effective skin penetration. The design must achieve a balance between **sharpness, durability, and flexibility** to prevent breakage and ensure complete penetration.

- **Scalability and High Production Costs**

Traditional microneedle fabrication methods, including lithography, micromolding, and laser cutting, are often intricate and costly. The challenge lies in scaling up for mass production while ensuring consistent quality. There is a need for cost-effective and reproducible fabrication techniques to enhance commercial viability.

- **Drug Loading and Release Control**

The small size of microneedles limits their drug loading capacity. Achieving controlled and sustained drug release is particularly challenging for hydrophilic drugs. Some drug formulations may experience degradation during the fabrication process or while in storage.

- **Skin Penetration and Variability**

Successful penetration is influenced by microneedle geometry, insertion force, and skin characteristics (such as thickness and hydration). Variability in skin types and individual patient differences can impact drug absorption rates.

- **Sterility and Stability**

Ensuring the sterility of microneedles is crucial to prevent infections, which complicates the production process. Additionally, stability concerns may arise from moisture uptake, polymer breakdown, or a decline in drug efficacy over time.

- **Regulatory and Safety Concerns**

Microneedles are classified as medical devices and drug delivery systems, necessitating regulatory clearance. Comprehensive long-term studies on safety and effectiveness are essential prior to their widespread clinical application. There is also a risk of skin irritation, allergic responses, or inadequate drug absorption.

While microneedles hold significant promise, their development is hindered by challenges related to material selection, scalability, mechanical integrity, drug loading, and regulatory compliance. Addressing these issues will require innovations in manufacturing processes, cost-efficient production strategies, and thorough clinical evaluations to guarantee safety and effectiveness.

7. CONCLUSION

The development of microneedle products is likely to take place in the near future. In this article, we have discussed the different types of microneedles, the fabrication methods used for it, and the challenges they face. Unlike hypodermic needles, microneedles are non-invasive in nature and has increased patient compliance. Further improvement of current microneedles devices will increase the transdermal delivery system. Considering the challenges that microneedles face, further investigations on the fabrication methods should be addressed properly. Hence, techniques associated with microneedle delivery should be investigated further.

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