J Pharm Res Sci Technol (2025) Vol 9 (1)

Journal of Pharmaceutical Research Science &Technology

journal homepage: https://ijpp.edwiserinternational.com

Review Article

Dissolving microneedles: an advanced approach for transdermal drug delivery

Shubham Tandon*, Rajesh Kumar, Ajeet Pal Singh and Amar Pal Singh

Department of Pharmaceutics, St. Soldier Institute of Pharmacy, Lidhran campus Behind IT, Jalandhar-Amritsar Bypass, Jalandhar, Punjab-144001, India

ARTICLE INFO

Received 03 May 2025
Revised 10 June 2025
Available Online 15 June 2025

Keywords:
Dissolving Microneedles (DMNs)
Transdermal Drug Delivery
Minimally Invasive Technology
Biodegradable Microneedles
Clinical Applications of Microneedles

ABSTRACT

Dissolving microneedles (DMNs) are tiny, polymer-based needles designed for minimally invasive drug delivery. Traditionally, DMN arrays are mounted onto patches to aid their insertion into the skin. Microneedles are revolutionizing transdermal drug delivery by providing a minimally invasive and efficient way to administer therapeutic agents. These microscopic needles—available in solid, hollow, coated, and dissolving forms—work by creating microchannels in the skin to enhance drug absorption. In contrast, dissolving microneedles (DMNs) offer superior drug-loading capabilities, easy fabrication, biodegradable properties, and the potential to be made entirely from the active pharmaceutical ingredient, eliminating the need for extra excipients. "Microlancer," an innovative micropillar-based system that enables self-administration of DMNs. This novel approach ensures rapid and efficient drug delivery, achieving an impressive 97 ± 2% delivery efficiency in less than a second, regardless of skin type or hair presence. This review explores the latest developments and future directions of DMNs, focusing on their advantages, challenges, and manufacturing techniques. The diverse applications of DMNs in areas such as cosmetics, vaccine delivery, diagnostics, cancer therapy, pain management, diabetes treatment, and dermatological disorders are discussed. Additionally, it highlights ongoing clinical trials, commercial advancements, and existing barriers to large-scale adoption, providing insight into the evolving landscape of dissolving microneedle technology. However, variations in skin elasticity and hair density often prevent complete insertion, leading to suboptimal drug delivery.

*Corresponding author: Shubham Tandon, Research Scholar, St. Soldier Institute of Pharmacy, Lidhran Campus, Behind NIT(R.E.C.), Jalandhar-Amritsar bypass NH-1 jalandhar-144011, Punjab, India.

https://doi.org/10.31531/jprst.1000188

Introduction

Transdermal drug delivery offers a significant advantage over oral and systemic administration by circumventing challenges such as fluctuating pH

levels, enzymatic degradation, and first-pass metabolism in the liver. Unlike hypodermic injections, which can cause pain and pose risks of needle-stick injuries, transdermal methods provide a non-invasive alternative for drug administration [1].

The skin, a crucial component of the integumentary system alongside hair follicles, nails, and glands, serves as a dynamic organ rather than just a passive barrier [2]. Beyond its protective role, the skin actively participates in immune defense, inflammatory responses, and tissue repair, while also acting as a diagnostic window for systemic diseases [3]. Historically considered a major obstacle to drug delivery, the skin has now become a focal point of innovation, fostering advancements in transdermal and intradermal therapeutic technologies [4,5].

Despite its advantages, transdermal drug delivery presents formulation challenges, as only small, lipophilic molecules typically under 500 Da can passively diffuse through the stratum corneum to reach systemic circulation at therapeutic levels. To address these limitations, microneedle technology has emerged as a transformative approach for intradermal drug administration [6].

Microneedles are micro-scale structures (less than 1000 μm in length) with conical, pyramidal, or multifaceted designs that enable precise drug delivery [7]. By creating temporary microchannels in the outer skin layer, microneedles overcome the stratum corneum barrier, facilitating the transport of drugs that would otherwise be ineffective via conventional transdermal methods [8]. Their short length ensures penetration deep enough to enhance drug absorption while remaining shallow enough to avoid stimulating pain receptors [9]. This virtually painless application significantly improves patient adherence, making microneedles especially beneficial for individuals with needle phobia [10,11].

Types of Microneedles

Microneedles are designed using different materials and fabrication techniques, giving them distinct functional and structural properties. Based on the intended medical or cosmetic application, they can be classified into solid, coated, dissolving, hollow, and hydrogel-forming types. These microneedle systems are utilized for the administration of various substances, including vaccines, biologics, and small-molecule drugs. Each type employs a unique mechanism to effectively deliver therapeutic agents to the target site [12].

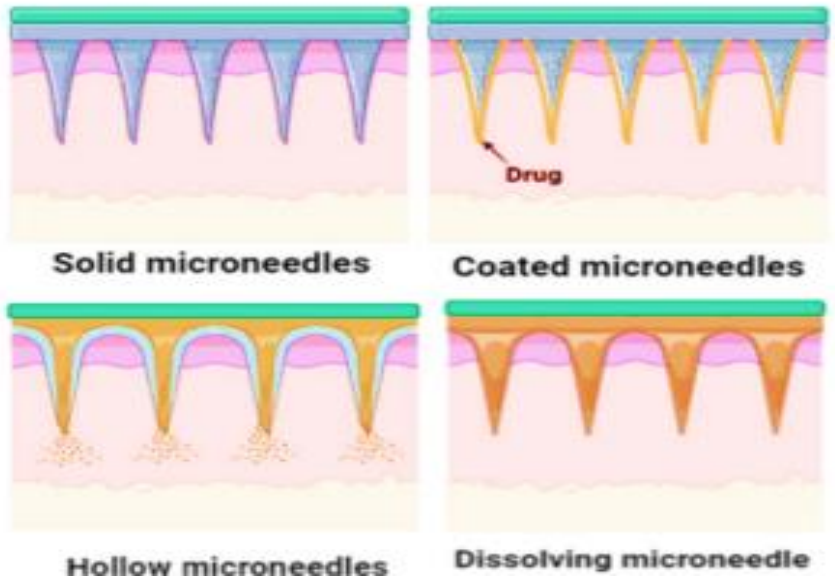

Figure 1: Types of microneedles: solid, coated, hollow and dissolving microneedles.

Microneedle Design

Over the past few decades, various microneedle designs have garnered considerable attention, each tailored to a specific drug delivery mechanism [13,14]. These designs can be broadly categorized into five types: (a) solid, (b) hollow, (c) coated, (d) hydrogel, and (e) dissolving microneedles, as illustrated in Figure 1.

Solid microneedles are typically manufactured using materials such as silicon, titanium, stainless steel, or certain polymers. They are often used in a "poke and patch" system, where the microneedles first create microchannels in the skin [14,15]. These needles are then removed, and a drug-loaded patch, cream, or solution is applied over the treated area to facilitate drug absorption (Figure 1).

Hollow microneedles, in contrast, contain a central channel with an opening at the tip. This allows for the direct injection of small volumes of drug formulations into the skin using a "poke and flow" method (Figure 1). Materials like silicon, ceramics, glass, and metals are commonly used in their fabrication. One of their main advantages is that they can remain in place to sustain drug delivery and prevent the microchannels from closing, unlike solid microneedles. However, they are prone to issues like channel blockage, which can be addressed by using designs with off-center bores [16,17].

Coated microneedles are designed to streamline the drug delivery process by using a "coat and poke" strategy (Figure 1c). In this method, the surface of the solid microneedles is coated with a thin layer of the active drug. Techniques such as dip coating, inkjet printing, and spray drying are commonly used. Challenges with this type include inconsistent coating, unintentional drug deposition on the patch base, loss of the drug during insertion, and limited drug loading due to coating thickness and needle size [18,19].

Hydrogel microneedles are made from hydrophilic, crosslinked polymer networks that can absorb water and swell. Upon insertion into the skin, these microneedles interact with interstitial fluid, expanding to form channels that facilitate drug diffusion through the swollen matrix [20].

Table 1: Methods of administration and therapeutic uses of various microneedle types [12].

Type of Microneedles	Delivery Strategies	Applications
Solid	The poke-and-patch method involves the application of numerous microneedles to create pores as a preparatory step. Following this, a traditional drug formulation is applied to the skin surface.	Skin pre-treatment for the delivery of potassium chloride, insulin, vaccines, cosmetics, and antipsychotic medication; monitoring of glucose and lactate levels; urea sensing.
Coated	The coat-and-poke technique involves applying a water-soluble drug coating on solid microneedles. This coating dissolves during administration, depositing the drug directly into the skin.	Delivery of proteins, vaccines, parathyroid hormone, insulin, desmopressin, and dexamethasone; sampling, isolation, and identification of biomarkers; monitoring of glucose.
Dissolving	The poke-and-dissolve method utilizes biodegradable or water-soluble microneedles encapsulating drugs. These microneedles dissolve upon application, releasing their therapeutic payload into the skin.	Delivery of vitamin B12, vaccines, therapeutic peptides, adenosine, doxorubicin, triamcinolone acetonide, near-IR photosensitizer (Redaporfin™), genes, and sodium nitroprusside in combination with sodium thiosulfate, tofacitinib, flurbiprofen axetil, epidermal growth factor, and ascorbic acid.
Hollow	The poke-and-flow method involves microneedles with a hole in the center or side of their structure, allowing the drug to flow across the skin.	Delivery of teriflunomide, ceftriaxone sodium, mRNA, and vaccines; cell therapy; monitoring of glucose; synthetic amphetamine-type substance sensing; dermal interstitial fluid sampling and sensing.
Hydrogel-forming	The poke-and-release method utilizes water-insoluble microneedles injected into the skin, gradually releasing the encapsulated therapeutic molecule. The patch remains on the skin after application.	Delivery of albendazole, sildenafil citrate, metformin hydrochloride, methotrexate, and tuberculosis drugs; dermal interstitial fluid sampling.

Current Approaches for Dermal Drug Delivery

Active transdermal delivery systems (TDDS) aim to improve the efficiency and consistency of drug penetration into the skin. Unlike traditional topical methods, these systems apply external stimuli — such as mechanical forces, electrical currents, or physical means — to temporarily increase skin permeability, thereby enhancing the absorption of drugs and biomolecules [21].

Iontophoresis

Iontophoresis is a technique that enhances the penetration of drugs through the skin, particularly for compounds with low natural permeability or poor absorption. This method facilitates the movement of charged molecules across biological membranes by applying a mild electrical current (typically less than 0.5 mA/cm²). By leveraging electrochemical potential gradients, iontophoresis has been effectively used for the transdermal transport of both ionic and certain non-ionic drugs in vivo [22].

Several factors influence the success of this method, including the drug's charge, molecular mobility, valence, and its overall chemical properties, as well as the specific parameters of the electrical current applied. Unlike traditional drug delivery methods that are largely influenced by the body's biological variability, iontophoresis depends more on the electrical current, making its performance more predictable. Additionally, this technique can be integrated with electronic systems to prompt users to adjust their dosage schedules, thereby potentially improving adherence to treatment regimens [23].

Sonophoresis

Sonophoresis is a technique that enhances drug delivery through the skin by using ultrasonic waves. This method significantly improves transdermal drug absorption, especially when low-frequency ultrasound (typically between 20 kHz and 100 kHz) is applied, as it has been found to be more effective than high-frequency ultrasound. Key ultrasound parameters — such as intensity, duration of exposure, frequency, and pulse characteristics — all influence how well a drug penetrates through the skin barrier [24].

Clinically, sonophoresis has been utilized to deliver medications for ocular conditions and to administer enzymes like papain, as well as drugs used to manage blood pressure. Additionally, antibiotics such as tetracycline, biomycin, and penicillin have been successfully used via this method to treat various dermatological conditions. Emerging research suggests that ultrasound can dramatically increase the skin permeability of large molecules, including proteins like insulin, by up to 5000-fold, indicating its strong potential for non-invasive delivery of macromolecular therapeutics [25,26].

Magnetophoresis

Magnetophoresis, also known as magnetic drug targeting, is a method used in dermal drug delivery to direct therapeutic substances to specific skin regions with high precision. This technique utilizes externally applied magnetic fields to steer and concentrate therapeutic agents exactly where they are needed. It typically involves magnetic nanoparticles — commonly made from iron oxide — that are loaded with active compounds such as drugs or biological growth factors. These particles are then incorporated into topical delivery systems like gels or creams, allowing for controlled and localized treatment [27].

Electroporation

Electroporation is a technique that temporarily increases skin permeability by applying short bursts of high-voltage electric pulses (typically between 100 and 1000 V/cm), which create transient aqueous pores within the lipid layers of the skin barrier. This method can enhance the transdermal transport of charged molecules by up to 10,000 times compared to passive diffusion. The efficiency of delivery is influenced by both the electrical parameters used and the chemical and physical properties of the drug molecule.

Although high-voltage pulses are generally well-tolerated in vivo, they may induce muscle contractions, making electrode and patch design critical for reducing patient discomfort during treatment. Research has shown that electroporation enables the effective delivery of large and complex biomolecules — including peptides, oligonucleotides, polysaccharides, and even genetic material — through the skin [28].

Dermal Ablation

Dermal ablation involves the targeted removal or disruption of specific skin layers and is commonly used in both therapeutic and cosmetic contexts. This technique helps to improve skin appearance or prepare the skin for enhanced drug delivery. One widely used method is dermabrasion, a procedure designed to improve skin texture by carefully exfoliating the

outermost layer, thereby reducing visible imperfections such as scars and fine lines.

Other forms of dermal ablation include laser-based treatments, where focused, high-energy laser beams are applied to selectively heat or remove sections of the skin. These methods are employed not only for aesthetic improvement but also to enhance the permeability of the skin, facilitating better absorption of topically applied medications [29].

Jet Injectors

Jet injectors are needle-free delivery systems used in dermal applications to administer medications or vaccines through the skin. These devices operate by generating a high-speed, narrow stream of liquid capable of penetrating the skin and delivering therapeutic agents without the need for a traditional syringe. This method offers a valuable alternative for individuals with needle anxiety and helps minimize the risk of accidental needle injuries among healthcare professionals.

The high-pressure liquid jet enables fast and efficient drug administration, targeting the upper layers of the skin with precision and reducing discomfort often associated with conventional injections [30].

Table 1: Dermal drug delivery techniques**,** showing each method alongside its mechanism and primary application

Method	Mechanism	Key Advantage	Common Applications
Iontophoresis	Electrical current	Controlled delivery of ionic drugs	Hormones, anti-inflammatories
Sonophoresis	Ultrasound waves	Delivery of large biomolecules	Insulin, antibiotics
Magnetophoresis	Magnetic field + nanoparticles	Targeted and localized delivery	Cancer therapy, wound healing
Electroporation	High-voltage pulses	Enhanced delivery of macromolecules	Gene therapy, peptides
Dermal Ablation	Skin layer removal	Boosts skin permeability	Cosmetics, scar treatment
Jet Injectors	High-pressure fluid stream	Needle-free, quick administration	Vaccines, insulin

Chemical Enhancers

Chemical enhancers are agents used to improve drug absorption through the skin by modifying the barrier properties of the stratum corneum. These compounds function by disrupting the lipid structure, enhancing drug solubility, or increasing drug partitioning into the skin. An ideal chemical enhancer should be cost-effective, chemically stable, and possess good solvent properties. It should also be non-toxic, non-irritating, non-allergenic, and free from color, odor, or taste. Additionally, it must be pharmacologically inactive to ensure it does not interfere with the drug's therapeutic effect.

Various classes of chemical enhancers — including alcohols, fatty acids, surfactants, and terpenes — each have specific advantages and limitations in their ability to facilitate transdermal drug transport [31].

Nanocarriers

Nanocarriers—colloidal systems typically under 500 nanometers in size—offer several key advantages in transdermal drug delivery. These include enhanced physicochemical stability of encapsulated drugs, sustained and controlled release, and improved drug permeation at targeted skin sites. Due to these properties, nanocarriers have become an essential component of advanced transdermal delivery systems.

Lipid-based nanocarriers are especially prominent in this field and include various formulations such as solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), niosomes, liposomes, and nanoemulsions. These nanosystems not only aid in stabilizing drugs but also facilitate deeper and more efficient skin penetration.

Hair follicles serve as important pathways for dermal and transdermal absorption. Research indicates that the extent of follicular penetration is largely influenced by the nanoparticle size, rather than the specific type of nanoparticle used [32].

Mechanism of Dissolving Microneedles (DMNS)

The success of topical drug delivery depends on diffusion processes. In microneedle-based systems, the skin undergoes temporary disruption, allowing for

improved drug penetration. These devices contain thousands of tiny needles arranged on a small patch, similar to conventional transdermal patches, and are designed to administer precise drug doses for therapeutic effectiveness [33].

Upon application, microneedles puncture the skin and gradually dissolve, creating microchannels that facilitate drug absorption while enabling interstitial fluid to escape. Additionally, drug diffusion can occur through a dry backing layer, which becomes hydrated by interstitial fluid, enhancing the drug's movement into the skin [34].

To improve drug release efficiency, researchers are developing polymer-based microneedles with controlled-release properties. Unlike fast-dissolving variants, these microneedles slowly release drugs over time, potentially reducing side effects and decreasing the need for frequent administration. Different types have been developed, such as slow-dissolving, degradable, and bioresponsive microneedles, each offering a distinct approach to regulated drug delivery [35].

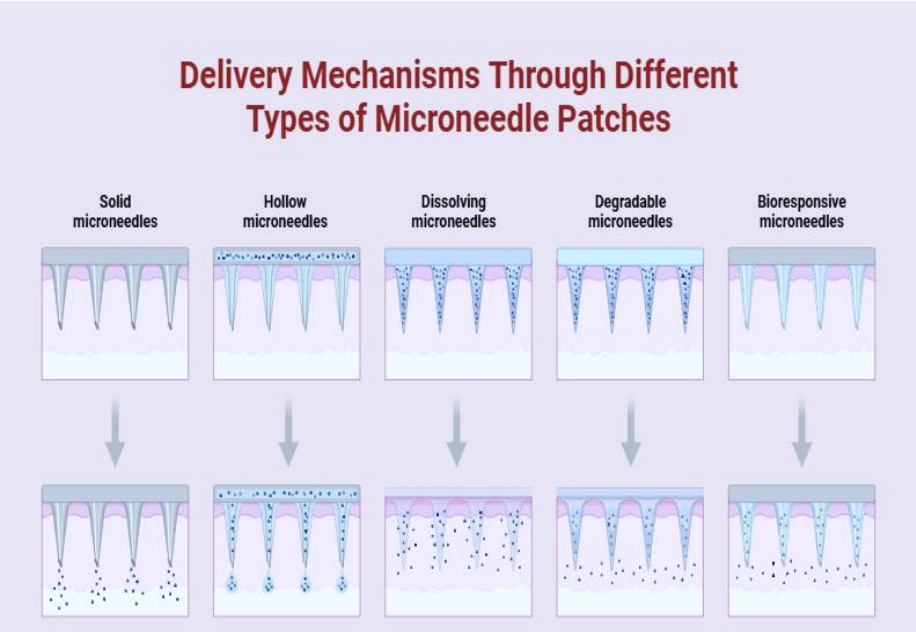

Figure 2: Graphical representation of the different types of microneedles typically discussed in the literature. Including: (a) solid, (b) hollow, (c) dissolving, (d) degradable, and (e) bioresponsive microneedles.

Biocompatibility is a key factor in ensuring the safety of DMNs, as materials must not trigger adverse skin reactions. Safety evaluations focus on using biodegradable or excretable materials to prevent long-term accumulation in tissues or organs. However, the effects of repeated microneedle use over time are still under investigation. Rotating application sites may help mitigate potential risks associated with continuous use [36].

Applications of Dissolving Microneedles

Biotherapeutic agents such as peptides, proteins, hormones, and natural compounds often face significant challenges in oral administration due to extensive first-pass metabolism. As a result, hypodermic injections remain a primary delivery route, despite the discomfort and invasiveness associated with needle use.

To address these limitations, microneedle (MN) patches have emerged as a promising alternative. These systems enable transdermal drug delivery in a minimally invasive, painless, and user-friendly manner—making them ideal for self-administration. Transdermal delivery via microneedles has thus become a focal point in therapeutic development across multiple disease areas.

Applications of Microneedles in Cosmetics

Microneedles (MNs) have emerged as a promising and innovative approach in dermatology, offering minimally invasive, cost-effective treatment options for various skin conditions. Their ability to stimulate healing through controlled physical trauma—without

altering skin morphology—has demonstrated therapeutic potential in managing atrophic scars, actinic keratoses, pigmentation disorders like melasma, alopecia, acne, and burn scars. MNs are especially effective in treating acne scars and stretch marks, with procedures involving dermarollers enhancing collagen production over multiple sessions. Compared to laser treatments, MNs provide a safer and more accessible option for managing hypertrophic and burn scars by reorganizing collagen fibers. In anti-aging therapy, MNs combined with radiofrequency (RF) and extracellular matrix compounds have shown improved results in reducing periorbital wrinkles, enhancing skin hydration, elasticity, and thickness. For hair-related disorders such as alopecia areata (AA) and androgenetic alopecia (AGA), MNs have proven beneficial by inducing collagen production and enhancing the efficacy of topical treatments like corticosteroids and minoxidil. Studies reveal that combining MNs with these agents leads to significantly better hair regrowth outcomes, earlier visible improvements, and fewer side effects compared to conventional treatments alone [37].

.

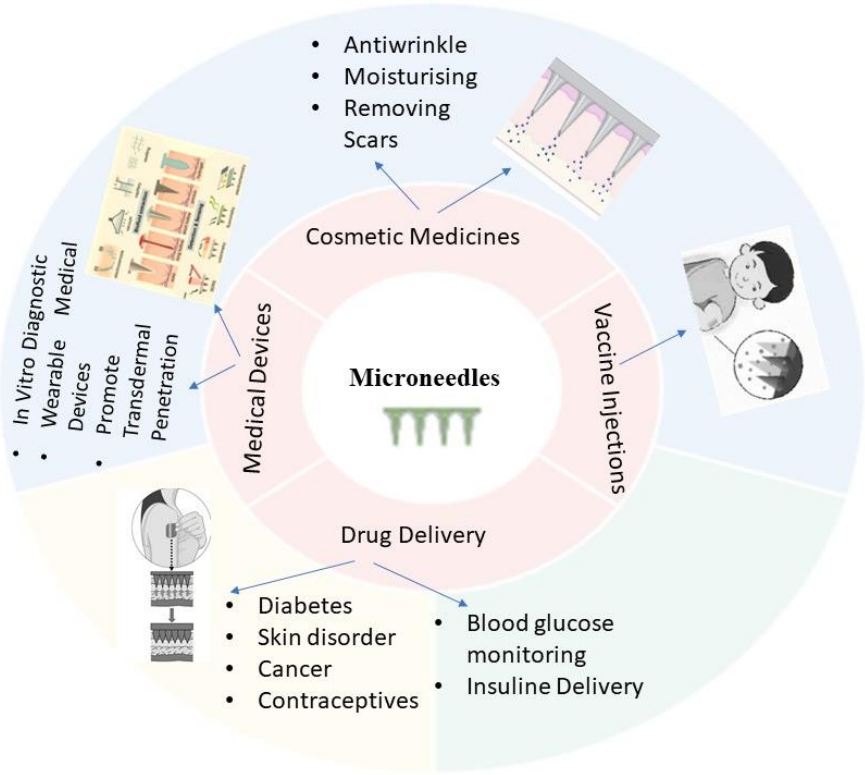

Figure 3: Application fields of MNs: drug delivery, cosmetic medicine, and medical devices.

Ophthalmic Drug Delivery (Allergic Conjunctivitis)

DMNs loaded with nano-spanlastics containing ketotifen fumarate have shown promise for localized ocular drug delivery, providing sustained drug release for allergic conjunctivitis [38].

Cancer Therapy

Conventional cancer therapies, including surgery, chemotherapy, and radiation, often result in severe side effects and do not prevent tumor relapse. In contrast, microneedle patches offer a more controlled and patient-friendly approach, combining ease of use with targeted delivery and potential for synergistic treatment effects [39].

For instance, **Dong et al.** developed microneedles composed of hyaluronic acid (HA) that dissolve upon insertion into the skin. These arrays co-deliver doxorubicin (a chemotherapy agent) and gold nanocages, enabling a combined chemotherapy and photothermal therapy approach specifically for superficial tumors [39,40].

In the field of cancer immunotherapy, **Ye et al.** introduced an HA-based microneedle system encapsulating anti-PD1 antibodies and 1-methyl-d,l-tryptophan (1-MT). This system blocks the immune-suppressive enzyme IDO and overcomes tumor immune evasion. The targeted release is triggered by the elevated hyaluronidase levels in the tumor

microenvironment, ensuring precise delivery of immune modulators [41].

Similarly, **Chen et al.** demonstrated a dissolvable microneedle patch made from poly(vinyl alcohol)/polyvinylpyrrolidone (PVA/PVP) that carries both photothermal nanoparticles and anti-cancer drugs. Their platform achieved complete eradication of 4T1 tumors within a week, with no recurrence observed [42].

To enhance cancer vaccination strategies, **van der Maaden et al.** created a hollow microneedle system for delivering synthetic long peptides as part of therapeutic cancer vaccines. Compared to conventional intradermal injections, this approach requires significantly smaller volumes, thereby improving both immune response and formulation efficacy [43].

RNA interference (RNAi) offers another innovative direction. **Tang et al.** evaluated microneedles for the delivery of siRNA directly into tumors, effectively inhibiting tumor growth by silencing specific gene targets [44].

Further expanding the scope of nucleic acid delivery, the **McCarthy group** introduced a microneedle platform using RALA peptides to encapsulate plasmid DNA encoding E6/E7 antigens. Their dissolving microneedle patch successfully delayed tumor initiation and slowed tumor progression, offering a novel route for DNA-based cancer immunotherapy [45].

Diabetes Management Using Microneedle Technologies

Managing diabetes, particularly through multiple daily insulin injections, can be complex and burdensome, often reducing patient adherence. In addition, frequent injections around mealtime increase the risk of hypoglycemia, creating an urgent need for more efficient, safer delivery methods [46].

To address these issues, **Yu et al.** developed an innovative glucose-responsive microneedle patch designed to manage type 1 diabetes by delivering insulin in a regulated and painless manner. This smart patch utilizes glucose oxidase, an enzyme that catalyzes the conversion of glucose to gluconic acid, consuming oxygen in the process. Under hyperglycemic or oxygen-deprived conditions, hydrophobic 2-nitroimidazole groups are reduced to hydrophilic 2-aminoimidazoles, causing the breakdown of hyaluronic acid-based vesicles and triggering insulin release. The system, composed of self-assembled synthetic vesicles, allows rapid and responsive insulin delivery in a needle-free format, enhancing patient comfort and safety [47].

For type 2 diabetes, **Chen et al.** introduced a pH-sensitive microneedle patch using alginate as the base material to deliver exendin-4 (Ex4), a peptide used in diabetes therapy. This patch incorporates two types of mineralized nanoparticles: one containing glucose oxidase (m-GOx), which produces hydrogen ions under high glucose conditions, and another containing Ex4 (m-Ex4), which dissolves in acidic environments to release the drug. This design enables a sequential, condition-responsive release of Ex4, minimizing the need for multiple daily doses and improving long-term glucose regulation [48].

Further advancing personalized diabetes care, **Lee et al.** created a wearable microneedle-integrated electrochemical device capable of both real-time health monitoring and therapeutic delivery. The patch continuously measures parameters such as pH, glucose concentration, humidity, and body temperature from sweat. Upon detecting abnormal glucose levels, the device thermally activates the release of metformin through the skin. Constructed from a stretchable, waterproof silicone film, the system includes multiple layers: a sweat management layer, a sensor module, and a drug delivery layer. Importantly, it transmits collected data wirelessly, enabling real-time point-of-care (POC) monitoring and personalized intervention strategies for diabetes management.

These microneedle and wearable platforms signify a major step toward non-invasive, adaptive, and patient-centric approaches to diabetes treatment, with potential to greatly enhance therapeutic outcomes and user compliance [49].

Obesity and Adipose Tissue Dynamics

Adipose tissue in the human body exists in two primary forms: **brown adipose tissue (BAT)** and **white adipose tissue (WAT)**. BAT is metabolically active and is primarily involved in generating heat, thereby contributing to increased energy expenditure. In contrast, WAT serves as a storage site for excess calories, which can lead to weight gain. Moreover, the accumulation of WAT is often associated with the production of harmful substances such as reactive oxygen species and free fatty acids, potentially worsening metabolic health.

Among natural compounds with potential anti-obesity effects, **caffeine**—commonly found in tea and coffee—has shown promising results. It has been reported to support weight management by promoting fat metabolism, without causing adverse effects in humans [50,51].

Microneedle-Based Vaccine and Antibody Delivery

Traditional vaccine and antibody administration typically relies on hypodermic, intramuscular, or intradermal injections. While effective, these methods often involve discomfort, pain, and anxiety related to needle use, which can deter some individuals from receiving vaccinations. To address these limitations, needle-free technologies—including liquid jet injectors and microneedle systems—have garnered considerable attention. These alternatives aim to reduce pain, improve patient compliance, and simplify administration. One significant challenge in traditional vaccine delivery is maintaining antigen stability, especially at elevated temperatures. Innovations in vaccine formulation, including combinations of three-component systems for hepatitis B, have shown promise in extending vaccine shelf-life and enhancing effectiveness when delivered via injection. Microneedle arrays, by creating temporary microchannels in the skin, significantly enhance the transdermal transport of vaccine compounds. For example, Ding et al. demonstrated that microneedle delivery of cholera toxin resulted in a stronger immune response than conventional intramuscular injection.

Among various microneedle types, dissolving microneedles require careful optimization to ensure complete skin penetration and timely dissolution. Li et al. reported that maltose-based microneedles could deliver monoclonal antibodies in just one minute—much faster than traditional solid microneedles, which may take up to 24 hours. These dissolvable systems are also effective for administering small amounts of hormones and organic molecules, offering a flexible platform for various therapeutic agents [51-53].

Vaccination (e.g., Influenza, Hepatitis B)

DMNs offer pain-free and self-administrable vaccine delivery. Studies demonstrate improved immune responses using DMNs for influenza and hepatitis vaccines, making mass immunization more feasible.

Hormonal Therapy

Hormone-loaded DMNs (e.g., estrogen, testosterone) have enabled controlled hormone replacement therapies for conditions such as menopause or hypogonadism, ensuring improved pharmacokinetics over oral formulations.

Psychiatric Disorders (Antipsychotic Delivery)

Long-acting injectable forms of antipsychotics delivered through DMNs can enhance patient adherence and therapeutic outcomes in schizophrenia and bipolar disorders.

Neurological Disorders (e.g., Parkinson's)

DMNs are used for delivering levodopa or dopamine agonists transdermally, bypassing gastrointestinal degradation and improving motor function consistency in Parkinson's patients.

Cosmeceuticals & Dermatology

DMNs are being increasingly adopted in cosmetic dermatology for anti-aging compounds, hyaluronic acid, and peptides, facilitating deeper skin penetration and improved efficacy.

Antibiotic Delivery

Antimicrobial peptides and antibiotics loaded into DMNs are being explored for treatment of skin infections like MRSA, enabling localized and effective bacterial eradication [54].

Personalized Medicine Platforms

Emerging work in the design of DMNs allows drug-polymer customization, enabling patient-specific drug profiles and dosages through 3D printing technologies [55].

Table 2: Examples of Different Drug Classes Potentially Suitable for the Preparation of Dissolvable Microneedles Made Exclusively from the Active Pharmaceutical Ingredient
Adapted from Patent no. WO202025021OA1

Class of Medicinal Compound	Examples of Compounds with Suitable Properties
Antifungals	Itraconazole, Clotrimazole, Ketoconazole, Fluconazole
Corticosteroids	Oestradiol, Betamethasone valerate, Testosterone
Anti-inflammatory Drugs	Celecoxib, Diclofenac, Sulindac, Indomethacin

Antimicrobials and Antibiotics	Cefuroxime axetil, Chloramphenicol
Cardiovascular and Antihypertensives	Carvedilol, Nifedipine
Autonomic Nervous System and Psychiatric Drugs	Droperidol
Antilipidemics	Probucol, Simvastatin
Gastrointestinal	Famotidine, Omeprazole
Anti-migraine	Zolmitriptan

Table 3: Microneedle in a clinical trial [56].

Disease/Condition	Therapeutic Agent	Type of MNs	Status	Phase
Oral Cavity Disease	–	Hypodermic needle	Completed	Not Applicable
Cystic Fibrosis	Pilocarpine	Pilocarpine microneedle patch	Completed	Not Applicable
Solar Lentigines	–	Ultra-Brightening Spot MN Patch	Completed	Not Applicable
COVID-19 (Vaccination/Infection)	–	Solid microneedle skin patch	Recruiting	Phase 2
Wrinkle	Hyaluronic acid	Soluble Hyaluronic Acid MN	Recruiting	Not Applicable
Skin Cancers – Squamous Cell Carcinoma	Doxorubicin	Microneedle Array Doxorubicin	Not Yet Recruiting	Phase 2
Local Anaesthesia	Lidocaine	Microneedle device (MinronJet 600)	Completed	Not Applicable
Keratosis	–	Microneedle Roller	Completed	Not Applicable
Allergic Reaction to Nickel	–	Gold-/Silver-coated or uncoated MNs	Completed	Not Applicable
Androgenetic Alopecia	Minoxidil	Microneedling Roller	Unknown	Phase 1
Acne Scar	–	Laser MN	Unknown	Not Applicable
Crow's Feet Wrinkles	–	TEOSYAL® MicronJet®	Phase 4	–
Latent Tuberculosis	–	TST vs. Patch (PDMN) Test	Not Yet Recruiting	Not Applicable
Acne Treatment	–	MicroPen + Universal Peel	Completed	Not Applicable
Whitening	–	AIV'IA Ultra-Brightening Spot MN	Recruiting	Not Applicable
Wrinkle Eliminating	–	Secret RF	Active	Not Applicable
Melasma	Trichloroacetic acid	Microneedle	Unknown	Not Applicable

Table 4: Key Recent Findings on Immunobiological Administration *via* Microneedles.

Microneedle Type	Material	Vaccine (Type)	Key Finding	Ref.
Dissolving microneedle	Hydroxyethyl starch 70000	Hepatitis B surface antigen (protein)	Maintained antigenicity for 6 months at 50 °C with only a 10% loss	57
Dissolving microneedle	Hyaluronic acid	Live attenuated BCG (bacteria)	Caused less inflammation and bruising than intradermal injection	102
Dissolving microneedle	Sucrose	Rabies vaccination (nucleic acid)	Achieved protective effect with a ten-fold lower dose than standard intramuscular	103

			injection	
Dissolving microneedle	Poly-vinyl alcohol	Influenza (virus)	Enhanced immunogenicity and potential to increase vaccine coverage	104

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethical Approval

Not applicable.

Data Availability

The raw data supporting the conclusions of this manuscript will be made available on genuine request.

Funding

This project did not receive funding from any public or private organization.

References

1. M.R. Prausnitz, R. Langer, Transdermal drug delivery, Nat. Biotechnol. 26 (11) (2008) 1261–1268.
2. Y. Gilaberte, L. Prieto-Torres, I. Pastushenko, ´ A. Juarranz, Anatomy and Function of the Skin, Elsevier, 2016, pp. 1–14.
3. R. Wong, S. Geyer, W. Weninger, J.C. Guimberteau, J.K. Wong, The dynamic anatomy and patterning of skin, Exp. Dermatol. 25 (2) (2016) 92–98.
4. K. Kabashima, T. Honda, F. Ginhoux, G. Egawa, The immunological anatomy of the skin, Nat. Rev. Immunol. 19 (1) (2019) 19–30.
5. Toulon, L. Breton, K.R. Taylor, M. Tenenhaus, D. Bhavsar, C. Lanigan, R. Rudolph, J. Jameson, W.L. Havran, A role for human skin–resident T cells in wound healing, J. Exp. Med. 206 (4) (2009) 743–750.
6. Brambilla D, Luciani P, Leroux J-C. Breakthrough discoveries in drug delivery technologies: the next 30 years. J Contr Release 2014;190:9–14.
7. Porsolt, R. D., Bertin, A., & Jalfre M(. "Behavioral despair" in mice: A primary screening test for antidepressants. Archives, 229(2), 327–336. Int Pharmacodyn Thérapie. Published online 1978.
8. Mdanda S, Ubanako P, Kondiah PP, Kumar P, Choonara YE. Recent advances in microneedle platforms for transdermal drug delivery technologies. Polymers 2021;13(15):2405.
9. Chiang B, Venugopal N, Edelhauser HF, Prausnitz MR. Distribution of particles, small molecules and polymeric formulation excipients in the suprachoroidal space after microneedle injection. Exp Eye Res 2016;153:101–9.
10. Hao Y, Li W, Zhou X, Yang F, Qian Z. Microneedles-based transdermal drug delivery systems: a review. J Biomed Nanotechnol 2017;13(12):1581–97.
11. Li QY, Zhang JN, Chen BZ, Wang QL, Guo XD. A solid polymer microneedle patch pretreatment enhances the permeation of drug molecules into the skin. RSC Adv 2017;7(25):15408–15.
12. Oliveira C, Teixeira JA, Oliveira N, Ferreira S, Botelho CM. Microneedles' Device: Design, Fabrication, and Applications. Macromol. 2024;4(2):320-355. doi:10.3390/macromol4020019
13. Yang D, Chen M, Sun Y, Jin Y, Lu C, Pan X, et al. Microneedle-mediated transdermal drug delivery for treating diverse skin diseases. Acta Biomater 2021; 121:119–33.
14. Dabholkar N, Gorantla S, Waghule T, Rapalli VK, Kothuru A, Goel S, et al. Biodegradable microneedles fabricated with carbohydrates and proteins: revolutionary approach for transdermal drug delivery. Int J Biol Macromol 2021; 170:602–21.
15. Aldawood FK, Andar A, Desai S. A comprehensive review of microneedles: types, materials, processes, characterizations and applications. Polymers 2021;13(16): 2815.
16. Shravanth SH, Osmani R, L J, Anupama VP, Rahamathulla M, Gangadharappa H. Microneedles-based drug delivery for the treatment of psoriasis. J Drug Deliv Sci Technol 2021;64:102668.
17. Carcamo-Martínez A, Mallon B, Domínguez-Robles J, Vora LK, Anjani QK, Donnelly RF. Hollow microneedles: a perspective in biomedical applications. Int J Pharm 2021;599:120455.
18. Lee KJ, Jeong SS, Roh DH, Kim DY, Choi H-K, Lee EH. A practical guide to the development of microneedle systems–In clinical trials or on the market. Int J Pharm 2020;573:118778.
19. Mahant S, Sharma AK, Gandhi H, Wadhwa R, Dua K, Kapoor DN. Emerging trends and potential prospects in vaginal drug delivery. Curr Drug Deliv 2023;20(6): 730–51.
20. Makvandi P, Maleki A, Shabani M, Hutton AR, Kirkby M, Jamaledin R, et al. Bioinspired microneedle patches: biomimetic designs, fabrication, and biomedical applications. Matter 2022;5(2):390–429.

21. Bird D, Ravindra NM. Transdermal drug delivery and patches—an overview. Medical Devices & Sensors 2020;3(6):e10069.
22. Li Y, Yang J, Zheng Y, Ye R, Liu B, Huang Y, et al. Iontophoresis-driven porous microneedle array patch for active transdermal drug delivery. Acta Biomater 2021;121:349–58.
23. Andreu A, Su P-C, Kim J-H, Ng CS, Kim S, Kim I, et al. 4D printing materials for vat photopolymerization. Addit Manuf 2021;44:102024.
24. Cevc G. Lipid vesicles and other colloids as drug carriers on the skin. Adv Drug Deliv Rev 2004;56(5):675–711.
25. Bharkatiya M, Nema R. Skin penetration enhancement techniques. J Young Pharm 2009;1(2):110.
26. Zhao YL, Murthy SN, Manjili MH, Guan L, Sen A, Hui SW. Induction of cytotoxic T lymphocytes by electroporation-enhanced needle-free skin immunization. Vaccine 2006;24(9):1282–90.
27. Denet A-R, Vanbever R, Preat V. Skin electroporation for transdermal and topical delivery. Adv Drug Deliv Rev 2004;56(5):659–74.
28. Al-Jumaily AM, Liaquat H, Paul S. Focused ultrasound for dermal applications. Ultrasound in medicine & biology. 2023.
29. Bekkers VZ, Bik L, van Huijstee JC, Wolkerstorfer A, Prens EP, van Doorn MBA. Efficacy and safety of needle-free jet injector-assisted intralesional treatments in dermatology—a systematic review. Drug delivery and translational research 2023; 13(6):1584.
30. Patzelt A, Mak WC, Jung S, Knorr F, Meinke MC, Richter H, et al. Do nanoparticles have a future in dermal drug delivery? J Contr Release 2017;246:174–82.
31. Ghasemiyeh P, Azadi A, Daneshamouz S, Heidari R, Azarpira N, Mohammadi Samani S. Cyproterone acetate-loaded nanostructured lipid carriers: effect of particle size on skin penetration and follicular targeting. Pharmaceut Dev Technol 2019;24(7):812–23.
32. Damiri F, Kommineni N, Ebhodaghe SO, Bulusu R, Jyothi VGSS, Sayed AA, Awaji AA, Germoush MO, Al-malky HS, Nasrullah MZ, Rahman MdH, Abdel-Daim MM, Berrada M (2022) Microneedle-based natural polysaccharide for drug delivery systems (DDS): progress and chal.
33. Lee JW, Park J-H, Prausnitz MR (2008) Dissolving microneedles for transdermal drug delivery. Biomaterials 29(13):2113–2124. https://doi.org/10. 1016/j.biomaterials.2007.12.048.
34. Du G, Sun X (2020) Current advances in sustained release microneedles. Pharm Fronts 02(01):e11–e22. https://doi.org/10.1055/s-0040-1701435.
35. Quinn HL, Larrañeta E, Donnelly RF (2016) Dissolving microneedles: safety considerations and future perspectives. Ther Deliv 7(5):283–285. https:// doi.org/10.4155/tde-2016-0015.
36. Amarjitsing Rajput, Anuradha Patil, Priyanka Kandhare, Atmaram Pawar, Application of microneedle arrays in cosmetics: Promises, advances, and challenges, Medicine in Novel Technology and Devices, Volume 24, 2024, 100325, ISSN 2590-0935, https://doi.org/10.
37. Elhabal, S. F., et al. (2025). Nano-spanlastics-loaded dissolving microneedle patches for ketotifen fumarate. Drug Delivery and Translational Research.
38. Hu Q, Sun W, Lu Y, Bomba HN, Ye Y, Jiang T, et al. Tumor microenvironment-mediated construction and deconstruction of extracellular drug-delivery depots. Nano Lett 2016;16:1118e26.
39. Jeanbart L, Swartz MA. Engineering opportunities in cancer immu notherapy. Proc Natl Acad Sci U S A 2015;112:14467e72.
40. Ye Y, Wang J, Hu Q, Hochu GM, Xin H, Wang C, et al. Synergistic transcutaneous immunotherapy enhances antitumor immune re sponses through delivery of checkpoint inhibitors. ACS Nano 2016; 10:8956e63.
41. Chen MC, Lin ZW, Ling MH. Near-infrared light-activatable micro needle system for treating superficial tumors by combination of chemotherapyandphotothermaltherapy. ACSNano2016;10:93e101.
42. van der Maaden K, Heuts J, Camps M, Pontier M, van Scheltinga AT, Jiskoot W, et al. Hollow microneedle-mediated micro-injections of a liposomal HPV E743-63 synthetic long peptide vaccine for efficient induction of cytotoxic and T-helper responses. J Con.
43. Tang T, Deng Y, Chen J, Zhao Y, Yue R, Choy KW, et al. Local administration of siRNA through microneedle: optimization, bio distribution, tumor suppression and toxicity. Sci Rep 2016;6:30430.
44. Ali AA, McCrudden CM, McCaffrey J, McBride JW, Cole G, Dunne NJ, et al. DNA vaccination for cervical cancer; a novel technology platform of RALA mediated gene delivery via polymeric microneedles. Nanomedicine 2017;13:921e32.
45. Hou GY, Men LH, Wang L, Zheng Z, Liu ZQ, Song FR, et al. Quantitative analysis of urinary endogenous markers for the treat ment effect of Radix Scutellariae on type 2 diabetes rats. Chin Chem Lett 2017;28:1214e9.

46. Yu J, Zhang Y, Ye Y, DiSanto R, Sun W, Ranson D, et al. Micro needle-array patches loaded with hypoxia-sensitive vesicles provide fast glucose-responsive insulin delivery. Proc Natl Acad Sci U S A 2015;112:8260e5.
47. Chen W, Tian R, Xu C, Yung BC, Wang G, Liu Y, et al. Microneedle array patches loaded with dual mineralized protein/peptide particles for type 2 diabetes therapy. Nat Commun 2017;8:1777.
48. Lee H, Choi TK, Lee YB, Cho HR, Ghaffari R, Wang L, et al. A graphene-based electrochemical device with thermoresponsive microneedles for diabetes monitoring and therapy. Nat Nanotechnol 2016;11:566e72.
49. Yoneshiro T, Matsushita M, Nakae S, Kameya T, Sugie H, Tanaka S, et al. Brown adipose tissue is involved in the seasonal variation of cold-induced thermogenesis in humans. Am J Physiol Regul Integr Comp Physiol 2016;310:R999e1009.
50. Zheng G, Sayama K, Okubo T, Juneja LR, Oguni I. Anti-obesity effects of three major components of green tea, catechins, caffeine and theanine, in mice. In Vivo 2004;18:55e62.
51. Ding Z, Verbaan FJ, Bivas-Benita M, Bungener L, Huckriede A, van den Berg DJ, et al. Microneedle arrays for the transcutaneous im munization of diphtheria and influenza in BALB/c mice. J Control Release 2009;136:71e8.
52. Li G, Badkar A, Nema S, Kolli CS, Banga AK. In vitro transdermal delivery of therapeutic antibodies using maltose microneedles. Int J Pharm 2009;368:109e15.
53. Kohale, N. B., et al. (2024). Microneedle Technology: A Promising Tool for Transdermal Drug Delivery. Biomedical & Cellular Archives. Access via EBSCOhost.
54. D'Amico, C., Ziegler, A. L., et al. (2024). Self-Nanoformulating Poly(2-oxazoline) and Poly(2-oxazine) Copolymers Based Amorphous Solid Dispersions as Microneedle Patch. Advanced Materials Technologies.
55. ClinicalTrial. Microneedles in clinicaltrials [Available from: https://clinicaltr ials.gov/. [Accessed 10 July 2024].
56. Poirier D, Renaud F, Dewar V, Strodiot L, Wauters F, Janimak J, et al. Hepatitis B surface antigen incorporated in dissolvable microneedle array patch is antigenic and thermostable. Biomaterials 2017;145: 256e65.