



A Review On Herbal Transdermal Patches

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ABSTRACT:

Transdermal drug delivery systems (TDDS) have emerged as a promising technology in the pharmaceutical industry, offering a non-invasive and patient-friendly approach to drug administration. In recent years, herbal TDDS patches have gained significant attention due to their potential to provide a safer and more effective alternative to synthetic drugs.

The increasing prevalence of life-threatening diseases has led to the development of numerous synthetic drugs, which often come with undesirable side effects. In contrast, herbal remedies offer a therapeutic approach that leverages natural medicinal properties with minimal adverse reactions. Transdermal drug delivery systems have emerged as a promising method to enhance the efficacy and reduce side effects of herbal medicine. Herbal TDDS patches are designed to deliver drugs through the skin, providing a controlled and sustained release of active pharmaceutical ingredients (APIs). This review provides detailed Knowledge of TDDS and Formulation method of herbal transdermal patche. This approach offers several advantages over traditional oral and injection-based drug delivery systems, including the avoidance of first-pass metabolism, increased patient compliance, and reduced gastrointestinal disorders.

Key Words : Herbal Drugs , Transdermal Pathes , Novel Drug Delivery System, Natural Product .

INTRODUCTION

At present, synthetic drugs form a major line of treatment in the management of many diseases and currently available as transdermal patches. Traditional medicine system is centuries old practice and again gaining importance. Hence, herbal products can be used to treat many diseases as transdermal patches. ^[1] Herbal medicines have become a vital component of mainstream healthcare, bridging traditional practices and ongoing research. These botanical compounds serve as a rich source of phytochemicals, harnessing bioactive substances with profound health benefits. ^[2] The present investigation was aimed to formulate transdermal films incorporating herbal drug components. Hence turning to safe, effective and time-tested Ayurvedic herbal drug formulation would be a preferable option. With this view transdermal films incorporating herbal drug components. Overall, it was observed that the well-known Ayurvedic drugs have been found to be effective through modern pharmaceutical formulation techniques. ^[3] The first transdermal system was FDA-approved in 1979 for preventing nausea and vomiting. Confirmation of percutaneous drug absorption can be established through measurable blood levels, detect excretion of the drug and its metabolites in urine, observing the patient's clinical response to the administered drug therapy. ^[4] Transdermal drug delivery systems are topically administered medicaments. Transdermal patches are pharmaceutical preparation of varying sizes, containing, one or more active ingredient, intended to be applied to the unbroken skin in order to deliver the active ingredient to the systemic circulation after passing

through the skin barriers, and it avoid first pass effect. Transdermal patch is a medicated patch that can deliver drugs directly into the bloodstream through the layers of the skin at a prescribed rate. In fact, patches are the most convenient method of administration. They are non-invasive, and treatment can last for several days and can be stopped at any time. They come in different sizes and contain multiple ingredients. When applied to the skin, the patch can deliver active ingredients into the systemic circulation via diffusion processes. Transdermal patches may contain high doses of active substances that remain on the skin for an extended period of time [5]

Comparison Between IV, Oral And TDDS

ADVANTAGES	IV	ORAL	TDDS
Avoid hepatic first pass effect	YES	NO	YES
Contant drug level	YES	NO	YES
Self administration	NO	YES	YES
Termination of therapy	NO	YES	YES

Dosage forms such as oral tablets and capsules are the most commonly used, but both forms experience instability due to the drug freezing in the stomach/enzyme before being metabolized. There are many other problems such as odour, taste, colour in the mouth. Many problems can occur while taking the drug; therefore, problems may occur during treatment. Sometimes patients act illegally. TDDS patches are controlled by sustained release, so they work for a certain period of time and the antibiotic is nonirritating and nonirritating. It is an attractive alternative to monitoring the drug delivery process. The delivery of drugs through the skin to achieve drug effect is often called transdermal drug delivery, unlike traditional creams. In order to deliver therapeutic drugs through human skin to produce effects in the body, the morphological, biophysical and physicochemical processes of the skin must be taken into account. Compared to oral and injection, transdermal drug delivery has the advantage of avoiding firstpass metabolism and increasing patient compliance. Transdermal drug delivery systems have attracted great attention in the last decade because they have many advantages over traditional drugs, especially oral controlledrelease drug delivery systems. Reduce frequency of application, do not press before passing, reduce gastrointestinal disorders, increase patient compliance. Transdermal delivery is defined as independent, discrete materials that deliver drugs through the skin to the body at a controlled rate when applied to intact skin. Transdermal delivery not only provides control and health management, but also allows continuous drug delivery with shortterm toxicity, eliminating pulsatile entry into the body that often causes adverse side effects and thus creates many new forms. Drug delivery systems. Transdermal drug delivery systems, controlled release, drug delivery to the body, etc. [6]

Definition:- Transdermal drug delivery system can deliver the drugs through the skin portal to systemic circulation at a predetermined rate and maintain clinically the effective concentrations over a prolonged period of time [7][8]

Herbal transdermal patches v/s synthetic transdermal patches

As the prevalence of life-threatening diseases grows, the pursuit of effective treatments has led to the development of numerous synthetic drugs. However, these pharmaceuticals often come with undesirable side effects. In contrast, herbal remedies offer a safer therapeutic approach, leveraging natural medicinal properties with minimal adverse reactions. Transdermal drug delivery systems have emerged as a promising method to enhance the efficacy and reduce side effects of herbal medicine. The increasing popularity of herbal remedies, driven by their therapeutic potential and low risk of adverse effects, has created a demand for innovative delivery systems. To unlock the full potential of natural medicines, researchers are working to optimize formulations for sustained and controlled release of active pharmaceutical ingredients (APIs), ensuring precise dosing and maximizing therapeutic benefits [9]

Advantages of Transdermal Drug Delivery Systems (TDDS):

Pharmacological Advantages

1. Sustained release: Provides consistent drug levels over an extended period.
2. Targeted delivery: Directly targets the affected area or tissue.
3. Reduced systemic side effects: Minimizes risk of gastrointestinal, hepatic, or renal side effects.
4. Improved bioavailability: Avoids first-pass metabolism, increasing bioavailability.
5. Rapid onset of action: Quick absorption through skin.

Patient-Centric Advantages:

1. Convenience: Easy to apply and remove.
2. Improved compliance: Reduces dosing frequency.
3. Pain-free administration: No injections or oral dosing.
4. Portability: Easy to carry and store.

Therapeutic Advantages:

1. Chronic pain management: Effective for managing chronic pain.
2. Local anesthesia: Provides localized numbing.
3. Hormone replacement therapy: Effective for hormone delivery.
4. Smoking cessation: Helps manage nicotine cravings.

Disadvantages of Transdermal Drug Delivery Systems (TDDS):

Pharmacological Disadvantages:

1. Skin permeability limitations: Variable skin permeability affects drug absorption.
2. Dose dumping: Risk of excessive drug release.
3. Skin irritation: Potential for allergic reactions or irritation.
4. Interindividual variability: Variable absorption rates among individuals.

Technical Disadvantages:

1. Formulation challenges: Difficulty in developing stable, effective formulations.
2. Manufacturing complexities: Requires specialized equipment and processes.

Patient-Centric Disadvantages:

1. Skin sensitivity: Potential for skin reactions.
2. Adhesion issues: Patch detachment or poor adhesion.

Therapeutic Disadvantages:

1. Limited drug candidates: Not suitable for all drugs or therapeutic areas.
2. Dose limitations: Limited dose range.
3. Duration limitations: Limited wear time.^{[10][11][12][13][14]}

Skin Structure

Before studying transdermal drug delivery system need to learn skin anatomy and physiology. Indeed, the skin is the body's largest organ, acting as a crucial protective barrier safeguarding the body from a range of external factors and

potential threats. Its large surface area, approximately 1.7 square meters in an average person, allows it to effectively shield the body from microorganisms, ultraviolet (UV) radiation, chemicals, allergens, and water loss. This protective function is vital for maintaining overall health and well-being. Additionally, the skin also plays a role in regulating body temperature, sensation, and the synthesis of vitamin D through exposure to sunlight. Taking care of the skin is essential to support its functions and maintain good health. The skin is commonly categorized into three primary layers:

- (a) The outermost layer, known as the epidermis;
- (b) The middle layer, referred to as the dermis; and
- (c) The innermost layer, called the hypodermis.^[15]

Here's a brief overview of each layer:

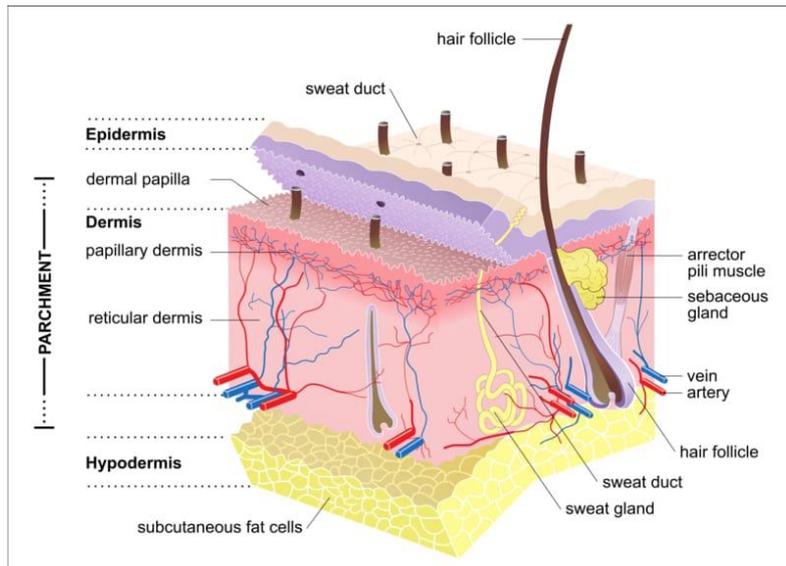


Fig 1: Layer Of Skin

EPIDERMIS

Your epidermis is the top layer of the skin that you can see and touch. Keratin, a protein inside skin cells, makes up the skin cells and, along with other proteins, sticks together to form this layer

The epidermis has several sub- layers, including:

1. Stratum corneum
2. Stratum granulosum
3. Stratum spinosum
4. Stratum basale

The old skin cells that your body sheds every day. You have new skin every 30 days.

Protects your body: Langerhans cells in the epidermis are part of the body's immune system. They help fight off germs and infections.

Provides skin color: The epidermis contains melanin, the pigment that gives skin its color. The amount of melanin you have determines the color of your skin, hair and eyes. People who make more melanin have darker skin and may tan more quickly.^{[16][17]}

DERMIS

The dermis makes up 90% of skin's thickness. This middle layer of skin:

Has collagen and elastin: Collagen is a protein that makes skin cells strong and resilient. Another protein found in the dermis, elastin, keeps skin flexible. It also helps stretched skin regain its shape.

Grows hair: The roots of hair follicles attach to the dermis. Keeps you in touch: Nerves in the dermis tell you when something is too hot to touch, itchy or super soft. These nerve receptors also help you feel pain.

Makes oil: Oil glands in the dermis help keep the skin soft and smooth. Oil also prevents your skin from absorbing too much water when you swim or get caught in a rainstorm.

Produces sweat: Sweat glands in the dermis release sweat through skin pores. Sweat helps regulate your body temperature.

Supplies blood: Blood vessels in the dermis provide nutrients to the epidermis, keeping the skin layers healthy.^[18]

HYPODERMIS

The bottom layer of skin, or hypodermis, is the fatty layer. The hypodermis:

Cushions muscles and bones: Fat in the hypodermis protects muscles and bones from injuries when you fall or are in an accident. Has connective tissue: This tissue connects layers of skin to muscles and bones.

Helps the nerves and blood vessels: Nerves and blood vessels in the dermis (middle layer) get larger in the hypodermis. These nerves and blood vessels branch out to connect the hypodermis to the rest of the body.

Regulates body temperature: Fat in the hypodermis keeps you from getting too cold or hot. epidermis: Acts as a protective barrier: The epidermis keeps bacteria and germs from entering your body and bloodstream and causing infections. It also protects against rain, sun and other elements.

Makes new skin: The epidermis continually makes new skin cells. These new cells replace the approximately 40,000 .^[19]

Routes of drug penetration through skin :

Drugs can penetrate the skin through several pathways, depending on their chemical properties and the type of formulation used. The main routes of drug penetration through the skin are:

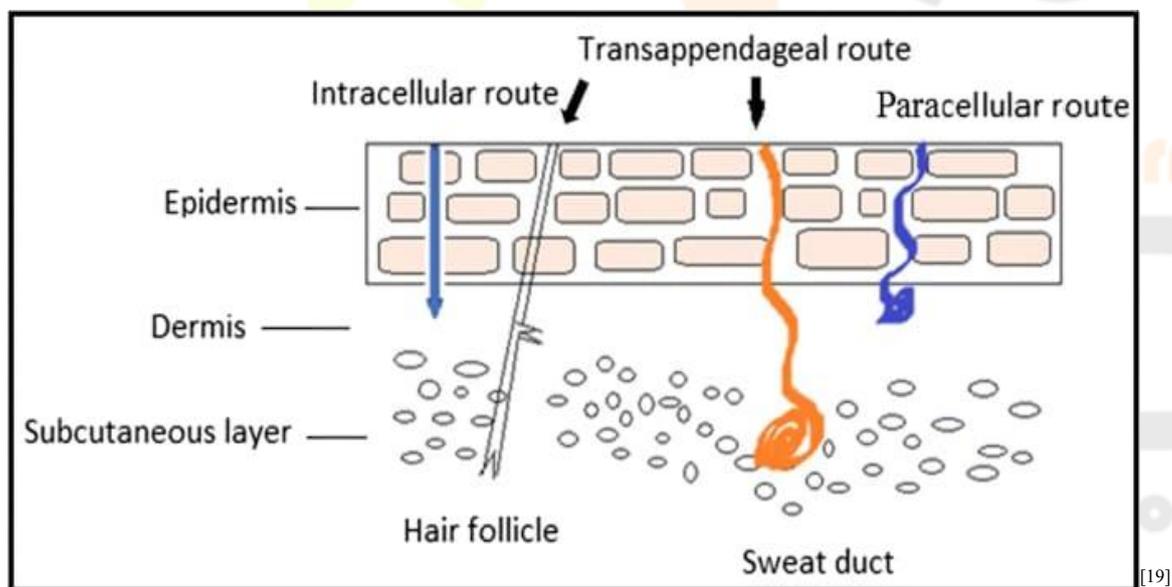


Fig2 : Different Routes Of Permeation.

1. Transcellular Route:

The drug passes directly through the skin cells (keratinocytes) of the stratum corneum, the outermost layer of the epidermis. This is the most common route for small, lipophilic (fat-soluble) drugs. The drug must traverse the lipid bilayer of the skin cells, which can be challenging for larger, hydrophilic (water-soluble) molecules. Lipophilic drugs are better able to diffuse through this route.

2. Intercellular Route (Between Cells):

This is the most common route for many drugs. Here, the drug travels through the spaces between the skin cells in the stratum corneum. The intercellular lipids (mainly ceramides, cholesterol, and fatty acids) form a barrier, and the drug must diffuse through these lipid layers. Hydrophilic drugs are often absorbed via this route, although lipophilic drugs can also pass through if their molecular size is small enough.

3. Transfollicular Route:

Hair follicles and sweat ducts can also serve as pathways for drug penetration. This route is less significant compared to the transcellular and intercellular routes, but it can become more important for certain drugs, especially when formulations are designed to target these structures. Drugs may enter the body through the sebaceous glands or sweat glands within hair follicles.

4. Intracellular Route (Within Cells):

This route involves drug molecules crossing directly through the cytoplasm of individual skin cells. This path is less common and may occur when the drug is formulated to enhance skin penetration, such as with iontophoresis or other technologies.

5. Via the Epidermis into the Dermis:

After crossing the outermost layers (epidermis), the drug may reach the dermis, where blood vessels are located, allowing for systemic absorption into the bloodstream. The dermis is more permeable than the epidermis, but still, the drug must traverse the layers of the epidermis first before reaching this deeper layer.^{[20][21][22][23]}

FACTORS AFFECTING TRANSDERMAL DRUG DELIVERY SYSTEM

According to the Physicochemical Properties of the Drugs

1. Partition Coefficients

Drugs possess both water and lipid solubility. Ideal partition coefficient for intermediate transdermal delivery is $\log K$. For highly lipophilic drug ($\log K > 3$), intracellular route is favourable, whereas for hydrophilic drugs ($\log K < 1$), it is permeated via transcellular route.

2. Molecular Size

Molecular size of the drug is inversely proportional to transdermal flux. The ideal molecular size of drug molecule for transdermal delivery is 400.

3. Solubility/Melting Point

Most organic solutes have high melting point and low solubility at normal temperature and pressure. Lipophilic drug permeates faster than hydrophilic substances, but it should also have aqueous solubility as needed in most of topical formulations.

4. Ionization

Unionized drug permeates the skin as according to pH-Partition hypothesis.

5. Diffusion Coefficient

Penetration of drug depends on diffusion coefficient of drug. At a constant temperature, the diffusion coefficient of drug mainly depends on properties of drug, diffusion medium and their interaction.

According to the Physicochemical Properties of Drug Delivery System

1. Release Characteristics

Drug release mechanism mainly depends on drug molecules which are dissolved or suspended in the delivery system and on interfacial partition coefficient or pH of the drug from delivery system to the skin tissue. If the drug is easily released from the delivery system, the rate of transdermal permeation will be higher.

2. Composition of Drug Delivery System

Composition may not affect release properties but may affect its permeability functionality. For example, methyl salicylate is more lipophilic than parent acid, i.e salicylic acid, and its percutaneous absorption is high when applied to skin in a lipoidal vehicle

3. Enhancement of Transdermal Permeation

Majority of drugs will not permeate into skin for therapeutic use. Some enhancers are used for synergistic action without showing its properties (eg. dimethyl sulphoxide, acetone, Propylene glycol and tetrahydrofuryl alcohol).

According to the Physiological Properties

1. Skin Barrier Properties in the Neonate and Young Infant

The skin surface of the newborn is slightly hydrophobic, relatively dry and rough when compared to that of older infants. Stratum corneum hydration stabilizes by the age of 3 months

2. Skin Barrier Properties in Aged Skin

There are some changes in the physiology of aged skin (465 years). The moisture content of human skin decreases with age. There is a destruction of the epidermal junction and consequently, the area available for transmission into the dermis is diminished.

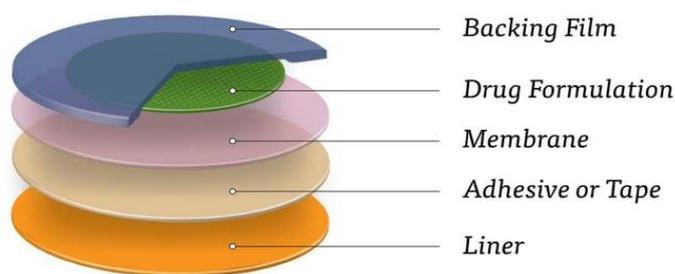
3. Race

Racial differences between black and white skins have shown some anatomical and physiological functions of the skin. In black skin, there is increased intracellular permeation due to higher lipid content and higher electrical skin resistance levels when compared to whites, but this difference is not detected in stripped skin.

4. Skin Temperature

The human body maintains a temperature of 32°C-37°C across the skin. Hence, increase in temperature leads to increase in diffusion through the tissue.^{[24][25]}

Components of a Transdermal Drug Delivery System (TDDS) :



[26]

Fig3: Components Of TDDS

1. Drug: The active pharmaceutical ingredient (API) or drug molecule that is intended to be delivered through the skin. The drug can be in various forms, such as a solid, liquid, or gel depending on its physicochemical properties and desired release profile.

Some of ideal properties of drug during preparation of transdermal patches are as follows:

- Dose should be low in weight (less than 20 mg/day).
- Oral bioavailability should be low,
- It should have narrow therapeutic window
- non-irritating and non-sensitizing
- Molecular weight: 400 Dalton
- Half life is less than 10 hrs.

2. Permeation Enhancers: These are substances that are included in the formulation to improve the permeation of the drug through the skin. Permeation enhancers can enhance the drug's solubility, disrupt the stratum corneum barrier, or alter the skin's lipid matrix to facilitate drug diffusion.

3. Adhesive Matrix: The adhesive matrix serves as the primary contact between the TDDS and the skin. It provides adhesion to the skin, holding the system in place during drug delivery. The adhesive matrix may be composed of natural or synthetic polymers, such as acrylics or silicones which allow for controlled drug release and permeation.

4. Backing Layer: The backing layer is a protective layer that covers the TDDS, providing mechanical support and preventing drug loss. It also protects the system from environmental factors, such as moisture and oxygen. The backing layer is typically made of impermeable materials, such as polyester or polyethylene.

5. Release Liner: The release liner is a protective layer that covers the adhesive matrix before application. It is removed prior to use to expose the adhesive surface for application to the skin. The release liner protects the adhesive from contamination and ensures proper storage and handling of the TDDS.

6. Control Membrane (optional): In some TDDS designs, a control membrane may be included between the drug reservoir and the adhesive matrix. The control membrane regulates the rate of drug release from the reservoir providing controlled and sustained drug delivery.

7. Reservoir (optional): In certain TDDS designs, a drug reservoir may be present. The reservoir is a compartment that contains the drug formulation and serves as the source of drug for delivery. It can be a separate layer or part of the adhesive matrix.

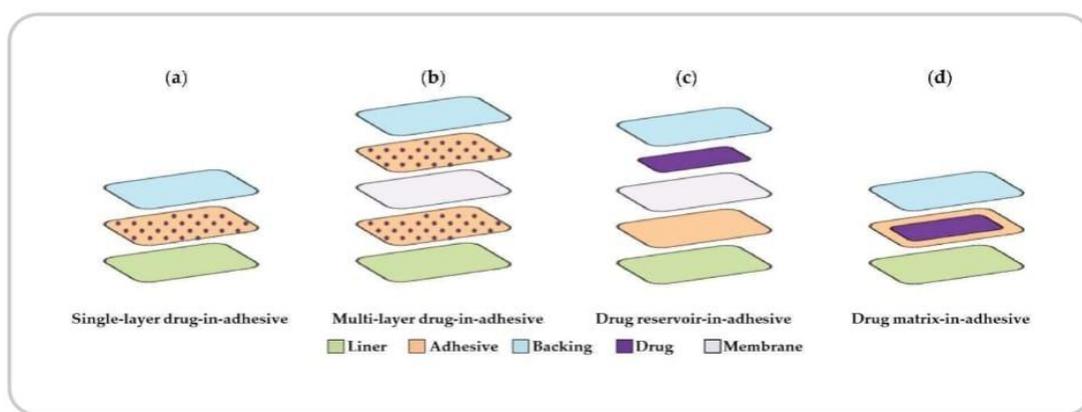
8. Pressure Sensitive Adhesive (PSA): Adherence of transdermal patch to the skin surface is increased by pressure sensitive adhesive. The major criteria for pressure sensitive adhesive is it should easily remove from the smooth surface and leave no residue on it. E.g. Silicon based adhesives and polyacrylates.

9. Plasticizers: They are used to reduce brittleness of polymer film. E.g. Glycerol, polyethylene glycol, propylene glycol.

10. Solvents: The examples of solvents used are chloroform, methanol, acetone, isopropanol & dichloromethane.

These are the fundamental components of a TDDS, but depending on the specific design and requirements of the system, additional components such as stabilizers, solvents, antioxidants, and penetration enhancers may be incorporated to optimize drug release, stability, and permeation properties.^{[27][28][29]}

Research Through Innovation



[30]

Types Of TDDS:

Fig4: Types Of TDDS

1. Single Layer Patch

- Structure: Consists of a single layer of adhesive material that contains the drug.
- Mechanism: The drug diffuses through the adhesive and into the skin.
- Uses: Suitable for drugs requiring simple, consistent release.
- Advantages: Easy to manufacture, consistent drug release rate.
- Limitations: Limited drug capacity; may not support controlled release.

2. Multilayer Adhesive Patches

- Structure: Has multiple layers, with at least one drug layer and other layers for controlled release or combination therapies.
- Mechanism: Each layer can release the drug at different rates or contain different drugs.
- Uses: Ideal for controlled-release or multi-drug therapies.
- Advantages: Better control of release rates; can incorporate multiple drugs.
- Limitations: More complex and costly; potential for skin irritation.

3. Reservoir Type Patch

- Structure: Contains a drug reservoir separated by a rate-controlling membrane.
- Mechanism: Drug diffuses through the membrane for controlled release.
- Uses: Suitable for long-term, controlled drug delivery.
- Advantages: Precise control over release rates; large drug capacity.
- Limitations: Risk of dose dumping if compromised; complex to manufacture.

4. Matrix Type Patch

- Structure: Drug is uniformly dispersed in a polymer matrix that adheres to the skin.
- Mechanism: The drug gradually diffuses from the matrix into the skin.
- Uses: Effective for sustained drug release.
- Advantages: Simpler design than reservoir patches; reduced dose dumping risk.

- Limitations: Release rate can decrease over time; less precise control.^{[31][32][33]}

PREPARATION METHOD OF HERBAL TRANSDERMAL PATCHES

The preparation of herbal transdermal patches involves the incorporation of active herbal components into a suitable polymer matrix for controlled transdermal delivery. Below is a general method for their preparation:

Materials Required

Active ingredient: Herbal drug extract

Polymers: Hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), or ethyl cellulose

Plasticizers: Glycerin or polyethylene glycol (PEG) to provide flexibility.

Solvents: Ethanol, water, or a mixture

Permeation enhancers: Dimethyl sulfoxide (DMSO) or propylene glycol

Backing membrane: Non-adhesive material like polyethylene

Release liner: Silicone-coated paper

Preparation Steps

Step 1: Preparation of the Polymer Solution

1. Dissolve the selected polymer(s) in a suitable solvent (e.g., water, ethanol, or their combination) under constant stirring until a uniform solution is obtained.
2. Add a plasticizer (e.g., glycerine) to improve the flexibility of the patch.

Step 2: Incorporation of Active Ingredients

1. Add the extract to the polymer solution.
2. Use a homogenizer or magnetic stirrer to ensure uniform dispersion.
3. Add permeation enhancers to improve skin penetration of the active compounds.

Step 3: Casting the Film

1. Pour the prepared solution onto a flat, non-stick surface or petri dish.
2. Spread the solution uniformly using a glass rod or film applicator to achieve a consistent thickness.

Step 4: Drying

1. Allow the film to dry at a controlled temperature (e.g., 40–60°C) in a hot air oven or under ambient conditions.
2. Ensure complete evaporation of solvents.

Step 5: Cutting and Layering

1. Cut the dried film into desired patch sizes.
2. Laminate the film onto a backing membrane.
3. Attach the release liner to the adhesive side of the patch.

Step 6: Packaging

1. Store the patches in airtight, moisture-proof packaging to maintain stability.
2. Label the packaging with necessary information, including dosage and instructions.^{[34][35][36]}

Evaluation Test of Herbal Transdermal Patch:

1. Organoleptic Characteristics: The physical appearance of developed patch was evaluated by using a naked-eye examination for its appearance, colour, clarity, flexibility, and smoothness.

2. Thickness: Thickness of patches was measured using micrometer screw gauge in different places on the plaster and average thickness was calculated.^[39]

3. Weight: Weight of 8 individual patches was determined using an electronic balance with sensitivity of 0.1mg and the average weight was calculated.^[36]

4. Moisture content: The prepared patch was out and weighed again, % moisture content was measured and calculated with the help of following equation.

$$\text{Moisture content} = (\text{Initial weight} - \text{Final weight}) / \text{Initial weight} \times 100$$

And

5. Moisture reuptake : was measured with the help of desiccators and humidity cabinet for 24 hours simultaneously.

$$\% \text{moisture reuptake} = (\text{Final weight} - \text{Initial weight}) / \text{Initial weight} \times 100^{[36]}$$

6. Folding endurance : A Particular area of the strip (2x2 cm) was cut uniformly and folded over and over until it broke. The value of the folding endurance was determined by the number of times the film was folded at the same location either to break the film or to develop visible cracks.^[37]

7. Tensile strength : The patch's tensile strength was determined using a tensiometer. It is made up of two grips for load cells. The lower one was fixed, while the upper one could be moved. Film strips measuring 2x2 cm were placed between the cell grips, and force was applied progressively until the film broke. The tensile strength was calculated using the dial reading in kilograms .

8. Percentage elongation break test : The percentage elongation break was calculated by noting the length just before the breaking point and the following formula was used to calculate the percentage elongation.

$$\text{Percentage Elongation} = 100 \times (\text{Final length} - \text{Original length}) / \text{Original length} \quad [38]$$

9. Weight uniformity test : The weight uniformity of randomly selected patches from each formulation was checked by digital weighing balance in triplicate. Every triplicate gave uniformity in weight and the average value was similar to an individual patch. So the mean value is zero in almost all the formulations and the patches showed minimum deviation in weight.^[40]

10. Flatness : In the flatness test for a transdermal patch, strips are cut from the center and both right and left sides of the patch. The length of each strip is measured, and the variation in length is calculated as percentage constriction using the following formula:

$$\% \text{Constriction} = (\text{Initial Length} - \text{Final Length}) / \text{Initial Length} \times 100$$

If the percentage constriction is 0%, it indicates 100% flatness, meaning that the patch maintains its smooth surface without any constriction over time.^[41]

11. Peel adhesion test: In this test, the force required to remove the patch from a surface is determined. The patch is applied to a steel plate, and then it is pulled away at a 180-degree angle from the surface. The force needed to detach the patch is measured, providing information about its adhesive strength.^[41]

12. Drug content : For estimating drug content, a required area of the patch is cut and is put into 100 ml phosphate buffer (pH 7.4) shaken continuously for 24 hrs. The solution is then subjected to ultrasonication for 15 minutes and after which it is filtrated and the drug content is analyzed by ultraviolet spectrophotometer at lambda max (λ_{max}) of 256 nm.^[42]

13.. Drug permeation study: Materials required Chemical and Reagents are Cellophane membrane, Open ended tube ,Buffer solution pH 7.4 and Distilled water. Equipments are Hot plate with magnetic stirrer and UV-visible spectrophotometer.

Procedure: The invitro diffusion rate of formulated transdermal patches was studied through an open-ended tube containing distilled water as the diffusion medium for 8 hours. The cellophane membrane was placed at the base of the

tube and dipped in the receptor compartment, which contains 200ml of 7.4 buffer solution. This was stirred at a medium speed and kept at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ by using Hot plate with magnetic stirrer. At regular intervals, samples were taken out and the same volume was refilled with fresh diffusion medium. A UV visible spectrophotometer with a wavelength range of 260-280nm was used to evaluate the samples.

14. Skin irritation test : Before applying the patch, the dorsal skin of a volunteer was washed with 70% ethanol. The patches were applied on right forearm for 24hrs. After 24 hours, the patches were removed and the forearms were cleansed with saline. The cutaneous responses were assessed by observing erythema, edema, pruritus and urticaria, skin allergy and irritation at 15 minutes, 1 hour and 24 hours after the test patch was removed.^{[43][44]}

CONCLUSION:

herbal TDDS patches offer a promising approach to drug delivery, providing a safer and more effective alternative to synthetic drugs. Further research is needed to optimize the formulation and delivery of herbal APIs through the skin, and to fully realize the potential of this technology in improving human health.

REFERENCE:

1. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1732004445072&u=%23p%3DC0yHILmROxYJ
2. https://wjpr.s3.ap-south-1.amazonaws.com/article_issue/1456749531.pdf
3. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1732004167436&u=%23p%3DxvmpJwCYagwJ
4. Kumar P, Sankar C, Mishra B. Delivery of macromolecules through skin. *Indian Pharm.* 2004;5(3):7-17
5. https://www.researchgate.net/publication/373367520_A_Review_on_Transdermal_Patches_of_Herbal_Drugs_for_Arthritis
6. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1732020590892&u=%23p%3DbezhFKPVenUJ
7. Gupta V, Yadav SK, Dwivedi AK, Gupta N. Transdermal Drug Delivery: Post, Present, Future Trends. *Int J Pharm Life Sci.* 2011; 12: 1096-1106.
8. Patel D, Patel N, Parmar M, Kaur N. Transdermal Drug Delivery System: Review. *Int J Bio Pharm Toxicol Res.* 2011; 1: 61-80.
9. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1731945214346&u=%23p%3DbezhFKPVenUJ
10. https://search.app?link=https%3A%2F%2Fwww.researchgate.net%2Fpublication%2F47740880_A_review_on_transdermal_patches&utm_campaign=aga&utm_source=agsadl1%2Cagsadl4%2Csh%2F%2Fgs%2Fm2%2F4
11. Zhang Y, Yu J, Kahkoska AR, Wang J, Buse JB, Gu Z, et al. Advances in transdermal insulin delivery. *Adv Drug Deliv Rev.* 2019;139:51-70.doi:10.1016/j.addr.2018.12.006
12. <https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/transdermal-patch>
13. Barry B. Transdermal drug delivery. In: Aulton E, editor. *The science of dosage forms design*, 2nd edn. . Churchill Livingstone, New York: Harcourt publishers; 2002. p. 499-533. 14
14. https://www.researchgate.net/publication/373555234_A_REVIEW_ON_TRANSDERMAL_PATCHES/link/64f18257c40f1d22df82d760/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVpY2F0aW9uIiwicGFnZSI6InB1YmVpY2F0aW9uIn19https://www.researchgate.net/publication/373555234_A_REVIEW_ON_TRANSDERMAL_PATCHES/link/64f18257c40f1d22df82d760/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVpY2F0aW9uIiwicGFnZSI6InB1YmVpY2F0aW9uIn19
15. https://journals.lww.com/jdnaonline/fulltext/2011/07000/anatomy_and_physiology_of_the_skin.3.aspx?cfchl_jschl_tk=2f35eb4663c32593535eb8171ede925fd9c57353-1616588383-0-AcrPdJ4XRv2JcuUv4WaJkDq3VYpNqq3331k1UdfM6K3HgL6wr_DeguTLStfT3vZ5kaDue_tCiCYWAFkX3RQm9UgS1sgd8j2NoxaiNfCn2rFz2MwchIJvxoLMg9S5-V6j9IiNNdwSO4IQHHsw629SN2Pr9e_6gYySnMNDb7yK_zjPfo4WifEppMS1mdJA41RDsmbfoPY6gkxYqWwpNS4bhY1vMliWCYuUc2Wfu7cnyVkQCCHN1C7Ls1zRD1_XpH69DWELEb0Smp2tpzNI7FWppLnVXvuyBqXr9oHpp5zfgk5kn_Ghsh8y-

- [Z6PaRI6WakQcngOiIvaqpgg63x8omKfbqavGMA3qvV5HM6pqvXHUPqoxK0JhZwsSwBZXStoJUe6VBygSdKYPEDdNZuKea3_UOoB59oJaqGvKe0G4EOPmt_ILDObGiIcpetDQmjHjYhiL9oaMVMBVjP1CRJg1mKyQo8mena3sM2jOFugsC8Bo45](https://www.researchgate.net/publication/37355234_A_REVIEW_ON_TRANSDERMAL_PATCHES/link/64f18257c40f1d22df82d760/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVudC9uIn19)
16. <https://www.sciencedirect.com/science/article/abs/pii/S0263931910001596>
 17. https://books.google.co.in/books?hl=en&lr=&id=n0y6NMnviLkC&oi=fnd&pg=SA3-PA1&dq=skin+anatomy+layers+epidermis&ots=y_Tx5hB510&sig=o_DX-cVk7YuyliXxQ9sd8F5uefA&redir_esc=y#v=onepage&q=skin%20anatomy%20layers%20epidermis&f=false
 18. https://journals.lww.com/jdnaonline/fulltext/2011/07000/anatomy_and_physiology_of_the_skin.3.aspx?cfchl_jschl_tk=2f35eb4663c32593535eb8171ede925fd9c57353-1616588383-0-AcrPdJ4XRv2JcuUv4WaJkDq3VYpNqq3331k1UdfM6K3HgL6wr_DeguTLStfT3vZ5kaDue_tCiCYWAFkX3RQm9UgS1sgd8j2NoxaiNfCn2rFz2MwchIJvxoLMg9S5-V6j9liNNdwSO4IQHHsw629SN2Pr9e_6gYySnMNDb7yK_zjPfo4WifEppMS1mdJA41RDsmbfoPY6gkxYqWwpNS4bhY1vMliWCYuUc2Wfu7cnyVkQCCHN1C7Ls1zRDl_XpH69DWELEb0Smp2tpzNI7FWppLnVXvuyBqXr9oHpp5zfgk5kn
 19. <https://images.app.goo.gl/RMN1r8KnNmBeacd16>
 20. https://www.researchgate.net/publication/37355234_A_REVIEW_ON_TRANSDERMAL_PATCHES/link/64f18257c40f1d22df82d760/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVudC9uIn19
 21. Arti Kesarwani, Ajit Kumar Yadav, Sunil Singh, Hemendra Gautam, Haribansh N Singh, et al. A review- Theoretical aspects of Transdermal Drug Delivery System. Bulletin of Pharmaceutical Research, 2013; 3(2): 78-89.
 22. Sampath Sampath Kumar KP, Debjit Bhowmik, Chiranjib B, RM Chandira A review Transdermal Drug Delivery System- A Novel Drug Delivery System and its market scope and opportunities. International Journal of Pharma and Bio Sciences, 2010; 1(2).
 23. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10142343/>
 24. Dr. Shailesh Sharma , Ms.Punam Gaba, Dr. Neelam Sharma, DR. Rahul Kumar Sharma, Nirali Prakashan.
 25. Dr . K. Jesindha Beyatricks , Mrs. Ashwini S. Joshi in Novel drug delivery systems by Nirali Prakashan , First edition 2020
 26. <https://images.app.goo.gl/3PEDQcWuLxzfyTSa7>
 27. https://search.app?link=https%3A%2F%2Fscholar.google.com%2Fscholar%3Fhl%3Den%26as_sdt%3D0%252C5%26q%3Dcomponents%2Bo%2Bherbal%2Btransdermal%2Bpatches%2B%26btnG%3D%23d%3Dgs_qabs%26t%3D1732102455885%26u%3D%2523p%253DV6d0yqshQZ4J&utm_campaign=aga&utm_source=agsadl1%2Cagsadl4%2Csh%2Fx%2Fgs%2Fm%2F4
 28. https://www.researchgate.net/publication/270015915_Transdermal_drug_delivery_system_An_overview
 29. <https://journals.innovareacademics.in/index.php/ajpcr/article/download/19909/12581>
 30. <https://www.google.com/imgres?imgurl=https%3A%2F%2F3-us-west-2.amazonaws.com%2Ftypeset-prod-media-server%2F0a77ff3f-7109-44f6-a6ea-7218a284a25cimage2.jpeg&tbnid=LX-YQjMQ2EBfbM&vet=1&imgrefurl=https%3A%2F%2Fwww.ijced.org%2Fhtml-article%2F21916&docid=UCIjCs4ICc-17M&w=1360&h=448&itg=1&hl=en-US&source=sh%2Fx%2Fim%2Fm5%2F4&kgs=1b24afd1951623b4&shem=abme%2Ctrie>
 31. https://www.researchgate.net/publication/37355234_A_REVIEW_ON_TRANSDERMAL_PATCHES/link/64f18257c40f1d22df82d760/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVudC9uIn19
 32. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10142343/>
 33. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1731938262368&u=%23p%3DbezhFKPVenUJ
 34. https://scholar.google.com/scholar?hl=en&as_sdt=0,5&q=herbal+transdermal+patches+&btnG#d=gs_qabs&t=1731938262368&u=%23p%3DbezhFKPVenUJ
 35. http://plantarchives.org/SPL%20ISSUE%20PDF/121-127_S-39_.pdf
 36. https://www.researchgate.net/publication/354801034_FORMULATION_DEVELOPMENT_AND_EVALUATION_OF_HERBAL_TRANSDERMAL_PATCH_FOR_FRACTURE_HEALING/link/61f9418c11a1090a79c7a776/download?tp=eyJjb250ZXh0Ijp7ImZpcnN0UGFnZSI6InB1YmVudC9uIn19
 37. <https://www.sciencedirect.com/science/article/abs/pii/S2210803321000142>
 38. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3252722/>

39. <https://pmc.ncbi.nlm.nih.gov/articles/PMC10819821/>
40. https://www.researchgate.net/publication/320802968_Formulation_and_evaluation_of_transdermal_patch_of_indomethacin_containing_patchouli_oil_as_natural_penetration_enhancerhttps://www.researchgate.net/publication/320802968_Formulation_and_evaluation_of_transdermal_patch_of_indomethacin_containing_patchouli_oil_as_natural_penetration_enhancer
41. Schuetz YB, Naik A, Guy RH, Kalia YN. Emerging strategies for the transdermal delivery of peptide and protein drugs. *Expert Opin Drug Deliv.* 2005;2(3):533-48.
42. https://www.researchgate.net/publication/320802968_Formulation_and_evaluation_of_transdermal_patch_of_indomethacin_containing_patchouli_oil_as_natural_penetration_enhancer
43. <https://www.ijfmr.com/papers/2023/6/10753.pdf>
44. <https://journals.innovareacademics.in/index.php/ijcpr/article/view/35716/20824>

