Sustainable Materials and Eco-Friendly Solutions in Transdermal Patch Development

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ABSTRACT

A cutting-edge medication delivery method called a Transdermal patch is intended to administer therapeutic substances via the skin for a systemic impact. Transdermal patches, in contrast to conventional oral or injectable pharmaceuticals, enable a non-invasive, regulated, and prolonged release of medication. These patches have several benefits, such as better patient compliance, fewer side effects, and circumvention of the liver's first-pass metabolism. Numerous medications, such as hormones, painkillers, nicotine, and antihypertensives, are frequently delivered via these patches. A substrate layer, a drug storage of matrix-like, a rate-controlling the membrane itself, an adhesive layer, along with a protective liner make up the fundamental components of transdermal patches.Recent developments in transdermal technology, including smart patches, nanoparticles, and microneedles, have increased the range of possible uses for this drug delivery technique and made it possible to administer insulin, biologics, and even vaccinations. Additionally, the incorporation of detectors and surveillance systems into transdermal pads creates new opportunities for real-time health management and tailored medication. Notwithstanding these developments, issues such medication stability, skin permeability, and the requirement for patient-specific formulations still exist. Though the future is trending toward more effective, focused, and flexible therapies, transdermal patches remain a potential option for managing chronic diseases and delivering non-invasive therapeutics.

1. INTRODUCTION

The goal of every biopharmaceutical researcher and firm is to develop a safe and effective medication delivery method. Drug administration via the transdermal method can provide both systemic and local therapeutic effects. Since transdermal drug delivery avoids gastrointestinal side effects and first pass metabolism, it is a desirable alternative to oral drug administration (1). Additionally, it can overcome the low patient compliance that is linked to other drug delivery methods. Self-administered transdermal drug administration enables the medication to enter skin that is healthy over a predetermined amount of time to

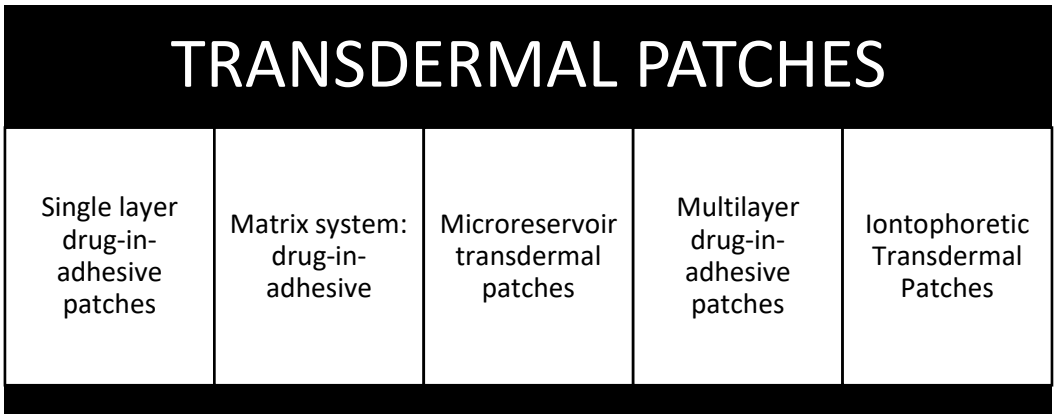
produce an individual as well as widespread impact.First-pass liver breakdown, enzymatic digestion, drug breakdown in environments with acidity, alimentary irritation, drug fluctuations, undesirable effects and therapeutic collapse, and the risk of disease transmission are just a few of the problems that transdermal delivery systems are intended to avoid. Additional benefits include regulated medication release, cheap cost, and patient compliance. Transdermal drug administration has several drawbacks, such as the potential for skin irritation, the inability to administer ionic medications, macromolecular agents, and the incompatibility with patients in stress or with low peripheral blood flow. Based on the size of the drug molecule and the absence of absorption enhancement material, transdermal delivery systems for drugs have been categorized into three generations.

Numerous permeation enhancer materials can be used to alter transdermal systems for drug delivery in order to alter the absorption of the medication profile in a predictable way. Different transdermal drug delivery systems, including vapour patches, membrane-moderated transdermal systems, matrix devices with drug-in-adhesive or matrix-dispersion infrastructure, and single or multilayer drugs in adhesive systems, have distinct mechanisms to regulate the drug release rate. As a result, the current review includes a concise overview of the different kinds of FDA-approved transdermal patches that are currently on the market, along with information on their designs, physicochemical characteristics, structural elements, preparation techniques, polymeric matrix components, and evaluation techniques needed for the assessments. The following describes the FDA-approved transdermal patches that are currently on the market. Transdermal patches are medicated adhesive patches that gradually release medication into the bloodstream through the skin. The regulated, prolonged release of medications made possible by these patches ensures therapeutic benefits without requiring frequent dosage. Percutaneous absorption is a key component of the transdermal patch mechanism. The active chemical in drugs (API), which usually targets the epidermis and dermis, is progressively released into the epidermal layers when administered topically (2). A systemic impact results from the API's absorption into the blood vessel walls and subsequent entry into the systemic circulation.

(Fig 1 Transdermal patches)

2. TYPES OF TRANSDERAL PATCHES

Transdermal patches are categorized according to their design, drug release mechanism, and mode of administration. The primary varieties of transdermal patches are listed below:



(Fig 2 Table of Transdermal Patches)

a) Single layer drug-in-adhesive patches

A reservoir for medication dispersion is only one layer of copolymer with sticky qualities. The single layer is covered with an impermeable backing laminate. The medication is released from the substrate laminate layer supporting the drug reservoir after being deposited in and adhering to the single polymers layer. Another instance of one-layered drug-in-adhesive patches that contains methylphenidate is the transdermal medication Daytrana® (3).

b) Multilayer drug-in-adhesive patches

A drug storage layer and a sticky layer make up layered transdermal patches, which allow for regulated medication release over time. Multilayer systems comprise both a permanent foundation layer and a temporary protective layer. Drug administration can be extended for a total of seven days with multilayer patches, which are used to provide hormone treatment, painkillers, and medications that promote quitting smoking (3).

c) Micro reservoir transdermal patches

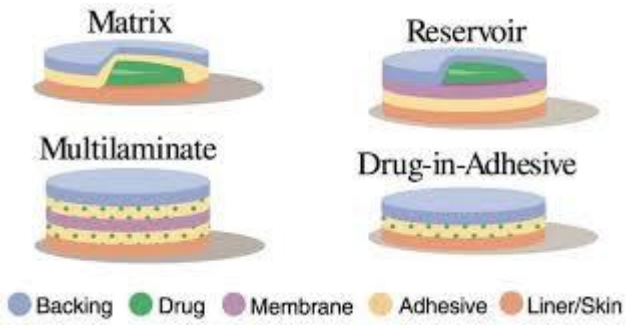
Matrix dispersion and a drug reservoir are combined in microreservoir transdermal patches. The reservoir is made by spreading the drug suspension uniformly on a lipophilic polymer after it has been suspended in a solution made up of hydrophilic polymer. When a large shear mechanical force is applied during dispersion, millions of tiny, impermeable spheres are formed. The drug level in bloodstream is kept constant by the drug release profile, which adheres to a 0-order amount of kinetic drug release. The use of crosslinking polymeric agents is typically necessary because the medication dispersion must be thermally inert (4).

d) Matrix system: drug-in-adhesive

A drug reservoir is made to disperse the medication over an adhesive polymer using just one layer or multilayered transdermal patches to do so. Using solvent casting or melting the sticky polymeric components, this drug-polymer mesh is applied to a waterproof backing layer.

e) Iontophoretic Transdermal Patches

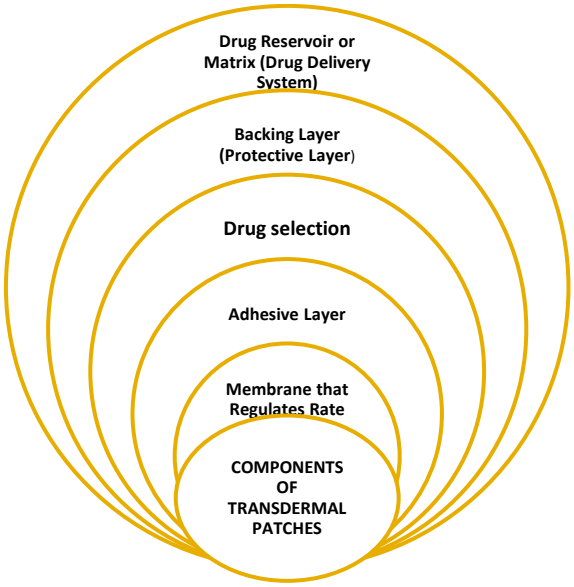
To improve the passage of molecules that are charged (ions) through the skin, these patches employ iontophoresis, a little electrical current.The medicine is driven into the skin by the electrical current, which increases the effectiveness of drug delivery, especially for hydrophilic (water-soluble) medications that would normally have trouble entering the skin (4).



(Fig 3 Types of Transdermal Patches)

3. STRUCTURAL COMPONENTS OF TRANSDERMAL PATCHES

Transdermal patches' structural elements are made to make it easier for APIs, which are active pharmaceutical ingredients, to be effectively delivered via the skin. Typically, a transdermal patch is made up of many layers, each of which has a distinct function to regulate medication release, offer adhesive qualities, and guarantee durability (5). The main structural elements of transdermal patches are listed below: (6)



(Fig 4 Table of the Components of Transdermal Patches)

- **Drug selection**

When designing patches for transdermal distribution, the physicochemical characteristics of medications must be taken into account. Medication solubility and diffusivity across the stratum corneum region of the skin are determined by hydrophobicity and ionization state, which are crucial considerations in medication selection (7).

- **Backing Layer (Protective Layer)**

Usually composed of synthetic fibers like polyethylene, which are polyester is polypropylene, or laminated films, the backing component is the outermost portion of the patch and serves to shield the patch and the medication from environmental elements like condensation, light, and air. It also helps keep the patch intact while in use. These materials are chosen for their strength, flexibility, and barrier-forming properties (8).

- **Drug Reservoir or Matrix (Drug Delivery System)**

a) Reservoir System: A rate-controlling membrane encloses a liquid or gel chamber that holds the medication. Through this membrane, the medication diffuses at a regulated pace (9).

b) Matrix System: The medication is distributed throughout a polyamide matrix-like, and it gradually permeates the matrix to reach the skin. The matrix itself regulates the drug release in this mechanism (9).

- **Membrane that Regulates Rate:**

The medicine is administered at a steady and regulated rate throughout time thanks to the rate-controlling membrane, which also controls the drug's release from the reservoir or matrix.Usually, silicone,

polyethylene, which are ethylene-vinyl acetate (EVA), or polyvinyl chloride (PVC) are used to make the membrane. The permeability of these materials to the particular drug is the basis for their selection (10).

- **Adhesive Layer**

The Adhesive Layer The patch will cling firmly to the skin thanks to the adhesive coating. It also regulates the absorption of the medicine by regulating what amount of the pharmaceutical will be released from the topical application to the flesh over time.Transdermal patches employ pressure-sensitive adhesives (PSAs), which include hydrocolloid-, silicone-, and acrylate-based adhesives. These adhesives are intended to minimize discomfort, be pleasant, and form a strong connection with skin (11).

- **Liner (Protective Release Liner)**

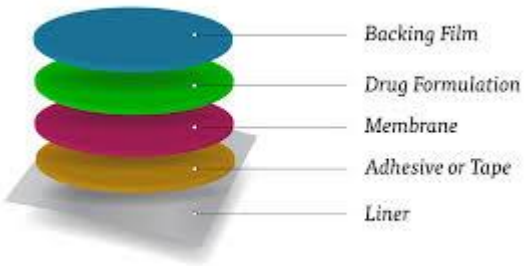
Prior to applying the patch, the liner—a protective layer—covers the adhesive. Prior to usage, it safeguards the medicine and the adhesive and stops the patch from adhering too quickly.Papers coated with silicone, polyethylene, or polypropylene are typically used. Whenever all is put to the skin, the user removes the liner.

- **Permeation Enhancers**

Although they are optional, penetration enhancers are frequently used to increase a drug's skin absorption, particularly for medications with limited skin permeability. These chemicals improve penetration by momentarily changing the skin's barrier characteristics.Urea, propylene glycol, ethanol, and surfactants are examples of common permeation enhancers (12). They are included in the formulation of the patch, frequently in the matrix or the adhesive layer.

- **Other excipients**

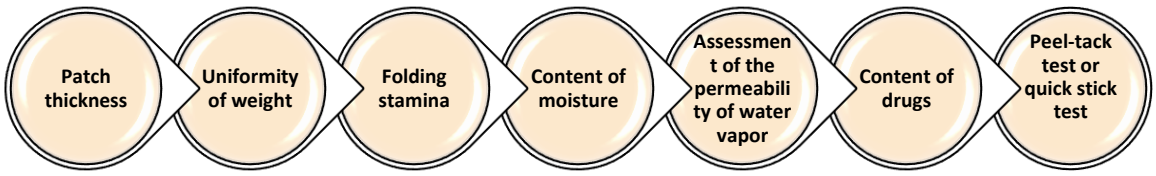
Plasticizers like dibutylpthalate and triethyl citrate are present in rates ranging from 5 to 20% to give transdermal patches their plasticity. Solvents used in the drug reservoir include methanol, ethanol, dichloromethane, and acetone.



(Fig 5 Components of Transdermal Patches)

4. CHARACTERIZATION AND ASSESSMENT TOOLS FOR TRANSDERMAL PATCH PREPARATION

Transdermal patches should be described and characterized using a variety of evaluation and development techniques, including dissolving, in vitro release of drugs, in vitro skin penetration, adhesive qualities, and excipient control (13). The tests listed below are in accordance with the Commission for Medicinal Products for Humanitarian Use's European Medicines Agency Recommendations on the manufacturing standards of transdermal patches. Additional physical, chemical, and biological tests, evaluations, and assessments—such as those pertaining to material interaction, patch thickness, weight uniformity, folding power, level of moisture, moisture uptake or weight gain, vaporization of water permeability, pharmaceutical content, flatness, stability, swell ability, and skin irritation tests—should also be carried out. These are detailed below (14-17).



(Fig 6 Table of the Evaluation of Transdermal Patches)

a) Patch thickness

Using a digital microscope screw gauge, measurements are taken at anywhere from three to five locations on the patch to determine its thickness. To ensure that the patch thickness is suitable, the mean depth and average variance of such numerous measurements are calculated.

b) Uniformity of weight

Weighing ten distinct, randomly chosen patches and computing the average bulk and standard deviation allows us to evaluate weight homogeneity. The weight of each patch shouldn't deviate much from the average weight (14).

c) Folding stamina

Rolling tenacity is the total amount of occasions the paper can be folded without breaking when a certain patch area is cut equally and folded repeatedly at the same spot until it breaks.

d) Content of moisture

A transdermal patch's moisture content is determined by precisely weighing it, putting it in a dryer with cemented chlorine dioxide for 24 hours, and then weighing it again. Equation (1) is used to determine the patch's percentage of moisture: Moisture content (%) Initial mass Final mass Initial = - mass ´ 100

e) Assessment of the permeability of water vapor

The moisture-vapor permeability (WVP) in a patch is measured using an organicair circulation oven, where: WVP = W/A (3), where W is the quantity of water vapor (g per 24 hours) that infiltrated the patch, A is the surface area (m2) exposed on the patch sample, and WVP is the water vapor permeability, given in g m–2 per 24 hours (15).

f) Content of drugs

A transdermal patch's medication content is determined by dissolving a particular patch region in a predetermined amount of a solvent. After being constantly shaken for up to 24 hours, the solution is ultrasonically sonicated for a predetermined amount of time and filtered. A suitable analytical approach is used to determine the drug content in the filtrate.

g) Assessing the adhesive qualities

Numerous tests, including peel force, adhesive strength, and tack tests, can be used to describe adhesive qualities. The drug's adhesive qualities in a transdermal formulation may be evaluated using both in vitro and in vivo testing (16).

h) Peel-tack test or quick stick test

In this test, an adhesive tape is pulled over the transdermal application at a 90° angle and 12 inches per minute. The peeling power required to break the adhesive-substrate connection is known as the tack value.

i) Strength in tensile

A tensiometer is used to measure tensile strength. A patch is attached to the tensiometer assembly, the weight needed to shatter it is calculated, and the patch's resulting elongation is measured (using the instrument's pointer). The patch's tensile strength is determined by taking the average of three patch readings. With a = patch width, b = patch thickness, L = patch length, ΔL = patch elongation at breakage point, and break force = weight (kg) needed for patch breaking, the formula for the patch's tensile strength is as follows: Tensile strength = break force / a ´ b (1 + ΔL/L) (17).

j) **Swell ability**A transdermal patch's swell ability is assessed by applying the sample to a Preweighed slip of plastic in a Petri dish with 50 mL of pH 7.4 phosphate buffer. Time t, which is typically about 30 minutes, is when sample absorption occurs.

5. CLINICAL USE OF TRANSDERMAL PATCHES ON THE CURRENT MARKET

S.no	DRUG	PRODUCT NAME	CLINICAL USE
01	Scopolamine	Transderm-Scop	Motion sickness
02	Nitroglycerin	Transderm-Nitro	Angina pectoris
03	Clonidine	Catapres-TTS	High blood pressure
04	Estradiol	Estraderm	Menopause
05	Fentanyl	Duragesic	Chronic pain
06	Nicotine	Nicoderm	Smoking cessation
07	Testosterone	Testoderm	Testosterone low level
08	Lidocaine/epinephrine	Iontocaine	Pain relief
09	Estradiol/norethidrone	Combipatch	Menopause
10	Lidocaine	Lidoderm	Pain relief
11	Norelgestromin	Ortho Evra	Contraception
12	Estradiol/levonorgestrel	Climara Pro	Menopause
13	Oxybutynin	Oxytrol	Overactive bladder
14	Rotigotine	Neupro	Parkinson's disease
15	Rivastigmine	Exelon	Dementia

Table 1

6. FUTURE PROSPECTIVE

Transdermal patches have the potential to significantly improve medicine delivery in the future by making it more effective, individualized, and adaptable. Transdermal skin patches have the ability to overcome several present constraints and broaden the scope of therapeutic applications because to advancements in the field of nanotechnology microneedles, programmable patches, and biologics (18). Better patient outcomes, more adherence to treatment plans, and more easily available and convenient therapy for a range of illnesses might result from this. These technologies will become more and more important in managing chronic illnesses and providing specific therapies as they develop (16, 17).

7. CONCLUSION

Transdermal patches are a non-invasive and practical substitute for conventional oral or injectable drugs, marking a significant breakthrough in drug delivery technologies. Their capacity to deliver regulated, reliable, and prolonged medication release over long stretches of time improves patient adherence and lowers the possibility of adverse consequences linked to high drug concentrations (19). For patients in need of long-term care, such as those with pain, hormonal imbalances, quitting smoking, or transdermal hormone replacement therapy, transdermal patches provide substantial advantages due to their capacity to avoid the gastrointestinal system and first-pass metabolism in the liver. Additionally, they offer a way to distribute medications like biologics, insulin, and vaccinations that would otherwise be challenging to give orally.Transdermal patches, which have the advantages of ease, accuracy, and patient-centered treatment, are becoming a more and more significant instrument in contemporary medicine. Drug delivery is anticipated to become safer, more efficient, and more patient-friendly as technology developments continue to play a major part in the treatment of a variety of ailments (20-21).

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