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Engineering Smart Drug Delivery: Evaluating Microneedle Patches As An Alternative To Traditional Injections

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ABSTRACT

Therapeutic efficacy, pharmacokinetics, safety, and adherence to the drug are important factors that are greatly affected by the route and method of administration. Many vaccines, biological therapeutics, peptides, proteins and other drugs are not suitable for oral or passive transdermal delivery, and require conventional parenteral routes of administration, namely intravenous, intramuscular, subcutaneous, or intradermal injection. However, repeated injections may lead to tissue damage, needle phobia, needle stick injuries, sharp waste, pain and anxiety and administration may require trained healthcare personnel. The restrictions have inspired the creation of minimally invasive drug delivery methods. A novel alternative that has been developed is the use of microneedle patches that can temporarily breach the stratum corneum and allow the injection of drugs into the superficial layers of the skin without the need to inject with the usual hypodermic needle. The various designs of the microneedles provide flexibility in drug delivery for different therapeutic needs, such as solid, coated, hollow, dissolving and hydrogel-forming microneedles. They have been shown to be capable of carrying vaccines, proteins, peptides, nucleic acids, as well as other therapeutic compounds. Safety, tolerability and patient acceptability have also been shown to be favourable in clinical studies, specifically for vaccination. There are, however, some drawbacks to microneedle patches, including the ability to carry a large amount of drugs, mechanical strength, skin variations, scalability of manufacture, formulation stability, regulatory issues, and limited clinical evidence from large-scale trials. The engineering principles, drug delivery efficiency, therapeutic uses, benefits and drawbacks, and future potential applications of microneedle patches are compared to conventional injectable routes. Available data indicate that microneedle patches are not likely to supplant injections, but may prove useful for specific vaccines and therapeutics for which minimally invasive and convenient delivery via a patch may offer clinical benefits that are likely to be self-administered.

KEYWORDS: Microneedles; microneedle patches; transdermal drug delivery; smart drug delivery; drug delivery systems; minimally invasive delivery; therapeutic technology

1. INTRODUCTION

The delivery of drugs to tissues is crucial in the treatment of disease and the efficiency of delivery is an important factor in determining the therapeutic effectiveness of a drug in addition to its pharmacological properties. Oral, topical, transdermal, inhalational, and parenteral routes are commonly used to administer medicines. Of these, the administration of biological therapeutics, vaccines, peptides, proteins, and drugs with low gastrointestinal absorption or high first pass metabolism are of particular importance. By intravenous (IV) administration, the drug is delivered directly into the system circulation and systemic drug exposure will be rapid and predictable (Dharadhar et al. 2018).

However, there are some practical and patient-related disadvantages to the conventional injections. Insertion may be uncomfortable and stressful for some people and needle phobia can make some people reluctant to get or follow up with treatment (Kaushik et al. 2001, McLenon and Rogers 2019). Chronic diseases that require long-term treatment are especially cumbersome to receive repeated treatments. Needles also generate conventional "sharps" waste and pose a risk of potential needlestick injury to healthcare workers. Many times there is a need for trained staff, sterile equipment and health-care facilities to administer injectable medications (Bhatnagar et al. 2017).

The skin is an interesting target for drug delivery because it has a network of blood vessels and immune cells, and is easily accessible. But the stratum corneum is an excellent barrier to the penetration of the majority of therapeutic molecules. Conventional passive transdermal delivery is thus mainly applicable to relatively small molecules, having the appropriate physicochemical properties. Most peptides, proteins and therapeutics based on nucleic acids are poor candidates of passive penetration through intact skin (Dharadhar et al. 2018).

To overcome this barrier, microneedles have been developed. They are micron-scale projections that are able to penetrate the stratum corneum and establish temporary channels for therapeutic agents to penetrate into the skin. Since the microneedles are much smaller than the conventional hypodermic needles, an appropriate system design can reach into the superficial layers of the skin without causing any harm to deeper tissues (Bhatnagar et al. 2017; Dharadhar et al. 2018; Haq et al. 2008).

Microneedle patches are microstructures that are a part of a patch-based application system. They can release drugs quickly, slowly, or when stimulated by a physiological event, depending on their design. They have been of great interest to pharmaceutical engineers and clinical investigators due to their self-administration and to their pain relief potential (Rouphael et al. 2017). Clinical trials have been reviewed, and the microneedle systems have evolved from experimental prototypes to human applications in the fields of vaccination, drug delivery, biosensing and dermatological treatment (Zhang et al. 2023).

The aim of this review is to critically assess the use of microneedle patches as an alternative or add-on method of delivery for selected therapeutic microneedles. They are discussed in detail with regard to their engineering design, mechanisms of drug delivery, therapeutic applications, safety, patient acceptance, challenges in manufacturing, and future potential. The big issue is whether or not microneedle patches

will become the alternative to traditional injections or whether they are more appropriately targeted to specific therapies in which their unique benefits can be leveraged.

2. CONVENTIONAL INJECTABLE DRUG ADMINISTRATION

2.1 Major Routes of Injectable Administration

There are a number of different ways to administer an injection, all of which can be broadly grouped into the following categories: intravenous (IV), intramuscular (IM), subcutaneous (SC) and intradermal (ID). IV injection involves the direct delivery of a drug into the bloodstream and is commonly used when the drug needs to be delivered into the system quickly and in a controlled manner. In IM injections, the drug is deposited into the muscle tissue and is used for vaccines and certain medications. SC injection involves injection below the skin; insulin and other biological medicines are often given. ID injection is injected into the skin, which is important for vaccination and diagnostic tests (Bhatnagar et al. 2017).

The injection route depends on the physicochemical properties of the drug, the pharmacokinetic profile of the drug, the therapeutic target and the dose of the drug. Despite the advances in injection delivery technology, injections continue to be a vital part of healthcare today.

2.2 Influence of Administration Route on Pharmacokinetics and Pharmacodynamics

The route and formulation used to administer a drug can substantially influence its pharmacokinetic and pharmacodynamic behaviour. Intravenous administration introduces the complete administered dose directly into the systemic circulation and therefore produces immediate systemic exposure, whereas intramuscular and subcutaneous administration require absorption from the injection site. The rate of absorption from these tissues depends on factors including local blood flow, formulation characteristics and physicochemical properties of the drug.

Important pharmacokinetic parameters include bioavailability, maximum plasma concentration (Cmax), time to maximum concentration (Tmax), area under the plasma concentration-time curve (AUC), and duration of systemic exposure (Ortega et al. 2013). Changes in these parameters may subsequently alter pharmacodynamic responses, including the onset, magnitude and duration of therapeutic action.

Microneedle-mediated intradermal administration introduces a drug into the epidermal or dermal environment rather than directly into muscle, subcutaneous tissue or the circulation. Consequently, absorption can be influenced by microneedle geometry, insertion depth, drug distribution within the array, dissolution or release rate, local blood and lymphatic transport, and the physicochemical characteristics of the therapeutic molecule. Therefore, demonstrating that a microneedle contains the intended drug dose is not sufficient; the amount actually delivered to the skin and its subsequent pharmacokinetic and pharmacodynamic profile must also be established.

2.3 Advantages of Traditional Injections

The main advantage of injections is that they are proven to be reliable. The bioavailability will be high or total, depending on the route of administration, and the dose administered can be relatively well controlled. IV injection is most effective for achieving rapid systemic absorption, while SC and IM injection can have extended absorption for appropriate formulations (Lee et al. 2011).

The ability to deliver products via injection is also underpinned by the development of manufacturing processes, clinical procedures and regulatory pathways. Healthcare staff have a wealth of experience in injections, and hospitals, clinics and pharmacies have infrastructure in place for storage and administration. These benefits make injections the industry standard by which new systems for novel drugs are measured.

2.4 Limitations of Traditional Injections

The drawbacks of injection therapy are most related to invasiveness, patient experience, and healthcare needs. The pain upon insertion and anxiety can be created by the injection, while repeated injections can harm compliance. This need for trained health-care professionals may cause a burden on treatment and limit access in resource-limited or remote areas.

Needlestick injuries are a job-related risk and discarded needles pose a sharp waste risk. The safety or absorption of the drug may also be influenced by an incorrect injection technique or by the wrong injection site. These restrictions are significant for vaccination programmes, and chronic diseases where patients might require multiple doses across many years.

2.5 Need for Alternative Drug-Delivery Systems

Traditional injections are a vital part of numerous treatments, but their needles and often the need for trained staff have led to the emergence of alternative delivery methods.

An ideal alternative to injections would be to have a drug delivery system that has good reliability, but is not as painful, invasive, and wastes resources and requires less training. To meet some of these requirements, there have been developments of microneedle patches which use microscopic structures to penetrate the skin without relying on the use of hypodermic needles, or syringes (Bhatnagar et al. 2017; Dharadhar et al. 2018).

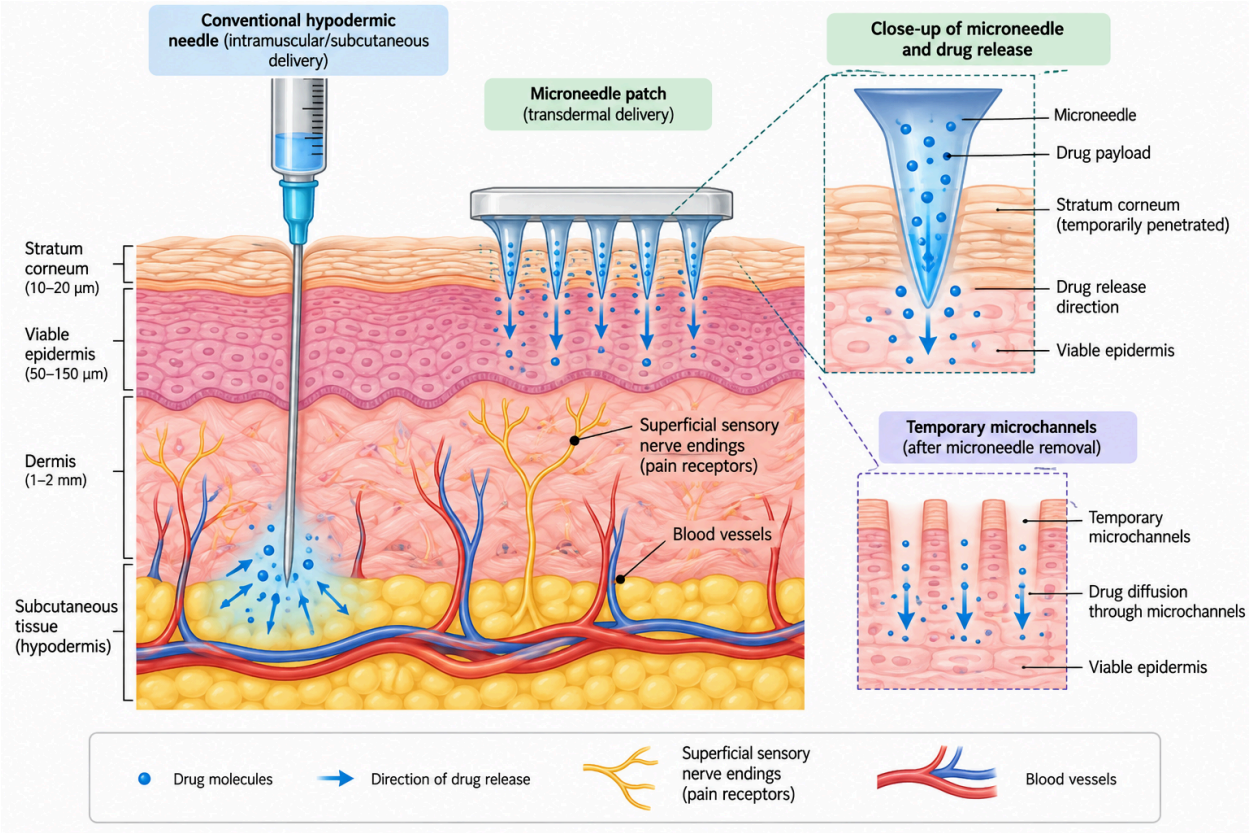
3. MICRONEEDLE PATCHES: DESIGN AND MECHANISM

3.1 Structure and Working Principle of Microneedles

In general, a microneedle patch is a patch made up of tiny projections (needles) attached to a base structure. The size, spacing, shape and substance of the projections can be designed based on the desired therapeutic use. The patch is applied to the skin and the microneedles push through the stratum corneum and make tiny holes in the outermost layer of skin (Haq et al. 2008; Bal et al. 2008).

The microchannels allow therapeutic agents to penetrate the stratum corneum and the viable epidermis and, depending on the depth of insertion and length of the microneedles, the superficial dermis. The drug can either be loaded into the microneedle or carried by a hollow channel or be released from a reservoir attached to the patch, depending upon the design. Once the skin is removed, the barrier function can slowly be restored over time. This method thus allows penetrating the skin without using the deeper penetration that is neces-sary with conventional injection needles (Dharadhar et al. 2018; Bhatnagar et al. 2017).

Figure 1. Skin structure and the principle of microneedle-mediated drug delivery



3.2 Types of Microneedles

The main function of solid microneedles is to penetrate the skin's outermost layer (stratum corneum) and create a pathway for increased skin permeability. They may be made of silicon, metals, ceramics or polymers. In some systems, the microchannels are formed, and the drug is deposited into them afterwards.

The therapeutic compound is coated on the surface of the coated micro needles. The coating will dissolve after it has been placed in the skin, and the drug will diffuse out of the coating into the target tissue. This is a design that can deliver relatively quickly and has been thoroughly studied in the context of vaccines.

Also, these systems are especially appealing as they can overcome the necessity of intact removal and disposal of microneedles.

Hollow microneedles have internal channels for the delivery of liquid formulations. They offer more control over the liquid dosing, but are more complex to make and can have issues including blockage and mechanical failure.

The microneedles swell once the interstitial fluid comes into contact with them and form gaps within the skin. This profile design may be beneficial for controlled and sustained delivery. With the variety of microneedle designs, researchers can select an architecture that can be matched with the drug properties and therapeutic needs (Moore et al., 2022; Frew et al., 2020).

Dissolving microneedles are commonly fabricated from water-soluble or biodegradable polymers containing the therapeutic compound within the needle matrix. Typically, the therapeutic compound is embedded in a water soluble or biodegradable polymer and the microneedles are fabricated using these materials. Once inserted, the microneedles dissolve in the interstitial fluid and deliver the payload into the skin. Dissolving systems can also decrease the amount of sharps needed to be disposed of as no intact needle is left after use. The hydrogels are usually a network of polymers that are crosslinked and absorb interstitial fluid and swell up after insertion without losing their structure. The matrix can increase in volume and create a pathway between the skin and a drug reservoir that permits slow diffusion while not necessarily dissolving the microneedle.

Table 1. Comparison of major materials used for microneedle fabrication

Material	**Principal advantages**	**Principal limitations**	**Common microneedle types**
Silicon	High stiffness; precise microfabrication; well-established lithographic processing	Brittle; relatively expensive fabrication; fracture concerns	Solid, hollow, coated
Stainless steel/titanium	High mechanical strength; good fracture resistance	Non-dissolving; potential sharps waste; more difficult drug incorporation	Solid, coated, hollow

Ceramics	High compressive strength; chemical stability	Brittle; relatively complex manufacture	Solid, porous, hollow
PVP/PVA and other synthetic polymers	Drug incorporation; tunable dissolution; scalable moulding potential	Mechanical strength depends strongly on composition and humidity	Dissolving, hydrogel-forming
Hyaluronic acid	Biocompatible; dissolving; suitable for incorporation of some therapeutics	Moisture sensitivity and formulation-dependent mechanical strength	Dissolving
Sugars/carbohydrate matrices	Rapid dissolution and biocompatibility	Hygroscopicity; possible thermal-processing limitations	Dissolving
Biopolymers such as gelatin/chitosan	Biocompatibility and biodegradability	Batch variability and formulation-dependent mechanics	Dissolving/hydrogel

3.3 Materials Used in Microneedle Fabrication

Microneedle performance is highly dependent on the type of material used. Silicon and metals offer excellent mechanical properties and good precision of manufacture, but may not be recommended if complete dissolution is required. The properties of polymers and sugars can be altered to make them attractive for the incorporation of drug molecules, as well as having biodegradability and controlled dissolution properties.

Several micro polymers like hyaluronic acid, polyvinylpyrrolidone, polyvinyl alcohol, carboxymethyl cellulose, chitosan, gelatin, and others have been studied as candidates for microneedle dissolution. There should be enough mechanical strength to penetrate the skin, but the material should be compatible with

the drug and the skin (Moore et al., 2022; Frew et al., 2020). The selection of the material is thus a compromise between mechanical resistance, manufacturability, biocompatibility, drug compatibility and the desired drug release profile. Metals like stainless steel and titanium offer strength and fracture resistance and so are good for solid, coated and hollow designs, but they do not dissolve after use. Silicon allows for very precise microfabrication, but is brittle and thus presents fracture issues. Polymers like polyvinylpyrrolidone, polyvinyl alcohol and hyaluronic acid, on the other hand, can be loaded with therapeutic agents and can be designed to dissolve or expand following insertion. Their mechanical properties, however, are much more sensitive to the polymer composition, molecular weight, crosslinking, water content and geometry of the microneedles.

3.4 Engineering Parameters Affecting Microneedle Performance

The height, sharpness, dimensions of the base of the microneedle, aspect ratio, the spacing and the density of the array of microneedles affect insertion efficiency. A microneedle's resistance to bending or fracturing is especially important, as mechanical strength is the key to its application (Davis et al. 2004). But larger dimensions, or pushing harder, may cause discomfort or damage to the tissues .

Additionally, there is variability in the properties of the skin. Penetration and drug transport may be affected by skin thickness, hydration, elasticity, anatomical location, age and disease. This means that laboratory performance is not necessarily a good indicator of clinical performance. For product development, standardized insertion and mechanical testing are therefore important for reliable product development (Dharadhar et al. 2018; Zhang et al. 2023).

3.5 Smart and Stimuli-Responsive Microneedles

In addition to passive or preprogrammed drug release, smart microneedle systems are being developed which will release the drug in response to the physiological conditions, including glucose concentration, pH, temperature and enzyme activity. The idea of these systems is to sense a biological state and deliver a therapeutic agent in response. One key example is glucose-responsive insulin microneedles, but the challenges of dose control, long-term performance, reproducibility and clinical validation are still significant (Yu et al. 2015; 2020).

4. EVALUATION OF MICRONEEDLE PATCHES

4.1 Drug-Delivery Efficiency

One of the biggest challenges for assessing microneedle patches is determining if they are able to provide a therapeutic dose that is reproducible and measurable. The microneedles provide mechanical penetration of the stratum corneum and allow the creation of transient microchannels through the barrier, which increases the transdermal and intradermal delivery. The microchannels increase the efficiency of therapeutic molecules that have poor passive skin permeability, such as peptides, proteins, nucleic acids and antigens of vaccines, to penetrate the viable skin layers as compared to intact skin. This is particularly true for peptides, proteins, nucleic acids and vaccine antigens (Nguyen and Nguyen 2023) .

The time required to release the needles varies from several minutes to extended delivery hours, days or even weeks in experimental formulations. The rapid dissolving polymeric systems can deliver their payloads in minutes following their insertion; for instance, PVP-based dissolving microneedles are reported to completely dissolve in about 3 min in experimental skin models (Lee et al. 2011). In contrast, drug diffusion or swelling of the polymers or degradation of the polymer matrix can be slower, resulting in sustained release that can be designed by other dissolving formulations of the same type as crosslinked hydrogels. A dual-release hepatitis B vaccine microneedle system, for instance, delivered a rapidly available fraction of the antigen within about 20 min and another fraction of the antigen in biodegradable polymeric tips that was released for over 55 days. Therefore, the terms rapid and sustained should be defined as a quantitative measure in each case and not just based on the type of microneedle.

The major drawback is that of drug loading capacity. Due to the small size of the microneedles, the volume of drug which can be contained in an array is limited. This is especially useful for strong chemicals for which only small amounts should be used. Conventional injections might be more appropriate for high dose therapies.

Incomplete insertion can also impact the efficiency of delivery of microneedle systems. There may be some variation in the dose due to application force and the skin characteristics. As a result, the study of engineering methods that enhance insertion reliability (Zhang et al. 2023) and that focus delivery of drugs at the tips of the microneedles (Nguyen and Nguyen 2023) is gaining in popularity.
Conventional injections nevertheless retain important advantages for therapies requiring large doses, immediate systemic exposure or tightly controlled infusion. Intravenous administration, in particular, cannot be considered functionally equivalent to current microneedle systems because it provides direct access to the systemic circulation. Microneedles are therefore most appropriately compared with conventional injection for applications in which intradermal or transdermal delivery can achieve the desired therapeutic exposure.

4.2 Patient Comfort and Acceptability

One of the most promising benefits of microneedle patches is that they are easy to accept by patients. Since the microneedles only penetrate superficial layers of the skin and are much shorter and thinner than traditional hypodermic needles, well-designed arrays may minimize stimulation of deeper nociceptive structures. In humans, pain levels have therefore been reported to be significantly lower after application of microneedles as compared to hypodermic needle insertion, but the level of sensation and discomfort will depend on the type of microneedle to be applied (Kaushik et al. 2001; Gill et al. 2008). Dissolving microneedle patches (Arya et al. 2017) have been reported to be well tolerated and easy to use in humans.

Clinical Vaccination Studies are an excellent source of evidence for patient acceptance. In a phase I influenza study conducted with 100 adults, the participants generally had a positive response to the microneedle patch vaccine, and ~70% were more likely to prefer using the patch for their future influenza vaccination than the other options offered in the study (Frew et al. 2020, Rouphael et al. 2017). The results suggest that minimising the mental and physical stress of the injection might be an important

benefit of microneedle technology. Some of the benefits of microneedle patches are that there may be less pain associated with them, less need to be trained in administering the shot, and less needle anxiety. They also have a patch format that affords opportunities for self-administration. This can be an important advantage for the chronic diseases that require chronic treatment. While this increased acceptability is a positive, it is only meaningful in the context of it being the right dose, taken consistently and having therapeutic benefits equivalent to current therapy.

4.3 Safety and Biocompatibility

The material, geometry, insertion force, drug formulation and skin contact time are all factors that determine the safety of microneedles. Complications that can occur are transient erythema, irritation, inflammation, allergic reactions, infection or mechanical failure.

So far, there has been good clinical evidence. A randomized trial of influenza vaccines using a high-density microarray patch was found to be safe and well-tolerated with the majority of adverse events being mild or moderate (Forster et al. 2020). In another clinical study, dissolving microneedles application resulted in minimal local reactions and human participants were okay with it (Arya et al. 2017).

However, safety in the short-term does not imply safety in the long-term. Different skin types, compromised skin barriers, repeated administration and extended exposure times to polymeric materials should be studied further (Vicente-Perez et al. 2017). For clinical adoption, it will be crucial to be able to reproduce the microneedle breakage, residual materials, skin recovery, and repeated dosing results for the acquisition to be standardized. The microneedle patches can help minimize the amount of sharps waste when compared to the amount traditionally used in injection products, since the needles dissolve after they are used. Such a feature may be useful in mass vaccinations and places where it is hard to dispose of sharps properly.

There remain, however, issues of backing materials, packaging and waste disposal when using microneedle patches. Their environmental benefits then must be evaluated over the entire life cycle of the product and not only based on comparing needle waste. Dissolving microneedles may additionally reduce conventional sharps waste because the needle projections dissolve following administration. However, the environmental impact of a microneedle product should be evaluated across its complete life cycle, including backing materials, applicators, packaging and manufacturing processes.

4.4 Drug Stability and Compatibility

Drug stability is a crucial factor since many of the biological therapeutics are temperature, moisture, pH and manufacturing condition sensitive. Drugs could be added to the dry-state matrices and so this formulation might have benefits in improving the storage stability.

One key area of interest is vaccines—some microarray patches are able to preserve the stability of vaccines which are difficult to preserve in the liquid media used for traditional vaccines. A clinical study of influenza showed that coating of the vaccine antigen onto a high-density microarray patch is

antigenically stable for a minimum of 12 months at 40°C (Forster et al. 2020). However, such stability data are formulation-specific and should not be generalized to all microneedle products. All drugs need to be monitored during the manufacture, storage, transportation and administration processes to ensure they remain biologically active and do not become inaccurate in their dosage.

4.5 Manufacturing and Scalability

One of the big challenges in commercialization is manufacturing. The dimensions, mechanical properties, drug loading, and dose uniformity are all critical parameters of microneedle arrays. Micro molding is widely studied, as it is capable of creating arrays with uniform geometry; however, it may be challenging to achieve micron scale cavity filling and to ensure uniform distribution of the drug.

Rapid prototyping and customized printing are possible with 3D printing and other advanced fabrication techniques. But there are several limitations in resolution, production rate, material compatibility, and cost that should be tackled before many of the lab fabrication approaches could be used for mass production (Olowe et al. 2022; Zhang et al. 2023).

In addition, manufacturing must meet requirements for sterility, packaging, stability, quality control and batch-to-batch reproducibility to be used clinically.

With the development of digital manufacturing technologies, such as three-dimensional printing, there is a possibility of tailoring microneedle geometry, drug loading and release profiles. In the future, personalized microneedles may be created based on individual patient-specific therapeutic needs.

But there's personalization, which adds complexity to manufacturing and regulation. There is a need to balance the advantages of individualized treatment with production cost, quality control, and scaling up.

4.6 Therapeutic and Clinical Applications

Currently, one of the most technically advanced uses of microneedle patches is for vaccination. ID vaccination could induce immune responses without the same burden of conventional vaccination and may enable antigen presenting cells within the skin to induce immune responses.

A high-density microarray patch was shown to be safe and generate immune responses comparable to or greater than IM injection in multiple vaccine groups in a Phase I clinical trial of influenza vaccination (Forster et al. 2020) . A subsequent phase 1/2 randomized trial was conducted in adults, toddlers and infants, in The Gambia, using the measles-rubella vaccine microneedle patch. 93% seroconverted for measles and 100% for rubella after patch administration of the vaccine in infants, with no severe or serious adverse events (Adigweme et al., 2024) reported.

In addition to vaccination, microneedles are under research for drug delivery of biopharmaceuticals, diabetes therapeutics, dermatological drugs, nucleic acids and localized treatments (Song et al. 2012). They are able to release molecules that might not be able to pass through the whole skin, which means

that they could be used in more ways than just traditional transdermal patches (Nguyen and Nguyen 2023).

4.7 Biosensing and Theranostic Applications

Biosensors and wearable electronics can also be combined with microneedles to provide simultaneous monitoring and therapy systems. The latest research activities have been directed towards the development of minimally invasive therapeutics and diagnostics systems (theranostics) based on microneedle platforms for sensing and therapeutic delivery (Wang et al., 2024).

In the future, systems could be adapted so they can communicate with smartphones or with other digital devices allowing for treatment response and adherence monitoring to be done remotely. This integration could possibly revolutionize the way microneedle patches can become a part of the connected healthcare system.

5. CHALLENGES AND LIMITATIONS

5.1 Technical and Engineering Challenges

There are still great technical challenges, such as mechanical strength and reliability on insertion. The microneedles need to be strong enough to penetrate the stratum corneum without bending or breaking the needle. Meanwhile, large dimensions and/or the depth of penetration can cause excess discomfort and tissue damage.

Another basic constraint is the loading capacity for drugs. The small size of each projection limits the amount of the drug that can be incorporated. Concentrated formulations, nanoparticles, multilayer systems and tip-loaded systems are being studied to address this issue (Nguyen and Nguyen 2023). However, high-dose drugs may not be appropriate for the conventional microneedle patches.

5.2 Biological and Patient-Related Challenge

The skin is highly variable both within and among people and anatomical sites. Thickness, hydration, elasticity, age, and disease can vary to impact insertion and drug transport. The technique of application can add to the variability, especially if patches are to be applied to oneself.

If repeated use is to be considered, this should be evaluated further. While repeated skin barrier disruption and repeated exposure to delivery materials have been shown to have good short-term tolerability from clinical studies, there is a need for more long-term research.

5.3 Manufacturing and Economic Challenges

For successful large-scale manufacturing, the dimensions of the microneedles and the uniformity of the drug distribution as well as their mechanical strength, sterility and stability is essential. Laboratory-based

fabrication methods do not always lend themselves to commercial production both economically and in terms of feasibility.

Scalable manufacture is still one of the critical issues that hinder the movement of the laboratory microneedle systems to become available clinical products (Olowe et al. 2022; Zhang et al. 2023).

5.4 Regulatory and Clinical Challenges

Microneedle products may possess attributes of pharmaceuticals and medical devices leading to complex regulatory issues. The authorities have to judge the quality of the drugs, mechanical strength, biocompatibility, sterility, dose uniformity and effectiveness.

While there have been a number of clinical trials that have yielded promising results, there are few studies that directly compare microneedle products with the standard injection therapies. Further diversity in the population, longer follow-up and clinically meaningful endpoints will be required to demonstrate generalizable therapeutic equivalence.

6. FUTURE RESEARCH AND CLINICAL TRANSLATION

Standardized testing, long-term safety, large-scale manufacturing, formulation stability, and well-designed clinical trials were suggested as areas of research that should be carried out in the future. Focus should be on the effectiveness of the therapy, patient adherence, safety, cost-effectiveness, and quality of life of direct comparisons instead of successful penetration of the skin.

Moving towards more integrated systems in the field will require coordinated advances in materials science, pharmaceutical formulation, microfabrication, and clinical research and regulatory science (Sultana et al. 2023; Zhang et al. 2023).

7. CONCLUSION

The microneedle patches are a promising engineering solution to enhance pharmaceutical delivery via minimally invasive penetration of the skin and controlled administration of the drugs. They are able to pass through the stratum corneum and offer opportunities to deliver poorly passively transdermal molecules, such as drugs, vaccines, peptides, proteins, and other molecules. The microneedle patches have some potential benefits over conventional injection, such as less sharp waste, ID administration, self-administration, and improved patient comfort.

They offer promising evidence of their translational potential from clinical studies. Vaccine trials have shown that influenza vaccines are safe, immunogenic and acceptable to the patient; and the 2024 measles-rubella (MMR) clinical trial in The Gambia has shown microneedle patch vaccines are feasible in infants and toddlers (Ikechukwu Adigweme et al. 2024; Forster et al. 2020) .

Although there have been advances, microneedle patches should not be considered as the replacement for injections at this time. The remaining barriers include limited drug loading capacity, differences in the properties of the skin, manufacturing issues, formulation stability, regulations and a limited number of large-scale clinical trials. Typical injection-based therapies will remain vital in high-dose therapy, IV therapy, and for the need for emergency systemic therapy.

The future is thus best complemented by a balance of the two. The microneedle patches will be most useful for specific vaccines, effective therapeutics, biological medicines and chronic therapies that would benefit from reduced pain, convenience, controlled delivery and/or self-administration. Microneedle patches, if developed further, could become a key element of future personalized medicine drug delivery systems, thanks to the advancement of smart materials, responsive drug-release systems, biosensor integration and scaling up of manufacturing.

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