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Transdermal Drug Delivery Systems: The Role Of Microneedles In Enhanced Therapeutics

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Abstract: Microneedles are an emerging technology for transdermal drug delivery, offering a minimally invasive and efficient alternative to traditional injections and topical formulations. All types of microneedles—solid, hollow, coated, and dissolving—function by penetrating the stratum corneum, creating microchannels that facilitate drug transport. Among these, coated and hollow microneedles have shown success but face challenges such as low drug loading capacity, pore blockage, and complex fabrication processes. In contrast, dissolving microneedles (DMNs) provide enhanced drug loading, simplified fabrication, and improved patient compliance. These microneedles, composed of biodegradable and water-soluble polymers, dissolve completely upon skin penetration, eliminating the risk of needle-stick injuries and biohazardous waste. Additionally, DMNs can be designed to release both small and large biomolecules, including peptides, proteins, and vaccines, ensuring controlled and sustained drug delivery. Notably, some dissolving microneedles can be formulated entirely from the therapeutic agent itself, eliminating the need for additional excipients and enhancing formulation efficiency. This article explores the materials, fabrication techniques, characterization methods, and applications of DMNs, highlighting their potential in vaccination, chronic disease management, and pain-free drug delivery. Furthermore, we discuss the current challenges associated with DMN technology, such as mechanical strength, drug stability, and large-scale manufacturing. Finally, we outline future research directions, emphasizing the role of DMNs in revolutionizing transdermal drug administration.

IndexTerms **- Transdermal Patches, Dissolving microneedle, Fabrication method of TDDS, Applications of TDDS**

INTRODUCTION

Transdermal drug delivery has been a subject of scientific exploration for centuries, dating back to ancient Roman ointment formulations and Galen's cold cream preparations. Over time, advancements in pharmaceutical technology have expanded the potential of transdermal administration, incorporating chemical permeability enhancers, iontophoresis, ultrasound cavitation, microdermabrasion, and microneedle technology to improve drug penetration. Unlike oral and systemic administration, transdermal delivery bypasses challenges such as pH variations, enzymatic degradation, and first-pass metabolism, offering a non-invasive, controlled-release alternative with improved patient compliance.[1][2] However, traditional transdermal patches are largely limited to lipophilic molecules (<500 Da), restricting their application for hydrophilic and macromolecular drugs. To overcome these limitations, microneedle (MN) technology has emerged as a promising approach, facilitating efficient drug delivery through the stratum corneum without pain or invasiveness. Microneedles are micron-scale structures (typically <10 µm in length) that create temporary microchannels in the skin, allowing for enhanced drug permeability and systemic absorption while minimizing discomfort. Unlike hypodermic needles, MNs provide a pain-free drug administration route, addressing issues of needle phobia, injection- site infections, and medical waste disposal.[3]-[5]

Over the years, the classification of microneedles has evolved, leading to the development of five major types:

1.Solid microneedles – Used to create micropores in the skin, followed by the application of a drug patch or solution.

2.Coated microneedles – Feature a drug coating on the needle surface that dissolves upon penetration, but leave behind biohazardous sharp waste.

3.Hollow microneedles – Contain a reservoir that allows for controlled drug injection but may suffer from pore blockage and stability issues.

4.Hydrogel-forming microneedles – Swell upon insertion into the skin, forming conduits between the drug reservoir and the systemic circulation.

5.Dissolving microneedles (DMNs) – Composed of biodegradable, water-soluble polymers, dissolving upon insertion and ensuring complete drug release without sharp waste.[7][8]

Among these, dissolving microneedles (DMNs) have gained significant attention due to their biocompatibility, ease of fabrication, and cost-effectiveness. DMNs are primarily made from maltose, polyvinylpyrrolidone (PVP), dextran, chondroitin sulfate, hyaluronic acid, and albumin, all of which dissolve upon skin contact, releasing the encapsulated drug. The "poke and release" mechanism of DMNs allows for precise, painless, and efficient drug delivery, making them particularly suitable for biologics, vaccines, and peptide-based therapies. Additionally, DMNs eliminate the need for medical supervision, making them an ideal self-administration tool for conditions requiring frequent dosing, such as diabetes and hormone therapy.[8][9]

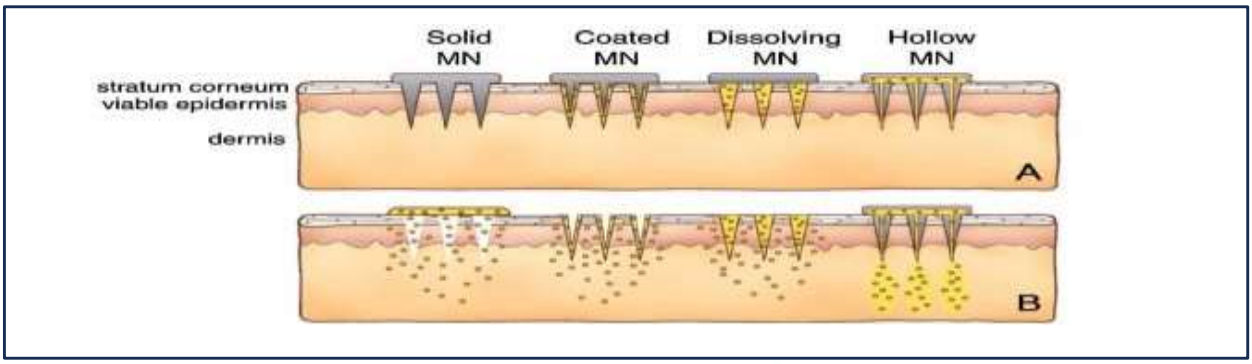

Figure no: 1 *different type of transdermal delivery method aspects along with release* [10]

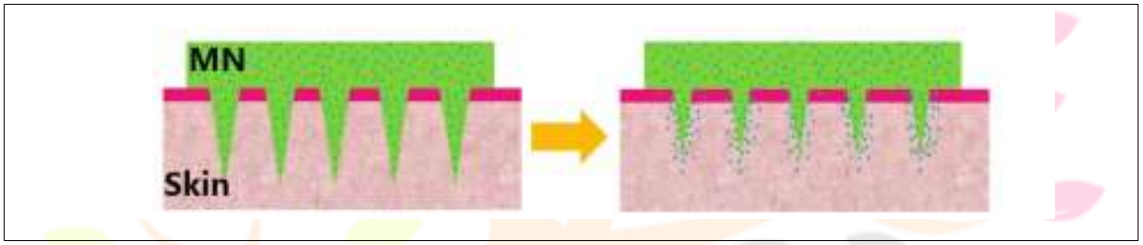

Figure no: 2 *dissolving microneedles* [10]

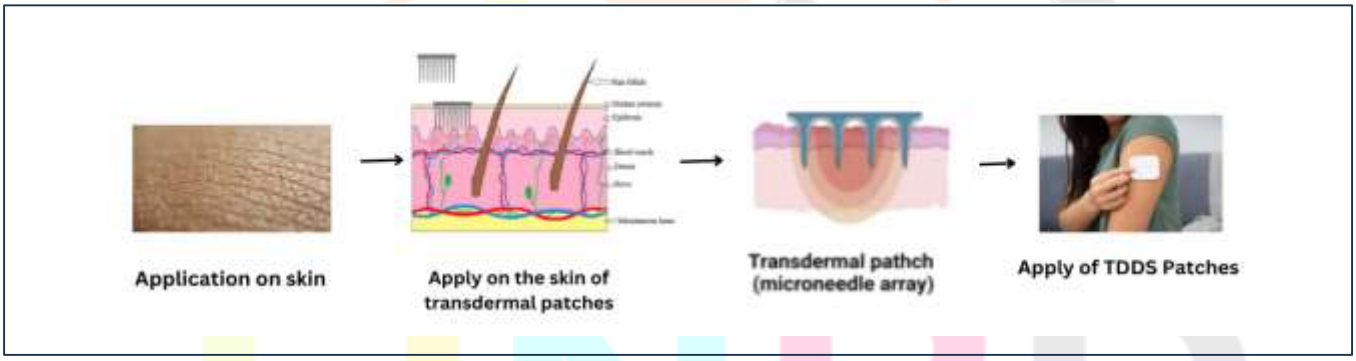

Figure no: 3 *Application of TDDS Patches on skin*

Method of Preparation of Dissolving Microneedles:

In the formulation of dissolving microneedles (DMNs), maintaining drug activity and stability is essential to ensure therapeutic effectiveness. Various physical and chemical factors can influence these properties, impacting the overall performance of the formulation. Additionally, the efficiency of DMNs can differ based on the manufacturing technique employed. Several methods are currently utilized for DMN fabrication, including micromolding, photolithography, droplet air blowing, spray deposition, and 3D printing. Among these, micromolding remains the most widely used approach due to its simplicity, cost-effectiveness, and ease of implementation.[11]

1. Micromolding:

Micromolding technology has significantly progressed, becoming a key method for fabricating dissolving microneedles (DMNs). This technique involves replicating microscale structures by filling micron-sized molds with materials, making it suitable for various substances, including polymers, metal alloys, and ceramics. Micromolding enables cost-effective mass production of components with intricate microscale features, achieving resolutions as fine as tens of nanometers. The preparation process of microneedles depends on the method of drug loading, which is typically classified into one-step and step-by-step approaches. Before fabricating microneedles, a template must be designed to serve as a mold, with its parameters determining the final shape and geometry of the microneedles. Polydimethylsiloxane (PDMS) is commonly used for mold preparation due to its beneficial properties, such as high-temperature resistance, corrosion resistance, and air permeability. Additionally, PDMS molds can be reused multiple times, improving production efficiency.[12][13]

For the fabrication of dissolving microneedles with a fully soluble needle body, a homogeneous mixture of the drug and matrix material is directly applied to the PDMS mold. The mixture is then subjected to vacuum and centrifugation to ensure complete filling of the microneedle cavities. Once dried, the microneedles are demolded and ready for use. In contrast, for microneedles with tip-loading, the drug solution is first introduced into the template, allowing it to fill the microneedle cavities through vacuum or centrifugation. After the drug solution dries, it is coated with a drug-free matrix material before undergoing a second drying process and demolding. Microneedles with a fully soluble body are simpler to manufacture, offer a higher drug-loading capacity, and are easy to handle. However, a drawback is the potential inefficiency in drug delivery, as medication near the base of the microneedle may not fully reach the subcutaneous layer, leading to wastage. In contrast, tip-loaded microneedles ensure precise drug delivery to the subcutaneous tissue, minimizing waste. However, the high drug concentration at the tip may influence penetration efficiency. while the micromolding process offers several advantages, the step involving vacuum or centrifugation for mold filling remains complex. Despite this, it effectively overcomes challenges related to surface tension and solution viscosity, ensuring optimal microneedle formation and performance.[14]

Advantages of Micromolding Method:

•High Precision and Reproducibility -Micromolding ensures the accurate replication of microneedle structures with consistent size, shape, and geometry, leading to uniform mechanical strength and penetration efficiency. This high level of precision enhances batch-to-batch reproducibility, a critical factor in pharmaceutical manufacturing.

•Cost-Effectiveness and ScalabilityThe reuse of molds and the ability to fabricate microneedles in large batches make micromolding economically viable for industrial production. The technique allows for high-throughput manufacturing, reducing production costs compared to other fabrication methods.

•Compatibility with a Wide Range of Materials- Micromolding supports the use of biocompatible and biodegradable polymers, such as polylactic acid (PLA), polyvinylpyrrolidone (PVP), chitosan, and hyaluronic acid, which dissolve in the skin after application, ensuring safe drug delivery.

•Customizable Drug Loading and Release Profiles- The technique allows for tailored drug incorporation, including one-step and stepwise drug loading. This flexibility enables controlled drug release kinetics, ensuring sustained and efficient drug delivery with minimal wastage.

•Minimal Drug Degradation- Micromolding operates under mild temperature and pressure conditions, making it suitable for heat-sensitive biologics, including peptides, proteins, and vaccines, without compromising their stability and therapeutic efficacy.

•Structural Integrity and Mechanical Strength- Micromolded microneedles maintain sufficient mechanical strength to penetrate the stratum corneum without breaking. This ensures effective drug delivery while preventing needle fragmentation, which could pose safety concerns.

Recent Advances in Micromolding:

Recently Innovative Mold Designs The introduction of double-penetration female molds (DPFM) has addressed challenges related to gas resistance and solution viscosity during fabrication. These molds, combined with positive-pressure microperfusion techniques (PPPT), enable high-precision DMN production with improved penetration efficiency. Additionally, Micromolding has been combined with microfluidic droplet technology to enable controlled drug release. This advancement allows for more precise drug delivery profiles, reducing variability and enhancing therapeutic effectiveness.[14][15]

2. Photolithography in the Fabrication of Dissolving Microneedles (DMNs)

Photolithography has emerged as a promising technique for the fabrication of microneedles (MNs), particularly in transdermal drug delivery applications. When combined with photoresponsive materials, this method enables the precise and efficient delivery of therapeutic agents, thereby improving drug efficacy and minimizing systemic side effects. This attribute makes photolithography-based MNs highly valuable in a range of medical applications, including cancer therapy, wound healing, and the diagnosis and treatment of chronic diseases such as diabetes.

Advantages and Limitations of Photolithography in DMN Fabrication

The photolithography process offers several advantages, making it an attractive choice for large-scale MN production. It is cost-effective, efficient, and scalable, allowing for high-throughput fabrication with minimal material waste. One of its key benefits is the ability to rapidly produce microneedle arrays without requiring post-drying steps, significantly reducing the overall production time. Additionally, this technique provides high precision and control over the shape, size, and aspect ratio of the MNs, which is crucial for achieving optimal skin penetration and drug delivery performance.

However, despite its numerous benefits, photolithography has certain limitations. A primary concern is its reliance on high-temperature processing conditions, which may adversely affect the stability and bioactivity of heat-sensitive drugs, limiting its applicability in the formulation of thermosensitive therapeutics. Addressing this challenge requires further research into alternative photoresponsive materials and low-temperature photopolymerization techniques that can preserve drug integrity.[16][17]

Recent Advances in Photolithography-Based DMN Fabrication

In recent years, several studies have explored innovative approaches to optimize photolithography for MN fabrication. Researchers developed a DMN patch using a mild processing method that combined thermal polymerization with photopolymerization. Their approach involved pre-polymerizing a vinyl acetone solution followed by a controlled heating and photolithography step. By optimizing the heating temperature and curing time based on viscosity measurements, they successfully created DMNs with enhanced structural integrity and drug-loading efficiency.[18]

Similarly, Researchers investigated conditions for fabricating high-aspect-ratio MNs using photopolymerization of polyethylene glycol diacrylate (PEGDA). By selectively crosslinking photocurable prepolymers using UV light, they optimized processing parameters to achieve MNs capable of efficiently penetrating the stratum corneum. These advancements demonstrate the

potential of photolithography in creating next-generation MNs with improved mechanical strength and drug delivery capabilities.[13]

3. Droplet-Born Air Blowing (DAB) method in the Fabrication of Dissolving Microneedles (DMNs):
The Droplet-Born Air Blowing (DAB) method has emerged as a novel and efficient technique for fabricating dissolving microneedles (DMNs), offering significant advantages over traditional fabrication methods. This review provides an in-depth analysis of the DAB method, its fabrication process, advantages, recent advancements, and future prospects. The DAB method involves shaping a drug-containing polymer solution into microneedles through controlled air blowing. This process operates under mild conditions, typically between 4 to 25℃, and achieves rapid fabrication within approximately 10 minutes, thereby minimizing potential drug degradation. The quantity of drug incorporated into the microneedles can be precisely controlled by adjusting the pressure and duration of the droplet dispenser. Subsequent air blowing molds these droplets into microneedles capable of effectively penetrating the skin. [19]

Advantages of the DAB Method
•Preservation of Drug Activity: The mild fabrication conditions inherent to the DAB method help maintain the stability and efficacy of sensitive biological drugs, reducing the risk of denaturation or loss of activity.
•Rapid Production: The DAB technique enables swift microneedle fabrication, enhancing production efficiency and scalability.
•Precise Drug Loading: By regulating dispensing parameters, the DAB method allows for accurate control over drug dosage within each microneedle, ensuring consistent and effective delivery.
•Elimination of Harsh Conditions: Unlike some traditional methods that may require high temperatures or UV exposure, the DAB process operates without such conditions, making it suitable for a broader range of pharmaceuticals.

Recent Advancements
Recent studies have demonstrated the efficacy of DAB-fabricated microneedles in delivering therapeutic agents. For instance, insulin-loaded microneedles produced using the DAB method exhibited a bioavailability of 96.6 ± 2.4%, comparable to that of subcutaneous injections, and effectively reduced blood glucose levels.
Additionally, research has explored the application of DAB in incorporating sensitive biopharmaceuticals, indicating its potential in preserving drug activity during fabrication. [20]

4.Centrifugal Lithography for Dissolving Microneedles (DMNs) Fabrication:
Centrifugal lithography is an advanced fabrication technique that combines centrifugal force and photolithography to create dissolving microneedle (DMN) structures. In this method, a drug-polymer solution is spread within a microneedle mold, where centrifugal force propels the solution toward the mold edges, forming well-defined microneedles. Once shaped, the polymer undergoes light curing to solidify the DMNs. This technique is particularly advantageous for drugs with unstable physicochemical properties or volatile compounds, as it helps preserve drug activity. However, the process requires a strictly controlled low-temperature environment to prevent degradation.

Advantages of the Centrifugal Lithography Method
•Preservation of Drug Activity – This method is particularly suitable for heat-sensitive and volatile drugs, as it operates under low-temperature conditions, reducing the risk of degradation.
•Uniform Microneedle Formation – The centrifugal force ensures even distribution of the polymer-drug solution within the mold, leading to consistent and reproducible microneedle structures.
•Enhanced Mechanical Strength – The curing process strengthens the microneedles, ensuring they have sufficient fracture resistance for effective skin penetration.
•Efficient Drug Loading – The technique enables precise control over drug incorporation, improving dose accuracy and therapeutic efficiency [21]

Recent Advancements
Centrifugal lithography has emerged as a pivotal technique in the fabrication of microneedles (MNs), offering precise control over microneedle geometry and drug loading. Recent advancements in this area have significantly enhanced the efficacy and versatility of MNs in biomedical applications. One notable development is the integration of centrifugal lithography with advanced materials to produce microneedles with superior mechanical properties and biocompatibility. Researchers have explored the use of various polymers and composites to fabricate microneedles that are both robust and capable of efficient drug delivery. These materials ensure that the microneedles can penetrate the skin effectively without breaking, thereby improving the reliability of transdermal drug delivery systems.[22]

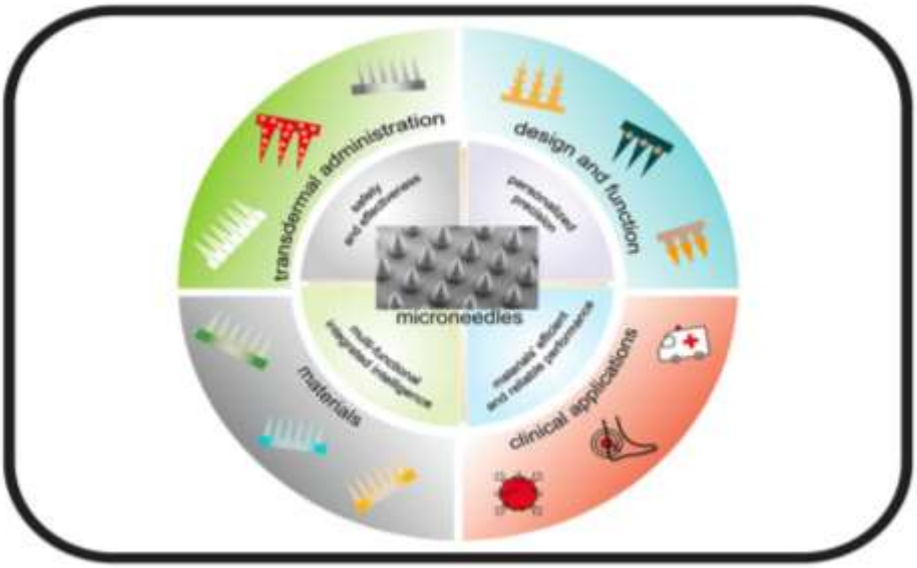

Figure no 4: microneedle design, clinical application and material used

Literature review of past prepared TDDS-Microneedle:

Sr No.	Drug Name	Observation	References
1	Insulin	Achieved 96.6% bioavailability through microneedle patch compared to subcutaneous injection.	Henry et al. (1998) [23]
2	Diclofenac Sodium	Controlled and sustained drug release was observed using polymeric microneedle patch.	Cunha-Filho et al. (2010) [24]
3	Human Growth Hormone (hGH)	Effective transdermal delivery of hGH with improved bioavailability.	Li et al. (2010) [25]
4	Lidocaine	Rapid local anesthesia with minimal pain sensation using dissolving microneedles.	Donnelly et al. (2012) [26]
5	DNA Vaccine	Increased immune response using microneedle-assisted transdermal delivery.	Prausnitz et al. (2010) [27]
6	Methotrexate	Effective treatment of rheumatoid arthritis using co-administration through microneedles.	Shende et al. (2019) [28]
7	Insulin	Higher bioavailability of insulin compared to subcutaneous administration.	Martanto et al. (2006) [29]
8	Paracetamol	Controlled drug release and rapid absorption through microneedle patches.	Kim et al. (2012) [30]

9	Naltrexone	Long-acting release achieved through dissolving microneedles.	Donnelly et al. (2012) [26]
10	Etanercept	Effective treatment of rheumatoid arthritis using microneedle patches.	Cao et al. (2019) [31]

Table no 1: Literature review of past prepared TDDS-Microneedle

Applications of Microneedle Patches in Various Medical Treatments:

1.Immunotherapies

Microneedle (MN) technology has shown great potential in immunotherapy by utilizing the skin as a delivery site due to its high concentration of antigen-presenting cells (APCs), such as dendritic cells, macrophages, and Langerhans cells. These cells help initiate systemic immune responses by activating CD4+ and CD8+ T and B cells. To enhance preventative cancer immunotherapy, researchers have developed biodegradable MN patches that combine hyaluronic acid (HA) with antigenic peptides. In one study, an HA-based MN patch was loaded with the cytotoxic T-cell epitope peptide SIINFEKL, allowing efficient transdermal antigen delivery. The results showed that HA-SIINFEKL conjugates remained in the administration site for over 24 hours, significantly reducing tumor formation in a B16 melanoma mouse model by stimulating strong antigen-specific T-cell responses. Additionally, a novel MN patch composed of glucose oxidase (GOx) and HA-encapsulated dextran nanoparticles carrying an anti-PD1 antibody (aPD1) was designed. When applied, GOx converts blood glucose into gluconic acid, lowering the pH and triggering the self-dissociation of nanoparticles, thereby releasing aPD1. Furthermore, dissolvable MNs have proven effective in transdermally delivering DNA to APCs, enhancing immune response efficiency. However, challenges remain in increasing the loading capacity of DNA delivery vectors within MN systems. Another study investigated the transdermal administration of human IgG using MN arrays, demonstrating that higher MN concentrations and longer MN lengths significantly improved the delivery of IgG across the skin.[32]

2.Microneedle Patches for Photoaging Skin Treatment

Skin photoaging, caused by prolonged UV exposure, leads to oxidative stress, collagen degradation, and structural skin damage. While conventional treatments like retinoids, antioxidants, and laser therapies offer temporary results and potential side effects, MN patches provide a minimally invasive and effective transdermal drug delivery alternative. MN patches create microchannels in the skin, allowing for localized and controlled drug release, which enhances absorption, collagen regeneration, and overall skin rejuvenation. One promising approach is the use of MN patches to deliver extracellular vesicles (EVs) derived from adipose stem cells (ADSC-EVs), which have shown anti-inflammatory and collagen-boosting properties. MN patches loaded with COL1A1-mRNA-encapsulated EVs significantly enhance collagen production and improve skin elasticity more effectively than injections. Additionally, protein-based MN patches, such as those incorporating adipose collagen fragments (ACF) or fibroblast growth factors (FGF-2 and FGF-21), have demonstrated long-lasting antioxidant effects and the ability to reverse UV-induced cellular damage. Another novel application involves MN patches loaded with living Chlorella microalgae. These patches continuously produce oxygen through photosynthesis, reducing oxidative stress and inflammation while enhancing collagen synthesis and minimizing wrinkles. Clinical studies have also validated the effectiveness of dissolvable MN patches (DA-MNP) containing hyaluronic acid, peptides, and vitamin C derivatives, which improve skin hydration, elasticity, and wrinkle reduction with minimal side effects. [33]

3.Cancer Treatment Using Microneedle Patches

Conventional cancer treatments such as chemotherapy, radiation, and surgery often lead to severe side effects, acute toxicity, and potential tumor recurrence. MN patches offer a minimally invasive and controlled alternative for drug delivery, improving treatment outcomes and reducing systemic toxicity. Researchers have developed HA-based dissolving MN arrays containing doxorubicin (DOX) and gold nanocages to combine chemotherapy with photothermal therapy for enhanced superficial tumor treatment.[34] Cancer immunotherapy has also advanced with the development of MN patches encapsulated with anti-PD1 antibodies (aPD1) and 1-methyl-D,L-tryptophan (1-MT), which prevent immune evasion and block the immunosuppressive enzyme indoleamine 2,3-dioxygenase (IDO). This synergistic transcutaneous delivery system enhances melanoma immunotherapy by enabling HA-based MN patches to dissolve in the tumor microenvironment.[35] Another innovative approach utilizes dissolvable MN patches composed of poly(vinyl alcohol)/polyvinylpyrrolidone (PVA/PVP), supporting photothermal nanoparticles and anti-tumor drugs to eradicate 4T1 tumors within one week without recurrence.[36] Additionally, hollow MN injection systems have been designed to deliver synthetic long peptides for therapeutic cancer vaccines. Compared to traditional intradermal injections, these MN patches improve vaccine immunogenicity by allowing lower-volume, targeted delivery. RNA interference (RNAi) has also been explored for targeting cancer-related genes, with MN patches demonstrating successful siRNA delivery to inhibit tumor progression. A breakthrough in this field is the use of RALA peptides encapsulated with the E6/E7 plasmid DNA in dissolvable MN patches, effectively delaying tumor growth in therapeutic models.[37]

4.Obesity Management Using Microneedle Patches

Obesity involves an imbalance between brown adipose tissue (BAT), which promotes energy expenditure, and white adipose tissue (WAT), which stores excess fat. Recent studies have explored the potential of MN patches for weight management by delivering anti-obesity agents through the skin. HA-based dissolving MN patches loaded with caffeine, a known metabolic enhancer, have demonstrated significant weight loss effects in high-fat diet-induced obese mice. [38]-[39] Additionally, MN patches have been designed to release browning agents such as β3-adrenoceptor agonists and thyroid hormone T3, converting WAT into BAT to boost energy expenditure and prevent weight gain. This controlled transdermal delivery method enables long-

term obesity management.[40] A more advanced approach involves a locally induced browning patch encapsulating rosiglitazone (Rosi), which not only inhibits fat accumulation but also enhances insulin sensitivity. This HA-based MN system contains nanoparticles encapsulating Rosiglitazone, glucose oxidase to create an acidic environment, and catalase to remove unwanted hydrogen peroxide. The resulting system effectively promotes white fat metabolism, leading to reduced adipose tissue.[41]

5.Microneedle Patches for Arthritis Treatment

Rheumatoid arthritis (RA) is a chronic autoimmune condition that causes joint inflammation and pain. Conventional treatments, such as subcutaneous injections of etanercept (a TNF-α inhibitor), have limitations due to poor patient compliance, adverse effects, and infection risks. To address these challenges, researchers have developed etanercept-loaded dissolvable MNs crosslinked with HA, ranging in size from 50 to 900 µm, to enhance biocompatibility and anti-inflammatory efficacy.[42] Another innovative approach is the development of methotrexate-loaded MN arrays containing PLGA microspheres of folic acid to improve drug bioavailability and reduce the required dosage [43]. Additionally, a hydrogel MN system was created to deliver aptamer DTA6, which blocks the DEK protein, a key factor in neutrophil formation in RA. This system enhances aptamer stability for up to 72 hours and effectively protects joints and bones from erosion in collagen-induced arthritis models.[44]

6.Ophthalmic Applications of Microneedle Patches

Ophthalmic drug delivery is challenging due to anatomical barriers, limited bioavailability, and rapid drug clearance. Conventional treatments often require high drug concentrations, increasing the risk of toxicity. MN patches have been developed to deliver drugs directly to affected ocular tissues, bypassing the cornea, blood-aqueous barrier, and tear film. [45] Studies on scleral drug delivery using MN patches in rabbits demonstrated prolonged drug retention in the eye for up to two months, compared to one-day retention with conventional formulations. Ex-vivo research further confirmed that MN patches can successfully deliver 6-aminoquinoline into the sclera without clogging pores.[46] For glaucoma treatment, MN patches have been developed with sizes ranging from 400 to 700 µm, enabling sustained intraocular drug delivery while reducing aqueous humor production and improving absorption rates. A study using stainless steel MNs loaded with pilocarpine demonstrated a 45-fold increase in drug absorption. Another approach combined sulforhodamine with hollow MNs, using borosilicate micropipette tubes to limit drug administration to 10–35 µL, ensuring precise dosing and prolonged therapeutic effects.[47]

Challenges:

Extensive research is currently being conducted to explore the impact of microneedles (MN) on transdermal drug delivery. These micron-sized needles hold significant potential for enhancing drug transport across the skin. However, for their widespread clinical adoption, several challenges must be addressed. These include issues such as skin irritation, the risk of microbial contamination, and the need to achieve therapeutically relevant drug concentrations.

Further obstacles include the limited availability of suitable biomaterials, inadequate mechanical strength of some MN, difficulties in controlling drug release, and restrictions on drug loading capacity. Potent drugs that require lower doses, as well as vaccines, appear to be the most promising candidates for delivery via microneedles in effective concentrations. Another key challenge is the transdermal delivery of macromolecules, particularly those derived from biotechnological advancements. These molecules often possess high molecular weights and significant hydrophilicity, making skin penetration particularly difficult.

Additionally, concerns have been raised regarding the mechanical strength of certain microneedles, particularly those made from silicon or specific polymers, which may not provide sufficient force to effectively pierce the skin. Ideally, microneedles should be designed to require minimal insertion force while exhibiting high fracture resistance. Furthermore, the conventional two-step application process, where the skin is first porated using MN before applying a drug-loaded patch, can be cumbersome. In this context, hydrogel-forming microneedles have emerged as a promising alternative, offering a simplified and efficient approach.

Another crucial factor to consider is the need to optimize penetration enhancement while maintaining a pain-free experience for the patient. Striking the right balance between these aspects will be essential in advancing microneedle technology for broader clinical applications.[48]

Future Perspectives and Outcomes

Microneedle (MN) technology is rapidly advancing, with ongoing research aimed at enhancing drug delivery efficiency, patient comfort, and clinical applicability. Smart microneedles equipped with biosensors enable real-time monitoring of biomarkers and controlled drug release in response to physiological triggers, improving precision medicine. Additionally, combining microneedles with nanoparticles and hydrogels enhances drug stability, bioavailability, and sustained release, particularly for biologics and macromolecules. The advent of 3D printing has facilitated the fabrication of customized microneedles with precise drug loading, while biodegradable materials help reduce medical waste and improve patient compliance. Furthermore, microneedles are being explored for personalized medicine, with the potential to tailor drug dosages based on genetic profiles, while diagnostic microneedles enable non-invasive biomarker analysis for early disease detection. These innovations are paving the way for more efficient, patient-friendly, and scalable microneedle-based therapies.[49]

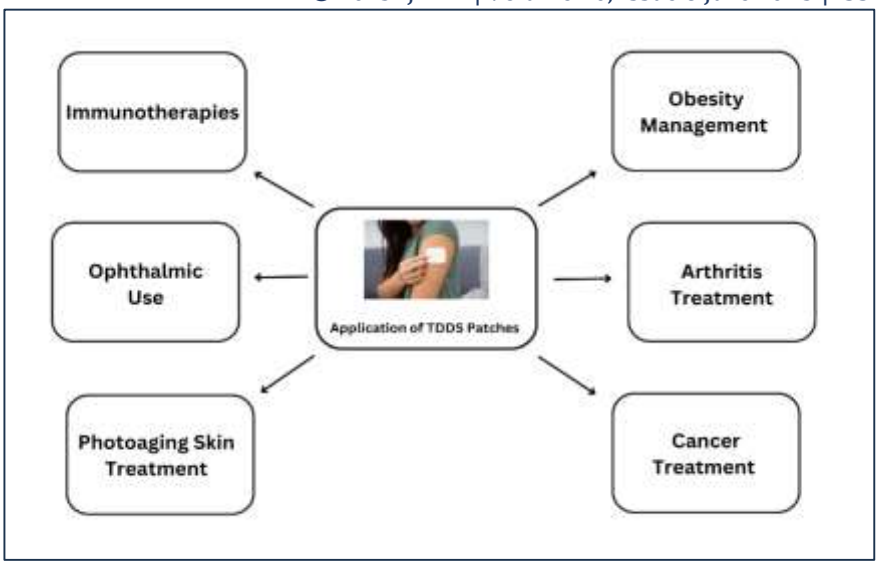

Figure no: 5 *Application of Transdermal Microneedle Patches*

Conclusion:

The advancements in transdermal drug delivery systems (TDDS) have positioned microneedle (MN) technology as a highly promising alternative to traditional drug administration methods. Microneedles, particularly dissolving microneedles (DMNs), have demonstrated superior biocompatibility, ease of fabrication, and improved patient compliance compared to hypodermic injections and conventional transdermal patches. Their ability to efficiently deliver both small and large biomolecules, including peptides, proteins, and vaccines, highlights their versatility in modern medicine. Various fabrication techniques, including micromolding, photolithography, droplet air blowing, and centrifugal lithography, have significantly enhanced the mechanical strength, drug-loading capacity, and controlled-release properties of microneedles. These innovations have paved the way for improved therapeutic outcomes in areas such as vaccination, chronic disease management, cancer treatment, and dermatology. The incorporation of biodegradable and water-soluble polymers has further minimized biohazardous waste, making microneedles an environmentally sustainable solution. Despite these advancements, challenges remain in optimizing drug stability, enhancing mechanical integrity, and scaling up manufacturing for commercial production. Future research should focus on smart microneedle systems, personalized medicine applications, and nanotechnology integration to further refine transdermal drug delivery. With continued technological innovations, microneedles have the potential to revolutionize painless, efficient, and controlled drug administration, improving patient outcomes across multiple therapeutic domains.

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