A Review on Herbal Transdermal Patches

D.S. Bhujbal, S. A. Kanase, V. V. Kunjir

Department of Pharmaceutical Chemistry , Rajgad Dnyanpeeth's College of Pharmacy, Bhor-412206, Maharashtra, India

ABSTRACT

Drug delivery technologies receiving attention from pharmaceutical industries. The main aim of developing alternative drug delivery technologies is to increase efficiency and safety of drug and provide more patient compliance. The transdermal patch is medicated adhesive patch which have coating of drug and is then placed on skin to deliver the drug in the blood stream through the skin. The synthetic drug are developed to treat complicated disease but these medication are related to many side effects and herbal source on other hand is more effective and no harmful effects comparatively. In this present review, we have summarized all the marketed herbal patches and published work on TDDS patches using medicinal plants. So this TDDS is useful innovation in transforming drug delivery particularly in bedridden patient.

Keywords: *Transdermal drug delivery system, Transdermal Herbal patch, Drug delivery technologies, Adhesive patch, Herbal agents*

1.Introduction

The transdermal delivery is a relatively simple technology. Transdermal drug delivery systems are defined as self-contained discrete dosage forms which applied to the intact skin, deliver the drugs, through the skin, at controlled rate to the systemic circulation.[1,2] In this system medicated adhesive patches are prepared which when placed on skin it delivers therapeutically effective amount of drug across the skin. They are accessible in different sizes & having more than one components. Transdermal drug delivery systems are used in management of angina pectoris, smoking cessation & neurological disorders and also in skin disorders.[3]

Advantages:

1. Increases bioavailability by avoiding hepatic and pre systemic metabolism.
2. Trouble and Inconveniences of IV therapy are avoided.
3. Reduction in dosing frequency.
4. Easy termination of drug therapy because drug administration stops with patch removal.
5. Improve patient compliances.
6. Improved therapeutic efficiency by avoiding the peaks and troughs in systemic drug levels associated with conventional drug delivery.
7. Self-administration is possible.
8. Minimization of side effects.

Disadvantages:

1. Limited only to potent molecules are suitable candidates for transdermal delivery.
2. At site of application some patients may develop contact dermatitis.
3. It is not suitable for drugs requiring high blood levels.
4. It may be uneconomical.
5. Transdermal route of administration is unsuitable for drugs that irritate or sensitize the skin.

1.2. Skin Structure And Anatomy [5]

The structure of skin is very complex and its properties helps into efficient outermost protection against external and environmental factors. It also helps to maintain the homeostasis of human body. This Function is mainly played by the outermost layer of epidermis which is stratum corneum.

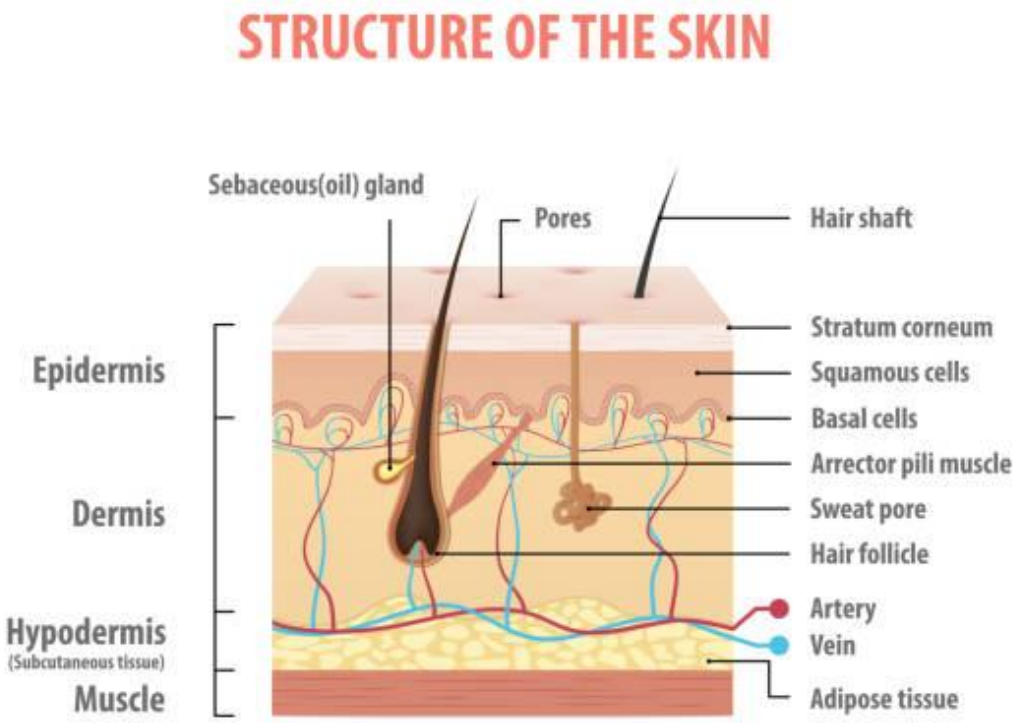

Fig.1. Structure of the skin

Download:https://media.istockphoto.com/id/953892302/vector/vol-2-structure-of-the-skin-info-graphics-illustration-vector-on-whitebackgroundbeauty.jpg?s=612x612&w=0&k=20&c=SqOUBKGWPsxM_LRJYPsVxPVGr7dffGc6uPbt9817nBY=

1.2 a) Epidermis:

Epidermis is keratinized stratified squamous epithelial layer which is obtain from ectoderm. It forms outermost layer of the skin. In the skin, if skin area is non hairy then there the epidermis is thick and skin has hair then the epidermis is thin. Epidermis has 2 types of cells they are keratinocytes and melanocytes. The keratinocytes are the major cells. Epidermis is made up of various layers like stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, stratum basale.

1. **Stratum Corneum:**
   The size of stratum corneum is 15-20 um. Stratum corneum is outermost layer of epidermis which has several layers of keratinized flat dead cell which continuously sheds off the skin and they have straight contact with the environment. Penetration of substance from environment and insensible loss of body water from surface to the environment is prevented by stratum corneum.
2. **Stratum Lucidum:**
   Stratum lucidum is present where skin is thick and lack hairs in specific area of body. It has the layers of keratinized compact dense cells.
3. **Stratum Granulosum:**

Stratum granulosum is below stratum lucidum. It has 3-5 layers of flat cells and non-membrane bound, irregular shaped, keratohyalin granules. Keratohyalin granule has structured protein profilaggrin which are included in keratinization and barrier function of skin.

4. **Stratum Spinosum:**
   It contain different layers of irregular polyhedral shaped cells. The uppermost layer has small granules or membrane coating granules.
5. **Stratum Basale:**
   It is also called as Stratum Germinativum which is consists of single layer made of columnar or cuboidal in shape.

1.2.b) Dermis:

Dermis is consists of network of collagen and elastin fibres enclosed in mucopolysaccharides matrix which has blood vessels, lymphatic nerve endings, etc. Dermis supports epidermis which is mesodermal in origin. The size of dermis is 3-5 mm. It carries the network of dense irregular tissue and extend from basement membrane to hypodermis.

1.3. c) Drug permeation through skin:[5]

Follicular epithelium and sebaceous gland absorb the drug. Diffusion through intact stratum corneum occurs when steady state is achieved. Drugs penetrates in skin through two routes and which are

1. **Trans epidermal route:** The drug penetrate through two routes such as transcellular and intercellular.
2. **Trans follicular route:** The drug is transported through sweat gland or hair follicles. Trans follicular route has high permeability.

1.3.Basic Components of Transdermal Drug Delivery System:[3]

1. Polymer matrix or Drug reservoir
2. Drug
3. Permeation enhancers
4. Pressure sensitive adhesive
5. Backing laminate
6. Release liner
7. Plasticizer and solvents

1. Polymer Matrix or drug reservoir:

It is synthesized by dispersing the drug in liquid or solid state synthetic polymer base. It should have biocompatibility and chemical compatibility with the drug and other substances of the system like penetration enhancers. Polymer are classified as-

1. Natural polymer: e.g. zein, gelatin, waxes, gums, natural rubber and cellulose derivatives etc.
2. Synthetic Elastomers: e.g. polybutadiene, butyl rubber, silicon rubber, polyisobutylene, acrylonitrile, neoprene, etc.
3. Synthetic Polymers: e.g. polyurea, polyvinylalcohol, polyvinylchloride, polyethylene, polypropylene, polyacrylate, polyamide, etc.

2.Drugs:

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 be non-irritating and non-sensitizing.
- Molecular weight: <400 Dalton
- Half life is less than 10 hrs.

3.Permeation Enhancers:

The chemical components which improve the permeability of stratum corneum so as to attain therapeutic levels of the drug. Penetration enhancers by interacting with stratum corneum improve the permeability.

Ideal Properties:

- Non-toxic, non- irritating and non-allergic.
- It should not attach to receptor site.

4.Pressure Sensitive Adhesive (PSA)

Adherence of transdermal patch to the skin surface is increase 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**.**

5.Backing laminate:

It is used as supportive material. It is impermeable to drugs and also to permeation enhancers. They should prevent the release of drug surface which is not in contact with skin. They should be chemically compatible with the drug and excipients.

e.g. Vinyl, polyethylene, polyester films and metallic plastic laminate.

6.Release liner:

This is the primary packaging material that can protect the patch during application. It is made up of base layer which may be non-occlusive or occlusive. E.g. Teflon, Silicon, Polyester.

7.Plasticizers:

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

8.Solvents:

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

1.3 A) Types Of Transdermal Patches:[5,6]

1.Single layer patches: In this type adhesive layer is responsible for releasing the drug and also adhere various layers together. Adhesive layer in patch contains drug. The adhesive layer is between release liner and backing laminate.

2.Multilayer adhesive patches: It contains one or more layer and it is also similar to single layer patches. One layer is responsible for control release of drug from adhesive layer and one of other layer for immediate drug release. Diffusion capacity and membrane permeability affect drug release.

3.Reservoir Type patch: In this of type, drug reservoir is sandwiched between drug impermeable membrane and rate controlling membrane. Drug can be in the form of solution, suspension, gel or dispersion in polymer matrix in the reservoir compartment. The drug releases only through rate controlling membrane. It can be non-porous or microporous.

4.Matrix Type Patch: Drug reservoir is prepared by dispersing the drug homogeneously in a hydrophilic and lipophilic polymer matrix. The medicated polymer is moulded on a medicated disc. It is also known as monolithic device.

5.Vapour Patch: The adhesive layer in this patch has two purposes: It adheres the several layers together and also releases vapours. The primary and common use of these vapour patches is decongestion The essential oils are released by these vapour patches for maximum six hours. Some vapour patches are designed to improve sleep .3quality and help people stop smoking.

1.3.B) Factors Affecting Transdermal Patch:[7]

A] Biological Factors:

1) Skin condition:

The intact skin and diseased condition of patient alters the skin condition.

2) Species differences:

Thickness of subcutaneous, hair follicles vary from species to species which affects penetration through the skin.

3) Lipid film:

Formation of thin film of skin occurs by excretion of sebaceous gland.

4) Skin age:

The permeability of younger skin more than older skin.

5) Regional skin site:

The thickness of skin, nature of stratum corneum changes from site to site which affects penetration.

6) Skin metabolism:

Skin metabolism decide effectiveness of drug penetrated through the skin.

B] Physicochemical factors:

1) Skin hydration:

Transdermal penetration can be increased by hydration of subcutaneous layer. Hydration increases permeation through the skin.

2) Temperature and pH:

The diffusion coefficient is directly proportional to temperature. pH affects the rate of absorption of acidic or basic drug. Medium pH is suitable but high or low pH causes damage to the skin.

3) Diffusion coefficient:

Diffusion coefficient of the drug affects the penetration of drug. Diffusion coefficient of the drug depends on properties of drug, diffusion medium at constant temperature.

4) Drug concentration:

The concentration of drug will be more across the barrier if concentration gradient will be higher.

5) Partition coefficient:

The ideal value of partition coefficient should be 1 or more than one.

6) Molecular size:

Drug permeation is inversely proportional to molecular size. Smaller molecules penetrate rapidly than larger ones.

1.4. Herbal Transdermal Patches V/S Synthetic Transdermal Patches

As time has passed, we have encountered numerous life-threatening diseases. To control and treat them, we have created the wide variety of synthetic drugs that are helpful in treating the illness, but they also come with several side effects. Consequently, using herbal remedy is a safer approach to therapy in comparison. Transdermal drug delivery has the ability to increase the potency and lessen its side effects in herbal medicine. The usage of herbal remedies has increased recently due to their greater medicinal properties and almost no side effects on the body. Still, making natural medicines requires certain adjustments to provide appropriate quantities of API through sustained and controlled release of drug.[8]

1.5. General Method of Preparation of Herbal Transdermal Patches

1.5.1.Extraction of Medicinal plants:[9]Medicinal plants are extracted and processed for experimental purposes or as herbals. Extraction of medicinal plants is for separating active plant material or secondary metabolites such as alkaloids, flavonoids, terpenes, saponins, glycosides and steroids from inactive material using an appropriate solvent and standard extraction procedure.

Solvents of extraction

The solvent used in extraction of medicinal plants are called as menstruum. The solvent choice depends upon availability of solvents, type of plant, part of plant to be extracted and nature of bioactive compounds.

Properties of solvent of extraction:

1. Water: It is polar solvent and used in the extraction of polar compounds.
   Advantage: It is cheap, nontoxic, nonflammable and highly polar.
   Disadvantage: It promotes bacterial and mold growth. It may cause hydrolysis.
2. Alcohol: It is also a polar solvent and is used in extraction of polar secondary metabolites.
   Advantages: It is self- preservative at concentration above 20% and it is non-toxic at low concentration.
   Disadvantages: It does not dissolve in fats, gums and wax. It is flammable and volatile.
3. Chloroform: It is nonpolar in nature and could extract compounds such as terpenoids, flavonoids, fats and oils.
   Advantage: Colorless, has a sweet smell and is soluble in alcohols.
   Disadvantage: It has sedative and carcinogenic property.
4. Ether: Ether is nonpolar solvent and is used in extraction of compounds such as alkaloids, coumarins, fatty acid and terpenoids.
   Advantage: Ether is miscible with water and has low boiling point.
   Disadvantage: Flammable in nature and highly volatile.
5. Ionic solvent (Green solvent): It is highly polar in nature and extremely heat stable. It is unique solvent of extraction.
   Advantage: It is suitable for microwave-assisted extraction and nonflammable in nature.
   Disadvantage: It is not used in formulation of tincture.

Factors are considered in selecting solvents of extraction

1. Selectivity
2. Safety
3. Cost
4. Reactivity
5. Recovery
6. Viscosity
7. Boiling temperature

1.5.2.Commonly used methods in the extraction of medicinal plants[10]

Factors are considered in choosing extraction method are as follows,

1. Stability to heat
2. Nature of solvent
3. Cost of the drug
4. Duration of extraction
5. Final volume required
6. Intended use

1.Maceration

It is very simple extraction method having disadvantage of long extraction time and low extraction efficiency. It is used for extraction of thermolabile components.

2.Infusion

It is an extraction process such as maceration. It is good method for preparation of fresh extract before use. Infusion is used for extraction of bioactive constituents that are readily soluble.

3.Percolation

Percolation is more efficient method than maceration and it is continuous process. The apparatus used in this process is known as percolator. In this method saturated solvent is constantly being replaced by fresh solvent.

4.Decoction

It is a process of continuous hot extraction using specified volume of water as solvent. This method is useful in extraction of heat stable and water soluble plant material.

5.Soxhlet Extraction or Continuous Hot Extraction

This is an automatic continuous extraction method. It has high extraction efficiency which require less time and solvent consumption than percolation or maceration. Period of extraction is long and high temperature in Soxhlet extraction will increase the possibilities of thermal degradation. It is not suitable for thermolabile substances and suitable for plant material that is partially soluble in the chosen solvent and plant materials with insoluble impurities.

6.Microwave-assisted extraction

It is advanced extraction method in preparation of medicinal plants. Microwaves generate heat by interacting with polar compounds in the plant matrix following the ionic conduction and dipole rotation mechanisms. Increasing the extract yield, decreasing the thermal degradation and selective heating of vegetal material are major advantages of microwave assisted extraction.

1.6. Method of Preparation of Transdermal Patches:[7]

The most commonly used method for preparation of patches is solvent casting method. The polymer and minimum amount of solvent is taken in beaker. Then mix 2/3rd of solvent with other polymers and was added firstly with the help of stirring at low rpm. After some time stir with high speed. Then the plasticizer was included and homogeneously mixed. The drug was added with enduring agitation and make up the volume. The films are cast on suitably made and fabricated glass mould. The films are dried at 40^{0}C in the oven. By using sharp blade the films were removed. The dried films were enclosed in butter paper and stored in closed container. The container is placed away from light and in cool place.

1.7. Evaluation Test: [2,5,6]

1) Organoleptic Characteristics:

In this, Organoleptic characteristics were studied such as colour, odour, texture and appearance.

2) Surface pH determination:

In this test, the pH of surface of transdermal patches is determined by using pH meter.

3) Drug Excipients Interaction Studies:

Interaction studies are carried out to determine the drug and excipients are compatible to produce stable product. This studies are performed by using UV, FTIR studies, thermal analysis and chromatographic methods.

4) Drug Content:

Dissolved the specific area of patch in solvent in specific volume. Then filter the solution through filter medium. Lastly, analyse the drug content by using UV or HPLC technique.

5) Weight Uniformity:

Before testing, the patches are dried at 60^{0}C for 4 hrs. The patch is cut into the different parts. The pieces of patch are weigh in digital balance. Calculate the average weight and standard deviation value.

6) Thickness of patch:

The thickness of patch is calculated using digital micrometer. It measures average thickness of patch and standard deviation for the same to assure the thickness of patch.

7) Flatness Test:

Three strips are to be cut in which one from right side, one from left side and another from center. Calculate the length of each strip if there is variation in length because of non-uniformity in flatness was calculated. Variation is calculated by determining percentage constriction.

8) Percentage Moisture Uptake:

The weighed patches are placed in desiccators at room temperature for 24 hrs having saturated solution of potassium chloride. The patches are reweighed after 24 hrs and calculate percentage moisture uptake by given formula,

% moisture uptake = [Final weight-Initial weight/Initial weight] × 100

9) Moisture Loss:

Individually weigh the prepared patches and placed in desiccator containing calcium chloride at 40^0C. reweigh the patches after 24 hrs and calculate the Percentage moisture loss by using given formula,

% Moisture loss = [Initial weight – Final weight/ Final weight]× 100

10) Folding Endurance:

In this, patch is repeatedly folded at same place until it breaks. Folding endurance value is measured by determining the number of times the patch is folded at same place without breaking.

11) Percentage elongation break test:

In this test, length just before the break point is calculated. The percentage elongation is calculated by using given formula,

Elongation Percentage = [L1 -L2/ L2] × 100

12) Polariscope Examination:

It is used to determine the drug crystals from patch by using polariscope. The specific area of patch is placed on object slide and observe the drug crystals to differentiate whether the drug is present in amorphous or crystalline form.

13) Probe tack test:

The tip of clean probe is brought in contact with adhesive and then the bond is formed between adhesive and probe. Probe tack test determine the force required to pull the probe away from adhesive at predetermined rate is calculated as tack.

14) Peel adhesion test:

In this test, force required to remove the adhesive from the test substrate. If there is no residue on substrate then the test is passed.

15) Water Vapor Transmission Rate:

The transmission cells used are made up of glass vials. The transmission cells are cleaned and dried in oven at 100^0C for some time. 1g of calcium chloride is kept in the cells and polymer fixed over brim. The transmission cells were weighed accurately and placed in a desiccator having saturated solution of potassium chloride to control relative humidity of 84%. The cells are reweighed and water vapor transmission rate is calculated by using given formula,

Water Vapor Transmission Rate = Final Weight – Initial weight/ time × Area

16) Skin irritation study

Healthy rabbits are selected for skin irritation and sensitization study. The average weight of rabbit selected should be 1.2 -1.5 kg. Clean the dorsal surface of rabbit and remove the hair then clean the area by using rectified spirit. The formulation is applied to the skin. After 24 hrs. patch is removed and observe the skin and classified into 5 classes on the basis of severeness of injury.

17) In-vitro drug release studies:

The paddle over disc method is used for evaluation of release of drug from the patches. Patches are cut into definite shape and weighed. These patches are fixed over the glass plate with an adhesive. The glass plate is kept in 500ml of the dissolution medium or phosphate buffer and apparatus is equilibrated to 32± 0.5^0C. Then set the paddle at

distance of 2.5 cm from the glass plate and used at speed of 50rpm. Sample is removed at suitable time interval upto 24 hrs and analyzed by using UV-spectrophotometer and HPLC method.

18) In vitro skin permeation studies:

In this test, diffusion cell is used. The full thickness abdominal skin of male wistar is used (Average weight 200 to 250g). Electric clipper is used for removing the hair from abdominal region. The dermal side of skin is cleaned to remove adhering tissue, equilibrated for for 1 hour in diffusion medium.

Diffusion medium is filled in diffusion medium and keep on a magnetic stirrer. By using thermostatically controlled heater maintain the temperature of cell at 32± 0.5^0C.Now, place the isolated rat skin piece between compartments of diffusion cell, in which epidermis facing the donor compartment. Remove the definite volume of sample at regular interval and replace the equal volume of fresh medium. Filtered samples are analyzed by HPLC.

1.8. Reported Herbal Transdermal Patches for Treatment of Various Diseases:

Table 1: Reported Herbal Transdermal Patches

Sr.no	Active constituent	Biological source	Method of preparation of patch	Reference
1)	Antiemetic therapy			
i)	Khardal, Zanjabeel, Podina and Sirka	*Brassica Nigra, Zingiber Officinale, Mentha Arvensis and Vineger*	Solvent evaporation Method	8
2)	Antidiabetic therapy			
i)	Extract of Hibiscus	*Hibiscus Rosasinensis*	Two different polymer in the ratio of (1:4) used for its preparation	8
ii)	Neem, Karela	*Azadirachta indica, Momordica charantia Linn.*	Solvent casting method	11
3)Anti-inflammatory				
i)	Ginger, Turmeric, Lavender, Katuvera, clove oil, wintergreen, Camphor, Menthol, Aloe vera, Turpentine.	*Zingiber officinale, Curcuma longa, Lavendula angustifolia, Aloe barbadensis*.	Matrix diffusion controlled systems, solvent casting method	8
3)Anti-microbial				
i)	Neem oil	*Azadirachta indica*	Solvent casting method	8
ii)	Tea tree oil	*Melaleuca alternifolia*	Solvent casting method	12
4)Anti-ischemic, Antioxidant, Anticancer, Antiviral				
i)	Indian Lotus	*Nclumbo nucifera*	Solvent Evaporation Method	8
5)Antirheumatic activity				
i)	Shalaki, Turmeric	*Boswellia Serrata, Curcuma longa*	Solvent casting method	8
ii)	Siegesbackiae herba extract	*Siegesbeckia pubescenes Makino*	Solvent Evaporation Technique	13
6)Antibacterial activity				

i)	Cissus Quadrangularis	*Cissus Quadrangularis*	Solvent evaporation method	14
ii)	Neem	*Azadirachta Indica*	Solvent Casting Method	15
7)Osteoarthritis				
i)	Curcumin	Extracted from rhizomes of *Curcuma longa*	Solvent casting technique	16
ii)	Curcumin, Arnica	Extracted from rhizomes of *Curcuma longa, Arnica Montana*	-	17
8)Wound healing				
i)	Tulsi, Aloe vera	*Ocimum sanctum, Aloe barbadensis*	Solvent evaporation method	5
ii)	Tubers extract of Momordica Cymbalaria	*Momordica Cymbalaria*	Solvent evaporation method	18
9)For Respiratory Relief				
i)	Ginger	*Zingiber Officinale*	--	19
ii)	Echinacea angustifolia DC. Lipophilic Extract	*Echinacea angustifolia*	Casting & drying Technique	20
10)Anti-Arthritic activity				
i)	Boswellic acid, Aloe vera	*Boswellia Serrata, Aloe barbadensis*	Solvent casting method	21
ii)	L. Strychnifolium	*Lysiphyllum strychnifolium*	-	22
11)Fracture Healing				
i)	P. bicalyculata	*Peristrophe bicalyculata*	Solvent casting method	23

1.9.Marketed Herbal Transdermal Patches:

Table 2: Marketed Herbal Transdermal Patches

Sr. No	Brand Name	Company	Content
1	Resto Patch	Eliph Nutrition Private Limited	Each 7 Sq. cm contains: Jatamanasi/Muskroot rhizome extract 10%, Sarpagandha root extract10%, Excipients q.s.
2	Zandu Ayurvedic Knee Pain Relief Patch	Indocoar Pharma Private Limited	Each 50 sq. cm patch, coated with 500 mg paste contains: Gandhapura Patra Taila 7%, Peppermint Satva (Mentha sp) 6.5%, Karpura 2.5%, Excipients q.s.
3	Zandu ayurvedic Feminine Pain Relief Patch	Indocoar Pharma Pvt. Ltd.	Each 100 sq. cm patch, coated with 1 gram paste contains: Peppermint Satva (Mentha sp) 15%, Tailaprana taila(Eucalyptus globulus Labill) 5%, Kundur (Boswellia serrata)
4	Diabetic Patch	Sumifun	Rehmannia, Scutellaria, Alfalfa, Hawthorn, Yam

6	Energy Patch	The Patch brand	Caffiene, Taurine, Green Tea and B vitamins
5	Deep Cleaning Foot Patch	Qerinkle	Wormwood extract, Bamboo charcoal, Ginger Powder
6	Viopatch Herbal Pain Relief Patch	Unexo Life Sciences	Camphor, Menthol, Gandhapura oil, Eucalyptus & clove oil
7	Slim Patch	Balaji Devotee	Cassia seed, Mathorn, Poria cocos, Immature bitter orange, Scutellaria Baicalensis, Alisma orientalis, angelica sinensis.
8	Herbal Headache Relief Patch	Sirona	Menthol, Camphor, Eucalyptus oil, Clove oil

2.CONCLUSION:

Herbal drugs are easily available, eco-friendly in nature and cost effective, showing less side effect so to be serves as an alternative to synthetic drugs. It has been demonstrated that herbal drugs from natural origin can be employed in better form with increased efficacy by reducing dosing frequency, increase absorption and delivering to the target side via incorporating them through novel transdermal route. Various Herbal patches are available in market for antiemetic therapy, antidiabetic, anti-inflammatory, anti-microbial, respiratory relief, wound healing, antirheumatic, anti-arthritic therapy. Thus by reviewing we can conclude that transdermal drug delivery represents a useful innovation in transforming drug delivery particularly in bedridden patient. However more research has been going on herbal drug patches. thus herbal transdermal patches can be more explored for treatment of diseases like as cancer, hypertension etc. in upcoming years.

3.REFERENCES:

1. Rathva.S, Patel.N. Herbal Transdermal Patches: A Review. World Journal of Pharmaceutical Research. 2012; 6(13): 365-374.
2. Prabhakar.D, Shreekanth.J, Jayveera.K. Transdermal Drug Delivery Patches: A Review. Journal of drug delivery & therapeutics. 2013 ;3(4): 213-221. DOI https://doi.org/10.22270/jddt.v3i4.590
3. Sharma.N. Brief review on transdermal patches. Organic and medicinal chemistry international journal. 2018; 7(2): 555-707. DOI: 10.19080/OMCIJ.2018.07.555707
4. Gaikwad.A. A Transdermal Drug Delivery System: Formulation Aspects and Evaluation. Comprehensive Journal of Pharmaceutical Sciences. 2013; 1(1): 1-10.
5. Rajput.S. Formulation and Evaluation of Herbal Transdermal Patches in Treatment of Wound Healing. International Journal of Scientific Development and Research. 2022; 7(9): 2455-2631.
6. Alam.I, Alam.N, Singh.V, Alam.S, Ali.S. Type Preparation & Evaluation of Transdermal Patch: A Review. World Journal of Pharmacy & Pharmaceutical Sciences. 2013; 2(4): 2199-2233.
7. Yadav S, Pandey S, Yadav S, Saleem M. A review on: Transdermal Patches of Herbal drugs for Arthritis. IJPPR. 2021; 22: 201-218.
8. Mishra S, Verma P, Gupta S, Pandey S, Ojha S. Nanocarrier and Herbal Based Transdermal Patch: An Advantage Over Other Drug Delivery Systems. Annals Of Ayurvedic Medicine. 2022;11(2): 145-156. DOI:10.5455/AAM.11486
9. Abubakar A, Haque M. Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for experimental purposes. J Pharm Bioallied Sci. 2020; 12 (1): 1-10. doi: 10.4103/jpbs.JPBS_175_19
10. Zhang Q, Lin L, Ye W. Techniques for extraction and isolation of natural products: a comprehensive review. Chin Med. 2018; 13: 20. DOI: 10.1186/s13020-018-0177-x
11. Chauhan L, Vashisht S. Formulation And Evaluation Of Novel Herbal Antidiabetic Transdermal Patch. Innovations In Pharmaceutical And Pharmacotherapy. 2018;6(4): 61-64.
12. Minghetti P, Casiraghi A, Cilurzo F, Gambaro v, Montanari L. Formulation Study of Tea Tree Oil Patches. Natural Product Communications. 2009; 4(1): 133-137.

13. Quan p, Jiao B, Shang R, Liu C, Fang L. Alternative therapy of rheumatoid arthritis with a novel transdermal patch containing Siegesbeckiae Herba extract. Journal of Ethnopharmacology. 2021; 265: 113-294. DOI: 10.1016/j.jep.2020.113294

14. Das R, Kolhe S, Wadher K, Patil A, Umekar M. Development and evaluation of transdermal patches with Cissus Quadrangularis plant extract. International Journal of Life Science & Pharma Research. 2018; 8 (2): 29-34.

15. Reddy D, Bhanja S, Chauhan A, Kumar B, Panda D, Panigrahi B. Methanolic Extraction, Formulation and Evaluation of Herbal Transdermal Patches of Azadirachta indica A. Juss. Research J. Pharm. And Tech. 2021;14(7): 3710-3716. DOI : 10.52711/0974-360X.2021.00642

16. Kriplani P, Guarve K, Baghel U. Formulation Optimization and characterization of transdermal film of curcumin by response surface methodology. Chinese Herbal Medicines. 2021; 13: 274-285. https://doi.org/10.1016/j.chmed.2020.12.001

17. Kriplani P, Guarve K, Baghel U. Novel Herbal Topical Patch Containing Curcumin and Arnica Montana for the Treatment of Osteoarthritis. Current Rheumatology Reviews. 2020; 16 (1): 43-60. DOI: 10.2174/1573397115666190214164407

18. Saundharya P, Joseph J, Rajalakshmi G, Shamya M. Formulation of wound healing transdermal patch from tubers extract of Momordica Cymbalaria and its In-vitro Evaluation. Haya Saudi J life Sci. 2022;7(7): 224-233. DOI: 10.36348/sjls.2022.v07i07.004

19. Astuti R, Simamora S, Taswin M. Formulation and Evaluation of patch preparations for Respiratory Relief from a Blend of Extract and Essential oils of Ginger Rhizome. Journal of Drug delivery & therapeutics. 2022; 12 (4): 64-67. DOI https://doi.org/10.22270/jddt.v12i4.5448

20. Hasa D, Zakelj S, Grabnar I, Cilurzo F, Dall`acqua S, Riva A, Perisutti B, Voinovich. Echinacea angustifolia DC. Lipophilic Extract Patch for Skin Application: Preparation, In Vitro and In Vivo Studies. Pharmaceutics. 2020; 12(11): 1096. DOI:10.3390/pharmaceutics12111096

21. Shelke S, Jagtap P. Formulation and In- vitro Evaluation of transdermal patches of Anti-Arthritic Ayurvedic Medicinal Plants. Biosc. Biotech. Res. Comm. 2020; 13 (2): 803-808. **DOI:** http://dx.doi.org/10.21786/bbrc/13.2/63

22. Monton C, Sampaopan Y, Pichayakorn W, Panrat K,Suksaeree J. Herbal transdermal patches made from optimized polyvinyl alcohol blended film: Herbal extraction process, film properties and in vitro study. Journal of Drug Delivery Science and Technology. 2022; 69:1-10. DOI:10.1016/j.jddst.2022.103170

23. Kumar A, Rana M, Bisht M, Rana A. Formulation, Development and Evaluation of herbal transdermal patch for fracture healing. Indian Drugs. 2020; 57(09): 60-66. DOI:10.53879/id.57.09.12640