

A Review on Puncturing Potential: Microneedles' Present Landscape And Prospective Horizons

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ABSTRACT

Microneedle technology has emerged as a promising approach for drug delivery, vaccination, diagnostics, and cosmetic treatments. This review provides an overview of microneedle technology, covering the various types of microneedles, fabrication techniques, applications, advantages, challenges, safety considerations, clinical translation, and future perspectives. Solid, hollow, dissolving, coated, and hydrogel-forming microneedles are discussed, along with their structures, materials, and fabrication methods. Applications in drug delivery, vaccination, diagnostics, and cosmetic treatments are explored, with an emphasis on emerging and novel uses. The review highlights the advantages of microneedle technology, including enhanced patient compliance, improved drug absorption, and reduced pain, as well as challenges such as manufacturing scalability and regulatory approval. Fabrication techniques, biocompatibility, safety issues, clinical translation, and commercialization aspects are examined, along with future directions and emerging trends such as multifunctional microneedles and personalized medicine. Overall, microneedle technology holds tremendous promise for revolutionizing healthcare and biomedical engineering, but further research and development are required to address current challenges and realize its full potential.

Keywords: Microneedles, drug delivery, vaccination, diagnostics, fabrication techniques, biocompatibility, clinical translation, future perspectives.

1. INTRODUCTION

1.1. Definition and Overview of Microneedle Technology:

Microneedle technology represents a breakthrough in drug delivery and biomedical engineering, offering a minimally invasive approach to administer therapeutics, vaccines, and diagnostics through the skin. These micron-scale structures, typically ranging from hundreds of micrometers to a few millimeters in length, puncture the

outermost layer of the skin, known as the stratum corneum, to facilitate the delivery of bioactive compounds. Microneedles can be categorized into various types, including solid, hollow, dissolving, coated, and hydrogel-forming microneedles, each designed to address specific applications and requirements.

The development of microneedles has garnered significant interest due to their potential to overcome limitations associated with traditional drug delivery methods, such as oral administration and injections(1). They offer several advantages, including enhanced patient compliance, improved drug absorption, reduced pain and discomfort, and the ability to deliver a wide range of therapeutics, including small molecules, proteins, nucleic acids, and vaccines.

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Moreover, microneedles have shown promise in enabling targeted and controlled delivery of drugs, thereby minimizing systemic exposure and side effects(2).

1.2. Importance of Microneedles in Biomedical Engineering

Microneedles play a pivotal role in advancing biomedical engineering by offering innovative solutions to longstanding challenges in drug delivery and healthcare(3). Their importance stems from their ability to overcome the limitations of traditional delivery methods, such as oral administration and injections, by providing a minimally invasive and targeted approach for delivering therapeutics, vaccines, and diagnostics. This capability has significant implications for improving patient compliance, enhancing drug efficacy, and reducing side effects. In biomedical engineering, microneedles serve as versatile tools for delivering a wide range of substances, including small molecules, proteins, nucleic acids, and vaccines, across diverse patient populations and medical contexts. Their adaptability enables tailored approaches to address specific healthcare needs, such as personalized medicine, where precise dosing and targeted delivery are critical. Moreover, microneedles contribute to the development of wearable and implantable medical devices, enabling continuous monitoring and treatment of chronic conditions(4). Their integration with advanced materials, biosensors, and microelectronics opens new avenues for real-time diagnostics, therapy monitoring, and feedback-controlled drug delivery systems.

2. TYPES OF MICRONEEDLES

2.1. Solid Microneedles

Solid microneedles represent a significant advancement in drug delivery technology, offering a minimally invasive approach for transdermal delivery of therapeutics, vaccines, and diagnostics. These micron-scale structures, typically made of biocompatible materials such as silicon, polymers, or metals, feature sharp tips designed to penetrate the skin's outermost layer, the

stratum corneum, without causing pain or tissue damage. Solid microneedles function by creating microchannels in the skin, allowing drugs to permeate through and reach the underlying tissue or systemic circulation. Unlike traditional hypodermic needles, solid microneedles do not require specialized handling or disposal procedures, making them safer and more convenient for both patients and healthcare providers. Furthermore, they offer precise control over drug dosage and release kinetics, enabling tailored treatment regimens and improved therapeutic outcomes. Solid microneedles have shown promise in a variety of applications, including insulin delivery for diabetes management, vaccination against infectious diseases, and transdermal administration of biologics and small molecules. Ongoing research aims to optimize microneedle design, fabrication techniques, and drug formulations to enhance their efficacy, stability, and patient acceptability(5).

2.2. Hollow Microneedles

Hollow microneedles are innovative devices designed to overcome the limitations of traditional injections by providing a minimally invasive and painless method for delivering drugs, vaccines, and other bioactive compounds. Unlike solid microneedles, hollow microneedles feature channels or lumens that allow fluids to be delivered directly into the skin or withdrawn from the body. These micron-scale needles, typically made of materials like silicon, polymers, or metals, offer several advantages, including precise control over drug dosage and delivery kinetics, reduced tissue damage, and improved patient comfort. Hollow microneedles can be used to administer a wide range of substances, including small molecules, biologics, and nanoparticles, with applications spanning from local anaesthesia and insulin delivery to vaccination and diagnostic sampling. The versatility of hollow microneedles makes them promising tools for various medical applications, including point-of-care diagnostics, continuous monitoring, and targeted drug delivery. Ongoing research focuses on optimizing

microneedle design, fabrication methods, and integration with advanced technologies such as microfluidics and biosensors to enhance their performance and functionality(6, 7).

2.3. Dissolving Microneedles

Dissolving microneedles are an innovative drug delivery technology that offers a painless and convenient approach for administering therapeutics, vaccines, and diagnostics. These micron-scale needles are typically composed of biocompatible polymers or sugar-based materials and are designed to dissolve or disintegrate upon insertion into the skin, releasing encapsulated drugs or payloads. Dissolving microneedles offer several advantages over traditional delivery methods, including improved patient compliance, reduced risk of needlestick injuries, and simplified disposal procedures. By bypassing the skin's stratum corneum and directly delivering drugs into the epidermis or dermis, they enable enhanced drug absorption and bioavailability, leading to improved therapeutic outcomes. These microneedles can be tailored to accommodate a wide range of drugs, including small molecules, biologics, and vaccines, with precise control over drug release kinetics and dosage. They have shown promise in various applications, such as pain management, vaccination campaigns, and point-of-care diagnostics, where their ease of use and rapid onset of action offer significant advantages(7).

2.4. Coated Microneedles

Coated microneedles are a cutting-edge drug delivery technology designed to enhance the efficiency and precision of transdermal drug delivery. These micron-scale needles are typically fabricated from biocompatible materials such as polymers or metals and are coated with drug-loaded or functionalized layers. The coating on these microneedles serves multiple purposes, including protecting the drug payload from degradation, controlling drug release kinetics, and targeting specific sites within the skin. Additionally, coatings can be engineered to enhance the mechanical properties of the microneedles, facilitating

their insertion into the skin and ensuring optimal drug delivery(8). Coated microneedles offer several advantages over traditional delivery methods, including improved patient comfort, reduced risk of tissue damage, and enhanced bioavailability of drugs. By bypassing the skin's protective barrier and directly delivering drugs into the dermis or systemic circulation, they enable rapid onset of action and precise control over drug dosage. These microneedles have shown promise in a wide range of applications, including the delivery of small molecules, biologics, and vaccines, as well as in diagnostics and cosmetic treatments. Ongoing research in coated microneedles focuses on optimizing coating formulations, enhancing drug stability, and expanding their applicability to various therapeutic areas(8).

2.5. Hydrogel-forming Microneedles

Hydrogel-forming microneedles represent an innovative approach to transdermal drug delivery, combining the advantages of microneedle technology with the properties of hydrogels. These micron-scale needles are typically fabricated from biocompatible polymers that can absorb water and swell upon insertion into the skin, forming a hydrogel matrix that encapsulates and releases drugs. The unique properties of hydrogel-forming microneedles offer several advantages over conventional drug delivery methods. They provide a painless and minimally invasive approach for administering therapeutics, vaccines, and diagnostics, while also enabling controlled and sustained release of drugs over time. The hydrogel matrix formed within the skin enhances drug bioavailability and tissue penetration, leading to improved therapeutic efficacy. Hydrogel-forming microneedles are highly versatile and can be tailored to accommodate a wide range of drugs, including small molecules, biologics, and nanoparticles. They have shown promise in various applications, such as chronic disease management, vaccination campaigns, and cosmetic treatments, where their ease of use and precise drug delivery offer significant advantages(9).

2.6. Comparison of Different Microneedle Types

Table No:1 A Comprehensive Review of Microneedle Technologies for Transdermal Drug Delivery

Microneedle Type	Structure	Material	Drug Delivery Mechanism	Advantages	Disadvantages
Solid Microneedles	Micron-scale solid needles	Silicon, polymers, metals	Penetration of stratum corneum, drug diffusion	Simple fabrication, mechanical strength	Limited drug payload capacity, single-use only
Hollow Microneedles	Micron-scale needles with lumens	Silicon, polymers, metals	Fluid delivery or extraction	Precise dosing, versatile applications	Risk of clogging, complex fabrication
Dissolving Microneedles	Micron-scale needles with dissolvable matrix	Biocompatible polymers, sugars	Drug encapsulation and release upon dissolution	Pain-free application, enhanced bioavailability	Limited drug stability, formulation challenges
Coated Microneedles	Micron-scale needles with drug-loaded or functionalized coatings	Silicon, polymers, metals	Controlled drug release, protection from degradation	Enhanced drug stability, targeted delivery	Coating uniformity, potential delamination
Hydrogel-forming Microneedles	Micron-scale needles forming hydrogel matrix upon insertion	Biocompatible polymers	Drug encapsulation and sustained release	Enhanced tissue penetration, prolonged drug release	Hydrogel swelling, fabrication complexity

3. FABRICATION TECHNIQUES FOR MICRONEEDLES

3.1. Micromolding

Micromolding is a versatile and scalable fabrication technique used in the production of microneedles and other microscale structures(9). It involves the replication of micrometer-sized features from a master mold onto a substrate, typically using elastomeric materials such as polydimethylsiloxane (PDMS) or thermoplastics like polycarbonate or poly (methyl methacrylate) (PMMA). The process begins with the creation of a master mold, often fabricated using photolithography or other micromachining techniques. This master mold contains the desired microneedle geometry and is used as a template for replication. Liquid polymer precursor material is then poured or injected into the mold, where it undergoes curing or solidification to form the microneedle structures. After solidification, the molded substrate is demolded, resulting

in an array of microneedles with precise dimensions and geometries(10). Micromolding offers several advantages, including high throughput, cost-effectiveness, and the ability to produce intricate microstructures with high fidelity(11). It is widely used in research and industry for the fabrication of microneedle arrays, microfluidic devices, lab-on-a-chip systems, and other microscale components for biomedical, pharmaceutical, and diagnostic applications(12).

3.2. Lithography

Lithography is a fundamental technique in microfabrication used to pattern and transfer geometric features onto substrates with high precision and resolution(13). It encompasses a variety of methods, including photolithography, electron beam lithography (EBL)(14), and nanoimprint lithography (NIL)(15), each with its own unique advantages and applications. In photolithography, a photosensitive resist is deposited onto

a substrate and exposed to ultraviolet (UV) light through a mask containing the desired pattern. The exposed regions of the resist undergo a chemical change, allowing selective removal of the unexposed regions through development, leaving behind the patterned features. Electron beam lithography (EBL) utilizes a focused beam of electrons to directly write patterns onto a substrate coated with a resist material. This technique offers unparalleled resolution and flexibility, making it ideal for prototyping and research applications requiring nanoscale features(14). Nanoimprint lithography (NIL) involves pressing a stamp or mold containing the desired pattern into a thermoplastic resist on a substrate, transferring the pattern through mechanical deformation. NIL is capable of producing high-resolution patterns over large areas and is used in the fabrication of microfluidic devices, optical components, and nanoelectronics(15).

3.3. Laser Ablation

Laser ablation is a versatile technique used in various fields, including materials science, microfabrication, and biomedical engineering, to precisely remove or modify material from a target surface using a laser beam(16). In laser ablation, a focused laser beam is directed onto the surface of the material, generating a high-intensity energy pulse that causes rapid heating and vaporization of the target material. The process of laser ablation can be used for various purposes, including cutting, drilling, patterning, and surface modification(17). It offers several advantages over traditional machining methods, including minimal heat-affected zones, high precision, and the ability to process a wide range of materials, including metals, ceramics, polymers, and biological

tissues. Laser ablation is widely used in microfabrication processes such as micro structuring of semiconductor devices, fabrication of microfluidic channels, and patterning of biomaterials for tissue engineering applications(18). Additionally, it finds applications in biomedical research and clinical practice for procedures such as laser ablation therapy for cancer treatment, laser-assisted drug delivery, and laser-based diagnostics.

3.4. 3D Printing

3D printing, also known as additive manufacturing, is a transformative technology that enables the fabrication of three-dimensional objects layer by layer from digital design data(19). It offers unprecedented flexibility, speed, and customization compared to traditional manufacturing methods, making it increasingly popular across various industries, including aerospace, automotive, healthcare, and consumer goods(20). This digital model is then sliced into thin layers, and the 3D printer builds the object layer by layer, typically using materials such as plastics, metals, ceramics, or biomaterials. 3D printing offers several advantages, including rapid prototyping, cost-effectiveness for low-volume production, and design freedom to create complex geometries and customized parts. It also enables on-demand manufacturing, reducing lead times and waste compared to traditional manufacturing methods. In healthcare, 3D printing is revolutionizing medical device manufacturing, patient-specific implants, prosthetics, and anatomical models for surgical planning and education(21). In aerospace and automotive industries, it enables lightweight and complex components with improved performance and fuel efficiency.

3.5. Advantages and Limitations of Each Technique

Table No:2 Comparison of Microneedle Fabrication Techniques for Transdermal Drug Delivery Systems

Technique	Advantages	Limitations
Micromolding(22)	1. High throughput production	1. Limited to certain materials and geometries
	2. Cost-effective fabrication	2. Requires a master mold, which can be time-consuming and expensive
	3. Precise control over microneedle dimensions and geometries	3. Limited scalability for mass production
Lithography(23)	1. High resolution patterning	1. Expensive equipment and infrastructure
	2. Versatile applications in microfabrication	2. Complex process requiring expertise in photolithography or electron beam lithography
	3. Suitable for prototyping and large-scale production	3. Limited to planar substrates and small area patterning
Laser Ablation(24)	1. Minimal heat-affected zones	1. Limited to certain materials and thicknesses
	2. High precision and resolution	2. Limited scalability for large-area processing
	3. Versatile applications in materials processing and microfabrication	3. Potential for thermal damage to surrounding materials
3D Printing	1. Design freedom for complex geometries and customization	1. Limited resolution compared to lithography and laser ablation
	2. Rapid prototyping and on-demand manufacturing	2. Material limitations may affect mechanical properties and biocompatibility
	3. Reduced waste and lead times compared to traditional manufacturing methods	3. post-processing may be required for surface finishing and dimensional accuracy

4. APPLICATIONS OF MICRONEEDLES

4.1. Drug Delivery

Microneedles have emerged as a promising technology for drug delivery, offering several advantages over traditional methods such as oral administration and injections(25). By bypassing the skin's protective barrier, microneedles enable precise and targeted delivery of therapeutics, enhancing drug absorption and bioavailability while minimizing systemic side effects. This makes them particularly suitable for delivering drugs with poor oral bioavailability, large molecular size, or narrow therapeutic windows. Microneedles have shown promise in a wide range of drug delivery applications, including the delivery of small molecules, biologics, vaccines, and nucleic acids. They have been explored for the treatment of various medical conditions such as diabetes, cardiovascular diseases, cancer, and infectious diseases. Additionally, microneedles offer the potential for controlled and sustained release of drugs, enabling prolonged therapeutic effects and improved patient compliance. Furthermore, microneedle-based drug delivery systems can

be tailored to specific patient needs, offering personalized treatment regimens and dosage adjustments. Ongoing research aims to optimize microneedle design, formulation strategies, and fabrication techniques to further enhance their efficacy, safety, and versatility for drug delivery applications. Overall, microneedles hold great promise for revolutionizing drug delivery and improving patient outcomes in diverse therapeutic areas(26).

4.2. Vaccination

Microneedles have emerged as a promising tool for vaccination, offering several advantages over traditional needle-based methods(27). By delivering vaccines directly into the skin's immune-rich layers, microneedles can enhance immune responses and improve vaccine efficacy. This is particularly advantageous for vaccines requiring enhanced immunogenicity or dose sparing. Microneedle-based vaccination offers several benefits, including improved patient compliance due to painless and minimally invasive administration, reduced risk of needlestick injuries for healthcare workers, and simplified vaccine administration in

resource-limited settings without the need for trained personnel or cold chain storage. Furthermore, microneedles enable precise control over vaccine delivery, allowing for dose optimization, antigen sparing, and the potential for combination vaccines. They have been explored for a wide range of vaccine targets, including infectious diseases such as influenza, measles, and COVID-19, as well as for emerging applications in cancer immunotherapy and personalized vaccines. Ongoing research aims to further optimize microneedle-based vaccination strategies, including vaccine stability, scalability, and integration with adjuvants or immune-modulating agents to enhance protective immune responses. Overall, microneedles hold great promise for revolutionizing vaccination efforts and improving global health outcomes(28).

4.3. Diagnostics

By penetrating the skin's outermost layer, microneedles can access interstitial fluid, blood, or other biological fluids containing biomarkers indicative of various health conditions(29). One of the key advantages of microneedle-based diagnostics is their ability to offer a less invasive alternative to traditional blood draws, reducing patient discomfort and anxiety associated with venipuncture. Microneedles also offer advantages in terms of sample volume requirements, allowing for smaller sample sizes compared to conventional blood collection methods. Microneedle-based diagnostic platforms have been developed for a wide range of applications, including monitoring glucose levels in diabetes management, detecting infectious diseases such as malaria and HIV, and assessing biomarkers for cancer diagnosis and monitoring. Additionally, microneedles have been explored for point-of-care testing in resource-limited settings, offering rapid and cost-effective diagnostic solutions outside of laboratory settings(30).

4.4. Cosmetic Treatments

Microneedles have emerged as a novel approach in the field of cosmetic treatments, offering minimally invasive and effective solutions for various skin conditions and aesthetic

enhancements(31). By creating microchannels in the skin's surface, microneedles facilitate the delivery of cosmeceuticals, such as vitamins, peptides, growth factors, and hyaluronic acid, directly into the dermis or epidermis, where they can exert their beneficial effects. One of the key advantages of microneedle-based cosmetic treatments is their ability to enhance skin rejuvenation, improve texture, tone, and firmness, and address common concerns such as wrinkles, acne scars, hyperpigmentation, and stretch marks. Microneedling also promotes collagen production and enhances the absorption of topical formulations, leading to long-lasting improvements in skin health and appearance. Microneedle-based cosmetic procedures are versatile and customizable, allowing for tailored treatments based on individual skin types, concerns, and treatment goals. Additionally, microneedling is associated with minimal downtime and discomfort, making it a popular choice for patients seeking non-surgical and less invasive alternatives to traditional cosmetic procedures.

4.5. Emerging Applications

Microneedles have expanded beyond traditional applications, paving the way for innovative and emerging uses across various fields. One such application is in the field of biosensing, where microneedles are being explored as minimally invasive platforms for continuous monitoring of biomarkers in interstitial fluid or blood. These biosensing microneedles can detect analytes such as glucose, lactate, and ions, offering real-time monitoring for disease management, athletic performance optimization, and personalized healthcare. Another emerging application of microneedles is in the field of tissue engineering and regenerative medicine. Microneedles are being investigated as delivery vehicles for bioactive molecules, stem cells, and growth factors to promote tissue regeneration and wound healing(32). They offer precise control over the spatial distribution and release kinetics of therapeutic agents, enhancing tissue repair and regeneration in various clinical settings. Additionally, microneedles are being explored for drug

delivery to specialized tissues and organs, such as the eye, inner ear, and brain, where traditional delivery methods face challenges in accessing targeted sites. These targeted delivery approaches hold promise for treating ocular diseases, hearing disorders, and neurological conditions with improved efficacy and reduced side effects.

4.6. Case Studies Highlighting Successful Applications

Case studies showcasing successful applications of microneedles underscore their versatility and efficacy across various fields. In one notable example, microneedle-based influenza vaccination demonstrated improved immune responses compared to traditional intramuscular injection, highlighting the potential of microneedles for enhancing vaccine efficacy and compliance. In another case, microneedle patches loaded with lidocaine provided effective local anaesthesia for minor dermatological procedures, offering a painless and convenient alternative to needle-based anaesthesia. This demonstrates the utility of microneedles in pain management and procedural care. Furthermore, microneedle-based delivery of anti-inflammatory drugs has shown promising results in treating inflammatory skin conditions such as psoriasis and atopic dermatitis, offering targeted and localized therapy with reduced systemic side effects. In the field of biosensing, microneedle-based glucose monitoring systems have enabled continuous glucose monitoring for diabetes management, improving patient outcomes and quality of life(33).

5. ADVANTAGES AND CHALLENGES OF MICRONEEDLE TECHNOLOGY

5.1. Advantages:

5.1.1. Improved Patient Compliance

Microneedle technology offers several advantages that contribute to improved patient compliance in various healthcare applications. Firstly, microneedles provide a less invasive and painless alternative to traditional needle-based methods, reducing patient anxiety and fear

associated with injections(34). This painless administration can alleviate needle phobia, particularly in pediatric and needle-sensitive populations, enhancing overall treatment adherence. Moreover, microneedles eliminate the need for healthcare professionals to administer injections, empowering patients to self-administer medications at home. This convenience promotes patient autonomy, reduces healthcare burdens, and increases treatment accessibility, especially for chronic conditions requiring frequent injections. Additionally, microneedles enable precise and controlled drug delivery, ensuring accurate dosing and minimizing medication errors. This reliability enhances treatment efficacy and reduces the risk of adverse reactions, fostering patient trust in the therapeutic regimen. Furthermore, the simplicity of microneedle-based delivery systems facilitates user-friendly interfaces, making them suitable for point-of-care applications and remote healthcare settings. This accessibility encourages patient engagement and facilitates continuous monitoring and management of health conditions.

5.1.2. Enhanced Drug Absorption

Microneedle technology offers significant advantages in enhancing drug absorption, revolutionizing drug delivery across various medical fields. By bypassing the skin's protective barrier, microneedles create microchannels that facilitate the direct delivery of therapeutics into the underlying dermis or systemic circulation, thereby improving drug absorption and bioavailability. One key advantage of microneedles is their ability to enhance the permeation of drugs, particularly macromolecules like proteins and peptides, which typically have poor transdermal absorption. The microneedle-mediated delivery enables these drugs to bypass enzymatic degradation in the gastrointestinal tract and first-pass metabolism in the liver, resulting in increased systemic exposure and therapeutic efficacy(35). Moreover, microneedles offer precise control over drug delivery kinetics, enabling tailored release profiles to

optimize drug absorption and maintain therapeutic concentrations over extended periods. This controlled release capability reduces the frequency of dosing and enhances patient compliance, particularly for medications requiring frequent administration. Furthermore, microneedles can improve drug absorption in patients with compromised skin barrier function, such as the elderly or those with dermatological conditions, offering new therapeutic options and improving treatment outcomes

5.1.3. Reduced Pain and Discomfort

Microneedle technology offers a significant advantage in reducing pain and discomfort associated with drug delivery and medical procedures, enhancing patient comfort and compliance. Traditional needle-based methods often cause pain, fear, and anxiety in patients, particularly in paediatric and needle-phobic populations. Microneedles provide a minimally invasive and virtually painless alternative, as their micrometer-scale dimensions enable gentle penetration of the skin without stimulating pain receptors or nerve endings. Furthermore, the design of microneedles, with their fine and tapered structures, minimizes tissue trauma and damage, further reducing discomfort during insertion. This gentle approach to drug delivery enhances patient acceptance and adherence to treatment regimens, particularly for individuals requiring frequent injections or long-term therapy. Moreover, microneedle-based delivery systems can be engineered to incorporate pain-reducing techniques, such as topical anaesthetics or vibration stimulation, further mitigating discomfort during administration. Additionally, the elimination of needle-related phobia and anxiety enhances patient satisfaction and trust in the healthcare provider, fostering positive therapeutic relationships and improving overall treatment outcomes(36).

5.2. Challenges

5.2.1. Manufacturing Scalability

Manufacturing scalability poses a significant challenge in the widespread adoption of microneedle technology for mass production and commercialization. While

microneedles offer promising advantages in drug delivery, diagnostics, and other applications, their fabrication processes often require precise and intricate manufacturing techniques that may not be easily scalable to large volumes. Traditional micromolding and lithography methods used for microneedle fabrication are typically labor-intensive and time-consuming, making them unsuitable for high-throughput production(37). Additionally, these techniques may require expensive equipment and specialized expertise, further limiting scalability and increasing manufacturing costs. Furthermore, maintaining consistency and quality control in microneedle fabrication at scale presents additional challenges. Variations in material properties, microneedle geometries, and manufacturing processes can affect the performance and reliability of microneedle devices, posing challenges in achieving reproducibility and uniformity across large production batches. Addressing manufacturing scalability challenges requires the development of innovative fabrication techniques and scalable manufacturing processes tailored to microneedle production. Emerging approaches such as roll-to-roll manufacturing, additive manufacturing, and microfluidic-based fabrication offer promising solutions for high-throughput production of microneedle arrays while maintaining precision and quality control.

5.2.2. Skin Penetration Depth Control

Skin penetration depth control is a critical challenge in microneedle technology, as it directly impacts the efficacy, safety, and reproducibility of drug delivery and other applications. Achieving precise control over the penetration depth of microneedles is essential to ensure optimal delivery of therapeutics while minimizing tissue damage and discomfort. One of the main challenges lies in designing microneedles that can reliably penetrate the skin to the desired depth without causing pain or injury. Variations in skin thickness, elasticity, and composition among individuals present additional complexities in achieving consistent penetration depths across diverse

patient populations. Moreover, factors such as microneedle geometry, material properties, insertion speed, and application force influence the penetration depth and must be carefully optimized to ensure accurate and controlled delivery of drugs or sampling of biological fluids. Addressing the challenge of skin penetration depth control requires interdisciplinary approaches combining engineering, materials science, and dermatology(38). Advances in microneedle design, fabrication techniques, and insertion methods, along with computational modeling and in vivo testing, are essential for developing microneedle devices with improved penetration depth control and reproducibility.

5.2.3. Regulatory Approval and Safety Concerns

Regulatory approval and safety concerns represent significant challenges in the widespread adoption of microneedle technology for clinical and commercial applications. While microneedles offer promising advantages in drug delivery, diagnostics, and other biomedical fields, ensuring their safety, efficacy, and regulatory compliance is paramount for successful translation into clinical practice. One of the main challenges is establishing the safety profile of microneedle devices, particularly regarding their potential for skin irritation, allergic reactions, and infection risk. Microneedle materials and coatings must be thoroughly evaluated for biocompatibility, stability, and long-term safety to mitigate adverse effects on patients. Additionally, achieving regulatory approval for microneedle-based products requires adherence to stringent standards and guidelines set forth by regulatory agencies such as the FDA and EMA. Demonstrating the quality, safety, and performance of microneedle devices through preclinical studies, clinical trials, and comprehensive regulatory submissions is essential but often complex and time-consuming. Furthermore, the evolving nature of microneedle technology, with innovations in materials, designs, and applications, poses challenges in establishing standardized testing protocols and regulatory pathways for

product approval. Addressing these challenges requires collaboration among researchers, clinicians, regulatory agencies, and industry stakeholders to develop robust safety assessment methodologies, streamline regulatory processes, and establish clear guidelines for microneedle-based products(39).

6. BIOCOMPATIBILITY AND SAFETY CONSIDERATIONS

6.1. Skin Irritation and Tissue Response

Biocompatibility and safety considerations are paramount in the development of microneedle technology, particularly regarding skin irritation and tissue response. While microneedles offer a minimally invasive approach to drug delivery and diagnostics, ensuring their compatibility with the skin and tissues is crucial for avoiding adverse reactions and promoting patient safety. Skin irritation and tissue response are primary concerns when assessing the biocompatibility of microneedle devices. The insertion of microneedles into the skin can elicit local tissue reactions, including erythema, edema, inflammation, and discomfort. These responses may vary depending on factors such as microneedle design, materials, insertion depth, and application duration. To mitigate skin irritation and tissue response, thorough preclinical evaluation of microneedle devices is essential. This involves conducting in vitro and in vivo studies to assess the biocompatibility, cytotoxicity, and immunogenicity of microneedle materials and formulations. Additionally, histological analysis of skin tissue following microneedle insertion provides valuable insights into the tissue response and inflammatory reactions. Furthermore, optimizing microneedle design and fabrication processes can help minimize tissue trauma and irritation during insertion. Strategies such as tapering microneedle tips, selecting biocompatible materials, and incorporating anti-inflammatory coatings can enhance the safety and tolerability of microneedle devices(40).

6.2. Infection Risk and Sterility

Biocompatibility and safety considerations extend beyond skin irritation to include infection risk and sterility in microneedle technology. Despite their minimally invasive nature, microneedle devices present a potential risk of infection due to their penetration of the skin barrier, making sterility a crucial aspect of their design and manufacturing process(41). To mitigate this risk, microneedle devices must undergo rigorous sterilization procedures to ensure the absence of pathogens and contaminants. Sterilization methods such as gamma irradiation, ethylene oxide gas, or autoclaving are commonly employed to achieve sterility while maintaining the integrity and functionality of microneedle materials. Additionally, the design of microneedle devices should incorporate features to minimize the risk of infection, such as smooth surfaces, aseptic handling procedures, and sterile packaging. Furthermore, maintaining strict quality control measures throughout the manufacturing process is essential to prevent microbial contamination and ensure product safety and efficacy. By addressing infection risk and maintaining sterility, microneedle technology can uphold patient safety and promote confidence in its use for drug delivery, diagnostics, and other biomedical applications(42). Ensuring compliance with regulatory standards and guidelines for sterilization and aseptic processing is essential for achieving regulatory approval and market acceptance of microneedle-based products.

6.3. Immune Responses and Allergic Reactions

Biocompatibility and safety considerations in microneedle technology extend to immune responses and allergic reactions, crucial factors that can impact the safety and efficacy of microneedle-based device(43). Immune responses to microneedles may manifest as local inflammation, immune cell infiltration, or systemic immune activation. Factors such as microneedle design, materials, and insertion depth can influence the magnitude and nature of immune responses. While mild inflammatory responses are common and typically resolve spontaneously, excessive or prolonged inflammation may compromise treatment outcomes and patient comfort. Allergic reactions to microneedle materials or components present another concern, particularly for individuals with known allergies or sensitivities. Certain materials used in microneedle fabrication, such as metals, polymers, or adhesives, may trigger allergic responses ranging from localized dermatitis to systemic hypersensitivity reactions. To mitigate immune responses and allergic reactions, thorough biocompatibility testing of microneedle materials and formulations is essential. Preclinical studies assessing immune compatibility, hypersensitivity reactions, and inflammatory markers can provide valuable insights into the safety profile of microneedle devices. Additionally, careful selection of biocompatible materials and coatings, along with adherence to regulatory guidelines for medical device safety, can help minimize the risk of adverse immune reactions and ensure the safe use of microneedle technology in clinical practice(44).

6.4. Strategies for Enhancing Biocompatibility and Safety

Table No:3 Advancements in Biocompatible Microneedle Technologies: Strategies for Enhanced Safety and Efficacy

Strategy	Description
Material Selection	Choose biocompatible materials for microneedle fabrication, such as medical-grade polymers (e.g., polylactic acid, polyethylene glycol), biodegradable materials (e.g., hyaluronic acid, gelatin), or metals (e.g., stainless steel, titanium) to minimize adverse tissue reactions and allergic responses.
Surface Modification	Apply coatings or surface treatments to microneedles to enhance biocompatibility and reduce tissue irritation. Examples include hydrophilic coatings to improve insertion and reduce friction, anti-inflammatory coatings to mitigate immune responses, or antimicrobial coatings to prevent infection risk.
Sterilization Techniques	Implement sterilization methods such as gamma irradiation, ethylene oxide gas, or autoclaving to achieve sterility and ensure the absence of pathogens and contaminants on microneedle devices. Maintain strict quality control measures throughout the sterilization process to preserve microneedle integrity and functionality.
Design Optimization	Optimize microneedle design parameters, including length, diameter, aspect ratio, and tip geometry, to minimize tissue trauma, enhance insertion efficiency, and improve patient comfort. Consider factors such as needle tapering, bevel angle, and spacing to optimize penetration depth and reduce pain during insertion.
Preclinical Testing	Conduct comprehensive biocompatibility testing using in vitro and in vivo models to evaluate the safety profile of microneedle materials and formulations. Assess parameters such as cytotoxicity, inflammation, immune compatibility, and tissue response to identify potential adverse effects and ensure regulatory compliance.
Regulatory Compliance	Adhere to regulatory standards and guidelines set forth by regulatory agencies (e.g., FDA, EMA) for medical device safety and biocompatibility. Ensure compliance with Good Manufacturing Practices (GMP) and ISO standards throughout the design, manufacturing, and testing of microneedle-based products.

7. CLINICAL TRANSLATION AND COMMERCIALIZATION

7.1. Current Status of Microneedle Technologies in Clinical Trials

Microneedle technologies have gained significant traction in clinical trials across various medical fields, reflecting their potential to revolutionize drug delivery, diagnostics, and therapeutic interventions. As of [current year], numerous clinical trials are underway to evaluate the safety, efficacy, and feasibility of microneedle-based devices in diverse patient populations and applications. In drug delivery, clinical trials are investigating microneedle patches for transdermal delivery of vaccines, insulin, contraceptives, and other medications, aiming to improve patient compliance, reduce pain, and enhance therapeutic

outcomes. Additionally, microneedle-based systems are being evaluated for targeted delivery to specialized tissues and organs, such as the eye, inner ear, and mucosal surfaces, to address unmet clinical needs and overcome barriers to conventional drug administration routes. In offering potential advancements in disease management and personalized healthcare(45).

7.2. Commercial Products and Market Trends

Commercial products incorporating microneedle technology have witnessed significant growth and diversification in recent years, reflecting increasing demand for minimally invasive drug delivery, diagnostics, and cosmetic treatments. Microneedle-based patches, devices, and systems are now available across various market segments, with notable advancements in pharmaceuticals,

healthcare, and personal care industries. In the pharmaceutical sector, microneedle patches for transdermal drug delivery have garnered considerable attention for their potential to improve patient compliance and therapeutic outcomes(46). Commercial products include patches for insulin delivery, vaccination, pain management, and hormone therapy, catering to diverse patient needs and treatment regimens. In healthcare, microneedle-based biosensing platforms have emerged as valuable tools for continuous monitoring of biomarkers, offering real-time insights into health status and disease management. Commercial products encompass wearable sensors for glucose monitoring, lactate monitoring, and other diagnostic applications, enabling personalized healthcare solutions and remote patient monitoring. In the personal care industry, microneedle-based cosmetic treatments have gained popularity for their ability to rejuvenate skin, improve texture, and address various dermatological concerns. Commercial products include microneedle rollers, pens, and patches infused with skincare ingredients, offering consumers non-invasive alternatives to traditional cosmetic procedures. Market trends indicate continued growth and innovation in microneedle technology, driven by advancements in materials, fabrication techniques, and application domains. As microneedle products become increasingly accessible and diversified, they are poised to reshape healthcare delivery, diagnostics, and aesthetic treatments in the years to come(47).

7.3. Regulatory Pathways and Approval Processes

Regulatory pathways and approval processes for microneedle-based products are critical considerations in ensuring their safety, efficacy, and market accessibility. In the United States, the Food and Drug Administration (FDA) oversees the regulation of medical devices, including microneedle devices, through a rigorous premarket approval (PMA) or 510(k) clearance process. Classifying microneedle devices based on their intended use, risk profile, and technological characteristics is essential for determining the appropriate regulatory pathway(48). Microneedle devices intended for drug

delivery or diagnostic purposes may require submission of a PMA application, which entails comprehensive preclinical and clinical data demonstrating safety, efficacy, and quality control. Alternatively, devices with substantially equivalent predicates may qualify for 510(k) clearance, expediting the approval process. Internationally, regulatory approval processes for microneedle devices vary by country, with regulatory agencies such as the European Medicines Agency (EMA) in the European Union and the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan overseeing medical device approvals. Navigating regulatory pathways and approval processes for microneedle-based products necessitates close collaboration between manufacturers, regulatory consultants, and regulatory agencies(49).

7.4. Challenges in Scaling Up Production and Distribution

Scaling up production and distribution of microneedle-based products presents several challenges that must be addressed to meet growing demand and ensure widespread accessibility. One major challenge is optimizing manufacturing processes to achieve high throughput production while maintaining product quality and consistency. Traditional fabrication methods such as micromolding and lithography may be labor-intensive and time-consuming, requiring innovative approaches such as roll-to-roll manufacturing or automated assembly lines to increase efficiency. Additionally, sourcing raw materials and components for microneedle production at scale can be challenging, particularly for specialized materials or coatings. Ensuring a stable and reliable supply chain is crucial for uninterrupted manufacturing and timely delivery of products to market. Furthermore, establishing robust distribution networks and logistics infrastructure is essential for reaching diverse healthcare settings and consumer markets. Microneedle products may require specialized storage conditions or handling procedures, adding complexity to distribution channels and inventory management. Addressing these challenges requires

collaboration between manufacturers, suppliers, regulatory agencies, and distribution partners to develop scalable production processes, optimize supply chains, and implement effective quality control measures. By overcoming barriers to scaling up production and distribution, microneedle technology can realize its full potential in improving healthcare delivery and patient outcomes on a global scale(50).

8. FUTURE DIRECTIONS AND EMERGING TRENDS

8.1. Multifunctional Microneedles

Future directions in microneedle technology are increasingly focused on developing multifunctional microneedles capable of delivering multiple therapeutic agents or performing simultaneous diagnostic and therapeutic functions(51). This enables real-time monitoring of biomarkers or physiological parameters while delivering therapeutic agents, allowing for precise and personalized treatment adjustments based on individual patient responses. Additionally, multifunctional microneedles are being explored for targeted and combinatorial therapy approaches, where multiple drugs or therapeutic agents are co-delivered to specific tissue targets for synergistic effects or enhanced therapeutic outcomes. This strategy holds promise for treating complex diseases such as cancer, autoimmune disorders, and infectious diseases more effectively while minimizing side effects. Furthermore, advancements in materials science, microfabrication techniques, and biocompatible coatings are driving the development of multifunctional microneedles with enhanced capabilities and versatility. These innovations are poised to expand the scope of microneedle applications in healthcare and pave the way for personalized, patient-centric treatment approaches in the future(52).

8.2. Stimuli-Responsive Systems

Stimuli-responsive systems represent a promising future direction in microneedle technology, offering dynamic and adaptive capabilities for targeted drug delivery, diagnostics, and tissue engineering applications. These systems are

designed to respond to specific environmental cues or external stimuli, triggering controlled release of therapeutic agents or modulation of biological processes in a precise and timely manner. One emerging trend is the development of stimuli-responsive microneedles that can actively respond to physiological changes within the body, such as variations in pH, temperature, glucose levels, or enzyme activity(53). By incorporating responsive materials or smart coatings into microneedle designs, researchers aim to create devices capable of on-demand drug release or sensing based on real-time physiological signals, enabling personalized and dynamic treatment regimens. Furthermore, stimuli-responsive microneedles are being explored for applications in tissue engineering and regenerative medicine, where they can deliver growth factors, cytokines, or cell therapies in response to specific cues within the local tissue microenvironment. This approach holds promise for enhancing tissue regeneration, wound healing, and functional tissue repair in various clinical settings.

8.3. Personalized Medicine Applications

Future directions in microneedle technology are increasingly oriented towards personalized medicine applications, leveraging the unique capabilities of microneedles to tailor treatments to individual patient needs and characteristics. Personalized medicine aims to optimize therapeutic outcomes by considering factors such as genetics, lifestyle, and disease state, and microneedle technology offers promising avenues for advancing this approach(54). One emerging trend is the development of personalized drug delivery systems using microneedles, where drug formulations and dosages are customized based on patient-specific factors. By integrating biosensing capabilities or utilizing patient-specific data, such as biomarker levels or genetic information, microneedle devices can deliver precise doses of therapeutics at optimal times, maximizing efficacy while minimizing side effects. Additionally, microneedles are being explored for point-of-care diagnostics and monitoring applications in personalized medicine,

enabling real-time assessment of biomarkers, disease progression, or treatment responses. These devices offer convenient and minimally invasive solutions for monitoring chronic conditions, managing medication regimens, and facilitating early disease detection. Furthermore, advances in materials science and microfabrication techniques are driving the development of customizable microneedle arrays tailored to individual patient needs, such as varying needle lengths, geometries, or drug release profiles. This customization enhances patient comfort, treatment adherence, and therapeutic outcomes, ultimately advancing the paradigm of personalized medicine with microneedle technology(55).

8.4. Integration with Wearable and Implantable Devices

The integration of microneedle technology with wearable and implantable devices represents a promising future direction in biomedical engineering, offering enhanced capabilities for drug delivery, diagnostics, and health monitoring. By combining microneedles with wearable or implantable platforms, researchers aim to

create seamless and unobtrusive solutions for personalized healthcare management. One emerging trend is the integration of microneedle patches with wearable devices, such as smartwatches or adhesive sensors, for continuous monitoring of biomarkers or physiological parameters. Microneedles embedded within these wearable platforms can facilitate minimally invasive sampling of interstitial fluid or blood, enabling real-time monitoring of glucose levels, lactate levels, or other biomarkers relevant to health and disease. Additionally, microneedle-based implantable devices are being explored for sustained drug delivery or targeted therapy applications. These devices can be implanted beneath the skin or within specific tissue targets, providing controlled release of therapeutics over extended periods while minimizing systemic side effects. Integration with wireless communication technologies allows for remote programming and monitoring of implantable microneedle devices, enhancing patient convenience and treatment compliance.

8.5. Potential Impact on Healthcare and Biomedical Engineering

Table No:4 Transformative Potential of Microneedle Technologies: Advancing Healthcare Delivery and Therapeutic Outcomes

Potential Impact	Description
Enhanced Patient Compliance	Minimally invasive and painless microneedle-based drug delivery and diagnostics promote patient acceptance and adherence to treatment regimens, particularly for paediatric and needle-phobic populations, improving therapeutic outcomes and healthcare outcomes overall.
Personalized Medicine	Integration of biosensing capabilities and customizable drug delivery profiles enables tailored treatment regimens based on individual patient characteristics and disease states, advancing the paradigm of personalized medicine and optimizing therapeutic efficacy while minimizing adverse effects.
Remote Monitoring and Telemedicine	Wearable and implantable microneedle devices facilitate remote monitoring of biomarkers and physiological parameters, enabling real-time health assessment and disease management outside traditional healthcare settings. This promotes telemedicine and remote patient monitoring, improving access to healthcare and reducing healthcare disparities.
Targeted and Controlled Drug Delivery	Precise control over drug release kinetics and spatial distribution enables targeted delivery of therapeutics to specific tissues or organs, minimizing systemic side effects and maximizing therapeutic efficacy. Microneedle-based drug delivery systems offer potential advancements in treating localized diseases and overcoming biological barriers to drug delivery.
Point-of-Care Diagnostics	Microneedle-based biosensing platforms enable rapid and minimally invasive diagnostics at the point of care, facilitating early disease detection, monitoring of treatment responses, and management of chronic conditions. This enhances healthcare delivery by providing timely and actionable information for clinical decision-making and patient management.
Tissue Engineering and Regenerative Medicine	Microneedle-based delivery of bioactive molecules, stem cells, and growth factors promotes tissue regeneration and wound healing, offering potential applications in tissue engineering and regenerative medicine. Controlled release of therapeutic agents enhances tissue repair and regeneration, addressing unmet clinical needs in wound care and tissue reconstruction.

9. CONCLUSION

9.1. Summary of Key Findings and Insights

The review article provides a comprehensive overview of microneedle technology, exploring its evolution, current status, and future directions in healthcare and biomedical engineering. Key findings highlight the versatility and potential impact of microneedle-based devices across various applications, including drug delivery, diagnostics, tissue engineering, and personalized medicine. Microneedle technology offers several advantages, including minimally invasive administration, enhanced patient compliance, and targeted drug delivery, making it a promising tool for improving healthcare delivery and patient outcomes. Emerging trends such as multifunctional microneedles, stimuli-responsive systems, and integration with wearable devices underscore the innovation and potential for transformative advancements in personalized medicine and remote healthcare monitoring. Challenges such as manufacturing scalability, regulatory approval, and distribution logistics are also addressed, emphasizing the need for continued research and collaboration to overcome barriers to widespread adoption and commercialization.

9.2. Implications for Research, Industry, and Clinical

The implications of microneedle technology span across research, industry, and clinical practice, shaping the landscape of healthcare delivery and biomedical innovation. In research, continued exploration of microneedle technology holds promise for advancing our understanding of drug delivery mechanisms, biomarker detection, and tissue engineering. Future research efforts should focus on optimizing microneedle designs, materials, and fabrication techniques to enhance functionality, biocompatibility, and therapeutic efficacy. In industry, the commercialization of microneedle-based products presents opportunities for growth and innovation in pharmaceuticals, medical devices, and biotechnology sectors. Industry stakeholders should invest in scalable

manufacturing processes, quality assurance systems, and regulatory compliance to bring microneedle products to market and meet growing demand for minimally invasive healthcare solutions. In clinical practice, the adoption of microneedle technology offers transformative benefits for patient care, enabling personalized medicine approaches, remote monitoring, and targeted therapy delivery. Healthcare providers should integrate microneedle-based devices into clinical workflows, leverage their capabilities for improved diagnostics and treatment outcomes, and educate patients on the benefits of these innovative technologies.

9.3. Future Directions and Recommendations for Further Study

Future directions in microneedle technology present exciting opportunities for further study and innovation, paving the way for advancements in healthcare delivery, biomedical engineering, and patient care. One key area for further study is the development of next-generation microneedle designs with enhanced functionality and versatility. Researchers should explore novel materials, fabrication techniques, and coating strategies to optimize microneedle performance for specific applications, such as targeted drug delivery, biosensing, and tissue engineering. Additionally, there is a need for comprehensive preclinical and clinical studies to evaluate the safety, efficacy, and long-term performance of microneedle-based devices in diverse patient populations. Future research efforts should focus on addressing challenges such as biocompatibility, scalability, and regulatory approval to facilitate translation of microneedle technologies from bench to bedside. Moreover, interdisciplinary collaborations between researchers, engineers, clinicians, and industry partners are essential for driving innovation and overcoming technical barriers in microneedle technology. Collaborative initiatives can accelerate the development of integrated microneedle platforms, personalized medicine approaches, and point-of-care solutions for improving healthcare delivery and patient outcomes.

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مراجعة حول القدرة على الاختراق: المشهد الحالي للميكرونيديلز وآفاقها المستقبلية

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ملخص

تُعد تقنية الإبر الدقيقة نهجًا واعدًا لتوصيل الأدوية والتطعيم والتشخيص والعلاجات التجميلية. تقدم هذه المراجعة نظرة شاملة على تقنية الإبر الدقيقة، وتشمل الأنواع المختلفة من الإبر الدقيقة، وتقنيات التصنيع، والتطبيقات، والفوائد، والتحديات، واعتبارات السلامة، والترجمة السريرية، وآفاق المستقبل. يتم مناقشة الإبر الدقيقة الصلبة، والمجوفة، والقابلة للذوبان، والمطوية، وتلك المكونة من الهلام المائي، إلى جانب بنيتها، والمواد المستخدمة، وأساليب التصنيع. كما يتم استكشاف تطبيقات الإبر الدقيقة في توصيل الأدوية، والتطعيم، والتشخيص، والعلاجات التجميلية، مع التركيز على التطبيقات الناشئة والاستخدامات الجديدة. وتتناول المراجعة مزايا تقنية الإبر الدقيقة مثل زيادة التقبل من قبل المرضى، وتحسين امتصاص الدواء، وتقليل الألم، بالإضافة إلى التحديات مثل قابلية التصنيع على نطاق واسع والحصول على الموافقة التنظيمية. يتم مناقشة تقنيات التصنيع، والتوافق الحيوي، واعتبارات السلامة، والترجمة السريرية، وجوانب التسويق التجاري، إلى جانب الاتجاهات المستقبلية مثل الإبر الدقيقة متعددة الوظائف وتطبيقات الطب الشخصي. بشكل عام، تمتلك تقنية الإبر الدقيقة وعدًا كبيرًا لإحداث ثورة في الرعاية الصحية والهندسة الطبية الحيوية، لكن لا بد من إجراء المزيد من البحوث والتطوير لمعالجة التحديات وتحقيق كامل إمكاناتها.

الكلمات الدالة: الإبر الدقيقة، توصيل الأدوية، التطعيم، التشخيص، تقنيات التصنيع، التوافق الحيوي، الترجمة السريرية، آفاق المستقبل.

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