

Integrating Herbal Medicine with Transdermal Technology: A Comprehensive Review

Saurabh Balu Betalse¹, Snehal Anil Bhosale², Jyoti Bhimraj Bhujade³, Dr. Vandana Patil⁴

Yash institute of Pharmacy

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Abstract—A safe, non-invasive, and patient-friendly substitute for traditional administration methods is provided by herbal transdermal patches, an innovative drug-delivery technique. By avoiding hepatic first-pass metabolism and minimizing gastrointestinal adverse effects, these systems transport phytoconstituents straight through the epidermis into the systemic circulation. In order to maintain controlled, sustained release, a conventional herbal patch is made up of a polymeric matrix, drug reservoir, adhesives, permeability enhancers, and a protective backing layer. Lipid content, blood flow, moisture, pH, and the molecular properties of the herbal medication are among the physicochemical parameters that affect drug transport across the skin via transcellular, intercellular, or appendageal pathways. Although there are some drawbacks such as skin irritation, inconsistent permeability, and expensive formulation costs, transdermal patches have many benefits like increased bioavailability, consistent plasma levels, convenience of administration, and extended shelf life. Pain relief, anxiety, sleeplessness, inflammation, asthma, and quitting smoking are among the uses. Quality and efficacy are guaranteed by thorough examination, which includes thickness, folding endurance, medication content, moisture analysis, in-vitro diffusion, and stability investigations. Herbal transdermal patches have great promise for future therapeutic innovation given the rising demand for natural medicines.

Index Terms—Herbal transdermal patches; Components; Skin permeation; Application; and Future aspects.

I. INTRODUCTION

A transdermal patch is a medicated patch that can administer medication at a predetermined rate through the skin's layers and straight into the bloodstream. The goal of any drug delivery system is to deliver a therapeutic dose of medication to the right location in

the body while maintaining the appropriate level of drug concentration. In order to maintain optimum plasma drug levels for therapeutic efficacy, these systems deliver the drug at the proper rates. Transdermal patch provides constant blood levels, by first pass metabolism, improve patient compliance, and reduce dose dumping. This approach can prevent drug-related side effects, such as stomach discomfort. For transdermal distribution, the medication should have a small molecular size, good solubility in the carrier, short half-life, low dose, and appropriate lipophilicity.¹⁻⁵

1.1 Herbal Transdermal Patch: -

The drug should be delivered at a rate that aligns with the body's needs during the therapy term. Secondly, it should direct the active ingredient of herbal drug to the site of action. This system is known as herbal transdermal drug delivery system. When applied to intact skin, herbal transdermal drug delivery systems (Herbal patches) are self-contained, discrete dose forms intended to administer the medication via the skin at a regulated pace of systemic circulation. A number of benefits make herbal transdermal drug delivery systems attractive, including the ability to administer medications continuously, the avoidance of minimal intestinal irritation, and the avoidance of the inconsistent absorption and metabolic breakdown linked to oral treatments. They have a number of benefits over traditional formulations, including improved drug bioavailability, fewer systemic side effects, steady state drug levels, less frequent dosing, a simpler patient dosage schedule, and less variability in plasma drug levels. Maintaining a high drug concentration within the patch is essential for transdermal drug delivery because it produces a concentration gradient that promotes skin diffusion and guarantees a steady plasma drug level.⁶⁻¹⁰

1.2 Synthetic Transdermal Patch:-

The synthetic TDDS is a non-invasive administration approach that causes minimal pain and strain on the patient. Drugs can be safely and comfortably provided to youngsters or the elderly.¹¹ These patches are intended to be placed to the skin while providing a therapeutically effective amount of one or more active substances into the systemic circulation via the skin's layers.¹ Several medications have been administered to the skin for systemic therapy. In a broad sense, transdermal delivery system refers to all topically applied medication formulations that are designed to transport the active ingredient into general circulation.¹²

1.3 Herbal patch v/s synthetic patch:

Synthetic medications can help treat illnesses, but they also have adverse effects. As a result, employing herbal remedies is a safer way to therapy than other options. Transdermal drug delivery enhances the

effectiveness and reduces negative effects in herbal medicine. Herbal medicines are increasingly popular due to their medical benefits and minimal adverse effects on the body. Making natural medicines involves changes to supply adequate herbal medicines have been used effectively to manage several life-threatening disorders. The amounts of API through continuous and regulated release of the drug.¹³

II. COMPONENTS OF HERBAL TRANSDERMAL PATCHE

1. Liner:-
2. Drug:-
3. Adhesive (pressure-sensitive adhesive):-
4. Membrane (polymer matrix/drug reservoir):-
5. Backing laminates:-
6. Other excipients like permeation enhancers and others:-

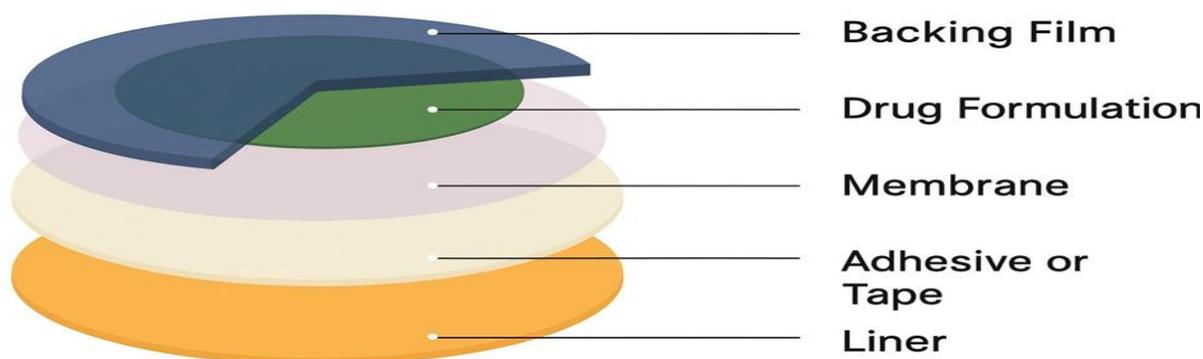


Figure 1: Components of Herbal Transdermal Patch

2.1 Liner

This kind of primary packaging is taken off when a transdermal patch is applied to the skin. The liner's primary purpose is to safeguard the dosage form while it is being stored.¹⁴ During storage, it protects the patch. Remove the lining before use. This aspect of primary packaging prevents medication loss from the polymer matrix.¹⁵

2.2 Drug

The transdermal drug delivery system (TDDS) is ideal for drugs that undergo increased GI tract first-pass metabolism and degradation, resulting in the limited

therapeutic value. Additionally, drugs with a short half-life (< 2 hours) require frequent dosing, which can result in patient non-compliance.¹⁴ The active compound is in direct contact with the release liner.¹⁵ Solvents and co-solvents help to dissolve or disseminate drug particles throughout the matrix, forming the drug reservoir. The medicine should be carefully chosen for the effective development of the TDDS.¹⁶

2.3 Adhesive (pressure-sensitive adhesive):-

A pressure-sensitive adhesive's principal role is to maintain intimate contact surrounded by the skin and the delivery system. Adhesive physicochemical properties are generally determined by the types and quantities of excipients used, primarily the mixture of the transdermal drug delivery system (TDDS), adhesive layer thickness, backing membrane thickness, residual solvent, and concentration of the active pharmaceutical ingredient (API).¹⁴ This component binds the patch elements and attaches it to the skin.¹⁵ It should not irritate or sensitize the skin on touch. The API should remain firmly adhered to the skin during the dose time, unaffected by actions. It ought to be easy to remove and leave no skin residue that is permanent. It ought to be in close link with the skin.¹⁶

2.4 Membrane (polymer matrix/drug reservoir):-

Polymers serve as the foundation of the TDDS, regulating the flow of medication from the system. To generate a drug reservoir, the medicine can be disseminated in a synthetic polymer that is either solid or liquid.¹⁴ The membrane regulates medication release from reservoirs and multilayer patches. It is typically comprised of chitosan and poly-2-hydroxyethylmethacrylate.¹⁵ A polymer matrix can be created by dispersing the medication in liquid or non-liquid form of synthetic polymers. To create a transdermal drug delivery system that virtual fits the numerous criteria, the polymer selection and design must be carefully considered. The polymer controls the device's release of the API. To get the best diffusion and release of the particular API, the polymer's molecular weight, glass transition temperature, and chemical activity must be carefully selected.¹⁶

2.5 Backing laminates

When utilizing the transdermal patch and the system, backing films are required. The film's function is to keep the system stable, support the active layer, and control skin penetration and resistance based on breathability or occlusion.¹⁴ It protects the patch from the environment, supports it, and enhances its flexibility and look.¹⁵ This is an impermeable material that protects the product when it is used on the skin surface. Metallic plastic laminates, plastic backings with absorbent pads, occlusive base plates, and sticky foam pads (flexible polyurethane) are some examples.¹⁶

2.6 Other excipients like permeation enhancers and others:

Permeation enhancer: - Permeation enhancers are chemicals that modify the skin's barrier to enable greater penetration of intended substances.¹⁶

III. DRUG ABSORPTION VIA SKIN

Because of its large surface area, the skin may be a location of drug absorption. Drug is released into the skin once drug-containing dosage forms are applied to it. However, medication absorption through the skin is extremely difficult since the first barrier must be overcome, the SC. The SC is structurally made up of dead keratinocytes that, along with the ceramide lipid component, form a thick structure characterized as a 'brick-and-mortar' arrangement. Keratin, an acidic or basic to neutral protein produced by keratinocytes, is the 'brick' of the SC, while lipids make up the 'mortar'. Corneodesmosomes are glycoprotein desmosomes that link keratinocytes.¹⁷

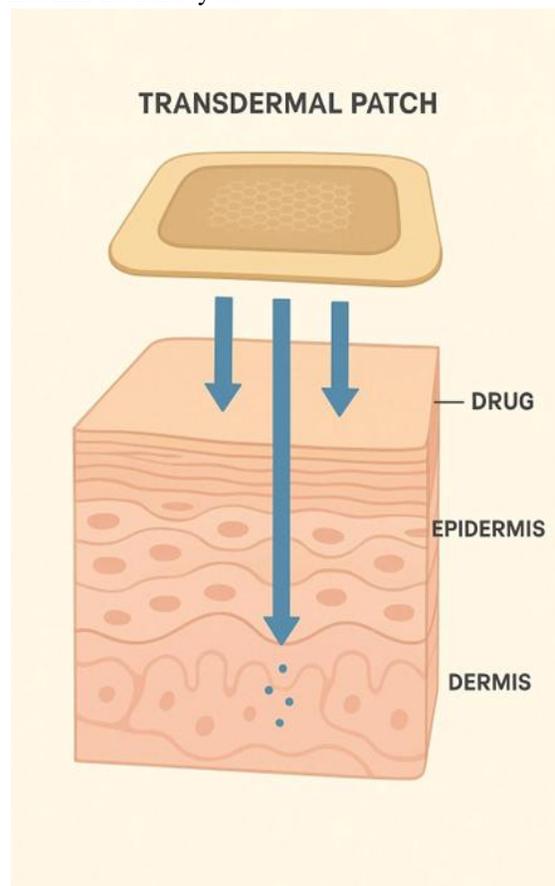


Figure 2: Drug penetration via skin

The two major steps of skin permeation include partitioning and diffusion across the stratum corneum (SC) and the epidermis, transit into the dermis, and finally systemic absorption or penetration into deeper tissues. The skin's outermost layer, or SC, is the most effective barrier to drug penetration. Many strategies have been used to improve medicine access to the lower skin layer and deeper tissues. Chemical and physical permeation enhancers have been created to aid in the transport of high medicine concentrations across the skin and into systemic circulation or deeper tissues.¹⁸

The herbaceous medicine meridian principle serves as the foundation for the meridian penetration point in the transdermal drug system. Agents accumulate through a meridian point to reach higher concentrations than those supplied via injection or oral route. According to research, agents absorbed by the meridian point principle differ from those absorbed through blood vessels; when a medicine penetrates through a meridian point, it treats the lesions directly rather than circulating throughout the body. In previous investigations on herbal medicines taken by a meridian point, the medicines were observed to go via the meridian-not scattered and disseminated to other areas.¹⁹

IV. FACTORS INFLUENCING HERBAL TRANSDERMAL PATCHES

4.1 Biological Factors:-

1. Skin condition: Many solvents, including methanol and chloroform, as well as acids and alkalis, harm skin cells and encourage penetration. Skin conditions change when a patient is ill. Although healthy skin provides a better barrier, penetration is impacted by the aforementioned factors.
2. Skin age: Younger skin is more permeable than older skin. Children are especially susceptible to pollutants absorbing via their skin. Therefore, one of the factors influencing drug penetration in TDDS is skin age.
3. Blood supply: Transdermal absorption may be impacted by modifications in peripheral circulation.
4. Regional skin site: Site-specific differences exist in skin thickness, stratum corneum composition,

and appendage density. These elements have a big impact on penetration.

5. Skin metabolism: The skin breaks down chemicals that cause cancer, hormones, steroids, and some medications. Therefore, the effectiveness of a drug that penetrates the skin is determined by skin metabolism.
6. Special differences: The penetration is affected by species-specific differences in skin thickness, appendage density, and keratinization.²⁰
7. Lipid film: By preventing moisture loss from the skin and supporting the preservation of the stratum corneum barrier function, the lipid film on the skin's surface serves as a safety layer. Defatting this film was observed to decrease transdermal absorption.
8. pH: Weak acids and bases dissociate to varying degrees depending on their pH and pKa or pKb values, and only unionized (neutral) molecules can easily penetrate the lipid membrane. Therefore, the pH-dependent effective membrane gradient will be determined by the concentration of unionized species.²¹

4.2 Physiological Factors:-

1. Skin hydration: Skin permeability dramatically increases when it comes into link with water. The most crucial element boosting skin penetration is hydration. Humectants are therefore applied transdermally.
2. Temperature and pH: As the temperature changes, the drug's penetration increases tenfold. As the temperature drops, the diffusion coefficient drops as well. The pH and pKa and pKb values determine how weak acids and weak bases dissociate. The drug percent in skin is driven by the percentage of unionized drug. Therefore, two crucial variables influencing medication penetration are pH and temperature.
3. Diffusion coefficient: The drug's diffusion coefficient determines its penetration. The features of the drug, the diffusion medium, and their interaction determine the drug's diffusion coefficient at a constant temperature.
4. Drug concentration: The concentration gradient across the barrier determines the flux, and the higher the drug concentration across the barrier, the greater the concentration gradient.

5. Partition coefficient: Good action necessitates the appropriate partition coefficient (K). High K drugs are not yet ready to exit the skin's lipid layer. Additionally, medications with low K will not pass through.
6. Molecular geometry and dimensions: Molecular weight and drug absorption are negatively correlated; tiny molecules absorb drugs more quickly than large ones.²⁰
7. Ionization: The pH-Partition hypothesis states that unionized drugs penetrate the epidermis.
8. Solubility/Melting point: The majority of organic solutes have low solubility and a high melting point at room temperature and pressure. Lipophilic medications penetrate more quickly than hydrophilic ones, but they also need to be somewhat soluble in water, which is necessary for the majority of topical formulations.²¹
7. Self-administration is feasible.
8. Reduction of adverse effects.¹³
9. This procedure is easy to use and only needs to be used once a week. A straightforward dosage schedule like this can help patients stick to their medication routine.
10. Patients who are not able to tolerate oral dosage forms can be served by transdermal medication delivery, which is an alternate method of administration.
11. It is quite beneficial for people who are unconscious or experiencing nausea.
12. Because transdermal distribution circumvents direct effects on the gastrointestinal tract, it can be a useful option for medications that disturb the gastrointestinal tract.
13. Drugs that are broken down by the gastrointestinal system's acids and enzymes might also be a viable target.
14. Transdermal administration avoiding first-pass effect, which is another restriction on oral medication delivery.
15. Transdermal drug administration is an excellent option for medications that need a comparatively constant plasma level.²³

V. IDEAL PROPERTIES OF HERBAL TRANSDERMAL PATCH

1. Two years is the maximum durability.
2. Little patch (less than 40 cm²).
3. Simple dosage planning (e.g., once weekly to once daily).
4. In terms of appearance, acceptable (i.e., a clear, white colour).
5. Simple to arrange.
6. The release liner is simple for both young and old patients to remove.²²

VI. ADVANTAGES OF HERBAL TRANSDERMAL PATCHES

1. Avoids pre-systemic and hepatic metabolism, increasing bioavailability.
2. IV treatment difficulties and inconveniences are avoided.
3. Decrease in the frequency of doses.
4. Medication therapy can be easily stopped because patch removal ceases medication administration.
5. Boost patient adherence.
6. Enhanced therapeutic effectiveness by avoiding the systemic drug level peaks and troughs that come with traditional medication delivery.

VII. DISADVANTAGES OF HERBAL TRANSDERMAL PATCHES

1. Only strong compounds are viable options for transdermal administration.
2. Some patients may get skin irritation at the application location.
3. It is not appropriate for medications that need elevated blood levels.
4. It might not be cost-effective.
5. Drugs that cause skin irritation or sensitization should not be administered transdermally.¹³
6. Ionic medications cannot be delivered by TDDS.
7. It is unable to develop for medications with big molecules.
8. TDDS is unable to provide pulsatile drug delivery.
9. If the medication or formulation causes skin irritation, TDDS cannot form.²³

VIII. APPLICATIONS OF HERBAL TRANSDERMAL PATCHES

Sr. No.	Drug	Category	Chemicals	Polymers	References
1	Withania coagulans	Antioxidant, anti-inflammatory and antidiabetic	Glycerol, citric acid	PVA	24
2	Ficus benghalensis fruit mucilage	Antidiabetic	Glycerine, eudragit, span-80, propyl paraben, methyl paraben, and water	PVA, HPMC, chitosan, PVP, PLA, PCL, PEG,	25
3	Aloevera	Anti-inflammatory	Glycerine, sodium alginate, water, and ethanol	HPMC and propylene glycol	2
4	Ginger	Anti-inflammatory	Peppermint oil, ethanol, water	HPMC, PVP	26
5	Garlic	Anti-inflammatory, Antibacterial, antioxidant and antifungal	Ethanol and water	Carbapol and ethylene vinyl acetate	27
6	Tulsi	Anti-inflammatory, antioxidant and anti-cancer	Pectin, sodium alginate, DMSO, glycerine, potassium dihydrogen orthophosphate ethanol water and NaOH	HPMC, PVA, PVP and carbopol	28
7	Neem	Anti-inflammatory and wound healing	Methanol, ethanol, water and glycerine	HPMC, ethyl cellulose, PEG-400 and propylene glycol	29
8	Fenugreek	Antidiabetic	Ethanol, disodium methyl sulfoxide and water	(HPMC) E15-LV, (HPMC) 15CPS, (HPMC) 50CPS and propylene glycol	3
9	Turmeric oil	Anti-inflammatory and antibacterial	Ethanol, water and chloroform	HPMC E50, poly vinyl alcohol and polyethylene glycol	30
10	Capsaicin extract and Mustard oil	Analgesic, anti-inflammatory and antioxidant	Water, alcohol, and naproxen	HPMC, PVP and PVA	31
11	Tridax procumbens	Anti-inflammatory and antidiabetic	Methanol, Hcl, NaoH, lead acetate solution, ammonia solution, ethanol and water	PVA and ethyl cellulose	32
12	Berberine	Antidiabetic	Ethanol, glycerine and water	Chitosan	33
13	Lavender essential oil	Anti-inflammatory	Ibuprofen, linalyl acetate, ethanol, water and linalool	HPMC, PVA and propylene glycol	34
14	Thespesia populnea	Anti-inflammatory	Ethanol, water and dimethyl sulfoxide	Polyvinyl pyrrolidone, polyethylene, polypropylene,	23

				polyvinyl alcohol, polyvinyl chloride, and polymethylmethacrylate.	
15	Green tea	Antioxidant, anti-inflammatory, anti-carcinogenic and anti-bacterial	Epigallocatechin 3-gallate, caffeine, ethanol, water and gallic acid.	PVA, HPMC and PGA	35
16	Kaempferia parviflora and Curcuma longa extracts	Anti-inflammatory	Methoxyflavones, ethanol and water	PVP	36
17	Marigold and Spinach	Anti-inflammatory	Water and ethanol	PVA and PGA	37
18	Yashtimadhu extract (Glycyrrhiza glabra L.)	Anti-ulcer, anti-inflammatory, antioxidant and wound healing	Methanol, distilled water	HPMC, polyethylene glycol 400 and 200	38
19	Hibiscus rosa sinensis	Anti-inflammatory, antioxidant, antidiabetic and antimicrobial	Potassium dihydrogen ortho phosphate, sodium hydroxide, anhydrous calcium carbonate, water and ethanol	Carbopol-940/pectin/sodium alginate, water and tween-80	39
20	Asparagus racemosus(s hetavari)	Antibacterial	Methanol and water	PEG 4000, PVA, PVP, EC, and HPMC	40
21	Piper betle L (Piperaceae)	Antioxidant and anticancer	2, 2-diphenyl-1-picrylhydrazyl, sulforhodamine B, ethanol and water	Pectin, hydroxyl propyl methylcellulose (HPMC), polyvinyl pyrrolidone K-90 (PVP-K90) and propylene glycol (PG)	41
22	Eplerenone	Anti-inflammatory	Water and ethanol	polyvinyl alcohol (PVA) and ethyl cellulose (EC)	42
23	Moringa oleifera leaf	Analgesic, antioxidant and anti-inflammatory	Glycerol and dimethyl sulfoxide, ethanol and water	HPMC, gelatin and polyethylene glycol 400	43
24	Nelumbo nucifera	hepatoprotective, hypoglycemic, lipolytic, hypocholesteremic, antipyretic, anti-	Sinomenine, glycerol, ethanol and water	PVA, PVP and polyethylene glycol	7

		inflammatory, antifungal, antibacterial, anti-inflammatory, anti-inflammatory, anti-ischemic, antioxidant, anticancer, antiviral, anti-obesity and diuretic			
25	Eucalyptus	Antimicrobial, anti-inflammatory, analgesic, antioxidant, respiratory (mucolytic and bronchodilatory), antidiabetic, antiviral, insecticidal and repellent, wound healing and neuroprotective	Glycerol, ginger oil, curcumin oil, ethanol and distilled water	HPMC K4M, EC 7 cps, PVP K30, and propylene glycol (PG), PVA and PEG-4000	44
26	Centella asiatic and Liquorice	Neuroprotective, cognitive enhancer, anti-inflammatory, wound healing, anti-anxiety (anxiolytic), antidepressant, hepatoprotective, antimicrobial, anticancer, antiulcer and cardio protective	Glycerol, ethanol and water	Hydroxypropyl methylcellulose (HPMC), carbapol 934, methanol and propylene Glycol	45
27	Amomum subulatum	Anti-inflammatory, antimicrobial, antioxidant and anticancer	Dibutyl phthalate, chloroform, methanol and essential oils, ethanol and water	Ethyl cellulose and polyethylene glycol (PEG 400)	46
28	Amla and Neem	Antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, antiviral, anticancer and antidiabetic	Ethanol, glycerine and water	PVA, HPMC, PEG and propylene glycol	47
29	Gokhru	Diuretic, anti-inflammatory, antioxidant and aphrodisiac	Distilled water, ethanol and glycerol	PVA, PVP and propylene glycol	48
30	Cardiospermum helicacabum and Aloe barbadensis	Anti-inflammatory, antioxidant, and antimicrobial	Chloroform, ethanol, glycerine and water	HPMC and tween 80	49

31	Datura	Sedative, anti-asthmatic and anti-inflammatory	Rose oil, ethanol, glycerine and distilled water	Propylene glycol, PVP and PVA	50
32	Piper betle and Psidium guajava Linn	Antibacterial, antifungal, antioxidant, antidiabetic and gastroprotective	Chloroform, ethanol, water and methanol	PEG-400, propylene glycol and HPMC	51
33	Crinum asiaticum	Anticancer, analgesic, anti-inflammatory, antiviral, antibacterial and antifungal	Paraben concentrate, ethanol and water	HPMC, poly vinyl alcohol and PEG-400	52
34	Olea europaea	Antioxidant, anti-inflammatory, antimicrobial, anticancer and antidiabetic	Propanediol, ethanol, water and glycerol	CMC and gua gum	53
35	Drypetes roxburghii	Anti-inflammatory, analgesic, antipyretic, antimicrobial and antioxidant	Methanol and water	HPMC	54
36	Pigeon pea (Cajanus cajan L.)	Antioxidant, anti-inflammatory, antimicrobial, and antidiabetic	Aquadest, ethanol and water	HPMC, polyethylene glycol-400, Propylene glycol and PVP	55
37	Eleutherine bulbosa Urb.	Anticancer, anti-diabetic, antibacterial, antifungal, antioxidant and anti-inflammatory	Dibutyl phthalate, Methyl paraben, ethanol and water	HPMC, PEG-400, propylene glycol and ethyl cellulose	56
38	Boswellia serrata	Anti-inflammatory, antioxidant and anticancer	Methanol, distilled water and glycerol	Ethyl cellulose, polyvinylpyrrolidone (PVP) and propylene glycol	57
39	Cissus quadrangularis	Bone healing, regeneration, anti-inflammatory, antioxidant activity and antimicrobial	DMSO, dibutyl phthalate, chloroform, water and methanol	HPMC (E15)	58
40	Wrightia tinctoria	Antimicrobial, anti-psoriatic, anti-inflammatory, anti-diabetic and wound-healing	Ethyl alcohol, ethanol, DMSO, glycerine and water	HPMC and pectin	59
41	Costus igneus N. E.	Anti-diabetic, antioxidant, anti-inflammatory, antimicrobial and hypolipidemic	Ethanol, methanol, brilliant green and water	HPMC and ethyl cellulose	60

42	Vitex negundo	Anti-inflammatory, analgesic, antioxidant and hepatoprotective	Ethanol, oleic acid, isopropanol, methanol, acetone, chloroform, sodium hydroxide, sodium bicarbonate, potassium chloride, calcium chloride dihydrate, sodium chloride, potassium hydrogen phosphate, water and disodium hydrogen phosphate	HPMC and PVP K30	61
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IX. EVALUATION TEST OF HERBAL TRANSDERMAL PATCH

9.1 Organoleptic Characteristics: -

A naked-eye assessment was conducted to assess the physical appearance, color, clarity, flexibility, and smoothness of the produced patch.

9.2 Physico-Chemical Evaluation: -

1. Patch thickness: -

A Vernier caliper was used to assess patch thickness uniformity in six locations. The average thickness of all six locations was found.

2. Surface pH determination: -

$$\text{Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} * 100$$

4. Percent drug content:

Patches were chopped into small fragments and submerged in a phosphate buffer solution (PH 7.4) for 24 hours. The entire solution was then ultrasonically processed for 15 minutes. After filtration, the drug content was determined spectrophotometrically at λmax using the necessary nm.

$$\text{Percent drug content} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} * 100$$

5. Folding endurance:

Folding endurance was measured by folding the patches repeatedly in the same spot even after they had broken. Folding endurance refers to the amount of times patches can be folded in the same location without breaking.

6. Uniformity of weight:

Five randomly selected patches from the same batch should be dried at 60°C for four hours. After that, the patch is placed on a digital balance to find its average weight.

7. Moisture uptake:

Weighed patches were placed in desiccators at room temperature for 24 hours in a saturated potassium chloride solution to maintain 84% relative humidity. After 24 hours, the patches were reweighed and the % moisture uptake was estimated using the procedure below.

$$\text{Percent moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} * 100$$

To test the pH of the patch, soak it in 1 cc of distilled water at room temperature for two hours before usage. Place the pH electrode on the patch's surface to record the pH value and let it to regulate itself for 1 minute.

3. Moisture content percentage:

The patches' percent moisture content was evaluated by weighing them after inserting them inside. Using a desiccator for 24 hours. The percentage moisture content can be computed using the following formula:

8. Percentage elongation test:

Applying external stress to patches causes strain and elongation, which increases with plasticizer concentration.

$$\text{Percent elongation} = \frac{\text{Increase in length of patch}}{\text{Initial length of patch}} * 100$$

9. Water vapour permeability test:

A standard air circulation oven can be used to determine water vapour permeability. The WVP can be calculated using the following formula.

$$\text{Water vapour permeability} = \frac{\text{Amount of vapour permeated through the patch}}{\text{Surface area}}$$

10. Flatness test:

Patches were divided into three longitudinal strips. The length of each strip was measured, and the difference owing to non-uniformity in flatness was computed using percentage constriction. 0% constriction equals 100% flatness.⁴⁹

$$\text{Percent constriction} = \frac{\text{Final length of each patch}}{\text{Initial length of each patch}} * 100$$

11. pH test:

The film's pH was measured using a pH meter. To determine pH, a 2x4 cm patch is dissolved in distilled water and a solution is created. The LT-5001 table top pH meter is used to determine pH levels.⁴⁵

12. Stability studies:

Stability investigations were carried out in accordance with ICH recommendations, storing TDSS samples at 40 degrees celsius and 75 percent relative humidity for 6 months. Samples were collected at 0, 30, 60, 90, and 180 days and tested for drug content.⁶

13. In-vitro drug release studies:

Franz diffusion cell at pH 6.8 was utilized for the produced matrix of each formulation in the in vitro release investigations. After the patches were attached to the Franz diffusion cell's mouth, the cell was continuously operated at 50 RPM at a maintained 37±0.5°C. At predetermined times, the samples were taken out and kept. The drug release pattern was then determined by analyzing each sample of each formulation using a UV-visible Spectrophotometer.

14. Tensile strength:

Tensile strength is a physical parameter that tells us how much tension is required to rupture a 2 cm by 2 cm patch. A tensiometer was used to measure it, and each formulation's reading was recorded in kilograms.⁶⁰

15. Skin irritation studies:

As stated in the CPCSEA Protocol (IAEC/2019-20/RP-05). The albino Wistar rats were housed in cages with usual laboratory diet and free access to water. The rats' dorsal abdominal skin was carefully

removed from the dorsal portion of their trunks within 24 hours of the study's conclusion by shaving, cutting, and avoiding any injuries. The exposed skin was wrapped with non-sensitizing microporous tape after transdermal patches containing the herbal remedy *Vitex negundo* were applied. The test patch composition was fixed across all test sites. The test locations were assessed for erythema, edema, or other potentially dangerous side effects in comparison to a drug-free blank patch and a histamine solution of 1 mg/mL (control). 1, 24, 48, and 72 hours following up application.⁶¹

X. FUTURE ASPECT FOR HERBAL TRANSDERMAL PATCH

Future research should concentrate on optimizing formulation procedures, increasing bioavailability, and assuring regulatory compliance in order to improve the commercialization of herbal transdermal patches. Innovations in herbal transdermal patches have opened up new drug delivery possibilities, providing a non-invasive, effective, and patient-friendly approach to herbal medicine. With continued breakthroughs in nanotechnology, smart polymers, and biosensor integration, herbal transdermal patches have enormous potential. For transforming healthcare and alternative medicine.⁹

The need for better patient adherence, regulated medication release, and improved therapeutic outcomes has led to considerable developments in transdermal patch technology in recent years. This

section examines some of the most recent developments in transdermal patch technology, emphasizing how they could transform medication administration in a number of areas of therapy.⁶²

It is anticipated that the merging of cutting-edge delivery technologies, digital health monitoring, and customized medicine approaches will influence the future of formulation science for smart transdermal herbal patches. Future formulations may include nano-sized herbal medicine carriers, such as solid lipid nanoparticles or nanostructured lipid carriers, to enhance phytoconstituents solubility, stability, and skin penetration due to the quick development of nanotechnology. Innovations in biodegradable and skin-friendly polymers, especially those made from sustainable plant sources, are anticipated to garner attention concurrently, allowing for improved patch flexibility and moisture control. 3D printing technologies, which enable accurate layering of herbal actives with controlled-release profiles customized to each patient's needs, may complement these developments.⁶³

10.1 Nanoformulations for Enhanced Permeation:

One promising method to get around the drawbacks of traditional transdermal drug delivery systems is nanotechnology. Lipid nanoparticles, polymeric micelles, and nanoemulsions are examples of nanoformulations that provide benefits like enhanced drug solubility, better skin penetration, and targeted delivery to particular skin layers. By encapsulating medications and improving their penetration through the stratum corneum, these nanostructures can increase therapeutic efficacy and decrease systemic side effects.

10.2 Wearable Technologies and Smart Patches:

Real-time monitoring of drug delivery parameters and patient adherence has been made possible by the combination of wearable technology and transdermal patches. Smart patches with sensors, microchips, and wireless connectivity can track the kinetics of drug release, keep an eye on physiological parameters, and give patients and healthcare professionals feedback. These developments allow for personalized medicine strategies catered to the requirements of each patient in addition to improving treatment results.

10.3 Microneedle-Mediated Delivery Systems:

Microneedles represent a minimally invasive approach to transdermal drug delivery, offering precise control over drug administration and enhanced patient

comfort. By creating micropores in the stratum corneum, microneedle arrays improve drug penetration without causing discomfort or tissue damage. These microneedle-mediated delivery systems have shown promise for delivering a wide range of therapeutics, including small molecules, biologics and vaccines with enhanced efficacy and reduced dosing frequency.

10.4 Hydrogel-Based Patches for Enhanced Adhesion and Drug Release:

Transdermal patches made of hydrogel provide benefits such better skin adherence, increased drug stability, and regulated release kinetics. The hydrophilic polymers used in these patches expand when they come into contact with skin moisture, creating a gel-like substance that sticks firmly to the application site. Both hydrophilic and hydrophobic medications can be included into hydrogel-based patches, providing a variety of drug delivery options while preserving patient comfort and compliance.

10.5 3D Printing Technology for Personalized Patches:

The creation of customized transdermal patches with exact control over patch geometry, medication dosage, and release kinetics has been made possible by developments in 3D printing technology. With benefits like dose titration, combination therapy, and quick prototyping of innovative drug delivery systems, 3D printing enables the on-demand production of patches customized to each patient's needs. This customized patch manufacturing process may maximize therapeutic results and reduce side effects.

10.6 Biodegradable and Biocompatible Materials:

Transdermal patch formulations that incorporate biodegradable and biocompatible materials have drawn interest because of their potential to lessen tissue irritation and their impact on the environment. Biodegradable polymers, like PLA and PLGA, can be used as drug carriers or matrix materials in transdermal patches, providing biocompatibility and controlled drug release. Sustainable drug delivery methods that put patient safety and environmental stewardship first are made possible by these environmentally friendly materials. In these, recent advancements in transdermal patch technology have propelled the field forward offering innovative solutions for enhanced drug delivery and patient care.⁶²

XI. CONCLUSION

Herbal transdermal patches offer controlled, long-lasting, and non-invasive delivery of medications by fusing the concepts of conventional herbal treatment with cutting-edge drug delivery technology and phytoconstituents. They improve patient compliance while overcoming significant disadvantages of oral dose forms, such as low bioavailability and first-pass metabolism. Research on drug release, physicochemical characteristics, and skin irritation verifies that well designed herbal patches can efficiently distribute active ingredients without irritating the skin. Their sustainability and safety are further reinforced by the use of natural polymers and environmentally friendly products. Herbal transdermal technology is expected to rise significantly thanks to new developments including hydrogels, microneedles, nanocarriers, and 3D-printed devices. These patches will be established as a safe, efficient, and long-lasting method in contemporary and alternative healthcare with the support of ongoing research and clinical validation.

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