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Design and Development of Microneedles Arrays for Minimally Invasive Therapeutic Delivery

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Abstract: Microneedles are a game-changer when it comes to drug delivery. They can bypass the liver's first-pass metabolism, which means the drug can be more effective and easier to administer. The way the skin is structured, with its different layers like the epidermis, dermis, and hypodermis, plays a big role in how well microneedles work. To make sure the process is painless, these tiny needles are designed to pierce just the outer layer of skin, called the stratum corneum, without triggering any pain receptors. This is important because it allows for controlled drug release, which can be a major advantage in treating various conditions. By simplifying the administration process, microneedles can make a big difference in people's lives.However, there are some downsides to consider - for instance, it can sometimes cause a bit of skin irritation, and making it can be tricky. Also, it has limited space for carrying drugs. Micro needles come in different types, like solid, hollow, dissolvable, swellable, and coated, each with its own unique features and uses. For instance, dissolvable micro needles are designed to safely break down after they're applied, which is really useful. On the other hand, swellable micro needles are great for releasing drugs over a longer period of time. Solid micro needles work by creating tiny channels in the skin, while hollow micro needles are used to deliver liquid medications directly into the body. Then there are coated micro needles, which have drugs attached to their surface, allowing for a more targeted delivery. Each type of micro needle has its own advantages, and they can be used in different ways to achieve specific goals, like improving drug delivery or reducing side effects. Metals, silicon, ceramics, and polymers are among the many materials used in fabrication; polymers are favored because of their mechanical strength, biocompatibility, and biodegradability. In order to promote drug diffusion into systemic circulation, the mechanism of action entails a brief disruption of the skin barrier. Dissolvable micro needle patches can be thrown away as non-sharp waste; proper patch disposal is essential for safety. Applications for micro needles are numerous and include the treatment of migraines, diabetes, cancer, hepatitis B vaccination, ocular drug delivery, and cosmetic procedures. Overall, microneedle systems represent a flexible transdermal platform with increasing relevance for future drug delivery applications.

Keywords: *Microneedle Patches, Drug Delivery, Dissolvable Microneedles, Patch Disposal, Ocular Delivery.*

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I. INTRODUCTION

Injectable systems remain the dominant route for administering biotherapeutics and vaccines; however, their routine use is associated with several clinical and practical limitations. It is possible to quickly, affordably, and directly inject almost any kind of chemical into the body. However, because hypodermic needles are challenging for individuals to use independently, patients who have received specialized training on safe needle disposal, correct injection technique, and other topics typically use them at home or in clinics [1]. Patient adherence is often compromised due to injection-related pain and psychological fear associated with needles [2-3]. Improper needle reuse continues to contribute significantly to the transmission of blood-borne infections, particularly in low-resource healthcare settings [4-5]. Although oral administration is generally preferred for its convenience, many therapeutic agents suffer from poor gastrointestinal stability and extensive hepatic metabolism. [6]. Other methods of administration have also been studied [7-8], but none work as well as direct injection with a needle.

Instead of avoiding needles, we and others have suggested making the needle smaller, down to the micron level, so that it can still deliver drugs effectively while making patients safer and more likely to follow instructions. A microneedle should be big enough to

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deliver almost any drug or small particulate formulation, but small enough to not hurt, scare, or require expert training to use. In addition, a microneedle allows precise tissue localization of delivery, such as within the skin, the suprachoroidal space of the eye, and the cell nucleus.

The intended effect, the type of disease, and the product type are the three factors that determine the drug's mode of administration. Although oral administration remains the most commonly used route, its effectiveness is limited for many modern therapeutics. This approach is widely used for long-term medications and is convenient for patients because it is simple to administer. Oral consumption also has negative effects on the liver and kidneys [9-10] . Parenteral routes include intravenous, intramuscular, intra-arterial, and subcutaneous methods as opposed to oral delivery. Because the parenteral route of administration is quicker and less uncomfortable, patients do not particularly prefer it [11]. On the other hand, compared to the parenteral method, the inhalation method is less painful and more comfortable. The drug goes straight into the lungs. This approach increases the drug's bio-availability. However, multiple doses per day are required due to the risk of overdosing through self-administration [9], [12-15].

➢ *An Overview of Skin Architecture:*

The skin functions as a complex biological barrier that regulates protection, absorption, and immune response. Skin makes up approximately 16% of an average sized human body and has a surface area of approximately 1.7 m2, putting it in the category of the most comprehensive and the best protection available on a body-wide level. The Skin will provide the body with an effective barrier against bacteria, ultraviolet radiation, chemicals and other potential hazardous materials, pollution, allergies, and the loss of excessive amounts of fluid. In addition to protection, the skin plays a key role in maintaining physiological stability. Each skin layer—epidermis, dermis, and hypodermis—plays a distinct role in determining mechanical strength, permeability, and drug transport behavior.

➢ *Epidermis:*

The epidermis is right on the surface—it's your body's first barrier against the outside world. Its thickness depends on where you look: about 0.8 mm on your palms and soles, but way thinner almost everywhere else. Most of the cells here are keratinocytes—around 95% of them, in fact. These cells produce keratin, a protein that's tough and waterproof, which helps keep your skin durable and flexible. The very top layer, the stratum corneum, faces the environment directly. This is the main shield, blocking things from getting in or out with its super tight mix of lipids and proteins. The stratum corneum is packed with flat cells called corneocytes, full of water, lipids, and keratin—all squeezed together to keep your skin protected. [16].

➢ *Dermis:*

Just under the epidermis sits the dermis—a much thicker layer, about two to three millimeters deep. This part of the skin packs in a ton of collagen, around 70%, plus elastin fibers [17]. That's what keeps your skin strong and stretchy. The dermis is loaded with blood vessels, which do all the hard work of delivering nutrients and oxygen not only to itself but also to the epidermis above. It's also where you'll find neurons, immune cells like macrophages, and lymphatic vessels. Thanks to all that, the dermis plays a vital role in immune defense, sensation, and clearing out waste. [18].

➢ *Hypodermis:*

The subcutaneous layer—people also call it the hypodermis—is that bottom part of your skin you don't really see but rely on a lot. It's loaded with fat cells, but these cells handle more than just energy storage. They cushion your organs, absorb shocks when you bump into things, and keep your body temperature even, working like built-in insulation. But there's more happening here than just fat storage. The hypodermis is buzzing with nerves and blood vessels, linking your skin to everything underneath. Actually, around half your body's fat is stored in this layer. Besides fat cells, you've got fibroblasts here to help patch up damaged tissue, and macrophages that defend against infections. So, your skin's not just a simple outer covering—it's a busy, active organ always working to keep you protected, regulate your body temperature, and help you sense the world around you. When it comes down to it, your skin really keeps everything in your body running smoothly. [19].

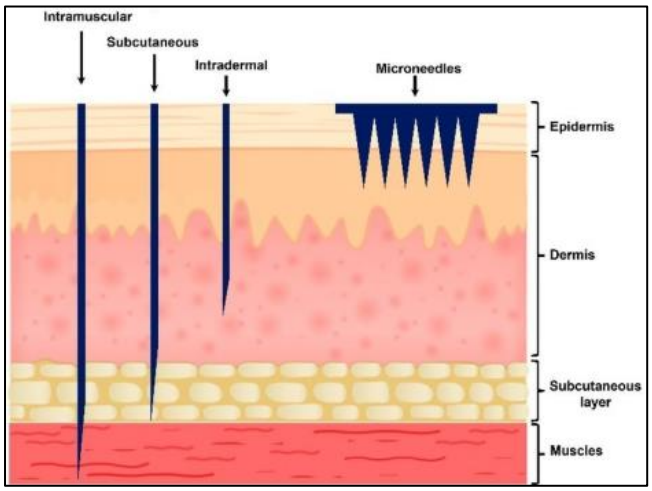

Fig 1 Schematic Showing Human Skin Layers and Micro-Needle Compared to Conventional Injection Method.

➢ *Advantages:*

- Microneedles are catching a lot of interest lately as a new way to deliver drugs through the skin. Unlike pills, which have to go through your gut and get processed by the liver—that's what's called first-pass metabolism—microneedle patches push the medicine straight through your skin [20] . This shortcut lets the drug get into your bloodstream faster and cuts down on wasted medicine or weird side effects from how your body breaks things down. People usually find the effects more consistent, and sometimes you don't need as high a dose.

- One big plus with microneedle patches is how gentle they are compared to regular shots or IV treatments. They

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barely break the skin, so people don't feel much pain, and there's a lot less anxiety. For anyone who dreads needles—which is a lot of folks, honestly—that's a huge relief and can make it much easier to stick with treatment. Kids, older adults, and patients who need regular medication end up benefiting the most. Another thing going for microneedle patches: they're simple to use. People don't need a nurse or doctor to help; they can just stick the patch on themselves, or someone with just a bit of training can do it. That makes everything a lot more flexible and accessible [21].

- This makes them ideal for use in community healthcare settings, remote areas, and even at home, potentially expanding access to medications and vaccines in underserved populations. From a scientific standpoint. Microneedles transiently disrupt the stratum corneum, thereby facilitating enhanced drug penetration into viable skin layers. —the outermost layer —in that blocks most drugs from penetrating [22].

- Microneedles poke tiny holes in your skin, opening up a direct path for medicine—whether it's small molecules, peptides, proteins, or even vaccines—to slip straight into the upper layers where your body can actually use it. Because the medicine goes right where it's needed, more gets absorbed, and you deal with fewer side effects spreading through the rest of your body. No detour through your stomach or liver, so the drugs stay stronger and work better.

- Since microneedles dodge the liver's usual filter, you end up with more reliable results, and the medicine packs more punch. But probably the biggest perk? They don't really hurt. Regular shots can sting or just plain scare people, especially if needles freak you out. Microneedles are so short they don't even reach the pain nerves, so most people barely feel them at all. That makes sticking to treatments a whole lot easier—whether you're a kid, older, or just someone who'd rather not deal with traditional needles.

➢ *Disadvantages:*

- Even with those benefits, microneedles still run into some real roadblocks—both technical and clinical—that keep them from catching on everywhere. Making microneedles isn't simple. You need the right materials: something that's safe for the body but tough enough to hold its shape and not break during use. That kind of balancing act ramps up how complicated and expensive they are to produce, which can make them tough to roll out in places with limited resources.

- Then there's the issue of getting dosing just right. The drug dose relies on things like how big the patch is, how many needles it has, and how well it can carry the drug. Sometimes, to actually get enough medicine, you have to use several patches on the same spot. That's not always practical or convenient for patients.

- Using microneedle patches isn't exactly straightforward. It takes time, it can be annoying, and the risk of skin reactions goes up. Even getting the drug levels right is a challenge—Rzhevskiy's team dug into that. Everyone's skin is different, and how you apply the patch isn't always the same. That messes with how much medicine gets in, so you might get too little or too much, which just means more chances for side effects [23]. And let's be real, people aren't all built the same. Bariya's work found that skin thickness changes a lot, not just between people, but across different body parts too. Age, health—those things only throw more variables into the mix. So, designing a microneedle patch that fits everyone perfectly? Not so easy.

- Getting the size and shape of micro-needles right makes all the difference. They need to hit the target beneath your skin without causing any damage. And honestly, it's not just the needles themselves—the patch's placement matters a lot. If you don't press it down firmly or evenly, those tiny needles won't break through, and the drug either spills out or just doesn't work.

- Keep slapping the patch on the same spot, and you're headed for problems. At first, you might not see anything wrong, but after a while your skin can turn red, get sore, or even develop bigger issues—especially if you already have sensitive skin or any skin conditions. The way the needles are built isn't just a detail—if they're off, nothing else about the patch really matters [24].

Let's talk about hollow microneedles. They're designed to send liquid drugs right into your skin, but there's a catch. If the tissue around the tip presses in as you insert them, the needle can clog fast. When that happens, the flow slows down to a trickle or just stops completely. At that point, you're not really getting the drug where it needs to go, which kind of ruins the whole idea.

Honestly, getting drugs to pass through skin is tricky no matter how you go about it. Microneedles sound nice, but they've got their own headaches—swelling, redness, some irritation or pain, and sometimes even infections if you skip disinfecting. There's also the chance your skin will react to the patch itself or to the medication. For most people, these problems are mild and clear up without much fuss, but you can't ignore them. They stick in your mind when you start thinking about patient safety and how to actually improve the technology. [25],[26].

II. TYPES OF MICRO-NEEDLES

➢ *Solid Micro Needles*

Solid micro-needles mechanically disrupt the stratum corneum , creating transient microchannels that facilitate drug diffusion . After that, you stick a drug patch on the skin, and the medicine travels through those little openings. This "poke-and-patch" technique gets drugs into the body by letting them diffuse from the patch through the micro-channels, or, if you use an electric current, the drugs can move even faster with iontophoresis. There's another method called

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"coat and poke." Here, the micro-needles are already coated with the drug before you press them into the skin, so all the medication sits right on the needle itself—there's no drug left behind on the skin's surface[27]. A twist on this is the "dip and scrape" approach: you dip the micro-needles in a drug solution, then drag them across the skin so the medicine gets left in the channels the needles create. If you look back, the first micro-needle was made by pressing it into a silicon wafer to deliver stuff inside cells in lab settings. Researchers started out using micro-needles on nematodes and other cells to boost molecule uptake and gene transfer. Later, they shifted focus to make micro-needles for drug delivery through the skin[28-29]. Now, there's a whole range of solid micro-needles out there. For example, Narayanan and Raghavan (2017) came up with solid silicon micro-needles for better trans dermal drug delivery, with an average height of 158µm, a base width of 110.5µm, and a sharp tip just 0.40µm wide[30].

In the study by Martin et al. (2012), members produced sugar glass micro-needles in a vacuum at low temperatures. The resulting sugar micro-needles were even strong enough to pierce human skin. Chaetal. (2014) used a different method to fabricate a micro-needle array by polymerizing acidic/methacrylate blend in a PDMS micro-molding. Other researchers fabricated a porous titanium micro-needle array (TPMA) by a modified metal injection molding at 1250°C for two hours. The only elements analyzed on the surface were titanium and oxygen. The array also perforated skin with not breakage. The philosophy behind micro needles is to damage skin as little as possible and make microscopic openings to allow the delivery of drugs to the upper derma and/or epidermis. Designed this way medications can even penetrate the circulatory system, as the micro needle delivery system is coated with a drug to allow it to cross even the skin barriers.

Micro-needles come in all sorts of heights—from 25 to 2000µm—and you'll find them made from all kinds of stuff: metals, silicon, glass, and both biodegradable and non-biodegradable polymers. Picking the right material matters a lot, since it affects how strong the micro-needles are, how flexible or permeable they can be, and ultimately, how well they deliver the drug. You'll see micro-needles made from ceramics, metals, silicon, glass, even carbohydrates. Researchers have looked into a bunch of different materials with good properties for making micro-needles—things like high mechanical strength and bio-compatibility. Metals, silicon, glass, ceramics, and polymers (including carbohydrates) are all in the mix. Metal micro-needles, for one, are reliable because they're strong, easy to make, and you can use cheap, FDA-approved metals like titanium, stainless steel, or nickel. People use techniques like laser cutting, wet etching, metal electroplating, or laser ablation to make them. And silicon? Its properties make it a favorite for micro-needle manufacturing.

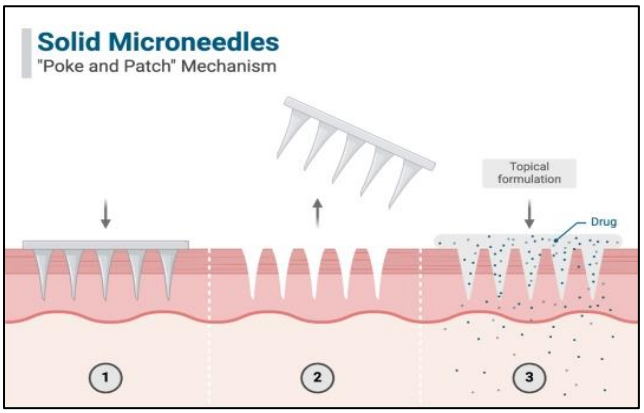

Fig 2 Mechanism of Drug Delivery Using Solid Micro-Needles Based on the Poke and Patch Approach

➢ *Hollow Micro-Needles:*

So here's how hollow micro-needles actually work: they've got a tiny hollow channel running through them, kind of like a straw, that carries medication straight from a reservoir in the patch down into blood vessels just under your skin. And they can move a surprising amount of fluid this way—up to 200µL, which is honestly pretty impressive for something so small. Think of it as a hypodermic needle's tiny cousin. You fill the bore at the tip with whatever drug you're delivering, stick the patch on, and the medication starts soaking into the top layers of skin almost right away—we're talking the epidermis and sometimes a bit deeper into the dermis. These aren't limited to simple drugs either. They can handle bigger, more complicated stuff too, like proteins, oligonucleotides, even vaccines.

Now, actually making these things is a whole other story [31]. It's genuinely tricky, especially once you try to make the needles longer and thinner. Solid needles have this internal support that keeps them sturdy, but hollow ones don't, so if the ratio of length to width gets too extreme, they get fragile fast [32]. Push one in at even a slightly wrong angle and it can just fail. And if someone's rough with the patch—slapping it on carelessly or yanking it off—you risk snapping a needle or messing up the whole delivery system. That's basically why most manufacturers just play it safe and keep the needles on the shorter side.

But here's why people put up with the hassle: hollow micro-needles create a real, direct pathway into skin or tissue—basically a mini hypodermic needle you can wear. That means you get precise, controlled delivery of liquid medication, with actual pressure behind it [58]. And it doesn't stop there. Down the road, these could potentially track how well a drug is soaking into the skin, help medication push past the eye's notoriously stubborn outer layer, or even pull small samples of fluid out of the body for testing.

What's kind of wild is that out of every micro-needle design scientists have played around with over the years, hollow ones are the only type that's actually made it to market. And the materials side keeps evolving too—there's now porous ceramic micro-needles that can deliver drugs at room temperature, no refrigeration needed, which opens up a whole new set of possibilities [59].

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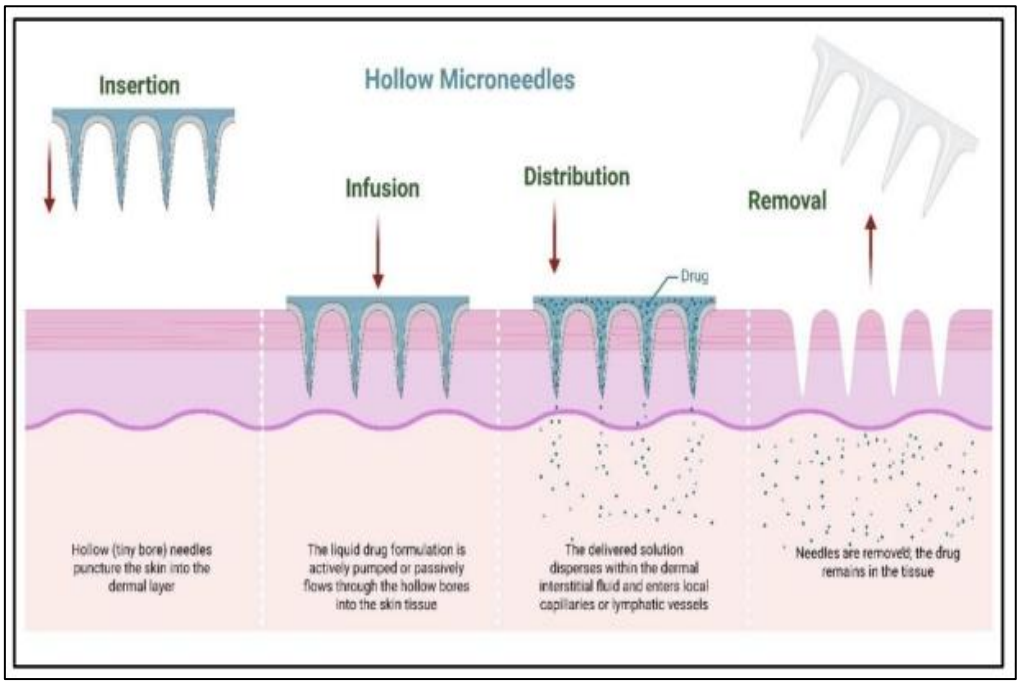

Fig 3 Mechanism of Transdermal Drug Delivery Using Hallow Microneedle

➢ *Dissolvable and Swellable Micro-Needles :*

Lately, researchers have started making micro-needles out of polymers that either swell up or dissolve. They load the drug straight into the needle during manufacturing. Once the micro-needle breaks through the top layer of skin, the polymer just melts away, releasing the medicine right where it's needed. Since the whole needle dissolves inside the skin, there's hardly any risk of needle-stick injuries afterward[60]. Swellable micro needle patches use hydrogels—materials that love water. These patches soak up moisture from the skin, causing the micro needles to swell and form little pores that let the drug spread out. An additional advantage is that the base plate beneath the micro-needles can function as a drug reservoir, and as the needles swell, they may enhance local microcirculation under the skin. Lately, designers have been experimenting with all kinds of drugs and polymers for these dissolvable and swellable micro-needles. Some of the latest versions can even pull out interstitial fluid from the skin—a pretty clever twist that uses the swelling effect for more than just delivering medicine[61]. These development highlights the growing versatility of polymer based micro-needle system.

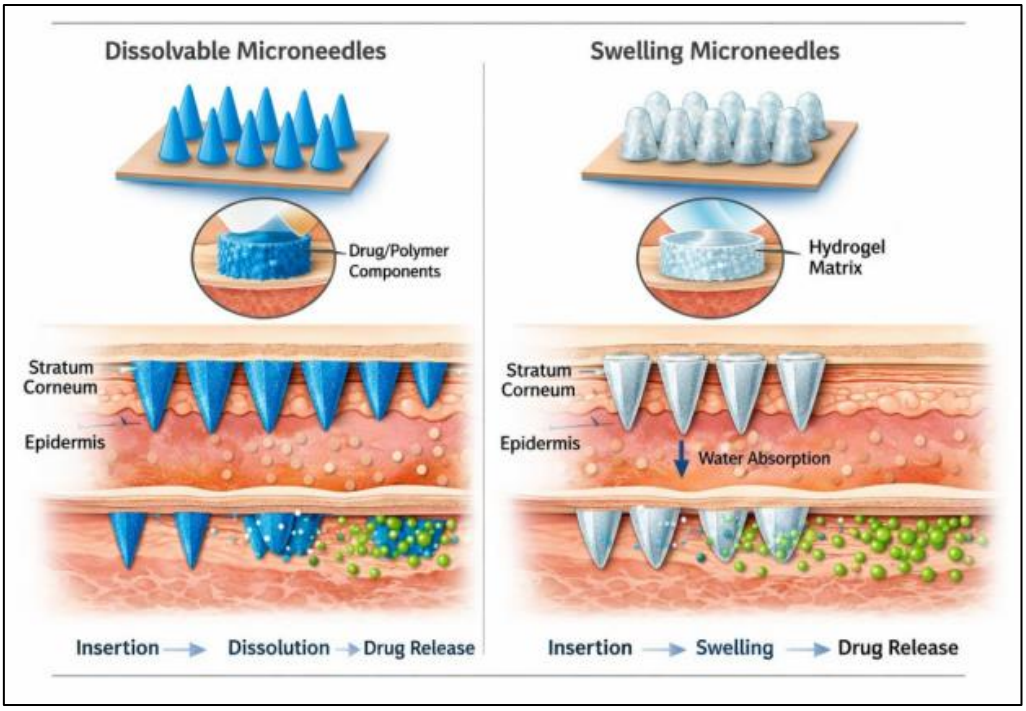

Fig 4 Mechanisms of Drug Delivery Using Dissolvable and Swelling Microneedle

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➢ *Coated Micro-Needles:*

A coated micro-needle array is an intricate device that, despite its fragile appearance, represents a sophisticated approach to drug delivery. Each array is composed of numerous tiny, sharp needles—each measuring just a few micrometers in width A coated microneedle array is an intricate device that, —protruding from a solid base. These slender needles are carefully coated with a thin film of therapeutic agent, which is mixed with water-soluble excipients to optimize the delivery process. The coating process itself is a subject of ongoing research, as scientists continually refine methods for applying an even, consistent layer of medication to the microneedle surfaces. The goal is to ensure that every needle carries just the right amount of drug, maximizing therapeutic efficacy and minimizing variability between doses. Researchers evaluate the performance of coated microneedle arrays by examining several critical factors. Chief among these are the adhesion and uniformity of the coating—since an uneven or poorly adhered layer could lead to inconsistent drug delivery—and the reproducibility of the coating process, which is essential for large-scale manufacturing. Most importantly, scientists assess whether the coated drug is efficiently transferred into the target tissue upon application. There is also interest in the versatility of these devices, as coated micro-needles have shown promise for delivering a diverse range of therapeutics, including peptides, small-molecule drugs, viruses for vaccination, and even micro-particles for sustained release. Different coating strategies have been explored to enhance performance.

In one experiment, researchers achieved a uniform coating over the entire micro-needle array—including the base—simply by dipping the patch into a specially formulated solution[62]. However, further studies revealed that selectively coating only the shafts of the micro-needles, rather than the entire device, yielded better results. Focusing the coating on the active region of the needles not only improved drug delivery efficiency but also significantly reduced waste, making the process more economical and environmentally friendly[63]. Typically, a coated micro-needle consists of a robust, solid needle core that does not dissolve in the skin. The surface of each needle is layered with the active pharmaceutical ingredient and water-soluble excipients[64]. These excipients play a crucial role: once the micro-needle array is inserted into the skin, the excipients rapidly dissolve in the interstitial fluid, prompting the drug coating to detach from the needle surface and diffuse into the surrounding tissue. In some designs, hydrophobic coatings are incorporated to facilitate the separation of the coating from the needle when it encounters the moist environment beneath the skin, further enhancing the release of the therapeutic agent. The rate at which the drug is released into the skin hinges on the solubility of the excipients in interstitial fluid[64].

Faster-dissolving excipients enable a more rapid onset of action, while slower-dissolving formulations can provide a more gradual release, depending on therapeutic needs. After the drug has been delivered and the coating has fully dissolved, it is essential to remove the micro-needle array from the skin. This ensures that no residual materials are left behind, reducing the risk of irritation or potential complications and confirming that the entire dose has been successfully administered. Hence , coated micro-needle arrays represent a promising advancement in transdermal drug delivery. Their ability to provide precise, minimally invasive, and potentially pain-free administration of a broad spectrum of therapeutics could transform how medications are given, improving patient compliance and opening new possibilities for self-administered treatments and mass vaccination campaigns. As research progresses, further refinements in coating techniques and formulations are likely to enhance their effectiveness, safety, and accessibility even further.

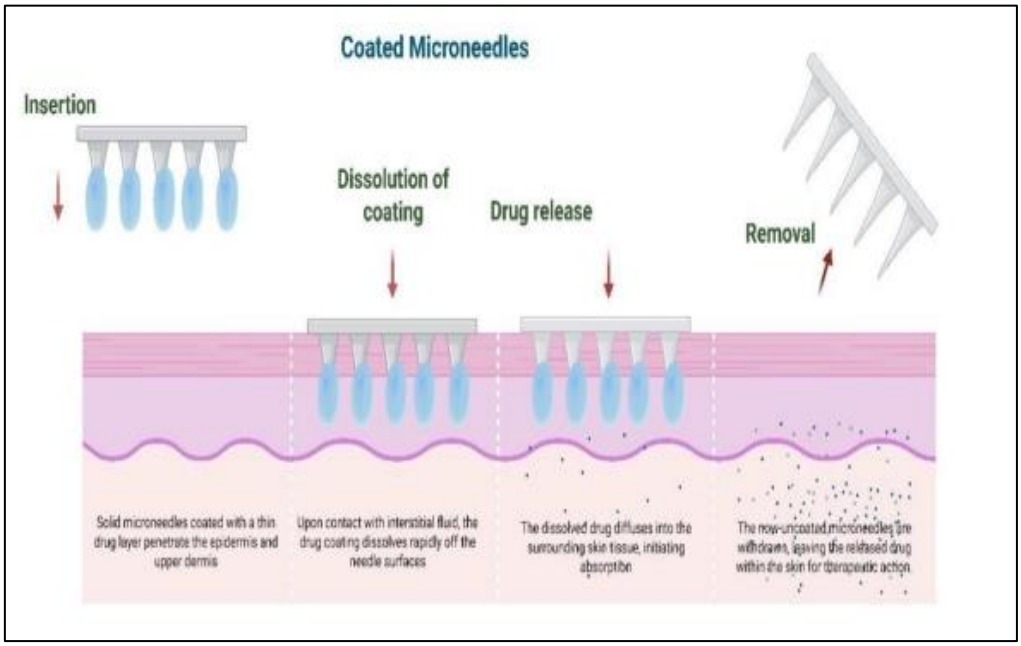

Fig 5 Mechanism of Transdermal Drug Delivery Using Coated Micro-Needles.

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III. MICRO-NEEDLE FABRICATION MATERIAL AND ITS PROPERTIES

➢ *Silicon:*

So, silicon's actually got some history here—it was the material behind the very first micro-needle, way back in the 1990s [33]. One quirky thing about it is that it's anisotropic, which is a fancy way of saying its properties change depending on which direction you're measuring in, thanks to its crystal structure. Depending on how that crystal lattice lines up, you get elastic moduli ranging anywhere from 50 to 180 GPa [34],[35],[36]. What that means practically is you've got a lot of design freedom—silicon can be shaped into needles of pretty much any size or form, which is a big part of why people like using it. It also scales well; you can produce these substrates with a lot of precision and in bulk. But here's the catch: it's expensive, and making the stuff is a real pain—labor-intensive, complicated, the whole nine yards. And then there's the brittleness issue. Silicon can crack or shatter, and if little fragments break off and end up stuck in someone's skin, that's obviously not great for their health [34].

➢ *Metal:*

When it comes to metal micro-needles, titanium and stainless steel are the go-to choices, though you'll occasionally see palladium, nickel, or palladium-cobalt alloys thrown into the mix [37]. Metals just tend to work well here—they're strong, and the body tolerates them fine. Since they don't snap or break as easily as silicon, they're honestly a better bet if you want something durable. Stainless steel was actually the first metal anyone tried for this [38], and titanium's since become a pretty solid alternative [34],[39].

➢ *Ceramic :*

Alumina (Al2O3) is a popular pick mainly because it just doesn't break down chemically—it forms this really tough oxide layer, thanks to strong bonding between the aluminum and oxygen atoms [40]. Other ceramics show up too, like gypsum and brushite [41]. And more recently, there's this newer material called Ormocer®, which is an organically modified ceramic—basically a copolymer with a 3D cross-linked structure [42]. The neat part is you can mess with its properties by changing up the organic components you use during polymerization. Most ceramic needles get made through micro-molding, where you basically pour ceramic slurry into a mold. It's a fairly cheap process, too, and it scales up without much trouble [34].

➢ *Silica glass:*

Glass is interesting because it lets you make all kinds of tiny, intricate shapes. It's biologically inert, so your body doesn't react badly to it, but it's also brittle, which is a real downside [43]. Borosilicate glass—the stuff made from silica and boron trioxide—holds up a little better and has more flexibility. The problem is these are usually made by hand, so it's a slow process [44]. Honestly, glass micro-needles haven't made it to the commercial market yet—they're mostly still just a research thing [34].

➢ *Carbohydrate :*

Maltose is probably the most common sugar used here [45], but you'll also see mannitol, trehalose, sucrose, xylitol, galactose, and different polysaccharides in play [46]. The process usually goes like this: you mold a carbohydrate slurry using silicon or metal templates, then pour in a drug-loaded carbohydrate mixture to actually form the needles [47]. Since the sugar dissolves gradually once it's in the skin, that dissolving speed is basically what controls how the drug gets released over time. These are cheap and pretty safe for people, which is nice, but they tend to break down at high temperatures, which makes manufacturing them a bit of a headache [34].

➢ *Polymer*:

There's a ton of different polymers used for micro-needles—stuff like PMMA [48], PLA [49], PLGA [50], PGA [44], polycarbonate [51], cyclic-olefin copolymer, PVP [52], PVA [52], polystyrene [53], poly(methyl vinyl ether-co-maleic anhydride) [54], and SU-8 photoresist [55], just to name a few. Generally, these polymers end up as either dissolving/biodegradable needles or hydrogel-based ones. They're not quite as strong as metal or silicon, sure, but they hold up better than glass or ceramic when it comes to durability [34],[35].

➢ *How Micro-Needles Works:*

When you apply the drug topically, the microneedle patch basically relies on diffusion to get things moving, and it creates a tiny, temporary break in your skin to do it. The design is actually pretty simple once you picture it—hundreds of little needles arranged in a grid on a small patch, kind of like the transdermal patches you'd already find at any pharmacy. The whole point is just to load in enough drug to actually trigger a real effect in the body. To get there, the needles have to punch through the stratum corneum, which is normally your skin's main line of defense against anything trying to get in. Once the drug makes it to the epidermis or the upper dermis, it can slip into your bloodstream and start working wherever it's needed. That's really why microneedle patches have become such a hot topic lately—they feel like a legit next step for transdermal drug delivery [56],[57].

➢ *Patch Disposal :*

Once you're done with a micro-needle patch, you have to think about how to throw it out safely. There's leftover drug, sharp points, and the fact that it touched your skin, so it's not just regular trash. Most of the time, these patches don't deliver every last bit of the drug. Sometimes that's fine, but other times it's a real problem—especially if the leftover medicine is strong or addictive[65]. You don't want kids, pets, or anyone else accidentally coming into contact with it, and you definitely don't want anyone misusing what's left. Used patches usually count as biohazardous waste since they've touched body fluids—mostly just a tiny bit, less than what you'd see on a used bandage[66]. They might also be labeled as sharp waste, depending on the type[67]. Dissolvable micro-needles generally lose their sharpness after use, so you probably don't need to worry about them being sharp waste. But the non-dissolving ones, especially coated micro-needles, are a different story. They're not as risky as used needles or

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scalpels, but they still need careful handling, and the rules for getting rid of them might not be the same. Regardless of microneedle type , appropriate disposal remains essential to ensure user and environmental safety. Stuff like sharps containers, biohazard bags, or special cases you can put the used patch in—these all help keep people and the environment safe.

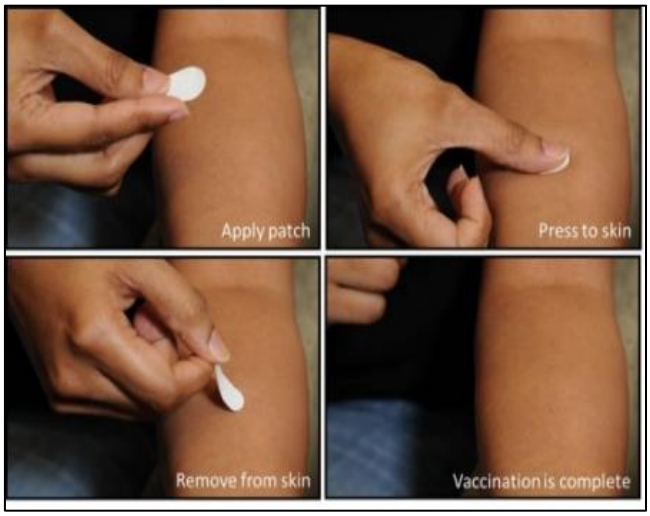

Fig 6 This Way the Used Micro-Needle Patches is Removed from the Skin and Disposed.

IV. APPLICATIONS

➢ *Migraines:*

There's a decent case building for microneedles as a way to handle migraines better—particularly for delivering a drug called dihydroergotamine—and honestly just improving day-to-day life for people who deal with these attacks regularly. And that's a lot of people. Severe, recurring migraines that blow up your work schedule, your social life, pretty much everything. Triptans do the trick for some, but plenty of patients either don't respond or can't stomach the side effects. Enter dihydroergotamine mesylate, DHE for short—an older-class drug that acts as a fallback option for moderate to severe cases. The issue is delivery: right now, it's either a shot under the skin or a nasal spray, and neither is particularly pleasant. Both bring discomfort along with side effects like nausea, congestion, soreness at the injection spot. On top of that, a good chunk of the drug never even makes it into circulation—low bioavailability, basically wasted potential. So, there's a clear opening for something better here: a way to give DHE that's self-administered, doesn't hurt, kicks in quickly, and actually gets absorbed properly [68]. Nail that, and you'd likely see people sticking to treatment more consistently, with less hassle and better results overall.

➢ *Diabetes:*

Microneedles might be a way out of the constant insulin-injection routine for people with diabetes—something that's still controlled but a lot less invasive. That daily injection cycle wears people down, and it's a big part of why some patients skip doses or end up with blood sugar that's harder to manage than it should be. Insulin at mealtimes matters a lot for avoiding dangerous drops in blood sugar, but when the process itself is uncomfortable and repetitive, people start slipping. That's part of what's driving research into glucose-responsive microneedle patches, which have already shown real promise in clinical trials with type 1 diabetics. These patches pick up on blood glucose changes and release insulin automatically, which tracks a lot closer to how the body naturally regulates things compared to manual dosing. There's also a "smart" patch built around self-assembling artificial vesicles—painless, simple, dependable—that could meaningfully change how people manage diabetes day to day. For type 2 diabetes, there's a separate pH-responsive patch made of alginate, packed with mineralized peptide and protein nanoparticles, designed to release insulin gradually. That cuts down on how many times a day someone has to inject, which eases both the physical strain and the mental toll that comes with it. Taken together, these aren't just convenience upgrades—they could genuinely improve long-term disease control simply by making people more likely to follow through with treatment [69].

➢ *Vaccination:*

Vaccine delivery through the skin is developing fast, and biodegradable microneedles are looking like a genuine turning point. One major thing keeping vaccination rates down is plain old fear of needles, and that fear leaves more people exposed to diseases that are otherwise preventable. Biodegradable microneedles sidestep that entirely—no pain, barely invasive, and they only need to penetrate the outermost skin layer, which happens to be full of immune cells anyway. So the immune response still kicks in, just without the usual anxiety of a traditional shot. It also makes rollout easier logistically, potentially opening the door to self-administered vaccines or delivery by people with minimal training. These patches aren't limited to one use case either—they've already been tested for flu, measles, and even COVID-19. Between a better experience for patients and easier logistics, microneedle-based vaccination looks like a strong candidate for pushing global immunization rates up [70].

➢ *Cancer:*

Cancer remains one of the hardest problems in medicine, largely because so many treatments are too toxic, miss their target, or lose effectiveness once resistance develops. Microneedles have drawn a lot of attention as a way to sharpen anticancer treatment, especially for skin cancers and tumors sitting close to the surface. Research has shown that self-degradable microneedles can deliver immune therapies steadily over time—things like anti-PD-1 antibodies—helping counter the ways tumors evade the immune system. By loading agents like anti-PD-1 and glucose oxidase into pH-sensitive dextran nanoparticles and delivering them via microneedles, researchers can get a very localized release right in the tumor's environment, boosting immune activity and shrinking the tumor [71]. Even older treatments benefit—topical 5-fluorouracil for basal cell carcinoma penetrates skin up to 4.5 times better when combined with solid microneedle pretreatment, leading to noticeably stronger tumor suppression [72]. There's also ongoing work with polymer microneedles aimed at delivering chemotherapy directly to skin tumors and other localized cancers, potentially offering stronger results with less damage

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elsewhere in the body. All of this suggests microneedle technology could genuinely reshape cancer treatment, particularly for the stubborn, hard-to-treat cases [73],[74].

➢ *Ocular Delivery:*

Getting drugs to the back of the eye is a genuinely difficult problem, mostly because of how many anatomical barriers stand in the way. Usually the drug just accumulates near the injection site instead of reaching the tissue it's meant for, which is a real obstacle for conditions like age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion. One approach that's helped is iontophoresis, which uses a mild electrical current to push nanoparticles toward the suprachoroidal space. Combine that with microneedles, and the results improve even more—over 30% of administered nanoparticles actually reach the back of the eye. That's a substantial improvement, and it points toward real potential for treating a range of eye conditions more effectively, possibly with fewer doses and fewer side effects elsewhere in the body. If this line of research keeps advancing, it could lead to far less invasive treatment options for a lot of vision-threatening diseases [75].

➢ *Cosmetics:*

The cosmetics industry has taken to microneedle technology quickly, mainly because of how effectively it delivers active ingredients into the skin. Things like vitamin C, eflornithine (used to slow unwanted hair growth), and retinyl retinoate (a vitamin A derivative for anti-aging) can all be pushed deeper into skin layers where they actually make a difference [76]. That boosts how well treatments work for blemishes, scarring, hyperpigmentation, and general skin rejuvenation. There's newer work too—like melanin encapsulated in phosphatidylcholine nanoliposomes—that improves how well active ingredients dissolve and absorb into the skin's lipid-rich layers, which is useful for things like uneven tone or sun damage. As this research matures, microneedle-based delivery seems likely to become a standard part of personalized skincare, giving people more customizable, minimally invasive options for dermatological concerns. Beyond just improving treatment effectiveness, this also means more of these issues could be handled safely outside a clinical setting [77],[78].

V. CONCLUSION

This article examines the development and present day applications of micro-needle patches for drug and vaccine delivery devices. The transdermal route offers a convenient, painless and minimally invasive alternative to conventional drug administration methods. The fact that future microneedle formulations may reduce dependence on cold-chain storage, improving accessibility in resource-limited regions will be extremely beneficial to the healthcare industry. It must lessen the transmission of blood-borne diseases, needle injuries, and medical waste from sharp objects in rural regions. Through regulated release into the bloodstream and avoidance of hepatic metabolism, micro-needle patches are a potential reagent delivery method that enhances medication delivery efficiency and adsorption. Furthermore, intracutaneous use of vaccine antigen-coated micro-needle patches may improve humoral immunity and T cell response. Micro-needle patches that deliver vaccine antigens right into the skin look promising for boosting both antibody and T cell responses. Given the high density of immune cells in the skin, microneedle-based vaccination remains a compelling strategy. However, additional clinical studies and manufacturing optimization are required before widespread clinical implementation can be achieved.

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