**Original Research Article**

# REVIEW ON: RECENT ADVANCEMENT OF MEDICATED PATCH

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**Abstract:**
Transdermal patches represent a non-invasive approach to drug administration, involving adhesive patches that efficiently transport specific medication doses through the skin and into the bloodstream. This method boasts several advantages compared to alternative administration routes, including its minimally invasive nature, patient convenience, and the capacity to bypass initial metabolic processing and the harsh acidic conditions of the stomach associated with oral drug ingestion. Over the years, transdermal patches have garnered significant interest and have been instrumental in delivering a range of medications, such as nicotine, fentanyl, nitro-glycerine, and clonidine, to address diverse medical conditions.
In recent times, the potential of transdermal drug delivery has expanded beyond conventional applications, encompassing the administration of biologics for various therapeutic purposes. This article provides a comprehensive survey of the available literature concerning the formulation and utilization of medical patches in the context of transdermal drug delivery. The primary focus is on recent strides in technological innovation that have given rise to novel advancements, notably in the realms of intelligent patches, degradable/biodegradable patches, high-capacity drug loading, release patches, and even patches crafted through 3D printing techniques.

## INTRODUCTION

The skin is vital for protecting the body from its external environment, acting as a highly effective barrier against the entry of substances. [1] The skin helps regulate body temperature and creates a protective barrier, shielding inner tissues from pathogens and environmental shifts. Its ability to renew itself aids in wound healing. As a result, higher doses of drugs are often needed for effective treatment, but these doses can lead to unintended reactions due to the drug's behavior in the body.

To address these side effects, delivering drugs directly to the affected area over time is seen as a promising method. [2]

A Transdermal Drug Delivery System (TDDS), commonly called a transdermal patch, is a flexible pharmaceutical device composed of multiple layers that can be adjusted in size. It contains one or more active substances and is formulated for application onto unbroken skin to facilitate the systemic absorption of these substances. [3] Transdermal drug delivery (TDD) is increasingly preferred over oral ingestion or injections of NSAIDs due to several reasons, presenting a safer and more preferable option.[4] It offers precise medication delivery by bypassing liver metabolism and quick absorption in the digestive system, thereby lowering the chances of internal bleeding and irritation.[5] It permits the medication to pass through the outermost layer of the skin (stratum corneum) and access both the epidermis and dermis layers, enabling therapy at both localized and systemic levels.[6,7]Moreover, transdermal drug delivery often removes the discomfort associated with administration and potential systemic side effects that might arise from oral ingestion. Wearing the transdermal patch is convenient, and the idea of "wearability" encompasses various factors affecting the wearer's comfort, including physical, psychological, and social aspects. Improving wearability and comfort involves the utilization of innovative materials and designs.[8]

The concept of transdermal medication delivery isn't recent. Its use in homemade medicinal treatments dates back to the early 1900s. Today, transdermal patches serve various purposes, including cosmetic, topical, and delivery systems. These patches signify a significant advancement resulting from the progress in skin science, technology, and expertise, established through trial and error, clinical observations, and evidence-based studies documented since ancient human records. This progression involves examining the development of different patch designs, their constraints, and the necessary qualities of actives for transdermal delivery.[9] The initial transdermal system designed for systemic delivery, a three-day patch dispensing scopolamine to alleviate motion sickness, received approval for use in the United States in 1979. [10]

A transdermal patch is a specifically designed, outer, ongoing, and extended-release medication format. To clarify:

- Specifically designed: precise and predetermined in its structure and composition.
- Outer: applied externally, not taken by mouth, inhaled, implanted, inserted, or injected.
- Ongoing: capable of maintaining drug release consistently, regardless of short half-life or narrow therapeutic window.
- Extended release: offering a dosage interval of up to a week between administrations.[11]

Pros and Cons of using transdermal patches: [12]

| Advantages | Disadvantages |
|---|---|
| Self-administered | Molecular size restriction |
| Alternative route | Low permeability limits |
| Improved patient compliance | Variation in barrier function |
| Flexibility of termination | High cost |
| Steady infusion | Local irritation |

**BASIC COMPONENT OF TRANSDERMAL PATCH** [13]

1. Backing and liners
2. Polymer matrix or matrices
3. The drug
4. Permeation enhancers
5. Adhesives

**1) Backing and liners** [14]

**Backing**

The outer adhesive layer of the transdermal patch, known as the transdermal liner, shields the formulation while it's being worn. When selecting a transdermal base, factors like its barrier characteristics, patient comfort, and appearance should be taken into account.

**Liners**

The transdermal release liner serves to protect both the adhesive and the drug formulation and must be taken off before applying the patch.

**2) Polymer Matrix** [15]

The polymer controls the release of the drug. Possible useful polymers for transdermal devices are.

Natural Polymers:

Cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch, etc.

Synthetic Elastomers:

Polybutadiene, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene- butadiene rubber, Neoprene, etc.

Synthetic Polymers are Polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate, Polyamide, Polyurea, Polyvinylpyrrolidone, Polymethylmethacrylate, Epoxy, etc.

**3) Drug** [13]

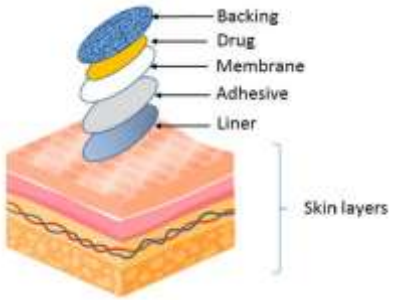
Careful selection of the drug is crucial for the successful development of a transdermal drug delivery system.

**4) Permeation enhancers** [16]

These substances are suggested to improve the transport through the polar pathway, particularly for hydrophilic drugs. The capacity of a surfactant to modify penetration relies on the nature of its polar head group and the length of its hydrocarbon chain. However, these compounds tend to irritate the skin, so it's crucial to strike a balance between enhancing penetration and causing irritation.

**5) Adhesives** [17]

Up until now, the attachment of all transdermal devices to the skin has been achieved using pressure-sensitive adhesive. This adhesive can be situated on the front or back of the device and can extend around its edges.




The basic component of a transdermal medical patch

**TRANSDERMAL PATCH DESIGN** [13,18]

The following criteria should be satisfied for a transdermal patch

i. Polymer properties like molecular weight, glass transition temperature, and chemical structure need to allow proper drug diffusion and release.

ii. The polymer should be stable, non-reactive with the drug, easy to manufacture into the desired product, and cost-effective.

iii. Both the polymer and its breakdown products must be safe for the body, non-toxic, and not cause any adverse effects.

iv. The drug's molecular weight should generally be below 1000 daltons.

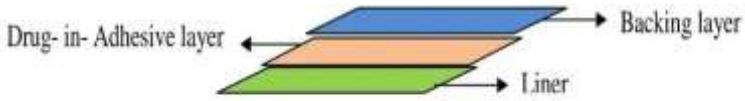
v. The drug should have an affinity for both lipid-based and water-based environments; extreme characteristics aren't favourable for successful skin drug delivery.

vi. It should strongly adhere to the skin during the dosing period without being displaced by activities like bathing or exercise.

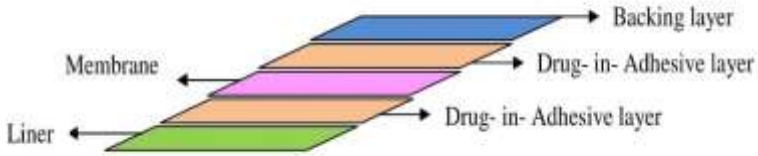
vii. It should be easily removable and not leave any residue on the skin that can't be washed off.

**TYPES OF TRANSDERMAL PATCHES**

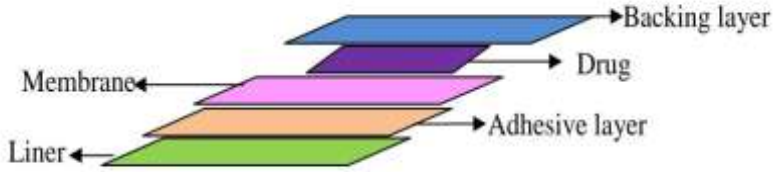
a) Single-layer drug in adhesive system: In a single-layer drug in adhesive system, the drug is incorporated within the adhesive layer. This layer not only binds the different components together but is also responsible for delivering the drug to the skin. The adhesive layer is encased by a temporary liner and a backing material. A standard example of this system is illustrated in the accompanying diagram. [19]



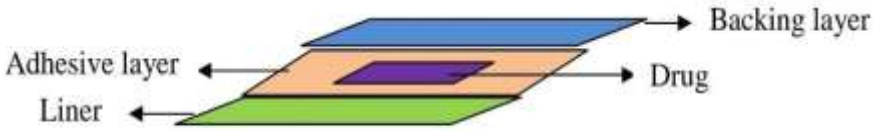

b) Multi-layer drug-in-adhesive system: The multi-layer drug-in-adhesive system resembles the single-layer design but incorporates multiple layers of drug-in-adhesive. This configuration is typically employed for extended-duration patches. As each layer closest to the skin completes drug delivery, it initiates diffusion through the subsequent layers, ensuring a continuous release over time.[20]




c) Reservoir System: Within this setup, the drug reservoir is positioned between the backing layer and the rate-controlling membrane. The drug is then discharged via the microporous rate-controlling membrane. The drug may exist as a solution, suspension, or gel, or it can be distributed within a solid polymer matrix within the reservoir space.[21]




d) Matrix patch: In a transdermal matrix patch, a drug-containing adhesive polymer matrix gradually releases the drug into the skin. Unlike a reservoir patch with a rate-controlling membrane, the rate of drug delivery in a matrix patch is determined by the formulation of the drug and polymer matrix. The active ingredient is uniformly distributed across the patch, reducing the likelihood of unintended or accidental release.[22]




## COMMON TRANSDERMAL PATCH DRUGS

The conventional transdermal patch primarily focuses on storing and releasing the drug. While it offers certain benefits, this method also presents several challenges and limitations, such as restricted dosage and modest release rates. Recent advancements in transdermal drug delivery have introduced innovative patch designs capable of precise drug sensing and release, increased drug loading, improved penetration, and enhanced release rates. Overall, the field of transdermal drug delivery is a vibrant area of ongoing research and development, showcasing numerous promising advancements on the horizon.[23]

Common transdermal patches/drugs and their unique features:

| DRUGS | INDICATIONS | REFERENCE |
|---|---|---|
| Diclofenac | Anti-analgesic | [24,25] |
| Nitroglycerine | Angina Pectoris<br>Relieve Pain After Surgery | [26,27] |
| Nicotine | Smoking Cessation | [28] |
| Dimenhydrinate | Nausea, Vomiting, and Dizziness caused by motion sickness | [29] |
| Duloxetine hydrochloride | Anti-depression | [30] |
| Testosterone | Hypogonadism in men | [31] |
| Scopolamine | Motion-sickness | [32] |
| Methylphenidate | Attention deficit hyperactivity disorder (ADHD) | [33] |
| Estradiol | Prevention of postmenopausal | [34,35] |
| Oxybutynin | Overactive bladder | [36] |
| Buprenorphine | Management of pain | [37] |
| Rotigotine | Parkinson's disease | [38,39] |
| Rivastigmine | Alzheimer disease | [40,41] |
| selegiline | Depressive disorder | [42] |
| Clonidine | High blood pressure | [43] |

## RECENT ADVANCEMENT OF TRANSDERMAL PATCH

### ➢ MICRONEEDLE BASED PATCHES

Biotherapeutics and vaccines are commonly administered through hypodermic needles, offering a quick, cost-effective, and direct means to introduce various molecules into the body. However, these needles pose challenges as they are not easily manageable by patients themselves. Hence, they are predominantly employed in clinical settings or by patients who have undergone specific training on proper injection techniques, safe disposal of needles, and related concerns. This reliance on specialized administration methods can restrict patient compliance.[44] The microneedle (MN) array is employed to penetrate the outer layer of the skin (stratum corneum) and deliver medication in a minimally invasive manner. These arrays consist of tiny needles, typically ranging from 25 to 2000 μm in height.[45] Microneedles (MNs) have found diverse applications in drug and vaccine delivery, cosmetics, and disease diagnostics. They come in various structural configurations, shapes, compositions, and materials, employing different manufacturing techniques.[46]
There are four types of microneedle-based patches as discussed below.

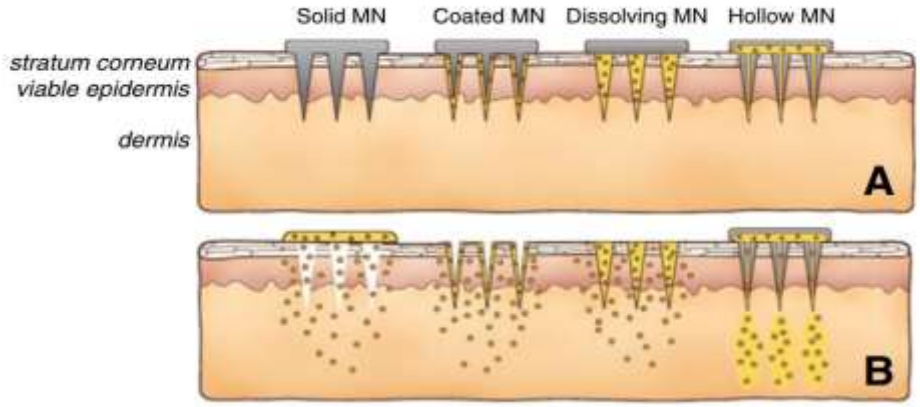
1.) Solid Microneedles: Microneedles serve as a pre-treatment method to create pores in the skin. These fine needles either pierce or abrade the skin, forming holes through which drugs can travel. This allows for localized skin effects or systemic delivery when absorbed by skin capillaries. Drugs can be administered onto the skin surface over these pores using a drug-loaded patch, similar to traditional transdermal drug delivery, or via semi-solid topical formulations like ointments, creams, gels, or lotions, commonly used for various skin treatments.[44]

2.) Coated Microneedles: The coated microneedle refers to a solid microneedle coated with a solution containing a drug. Usually, it contains a limited quantity of the drug, determined by the thickness of the applied coating. Effectively delivering a drug via coated microneedles relies on the

consistent and controlled application of a drug layer onto these microneedles.[46] A coated microneedle enables the minimally invasive delivery of proteins and DNA.[47]

3.) Dissolving Microneedles: Dissolving microneedles are traditionally fabricated by encapsulating the drug into biodegradable polymers. After penetrating the stratum corneum, the polymer forming the needle architecture dissolves and releases the entrapped drug.[48]

4.) Hollow Microneedles: Hollow microneedles are comprised of an internal void within each needle and a channel at the needle tip. This setup permits minute quantities of drug solutions to be injected into the skin through a "poke and flow" mechanism. Various materials such as ceramics, metal, silicon, and glass have been used to create hollow microneedles. The advantage of hollow microneedles becomes apparent when compared to a challenge associated with the "poke and patch" method. After the removal of solid microneedles applied onto the skin, the microchannels formed quickly heal, closing the openings.[49,50]




## ➢ SMART PATCH

A medical skin adhesive patch stands as a fundamental and adaptable tool utilized across various medical applications. Unlike conventional adhesive patches for the skin, modern developments have integrated several crucial functionalities of larger medical devices into a slim, flexible patch. These advancements leverage emerging nanomaterials and flexible electronic technologies.[51] Presently, diabetes impacts more than 285 million individuals globally and is anticipated to affect 1 out of every 10 people by 2030, as per the World Health Organization. The American Diabetes Association reports that in the United States alone, over 25 million people are affected by type 1 and type 2 diabetes.[52] For individuals with diabetes, maintaining precise and continuous monitoring of blood glucose levels over an extended period is a significant challenge.[53] Achieving consistent adherence to testing is challenging due to the uncomfortable and repetitive nature of the conventional finger-prick method commonly used.[54] To achieve this goal, our aim was to create a sensor platform called the "Smart Patch,"utilizing microneedles for continuous intradermal sensing that is painless.[52] Continuous glucose monitoring (CGM) offers comprehensive details that intermittent blood sampling cannot provide. It includes real-time, round-the-clock display of glucose levels, rate of glucose level changes, and alerts for current or potential hypo and hyperglycemia. This continuous monitoring yields extensive information about fluctuating glucose

levels, encompassing their scale, trends, duration, and frequency, ultimately enhancing the quality of treatment for individuals with diabetes.[55]

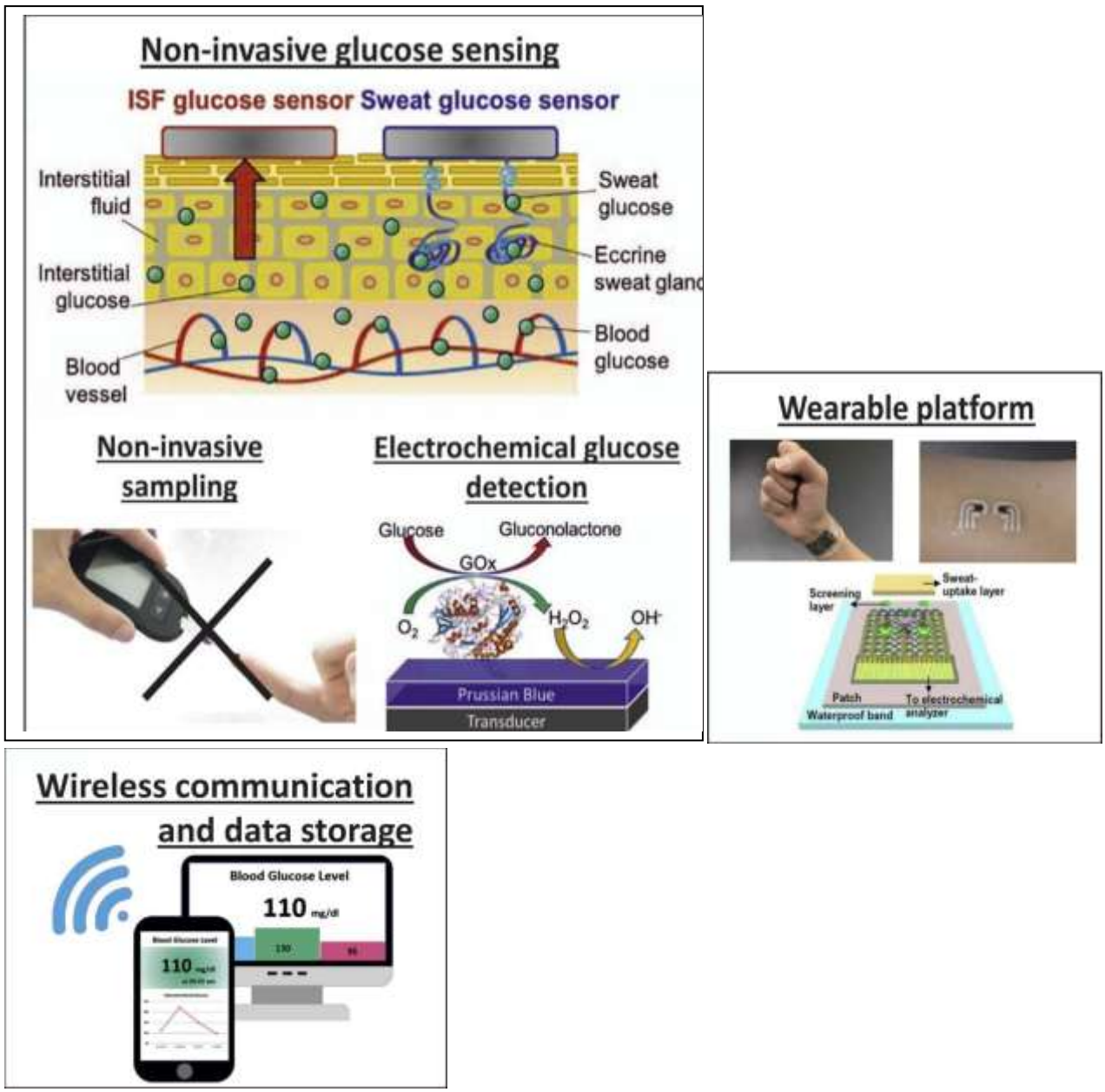



Illustration representing wearable epidermal glucose sensors. Visualization of wearable platforms arranged from left to right, reproduced from [source]. [56] Copyrighted in 2016 by Macmillan Publishers. Reproduced from [source] [57] Copyright 2014, American Chemical Society. Reproduced from. [58] Copyright 2017, American Association for the Advancement of Science

Wound care and its treatment have posed significant challenges for healthcare providers. Both short-term and long-lasting wounds pose a substantial risk to global health and economic stability. The increasing need exists for smart disposable patches capable of offering efficient and timely wound management. These patches utilize biochemical and physiological sensing to monitor parameters like pH levels, temperature, hydrogen peroxide, wound exudate volume, lactate, and glucose. [59] The pH level within a wound area serves as a crucial indicator for evaluating the progress of healing.[60] The wound's pH level is linked to protease activity, angiogenesis, and

bacterial infection, emphasizing the importance of continuous, real-time pH detection for monitoring the healing process. [61]

Sweat, an underexplored biofluid, holds significant promise as it contains biochemical details providing comprehensive insights into the body's dynamic metabolic functions. Its diverse makeup, comprising electrolytes, metabolites, hormones, proteins, nucleic acids, micronutrients, and external elements, fluctuates dynamically based on health status, stress levels, and dietary factors.[62] Continuous, non-invasive monitoring of biomarkers poses a distinctive challenge in sports, exercise science, and healthcare. This need arises to evaluate human performance, health, and overall well-being. For instance, tracking hydration levels and essential signs during sports activities can offer extensive insights into an individual's physiological capabilities and efficiency during stressful conditions.[63] Even during inactive moments such as sitting or sleeping, the production of sweat for thermoregulation occurs at notably lower rates compared to the higher rates observed during exercise. This lower secretion rate, often just a few nL min−1 cm−2, presents challenges in both collection and analysis compared to the much higher rates observed during physical activity, reaching hundreds of nL min−1 cm−2. Nevertheless, sweat generated near or during rest can offer distinct insights into body physiology, differing from exercise-induced, thermally induced, or chemically induced sweat, and is utilized for non-invasive assessment of body physiology.[64]

## ➢ THREE-DIMENSIONAL PRINTED PATCH (3D)

Specialists are using advancements in 3D printing to create customized transdermal patches tailored to address the specific needs of individual patients.[65] An example illustrating this is the use of 3D-printed patches for cardiac function recovery. Substantial scientific research has focused on reinstating myocardial cell displacement and curtailing ventricular remodeling following a heart attack (MI). Our study investigated the potential of a three-dimensional (3D) engineered fibrin patch infused with human umbilical cord blood-derived mesenchymal stem cells (UCBMSCs) to aid in restoring cardiac function after a heart attack. These UCBMSCs were genetically modified to express luciferase and fluorescent protein markers. They were then combined with fibrin to create a cohesive and viable structure, referred to as a fibrin-cell patch, affixed to the infarcted myocardial tissue in mice, constituting the MI-UCBMSC group.

Attachment of the patch to the heart has been verified. By employing non-invasive bioluminescence imaging, we observed the initial proliferation and differentiation of UCBMSCs within the engineered patch in post-heart attack mice belonging to the MI-UCBMSC group.[66]

Another study explores the application of 3D-printed patches in wound healing. Jang et al. investigated the potential of gelatin methacrylate (GelMA) as a viable option with adjustable physical characteristics. They successfully printed GelMA hydrogel containing a mimic peptide of vascular endothelial growth factor (VEGF) using a 3D bioprinter, benefiting from the hydrogel ink's capability to thin under shear. The resulting 3D hydrogel patch exhibited high porosity and water absorption properties. The slow release of the VEGF peptide from these patches showed promise in enhancing cell viability, proliferation, and the formation of tubular structures. This suggests that a 3D Gel-MA-VEGF hydrogel patch holds potential for applications in wound dressings. [67] Alternatively, 3D printing technology, known as Continuous Liquid Interface Production (CLIP), is utilized for the design and production of transdermal patches. [68]

# EXPLORING THE VERSATILITY OF TRANSDERMAL PATCHES: POTENTIAL APPLICATIONS AND BENEFITS

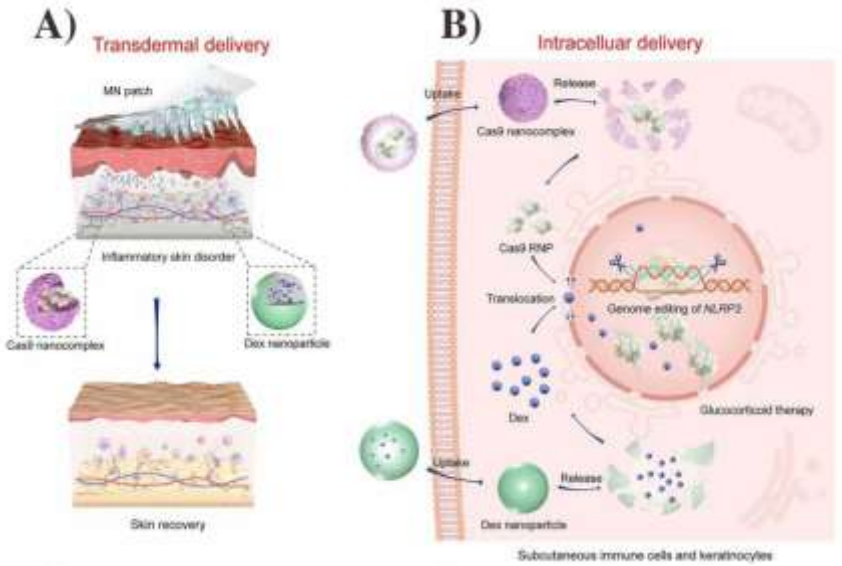
## ➢ TRANSDERMAL PATCH FOR VACCINATION

Vaccines have a historical origin dating back to the late 18th century. By the late 19th century, laboratory-based vaccine development became feasible. However, it wasn't until the 20th century that the development of vaccines using immunologic markers became achievable. [69] Vaccines, a biological tool enhancing immunity against specific diseases, stand as a paramount achievement in the field of medicine. Over time, numerous diseases like measles, rubella, tetanus, pertussis, and yellow fever have been effectively managed through conventional vaccines. While most injectable vaccines prove effective, they still present challenges related to pain, needle-associated ailments, or injuries.[70] The majority of vaccines are delivered via hypodermic needle and syringe injections, requiring a skilled healthcare professional for safe administration and disposal of sharps waste. Microneedle patches (MAPs) have emerged as a potential solution to enhance vaccination, particularly in developing nations, and are becoming a focal point of research in academic and industrial settings. These microneedles, measuring less than one millimeter in length, administer vaccines into the epidermis and dermis of the skin, unlike traditional injections that target deeper tissues in the muscle or subcutaneous space using hypodermic needles and syringes.[71] An effective illustration is the Dissolvable Microneedle Adhesive designed for influenza vaccination, specifically aiming at the skin's antigen-presenting cells. These microneedles, crafted from a biocompatible polymer, encapsulate an inactive influenza virus vaccine, penetrating the skin and dissolving rapidly within minutes. In studies with mice, this patch induced robust antibody and cell-mediated immune reactions, ensuring full protection against a severe challenge. These findings suggest a potential new method for simplified and safer vaccination, enhancing immune response efficacy through transdermal patches, potentially enabling broader vaccination coverage. [72] Researchers devised a microneedle-based patch for smallpox vaccination. In mice, this vaccine prompted the generation of vaccine-neutralizing antibodies within three weeks of application. These immunity levels were sustained for 12 weeks, exhibiting a notable increase. This suggests the potential for transdermal patches to function as an alternative vaccination delivery system and to support the persistence of IFN-γ secreting cells. [73]

## ➢ TRANSDERMAL PATCH FOR GENE THERAPY

Gene therapies involve introducing external nucleic acid into cells to produce therapeutic proteins, effectively treating various diseases. This approach has been applied in cancer therapy, tissue engineering, and modifying the characteristics of tumor cells, immune cells, and stem cells through the delivery of specific genes. Recent FDA approvals for treatments like anti-CD19 chimeric antigen receptor (CAR) T-cell therapy and LUXTURNA®, a gene therapy employing an adeno-associated virus vector for biallelic RPE65 mutation-related retinal dystrophy, have prompted extensive research into more effective gene delivery strategies. [74] Microneedles (MNs) are tiny, minimally invasive devices that puncture the stratum corneum (SC) and deliver therapeutic substances through diverse mechanisms.[75] MNs are commonly made from polymers, ceramics, steel, or silicon. They fall into various categories like biodegradable, rapidly dissolving, hydrogel-forming, bio-responsive, and hollow MNs. Their potential uses as carriers for immune/gene therapy in transdermal applications remain a focal point in ongoing biomedical engineering studies.[76]

The combined approach of gene therapy and photothermal therapy (PTT) has been extensively explored as a promising cancer treatment strategy. In efforts to deliver genes and photothermal agents precisely to tumor sites, a microneedle (MN) patch containing both p53 DNA and IR820 was created using a two-step casting process. Hyaluronic acid was utilized as a matrix, concentrating the p53 DNA and IR820 mainly at the tips of the microneedles to enhance efficiency and minimize waste. This MN patch effectively penetrated the stratum corneum and rapidly dissolved, facilitating the release of p53 DNA and IR820 at the subcutaneous tumor site.[77]




(A)Schematic of transdermal microneedle patch (B) intracellular pathway [76]

## ➢ TRANSDERMAL PATCH FOR INSULIN DELIVERY

Oral administration is a convenient and patient-preferred method for drug delivery when compared to injections. Yet, it's not suitable for macromolecules due to their limited oral bioavailability. This challenge is more pronounced for proteins and peptides as they are susceptible to enzymatic breakdown in the gastrointestinal tract and have low permeability across the intestinal epithelium. Various methods have been suggested to improve oral insulin bioavailability, such as using permeation enhancers, enzyme inhibitors, and encapsulation techniques like microspheres, nanoparticles, hydrogels, microemulsions, and liposomes.[78] Hollow microneedle patches (HMNPs) show significant potential for delivering drugs transdermally with efficiency and precision in a pain-free manner.[79] One example involves researchers developing a microneedle patch for insulin delivery, aiming to address the challenges posed by poor glucose control and insulin deficiency in diabetes. Type I diabetes often requires hypodermic injections of insulin due to its low oral bioavailability caused by poor absorption and hepatic metabolism in the gastrointestinal tract. However, self-injection concerns are common among diabetes patients. While alternate routes like nasal or ocular administration have been explored, they suffer from similarly low bioavailability as seen with oral delivery. As a result, microneedle (MN) patches loaded with insulin have been created to offer a simple, painless, and comfortable self-administered approach for managing blood sugar levels.[80]

## ➢ TRANSDERMAL PATCH FOR CARDIOVASCULAR DISEASES

As per the Centers for Disease Control and Prevention (CDC), cardiovascular disease (CVD) stands as the leading cause of mortality in the United States. Myocardial ischemia results in the swift demise of heart muscle cells, leading to the formation of an infarcted region and impairing contractile function. This loss of substantial functional tissue prompts the development of a fibrotic scar in the heart, aiming to compensate for the damage, eventually impacting the heart's overall performance.[81] Existing treatments for myocardial infarction (MI), such as bypass grafts, angioplasty, stents, and drug therapies, primarily offer symptomatic relief and don't address the fundamental issue of cardiomyocyte loss and replenishment during early-stage cardiomyopathy. As of now, the sole definitive solution remains a heart transplant, yet the scarcity of suitable donor hearts limits this option for the growing number of patients in need. Hence, there's a crucial need to develop an efficient therapy for repairing damaged heart tissue and preventing advanced heart failure. One potential approach involves the application of a temporary local patch directly onto the heart's surface, known as the cardiac patch.[82] Cardiac patches, composed of biomaterials, biological components, and occasionally combined with cells or medications, present a promising avenue for treating severe myocardial infarction (MI) and the ensuing heart failure.[83] Researchers developed a microneedle patch combined with cardiac stromal cells (CSCs) for the purpose of therapeutic heart regeneration. They designed a polymeric microneedle patch integrated with CSCs, known as MN-CSCs. These painless microneedle patches have proven to be efficient in delivering substances through the skin.[84]

## ➢ TRANSDERMAL PATCH FOR HORMONAL DEFICIENCIES AND CONTRACEPTIVES

Globally, OVER 100 million women opt for hormonal contraception for family planning,1 with over 12 million users in the United States exclusively. Combined oral contraceptives (OCs) are prevalent due to their proven effectiveness in clinical trials and established safety via post-marketing surveillance. There's a demand for reversible contraceptives offering a more convenient dosing regimen to improve patient adherence and achieve greater contraceptive efficacy in real-world usage.[85] Patient compliance with prescribed medications tends to be lacking, and contraception is no different. The patch, a small (2 cm2) adhesive square, releases 150 mg of the progestin norelgestromin and 20 mg of the estrogen ethinyl estradiol (EE) daily into the bloodstream. It can be placed on the upper outer arm, lower abdomen, upper torso, or buttocks, but should not be applied to the breasts.[86] The inaugural transdermal contraceptive patch, operating as a matrix system, received approval from the Food and Drug Administration in November 2000. It contained a combination of 6.0 mg norelgestromin (previously referred to as 17-deacetylnorgestimate) and 0.75mg ethinyl estradiol. Norelgestromin serves as the key active metabolite of norgestimate, a progestin previously utilized alongside ethinyl estradiol as an oral contraceptive (OC) starting from 1986.[87]

## Conclusion

The utilization of transdermal patch technology stands as a valuable and versatile approach to drug delivery, boasting clear advantages over alternative methods. By circumventing the digestive system and first-pass metabolism, these patches enable consistent and sustained drug dosing over extended timeframes. Widely employed in diverse indications such as chronic pain management,

motion sickness prevention, and hormone replacement therapy, transdermal patches have demonstrated their potential to revolutionize drug delivery.

In recent years, the field has witnessed remarkable progress, with the emergence of innovative patch technologies. These include smart patches that incorporate monitoring or responsive elements, dissolvable/biodegradable patches that offer environmentally friendly options, high-loading/release patches that enhance drug delivery efficiency, and 3D-printed patches that enable intricate design possibilities. These advancements extend the capabilities of transdermal patches, promising greater customization, efficiency, and patient-centered care.

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