



International Journal of Biopharmaceutics

Journal homepage: www.ijbonline.com

IJB

MICRONEEDLE-BASED DRUG-DELIVERY SYSTEMS: INNOVATIONS AND THERAPEUTIC APPLICATIONS

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ABSTRACT

Abstract: Microneedle-based drug-delivery systems have emerged as minimally invasive platforms capable of overcoming the limitations of conventional oral and parenteral administration. These micron-sized needles penetrate the stratum corneum without reaching deeper pain receptors, enabling efficient drug transport with minimal discomfort. Microneedles are classified as solid, coated, hollow, dissolving, and hydrogel-forming systems, each offering distinct advantages for drug loading and controlled release. Recent innovations in biocompatible materials, microfabrication techniques, and stimuli-responsive designs have expanded their applications in vaccines, insulin, peptides, proteins, anticancer agents, and dermatological therapies. Microneedles can improve drug bioavailability, provide targeted or sustained release, reduce systemic adverse effects, and increase patient adherence. Their integration with biosensors also enables simultaneous disease monitoring and treatment. Despite these benefits, limitations involving mechanical strength, dose capacity, large-scale production, sterility, stability, and regulatory approval remain. Continued technological and clinical development may establish microneedles as versatile platforms for personalized and effective therapy.

Key words: Microneedles; Transdermal drug delivery; Controlled drug release; Therapeutic applications.

INTRODUCTION

Microneedle-based drug-delivery systems have emerged as innovative platforms for administering therapeutic agents across the skin in a minimally invasive, safe, and patient-friendly manner. Conventional transdermal delivery is restricted by the stratum corneum, which acts as a highly effective barrier and limits the penetration of most drugs, particularly hydrophilic compounds and high-molecular-weight biological molecules. Microneedles overcome this limitation by creating microscopic pathways through the outermost skin layer without significantly stimulating deeper pain receptors or causing extensive tissue damage. These devices generally range from a few hundred micrometres

to approximately one millimetre in length and can provide efficient drug delivery while reducing the pain, anxiety, and need for trained personnel associated with hypodermic injections. (Sekar et al., 2024) Microneedle systems are commonly classified as solid, coated, hollow, dissolving, and hydrogel-forming microneedles according to their structure, materials, and mechanisms of drug release. Recent developments in polymers, metals, ceramics, silicon, microfabrication, and nanotechnology have improved their mechanical strength, biocompatibility, drug-loading capacity, and release characteristics. Microneedles have been investigated for delivering small-molecule drugs, vaccines, insulin, peptides, proteins, nucleic acids, anticancer agents, and long-acting therapeutic formulations. Their applications extend to diabetes management, immunization, cancer therapy,

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dermatological disorders, pain management, infectious diseases, and hormonal treatment. Furthermore, the integration of microneedles with biosensors and responsive materials has enabled real-time disease monitoring, feedback-controlled drug release, and personalized treatment. (Kenchegowda et al., 2025) These systems may improve bioavailability, avoid gastrointestinal degradation and first-pass metabolism, reduce systemic adverse effects, and enhance treatment adherence. However, limited dose capacity, variable skin penetration, mechanical failure, formulation instability, sterility requirements, manufacturing complexity, and regulatory uncertainty continue to restrict widespread clinical translation. Therefore, continued interdisciplinary research is necessary to optimize microneedle design, establish standardized quality-control methods, evaluate long-term safety, and support large-scale production. This review examines the major innovations, delivery mechanisms, therapeutic applications, challenges, and future prospects of microneedle-based drug-delivery systems.

Skin Anatomy and Barriers to Transdermal Drug Delivery

The skin is a complex, multilayered organ that protects the body from physical, chemical, and biological hazards while regulating temperature and preventing excessive water loss. It consists principally of the epidermis, dermis, and hypodermis. The outermost epidermal layer, known as the stratum corneum, is approximately 10–20 μm thick and represents the primary barrier to transdermal drug transport. It contains nonviable, keratin-filled corneocytes embedded within an organized lipid matrix composed mainly of ceramides, cholesterol, and free fatty acids. (Wu et al., 2021) This “brick-and-mortar” arrangement restricts the passage of hydrophilic compounds, macromolecules, and drugs with unfavorable physicochemical properties. Beneath the stratum corneum, the viable epidermis contains living keratinocytes but lacks blood vessels, whereas the underlying dermis contains capillaries, lymphatic vessels, nerves, hair follicles, and connective tissue. Drugs reaching the dermal microcirculation can enter systemic circulation while avoiding gastrointestinal degradation and hepatic first-pass metabolism. Conventional transdermal delivery generally favors potent, moderately lipophilic molecules with low molecular weight, balanced partition coefficients, and suitable melting points. Larger molecules, including proteins, peptides, vaccines, and nucleic acids, exhibit limited passive penetration. Skin thickness, hydration, age, anatomical location, disease, temperature, and interindividual variability further influence drug permeation. Hair follicles and sweat glands provide alternative pathways, but their limited surface area restricts their overall contribution. (Hashemi et al., 2024) Microneedles

overcome these biological barriers by creating temporary aqueous microchannels through the stratum corneum while minimizing contact with deeper pain receptors and blood vessels. These microchannels permit the delivery of substances that cannot cross intact skin efficiently. The resulting permeability enhancement depends on microneedle geometry, insertion depth, application force, formulation characteristics, and channel-closure time. Understanding skin structure and barrier function is therefore essential for designing microneedles that achieve reproducible penetration, appropriate drug deposition, minimal irritation, and effective local or systemic therapy.

Materials Used in Microneedle Fabrication

Material selection is a fundamental consideration in microneedle development because it determines mechanical strength, biocompatibility, drug compatibility, manufacturing feasibility, and release behavior. Early microneedles were commonly fabricated from silicon because established microelectronics techniques permitted precise control over dimensions and geometry. However, silicon is brittle, relatively expensive, and may fracture during insertion, raising concerns about retained fragments in the skin. Metals such as stainless steel, titanium, nickel, and palladium provide high mechanical strength and are particularly suitable for solid, coated, and hollow microneedles. Stainless steel and titanium are widely preferred because of their established medical use, corrosion resistance, and ability to withstand insertion forces. (Haider et al., 2023) Nevertheless, metallic microneedles may require complex manufacturing and careful evaluation of nickel sensitivity, coating uniformity, and safe disposal. Ceramics, including alumina and calcium phosphate, offer chemical stability, hardness, and potential biodegradability, but their brittleness can complicate production. Biodegradable and water-soluble polymers have become increasingly important for dissolving and hydrogel-forming microneedles. Frequently investigated materials include polyvinylpyrrolidone, polyvinyl alcohol, polylactic acid, polyglycolic acid, hyaluronic acid, carboxymethyl cellulose, chitosan, dextran, maltose, and sodium alginate. These materials can encapsulate drugs within the microneedle matrix and dissolve or swell following insertion, eliminating sharp waste and reducing fracture-related risks. Natural polymers generally provide favorable biocompatibility, whereas synthetic polymers offer greater control over mechanical and release properties. Sugars are also used because of their rapid dissolution, although heat sensitivity, hygroscopicity, and limited mechanical stability can present challenges. (Gera & Burra, 2022) Composite materials, nanoparticle-reinforced polymers, and stimuli-responsive hydrogels are being developed to combine adequate strength with controlled drug release. Selection

should account for toxicity, sterilization compatibility, moisture sensitivity, storage stability, degradation products, and scalability. Accordingly, successful microneedle fabrication requires balancing mechanical performance with biological safety, pharmaceutical functionality, and cost-effective manufacture.

Microfabrication and Manufacturing Techniques

Microneedle fabrication requires precise manufacturing methods capable of controlling needle length, tip sharpness, base diameter, spacing, internal structure, and overall array geometry. Traditional microfabrication techniques were adapted from the semiconductor industry and include photolithography, wet and dry etching, deep reactive-ion etching, laser cutting, and micromachining. Photolithography creates patterned masks on silicon substrates, while chemical or plasma-based etching removes selected material to produce accurately shaped needles. These techniques offer excellent dimensional control but may involve expensive equipment, clean-room facilities, multiple processing stages, and hazardous reagents. Metal microneedles can be manufactured using laser cutting, laser ablation, electroplating, wire-electrical-discharge machining, and metal injection molding. (Tan, 2025) After cutting, needles may be bent out of the substrate plane and sharpened through electropolishing or chemical treatment. Hollow microneedles require additional processes to form internal channels and openings without compromising mechanical integrity or fluid flow. Micromolding has become a widely used approach for producing polymeric, dissolving, and hydrogel-forming microneedles. In this method, a master structure is prepared and replicated using flexible molds, commonly made from polydimethylsiloxane. Drug-polymer formulations are introduced into mold cavities through centrifugation, vacuum application, pressure, or casting before drying and removal. Micromolding is comparatively economical, scalable, and compatible with temperature-sensitive therapeutic agents. Three-dimensional printing techniques, including stereolithography, digital light processing, two-photon polymerization, and fused deposition modeling, provide rapid prototyping and enable complex, patient-specific geometries. However, printing resolution, residual monomers, material selection, and production speed require careful optimization. (Wallis et al., 2020) Injection molding, hot embossing, and roll-to-roll processing are being explored for high-volume manufacture. Essential process controls include mold filling, drying conditions, dimensional consistency, tip formation, drug distribution, and microbial contamination. Industrial translation ultimately requires reproducible fabrication under good manufacturing practices, validated in-process controls, automated inspection, scalable packaging, and manufacturing

methods that preserve both microneedle integrity and therapeutic activity.

Drug Loading and Controlled-Release Strategies

Drug loading in microneedle systems is determined by microneedle type, therapeutic dose, drug stability, intended release pattern, and site of action. In solid microneedle systems, the skin is first punctured to create microchannels, after which a conventional formulation such as a gel, cream, solution, or transdermal patch is applied. Although this “poke-and-patch” strategy separates drug formulation from the device, microchannel closure and variable application can influence delivery. Coated microneedles carry the active pharmaceutical ingredient as a thin surface layer that rapidly dissolves after insertion. Coating formulations may contain viscosity enhancers, surfactants, stabilizers, and film-forming agents, but their loading capacity is limited by the available needle surface area. Hollow microneedles transport liquid formulations through internal channels using pressure, diffusion, or pump-assisted infusion, enabling dose adjustment but creating risks of leakage, blockage, or tissue compression. (Adeyemi, 2019) Dissolving microneedles incorporate drugs directly into water-soluble or biodegradable polymer matrices. Following insertion, interstitial fluid hydrates the matrix and releases the payload as the needles dissolve. Drug localization within needle tips can improve delivery efficiency and reduce wastage in the supporting base. Hydrogel-forming microneedles absorb interstitial fluid and swell to establish pathways through which drugs diffuse from an attached reservoir. Controlled release can be achieved by altering polymer composition, molecular weight, cross-linking density, porosity, degradation rate, needle geometry, or drug-polymer interactions. Nanoparticles, liposomes, nanoemulsions, microspheres, and inclusion complexes may be incorporated to protect unstable drugs and modify release kinetics. Layered, core-shell, and separable microneedles can provide biphasic, sustained, or sequential delivery. Stimuli-responsive systems release drugs in response to glucose, pH, temperature, light, enzymes, or inflammatory biomarkers. (Dick et al., 2020) Successful formulation requires uniform drug distribution, accurate dosing, adequate mechanical strength, and protection from heat, moisture, oxidation, and processing stress. Thus, rational integration of formulation science and device engineering is essential for achieving reproducible loading and clinically appropriate drug-release profiles.

Mechanical Strength, Skin Penetration, and Performance Evaluation

Microneedles must possess sufficient mechanical strength to penetrate the stratum corneum without bending, buckling, or fracturing while remaining

safe and comfortable for patients. Their mechanical behavior depends on material properties, needle length, base width, tip radius, aspect ratio, geometry, array density, and fabrication quality. Long or slender needles may provide deeper penetration but are more vulnerable to deformation, whereas wider needles generally offer greater strength but may increase tissue disruption. Mechanical testing commonly involves axial compression using a texture analyzer or universal testing machine to measure failure force and deformation. The force required for structural failure should substantially exceed the force experienced during application. Transverse testing may also be performed to evaluate bending resistance. (Tsuboko et al., 2024) Skin penetration is assessed using human or animal skin, synthetic membranes, multilayer films, or polymeric skin models. Common techniques include histological examination, optical coherence tomography, confocal microscopy, scanning electron microscopy, and staining of microchannels with dyes. Transepidermal water loss and electrical impedance measurements can provide indirect evidence of barrier disruption. Parafilm-based models are useful for preliminary comparisons, although they do not completely reproduce the elasticity and biological complexity of human skin. Insertion efficiency is influenced by application force, velocity, duration, supporting patch flexibility, and skin tension. Performance evaluation should also determine drug content, content uniformity, dissolution or swelling time, insertion depth, drug deposition, permeation rate, microbial limits, sterility, and stability. In vitro diffusion studies commonly use Franz diffusion cells, while pharmacokinetic and pharmacodynamic studies assess systemic exposure and therapeutic activity. (Takizawa et al., 2020) Skin recovery, erythema, edema, irritation, pain, infection risk, and channel-closure time should be examined during safety testing. Because no single model fully predicts clinical performance, a combination of mechanical, analytical, ex vivo, and in vivo methods is required. Standardized testing procedures and clinically relevant acceptance criteria are essential for comparing products, controlling batch quality, and supporting regulatory approval.

Delivery of Small-Molecule Drugs

Microneedles provide an effective approach for delivering small-molecule drugs that exhibit poor oral bioavailability, extensive first-pass metabolism, gastrointestinal instability, short biological half-lives, or inadequate passive skin permeability. Although conventional transdermal patches are suitable for selected lipophilic and potent drugs, the intact stratum corneum prevents efficient transport of many hydrophilic, ionized, or moderately sized compounds. Microneedles create temporary microchannels that enable these drugs to reach the viable epidermis or dermis, from which they may act

locally or enter systemic circulation. Small molecules can be administered through solid microneedle pretreatment followed by topical formulation, surface-coated arrays, hollow systems containing drug solutions, or dissolving microneedles that encapsulate drugs within polymer matrices. (Gandhat et al., 2025) Analgesics, local anesthetics, antihypertensives, contraceptives, antimicrobials, anti-inflammatory agents, and dermatological medicines have been investigated using these platforms. For rapid therapy, coated or rapidly dissolving microneedles can release drug within minutes. Sustained delivery may be achieved using slowly degrading polymers, cross-linked hydrogels, nanoparticles, microspheres, or drug reservoirs connected to hydrogel-forming arrays. Localized delivery can produce high drug concentrations at diseased skin sites while reducing systemic exposure and adverse reactions. In systemic therapy, microneedles may provide controlled plasma concentrations and reduce fluctuations associated with repeated oral doses. Drug candidates must nevertheless possess adequate potency because the limited dimensions of microneedle arrays restrict loading capacity. Crystallization, polymer incompatibility, chemical degradation, and uneven distribution can further affect dose accuracy and release. (Filho et al., 2023) Formulators may use solubilizers, cyclodextrins, salts, amorphous dispersions, or nanocarriers to improve loading and stability. Pharmacokinetic assessment is necessary because delivery rate depends on insertion efficiency, skin condition, formulation dissolution, and microchannel closure. By combining minimally invasive administration with adaptable release profiles, microneedles can broaden the range of small molecules suitable for transdermal delivery and improve convenience, adherence, and therapeutic effectiveness.

Delivery of Proteins, Peptides, and Biological Therapeutics

Proteins, peptides, antibodies, enzymes, and nucleic-acid-based therapeutics offer high specificity and substantial clinical value but are difficult to administer through conventional routes. Oral delivery is limited by enzymatic degradation, acidic conditions, poor intestinal permeability, and variable absorption, making repeated injections necessary for many biological products. Microneedles bypass the gastrointestinal tract and cross the stratum corneum through microscopic pathways, enabling biological therapeutics to reach viable skin layers while causing minimal discomfort. Coated microneedles can rapidly deliver potent biomolecules deposited on their surfaces, whereas dissolving microneedles protect and release encapsulated agents after contact with interstitial fluid. Hollow microneedles permit infusion of larger liquid doses, and hydrogel-forming devices can draw fluid from an external reservoir to support sustained delivery. Investigated payloads

include insulin, growth hormone, parathyroid hormone, monoclonal antibodies, erythropoietin, desmopressin, interferons, enzymes, DNA, messenger RNA, small interfering RNA, and gene-editing components. (Sekar et al., 2024) A major formulation challenge is preserving biological structure and activity during mixing, casting, drying, storage, sterilization, and release. Exposure to heat, organic solvents, interfaces, mechanical stress, moisture, and extreme pH may cause aggregation, oxidation, deamidation, or denaturation. Stabilizers such as trehalose, sucrose, mannitol, amino acids, surfactants, and buffering agents can improve stability. Low-temperature and vacuum-assisted manufacturing techniques may further protect sensitive molecules. Delivery efficiency also depends on molecular size, charge, tissue binding, degradation within the skin, and access to dermal capillaries or immune cells. Biomolecule loading is often limited by the small needle volume, requiring concentrated formulations or drug localization within the tips. Immunogenicity, local reactions, dose reproducibility, and long-term storage must be evaluated carefully. Despite these challenges, microneedles could reduce dependence on injections, simplify self-administration, improve adherence, and enable stable biological formulations that require less intensive cold-chain infrastructure.

Microneedle-Based Vaccine Delivery

Microneedle-based vaccination is a promising alternative to conventional intramuscular or subcutaneous injection because the skin contains abundant antigen-presenting cells, including Langerhans cells and dermal dendritic cells. Delivery of antigens to these immune-rich layers can induce strong humoral and cellular responses while potentially reducing the antigen dose required for protection. Coated microneedles deposit vaccine material rapidly after insertion, whereas dissolving microneedles release encapsulated antigens as their polymeric structures dissolve. Hollow microneedles can administer liquid vaccines intradermally, and solid devices may create microchannels before topical vaccine application. (Qiao et al., 2025) Microneedles have been investigated for influenza, hepatitis, measles, rubella, tuberculosis, polio, human papillomavirus, coronavirus disease, and other infectious diseases. They have also been studied for cancer vaccines and allergen-specific immunotherapy. Several advantages make these systems attractive for mass vaccination. Their minimally invasive nature may reduce needle fear, pain, and the requirement for highly trained personnel. Patch-like products can potentially support self-administration and simplify distribution during outbreaks. Dissolving devices leave no sharp waste, reducing needle-stick injuries, reuse, and transmission of blood-borne infections. Dry vaccine formulations may demonstrate improved thermal stability compared with liquid injections, thereby decreasing

dependence on refrigerated storage and transportation. However, vaccine potency must be preserved during fabrication, drying, sterilization, packaging, and prolonged storage. Accurate antigen loading, adjuvant compatibility, consistent skin insertion, and complete dose delivery are essential. (Bajwa et al., 2024) Skin pigmentation, age, anatomical site, immune status, and application technique may contribute to variability. Local redness, swelling, itching, and sensitization should also be evaluated. Regulatory assessment must consider both the vaccine and delivery device as an integrated product. With standardized manufacturing, applicator design, stability testing, and clinical validation, microneedle vaccine patches could increase immunization coverage, improve outbreak preparedness, and facilitate vaccination in remote or resource-limited settings.

Applications in Diabetes Management

Diabetes management frequently requires repeated blood-glucose monitoring and subcutaneous insulin injections, which may cause discomfort, fear, inconvenience, and poor treatment adherence. Microneedle technology offers minimally invasive strategies for insulin administration, glucose monitoring, and closed-loop therapy. Dissolving microneedles can encapsulate insulin within biocompatible polymers and release it after insertion into the skin. Hollow microneedles deliver liquid insulin into the viable epidermis or dermis, where abundant capillaries may promote rapid absorption. Hydrogel-forming microneedles can connect the skin to an insulin-containing reservoir, supporting prolonged administration without leaving polymer residues. Compared with conventional injections, these systems may reduce pain, simplify self-administration, and improve patient acceptance. More advanced “smart” microneedles are designed to release insulin in response to elevated glucose concentrations. Glucose-responsive mechanisms may employ glucose oxidase, phenylboronic acid derivatives, hypoxia-sensitive materials, or glucose-binding molecules. (Zahoor et al., 2021) When glucose increases, chemical or structural changes within the microneedle trigger insulin release, potentially reducing the risk of hypoglycaemia caused by excessive dosing. Microneedles can also sample dermal interstitial fluid for glucose measurement. Integration with electrochemical sensors, wearable electronics, wireless communication, and automated control algorithms could enable continuous monitoring and feedback-regulated insulin delivery. Nevertheless, significant challenges remain. Insulin must retain its biological activity during fabrication and storage, while each device must provide sufficient loading and reproducible delivery. Differences between interstitial-fluid and blood-glucose concentrations, physiological time lag, sensor drift, skin variability, and device adhesion may affect accuracy.

Glucose-responsive systems require rapid, reversible, and predictable behavior across clinically relevant glucose ranges. Biocompatibility of enzymes, nanoparticles, and degradation products must also be established. (Vats et al., 2025)Regulatory evaluation of combined sensor–drug devices is particularly complex. Continued research into stability, dose capacity, response kinetics, and long-term safety may allow microneedles to reduce the daily burden of diabetes management and support more personalized glycaemic control.

Applications in Cancer Therapy

Microneedle systems are increasingly being investigated in cancer therapy because they can deliver therapeutic agents directly to accessible tumors or immune-rich skin tissues while limiting systemic exposure. Conventional chemotherapy frequently produces dose-limiting toxicity because cytotoxic drugs circulate throughout the body and damage healthy tissues. Microneedles may concentrate drugs within localized lesions, particularly in melanoma, basal-cell carcinoma, squamous-cell carcinoma, and other superficial malignancies. Dissolving microneedles can encapsulate chemotherapeutic drugs, immune modulators, proteins, nucleic acids, or nanoparticles and release them after insertion. Hollow microneedles enable localized infusion, while hydrogel-forming systems may support prolonged administration from an attached reservoir. Drugs such as doxorubicin, paclitaxel, cisplatin, 5-fluorouracil, and immune-checkpoint-related agents have been explored in experimental microneedle platforms. Nanoparticles, liposomes, micelles, and nanoemulsions may be incorporated to improve solubility, cellular uptake, tissue retention, and controlled release.(Singh & Shukla, 2024) Microneedles can also deliver tumor antigens, adjuvants, cytokines, messenger RNA, small interfering RNA, and immune-stimulating compounds to activate local and systemic antitumor immunity. Stimuli-responsive devices may release their payloads in response to acidic pH, tumor-associated enzymes, reactive oxygen species, light, heat, or other features of the tumor microenvironment. Combination systems can integrate chemotherapy, photothermal therapy, photodynamic therapy, and immunotherapy within one patch. However, tumor heterogeneity, irregular tissue architecture, variable penetration, restricted loading capacity, and incomplete distribution may limit effectiveness. Some cancers are too deep or inaccessible for direct microneedle application. The stability of biological agents, safety of nanomaterials, local inflammation, and reproducibility of dosing also require careful investigation. Clinical translation will depend on demonstrating meaningful therapeutic benefit, consistent manufacturing, acceptable tolerability, and compatibility with existing oncology treatments. Properly designed microneedle platforms may ultimately provide

localized, sustained, and personalized cancer therapy with reduced systemic toxicity.

Microneedle-Based Biosensing and Theranostic Applications

Microneedles can access dermal interstitial fluid, a biological fluid containing metabolites, electrolytes, proteins, biomarkers, and drug molecules that reflect physiological and pathological conditions. This capability has encouraged the development of minimally invasive biosensors for continuous or periodic health monitoring. Hollow microneedles can withdraw small fluid volumes for external analysis, whereas porous and hydrogel-forming microneedles collect interstitial fluid through capillary action or swelling. Sensor-equipped solid microneedles can directly measure analytes within the skin using electrochemical, optical, colorimetric, or fluorescence-based techniques. Glucose monitoring is the most extensively studied application, but microneedle sensors have also been investigated for lactate, alcohol, electrolytes, pH, cortisol, inflammatory markers, therapeutic drugs, and disease-associated proteins. Integration with flexible electronics, microfluidic channels, smartphones, and wireless communication systems may provide real-time data and remote clinical monitoring. Theranostic microneedles combine diagnostic sensing with therapeutic delivery in a single platform. Such systems may detect a biomarker, process the signal, and release an appropriate drug dose through feedback-controlled mechanisms. (Zeng et al., 2023)Glucose-responsive insulin patches represent a leading example, while experimental systems are being developed for infection, inflammation, wound healing, cancer, and pain management. Smart materials can respond to pH, enzymes, temperature, light, reactive oxygen species, or electrical signals to regulate drug release. Despite their promise, interstitial-fluid concentrations may not always correspond directly to blood values, and physiological delays can affect clinical interpretation. Biofouling, sensor drift, calibration requirements, small sample volumes, tissue reactions, and motion-related artifacts may impair accuracy. Devices must also maintain skin contact, mechanical integrity, and sterility during extended use. Power supply, data security, wireless reliability, and integration of sensing and delivery components add further complexity. Rigorous validation against established clinical methods is essential. With improvements in analytical sensitivity, materials, electronics, and closed-loop control, microneedle theranostic systems may support personalized treatment and decentralized healthcare.

Regulatory Considerations and Manufacturing Challenges

The regulatory development of microneedle products is complex because these systems may be

classified as medical devices, medicinal products, or drug-device combination products depending on their composition, mechanism, and intended use. A solid microneedle used for skin pretreatment may be evaluated primarily as a device, whereas dissolving or coated microneedles containing active pharmaceutical ingredients require assessment of both formulation and device performance. Developers must establish the identity, strength, purity, quality, safety, and efficacy of the drug while demonstrating mechanical integrity, reliable insertion, accurate dosing, and safe skin recovery. (Nguyen, 2023) Critical quality attributes include needle dimensions, tip sharpness, array uniformity, failure force, insertion efficiency, drug content, content uniformity, dissolution or swelling behavior, release kinetics, microbial limits, and package integrity. Biocompatibility testing should evaluate cytotoxicity, sensitization, irritation, tissue damage, inflammation, degradation products, and risks associated with retained fragments. Sterilization presents a major challenge because heat, radiation, ethylene oxide, or other processes may alter polymers, weaken needles, degrade drugs, or reduce biological activity. Aseptic manufacture may therefore be necessary for sensitive products. Large-scale production must reproduce laboratory-level geometry and performance at commercially acceptable speeds and costs. Polymer viscosity, mold filling, drying, demolding, environmental humidity, and drug migration can cause batch variability. Automated optical and mechanical inspection methods are needed to identify incomplete needles, damaged tips, coating defects, and dimensional deviations. (Kumar Sarella et al., 2024) Packaging must protect microneedles from moisture, contamination, physical damage, and accidental use while remaining convenient for patients. Human-factors studies should evaluate application force, placement, wear time, removal, disposal, and the potential for misuse. Clinical trials must demonstrate consistent dose delivery across different skin types, ages, and anatomical sites. Limited harmonization of testing standards and regulatory expectations continues to slow development. Early engagement with regulatory authorities, quality-by-design principles, validated manufacturing processes, and internationally accepted performance standards will be essential for successful commercialization and widespread clinical adoption.

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CONCLUSION

Microneedle-based drug-delivery systems represent a significant advancement in pharmaceutical technology by combining the therapeutic effectiveness of injectable administration with the convenience and acceptability of transdermal delivery. By creating microscopic pathways across the stratum corneum, microneedles can deliver small-molecule drugs, proteins, peptides, vaccines, insulin, nucleic acids, anticancer agents, and other biological therapeutics that cannot efficiently penetrate intact skin. Solid, coated, hollow, dissolving, and hydrogel-forming microneedles offer distinct mechanisms of administration and can be adapted for rapid, sustained, localized, or stimuli-responsive drug release. Innovations in biodegradable polymers, microfabrication, nanotechnology, biosensors, and wearable electronics have further expanded their potential in vaccination, diabetes management, cancer therapy, dermatological treatment, disease monitoring, and personalized medicine. Their minimally invasive nature may reduce pain, needle-related anxiety, accidental injuries, and dependence on trained healthcare professionals while improving patient adherence and supporting self-administration. Nevertheless, several technical and regulatory challenges must be addressed before widespread clinical adoption. These include restricted drug-loading capacity, variable skin penetration, inadequate mechanical strength, biomolecule instability, sterilization difficulties, large-scale manufacturing limitations, and the absence of fully harmonized quality standards. Comprehensive evaluation of insertion performance, dose accuracy, biocompatibility, skin recovery, storage stability, and long-term safety remains essential. Regulatory frameworks must also account for the combined pharmaceutical and device-related characteristics of microneedle products. Future research should focus on scalable manufacturing, standardized testing, improved applicator designs, greater loading efficiency, and reliable closed-loop systems that integrate diagnosis with treatment. Well-designed clinical trials involving diverse patient populations will be necessary to confirm therapeutic benefits and user acceptability. With continued collaboration among pharmaceutical scientists, engineers, clinicians, manufacturers, and regulatory authorities, microneedles have the potential to transform conventional drug administration and become versatile platforms for safer, more precise, and patient-centred therapy.

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