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Formulation And Evaluation Of Transdermal Patch For Pain Management.

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ABSTRACT

The present study focuses on the formulation and evaluation of herbal transdermal patches incorporating Cissus quadrangularis, Thespesia populnea Linn, and Mentha piperita Linn. With increasing interest in alternative and non-invasive drug delivery systems, transdermal patches offer an effective route that bypasses first-pass metabolism and enhances patient compliance. The selected herbal extracts, known for their anti-inflammatory, antimicrobial, and analgesic properties, were subjected to phytochemical screening, confirming the presence of active constituents like alkaloids, glycosides, tannins, and flavonoids. Patches were formulated using rice and corn starch bases and evaluated for physicochemical parameters including weight uniformity, thickness and tensile strength, The optimized formulation demonstrated satisfactory physical characteristics, effective drug release, and minimal skin irritation. This study supports the potential of herbal-based transdermal systems as a promising alternative for sustained and targeted drug delivery.

Keywords- Transdermal patch, Anti-inflammatory patch, Painless drug delivery, Herbal drugs.

INTRODUCTION

Transdermal drug delivery systems (TDDS) offer a promising alternative to traditional oral dosage forms, which often face challenges such as instability in the stomach, enzymatic degradation, and unpleasant odour or tastes. These issues can lead to reduced patient compliance and efficacy. In contrast, TDDS patches provide a controlled and sustained release of medication, bypassing the digestive system and avoiding first-pass metabolism.The skin's unique morphological, biophysical, and physicochemical properties must be considered when designing TDDS. By understanding these factors, TDDS can effectively deliver therapeutic agents through the skin, providing a consistent and sustained release of medication. This approach has several benefits, including reduced frequency of application, minimized gastrointestinal disorders, and improved patient compliance.

Overall, transdermal drug delivery systems offer a reliable and efficient way to deliver medications, enhancing patient compliance and therapeutic efficacy. By leveraging the skin's natural properties, TDDS can provide sustained release, reduced side effects, and improved treatment outcomes.

Table 1: 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

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 anaesthesia: 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. Skin irritation: Potential for allergic reactions or irritation.

Patient-Centric Disadvantages:

1. Skin sensitivity: Potential for skin reactions.

2. Adhesion issues: Patch detachment or poor adhesion.

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.

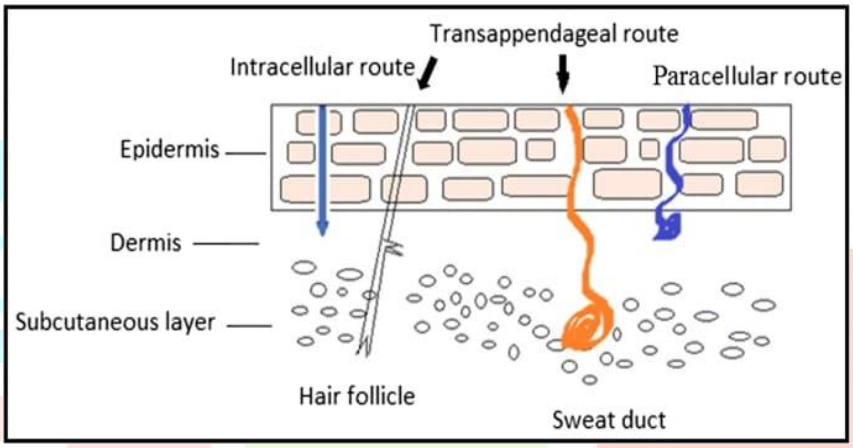


Fig1: Different Routes of Permeation.

Components of a Transdermal Drug Delivery System (TDDS):

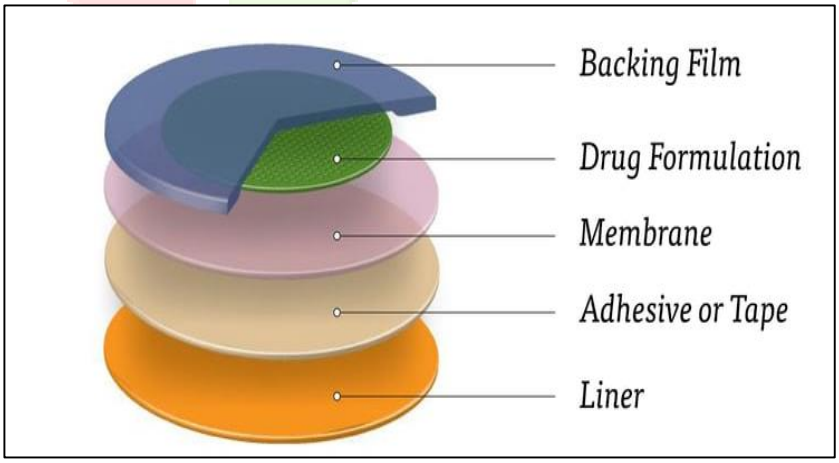


Fig 2: Components Of TDDS

Backing Layer - The outermost layer that protects the patch from external factors.

Reservoir- The layer that contains the medication, which is released over time.

Rate Controlling Membrane- A semipermeable membrane that regulates the release rate

of the medication.

Adhesive Layer- The layer that adheres the patch to the skin, ensuring consistent contact.

Release Liner- A protective layer that covers the adhesive layer until the patch is applied.

AIM- Formulation and Evaluation of Transdermal Patch.

OBJECTIVE -

1. To develop a novel, sustained-release herbal drug formulation that is more effective and convenient to use.

2. To design and develop a topical formulation using extracts of Cissus Quadrangularis, Thespesia Populnea Linn, and Mentha Piperita Linn for the effective treatment of condition.

3.To collect and authenticate the plant materials used in the study.

4. To investigate the phytochemical parameters of the plant powders.

5. To carry out the extraction process of the leaves/stems of the selected plant species.

6. Herbal Transdermal Patch Development and Evaluation: To prepare and evaluate a herbal transdermal patch formulation for its effectiveness and stability.

7. To formulate a stable and efficient transdermal patch containing cissus Quandragularis , Thespesia Populnea and Mentha Piperita extracts.

8. To evaluate the in vitro skin irritation and stability of the herbal extract from the transdermal patch.

LITERATURE REVIEW

A) Literature Review on TDDS

Shashi Kumar Yadav et al., (2013) formulated and evaluated of transdermal patch of Ayurvedic Antirheumatic Drug using Different polymers. 4 – day skin permeation study shows 81.44% release of drug from the formulation 7 containing polymers HPMC, Ethyl cellulose and PEG-6000 (10:10:1). Hence, this formula was considered to be the optimized formulation with good physicochemical properties, skin compatibility, and sustained drug release

Sahoo B et al. formulated the diclofenac transdermal patch by the solvent evaporation technique using of hydrophilic (hydroxyl propyl methyl cellulose): hydrophobic (ethyl cellulose) polymers in different ratios and glycerol as plasticizer. Different concentrations of oleic acid and isopropyl myristate were used to enhance the permeation of diclofenac.

Kansagra Hemanh et al., (2012) formulated and evaluated transdermal patch of Tetraconazole nitrate. The permeation studies illustrated that the ratio of polyvinyl pyrrolidone and ethyl cellulose 1:5 showed good controlled release. Higuchi and Korsmeyer-Peppas models were used for optimizing the formulation.

Sunil R. Rathva et al., (2012) carried out a review on Herbal transdermal patches. It has been found that drugs from herbal origin can be utilized with enhanced efficacy by incorporating in transdermal patches. Herbal transdermal patches aids to quit smoking, relieve stress, increase sexuality, insect repellent patches, detoxification, male energizer, postpone menopause are available in market.

Smt. Kishoritai Bhoyar College of Pharmacy Kamptee, Nagpur, Maharashtra, India. April 2018 Prepare and evaluate the transdermal patches of Cissus Quadrangularis extract. Cissus Quadrangularis Aqueous extracts were prepared using Maceration method. The transdermal patch was prepared by the

solvent evaporation method using hydroxy propyl methyl cellulose (HPMC E -15) in different concentrations Di butyl Phthalate and DMSO were used as plasticizers and permeation enhancer. The prepared transdermal patches were evaluated for their physiochemical characteristics such as physical appearance, weight uniformity, thickness, folding endurance; moisture content**.**

B) Literature Review on Bio Polymer

Kalyani Pathak, Ratna Jyoti Das, Riya Saikia, Aparoop Das and Mohammad Zaki Ahmad. November 2021. Assam Bora Rice Starch: A Promising Biopolymer for Pharmaceutical Applications. It is a natural, safe biopolymer with potential pharmaceutical applications due to its non-toxic, biocompatible, biodegradable, mucoadhesive, and non-immunogenic properties. With its high amylopectin content, it can be used as a matrix operator for controlled release drug delivery systems. The starch's physicochemical properties make it suitable for delivering drugs with poor physical and chemical qualities in a sustained or prolonged manner. Moreover, the absence of patent restrictions on Bora rice starch opens up opportunities for research and commercial development. Its potential applications also extend to nanotechnology, where it may enhance the delivery of water-insoluble pharmaceuticals by improving their physicochemical properties and altering their pharmacokinetics and pharmacodynamics**.** Overall, Assam Bora rice starch shows promise as a versatile biopolymer for advancing drug delivery systems.

U. Rasikha and P. A. Rajeswari August 2023, Rice-based edible films were developed at a lab scale level by extracting rice starch and using glycerol as a plasticizer to enhance flexibility and plasticity. The films were formulated with different glycerol concentrations (5ml and 10ml) and evaluated for functional properties such as thickness, tensile strength, elongation at break, moisture permeability, and moisture content. The results showed that the rice starch films were firm, transparent, and white in colour. While there was some microbial growth, it was within permissible limits (8 cfu/gm), with 3.5 cfu/gm and 5.2 cfu/gm observed for 5ml and 10ml glycerol concentrations, respectively. In comparison to rice starch films, potato starch-based edible films exhibited lower moisture absorption, moisture permeability, and good tensile strength.

Mingju Feng, Xiaoya Wang, Hua Xiong, Tingting Qiu, Hua Zhang, Fanghua Guo, Li Jiang, Yong Sun. 2021The study demonstrates that selenium-enriched brown rice protein hydrolysates, particularly the 1.0-3.5 kDa peptide fractions, exhibit potent anti-inflammatory activity by regulating NF-κB/MAPKs signalling pathways. The peptide fraction TSPHs-2, with the sequence ALLLQAVQSQYEEK, showed the most promising results. A positive correlation was found between selenium content and anti-inflammatory properties. These findings suggest that selenium-enriched brown rice protein hydrolysates have potential as functional foods or nutraceuticals for managing and preventing inflammation-related diseases.

C) Literature Review on drugs profile

Aadesh Kumar (2018) prepared Cissus quandragularis transdermal patches utilising various composition of polymer. Method uses for the fabrication was solved casting Various parameter of Transdermal were evaluated. The result show that formulation consisting drug reduce the healing process of fracture bone.

Somasundaram Ramachandran 2021 prepared and evaluate effect of alcoholic extract of Cissus quadragularis in the management of bone healing of Wistar albino rats. To find out the bone healing properties of alcoholic extracts of natural compounds. Later, animals were treated with the standard drug and alcoholic extracts of natural compounds. Calcium vitamin D3 tablets are used as a standard drug to find out the calcium supplementary effect of alcoholic extracts of natural compounds obtained from plants and fish. Later, animals were treated with the standard drug and alcoholic extracts of natural compounds. Calcium vitamin D3 tablets are used as a standard drug to find out the calcium supplementary effect of alcoholic extracts of natural compounds obtained from plants and fish.

Shobha Yadav, Shubham Pandey, Sandeep Singh Yadav, Mohammad Saleem (2021)

Give the information of Cissus quadrangularis and Mentha piperita transdermal patches used as an anti-inflammatory analgesic and antioxidant activity

Nilofar Abid Khan, Uttam Singh Baghel NeuroQuantology 20 (10), 3248, 2022 the prepared transdermal patches of ethanolic extract of Cissus quadrangularis were prepared by solvent evaporation method and by using HPMC (Hydroxypropyl methylcellulose), Ethyl Cellulose (EC), Dibutyl Phthalate, Ethanol and chloroform. Developed Patch formulation was evaluated by considering parameters such as organoleptic characteristics, weight uniformity, thickness, drug content, folding endurance, tensile strength, percentage of moisture content & in-vitro permeation study

Sripanidkulchai Journal of Drug Delivery Science and Technology 68, 103093, (2022) This study aimed to develop transdermal delivery of a combination of both extracts in matrix-patch formulations with five different volatile oils which possess analgesic and anti-inflammatory properties

S. Solomon, N. Murugananthamand M. M. Senthamilselvi. (2015) This study highlights the potential of Thespesia populnea as a valuable remedy for arthritic disorders due to its notable anti-inflammatory and antioxidant properties. The plant's therapeutic efficacy can be attributed to its rich composition of phenolic and flavonoid components.

R Ilavarasan et al. Nat Prod Res. 2012. This study demonstrates that Thespesia populnea leaf extracts exhibit significant analgesic and anti-inflammatory activities, as evidenced by their effectiveness in various pain test models and reduction of paw edema in rats. The findings suggest that both aqueous and ethanol extracts possess therapeutic potential for managing pain and inflammation, supporting the traditional use of Thespesia populnea in treating related conditions. These results warrant further investigation into the bioactive compounds and mechanisms underlying its analgesic and anti-inflammatory properties.

Mrunal K. Shirsat, Mahesh M. Thakare, Kalyani V. Amale, Aishwarya U. Kulkarni, Sandhya K. Shinde (2024) This analysis suggests that Thespesia Populnea leaf extract exhibits anti-inflammatory properties, likely due to its bioactive compounds, including lupeol, quercetin, and rutin. These compounds may work by inhibiting cyclooxygenase enzymes, stabilizing lysosomal membranes, or modulating other inflammatory pathways.

Paul Rita and Datta K. Animesh (2011) Mentha piperita, commonly known as peppermint, has been extensively studied for its analgesic properties. Research suggests that peppermint oil stimulates cold receptors, leading to analgesic effects. Studies have demonstrated its efficacy in reducing pain in various conditions.

PLANT PROFILE

Cissus Quandragularis

Cissus quadrangularis is a plant whose stems and roots are used for medicinal purposes. It's known for its potential benefits in supporting bone health and reducing inflammation.

Fig 4: Cissus Quandragularis.

- Botanical Name: Cissus Quadrangularis
- Synonym: Vitis quadrangularis, Vitis quadrangularis Wall.
- Common name: Devil's backbone, Hadjod, Asthisamharaka, Vajravalli
- Family: Vitaceae
- Active Phytochemicals: Ascorbic acid, beta-carotene, calcium, flavonoids, kaempferol, magnesium, phosphorus, potassium, quercetin, resveratrol, vitamin E.

Part used for Research: Stem

USES

1. **Bone health:** Cissus quadrangularis might be useful in transdermal patches for bone-related issues, such as osteoporosis or fracture healing.

2.**Anti-inflammatory:** The plant's anti-inflammatory properties could be beneficial in transdermal patches for pain management or skin inflammation.

3.**Wound healing:** Cissus quadrangularis might promote wound healing when incorporated into transdermal patches**.**

Thespesia Populnea Linn

Thespesia populnea Linn, also known as the Portia tree, is a plant used in traditional medicine for its various therapeutic properties.

Fig 5: Thespesia Populnea Linn.

- Botanical Name: T. Populnea Linn
- Synonym: Hibiscus bacciferus, Hibiscus populneus
- Common name: Portia tree, Bhendi tree.
- Family: Malvaceae
- Active Phytochemicals: Gossypol, quercetin, lupeol, Beta-sitosterol.

Part used for Research: Leaves

USES

1.**Anti-inflammatory:** Thespesia populnea has been studied for its anti-inflammatory properties.

2.**Antioxidant:** The plant is rich in antioxidants, which can help protect against oxidative stress.

3.**Antimicrobial:** Thespesia populnea has shown antimicrobial activity against certain microorganisms.

Mentha Piperita Linn

Mentha Piperita (Peppermint) as an Anti-Inflammatory and Analgesic Mentha piperita, or peppermint, has been traditionally used for its potential benefits in reducing inflammation and pain. Its anti-inflammatory and analgesic properties make it a potential natural remedy for various conditions.

Fig 6. Mentha Piperita Linn

- Botanical Name: Mentha Piperita Linn
- Synonym: Mentha piperita, Mentha balsamea
- Common name: Peppermint, Pudina
- Family: Liliaceae
- Active Phytochemicals: Menthol, menthone, eucalyptol, limonene, beta-pinene, alpha-pinene

Part used for Research: Leaves

USES

1.**Topical Analgesic:** Used in creams for muscle pain relief.

2.**Anti-inflammatory:** Thespesia populnea has been studied for its anti-inflammatory properties.

3.**Antioxidant**: The plant is rich in antioxidants, which can help protect against oxidative stress.

EXPERIMENTAL DESIGN

A) Collection

Plant materials were collected from the local area of Tal-Rahuri, Dist-Ahmednagar in January 2025. The collected plants were:

Table 2: Collection of Plant

Sr. No	Plant Name	Location
1	Cissus Quadrangularis	Mahatma Phule Krishi Vidyapeeth,Rahuri.
2	Thespesia Populnea Linn	Mahatma Phule Krishi Vidyapeeth,Rahuri.
3	Mentha Piperita Linn	Sweetyraj nursary At.Guha.Tal.Rahuri

The collected plant materials were thoroughly cleaned, and healthy leaves/stems were selected. The selected plant materials were dried under shade. Once dried, a sufficient quantity of leaves was powdered using an electric grinder. The powdered material was then sieved through a 60# mesh to obtain fine and coarse powders.

B) Authentication

The plant material was taxonomically identified and authenticated at the Department of Botany and Research Centre, Padmashri Vikhe Patil College of Arts, Science, and Commerce, located at A/ P-Loni kd, Tal-Rahata, Dist-Ahmednagar.Voucher specimens of the identified species were deposited in the form of herbarium sheets for future reference as following.

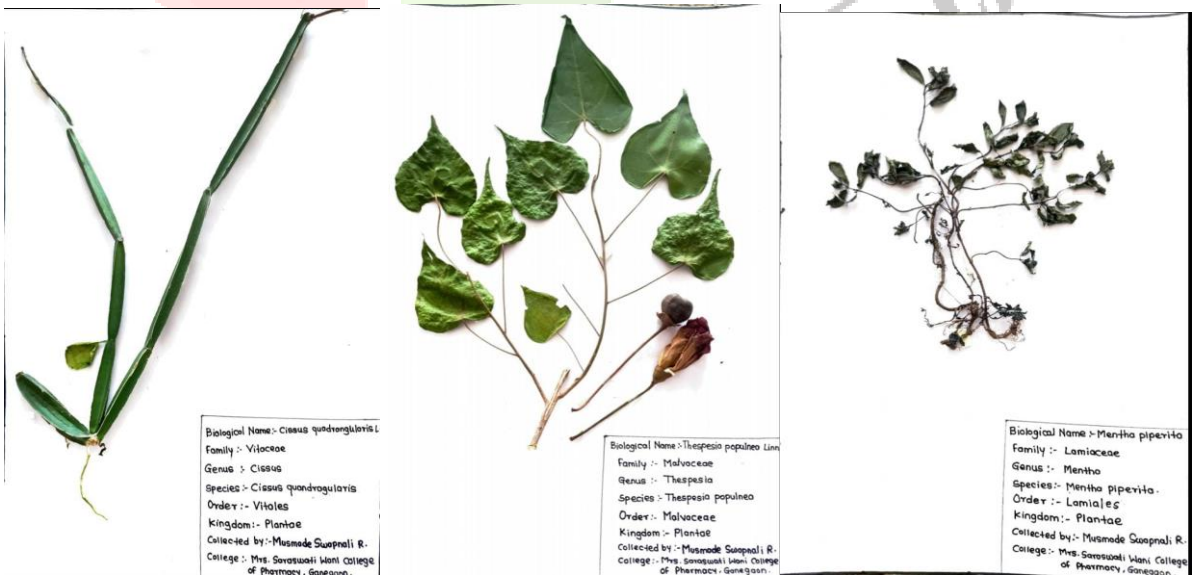


Fig. 8: Authentication of Herbal Drugs.

C) Solubility Testing

The solubility of the coarse powders of the three plant species was tested in various solvents. Acetone, Chloroform, Water, Alcohol, Petroleum ether.

Results:

The results showed that the powders of:

- Cissus Quadrangularis (steam)

- Thespesia Populnea (leaves)

- Mentha Piperita Linn (leaves)

were more soluble in alcohol compared to the other solvents tested.

Fig 9: Solubility Analysis of Herbal Drugs

D) Preparation of Herbal Extracts

The maceration process for Cissus Quadrangularis and Thespesia Populnea Linn

It was carried out by steeping the plant material in a solvent to extract the active ingredients. A suitable solvent ethanol was selected and the plant material was submerged in it. The mixture was left too steep for 7 days, with occasional agitation, allowing the solvent to extract the active ingredients. After the steeping period, the resulting liquid extract was filtered to remove any remaining plant material, and then concentrated through evaporation to produce a more potent extract.

Fig. 10. Extraction By Maceration (alcohol)

Soxhlet Extraction of Mentha Piperita Linn

The Soxhlet extraction of Mentha piperita was carried out to isolate its active phytochemicals. The dried leaves of Mentha piperita were first ground into a fine powder and then placed in a Soxhlet extractor. A suitable solvent, ethanol, was selected and poured into the extractor, allowing it to flow through the plant material. The extraction process was repeated for several hours, allowing the solvent to extract the active ingredients from the plant material. The resulting extract was then collected and concentrated through evaporation to produce a more potent extract. The extract was then stored in a cool, dry place for further analysis.

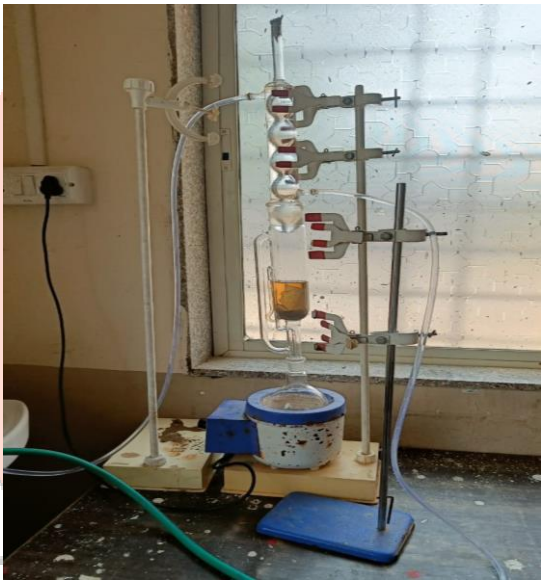


Fig 11: Soxhlet Extraction of Mentha Piperita.

Fig12: Filtered Extract of Herbal Drugs.

V) Phytochemical Screening of Plant Extracts

(- sign indicate Absent and + sing indicate present)

Table 3: Phytochemical Screening

Sr. no	Test Name	Procedure	Result		
			CQ	TP	MP
1.	ALKALOIDS	**Mayer's Test:** Add 1-2 ml of Mayer's reagent to 2-3 ml of the alcoholic extract. A cream precipitate indicates the presence of alkaloids.	+	+	+
2.	GLYCOSIDE	**Fehling's Test:** Add 1-2 ml of Fehling's solution to 2-3 ml of the alcoholic extract and heat the solution . A brick-red precipitate indicates the presence of glycosides.	+	-	+
3.	TANNIS	**A)Gelatin Test:** Add 1-2 ml of gelatin solution to 2-3 ml of the alcoholic extract. A white precipitate indicates the presence of tannins. **B) Ferric chloride test** : Add 1-2 ml of Fecl3 solution to 2-3 ml of the alcoholic extract. A green and purple precipitate indicates the presence of tannins.	+	-	-
4.	CARBOHYDRATE	**Fehling's Test:** Add 1-2 ml of Fehling's solution to 2-3 ml of the alcoholic extract. A brick-red precipitate indicates the presence of carbohydrates. **Molisch test** Add 1-2 ml of Molisch reagent to 2-3 ml of the alcoholic extract. Add concentrated sulphuric acid slowly .Observe the formation of a purple ring at the junction of the two liquids	+	+	-

5.	FLAVONOIDS	**Shinoda Test:** Add 1-2 ml of Shinoda reagent($Fecl_3$) to 2-3 ml of the alcoholic extract. A yellow, pink , purple precipitate indicates the presence of flavonoids.	+	+	+
6.	AMINO ACID	**Ninhydrin Test:** Add 1-2 ml of Ninhydrin reagent to 2-3 ml of the alcoholic extract. And heat the extract gently. A purple colour indicates the presence of amino acids.	-	-	-

Fig 13: Phytochemical Screening of herbs.

Fig.14: Rice Starch

Biological Source: Oryza sativa (Rice)

Synonyms: Selenium-fortified brown rice

Pharmacognosy Aspects

Anti-inflammatory activity: Selenium's antioxidant properties reduce inflammation.

Selenium content: Higher levels of selenium.

Antioxidant properties: Protects against oxidative stress.

Stability and Storage

Storage conditions: Cool, dry place

Packaging: Airtight containers

Shelf life: Dependent on storage conditions and packaging

Preparation method of rice starch

The preparation of rice starch involves several steps to extract and purify starch from rice grains. The process begins with rice selection and cleaning, followed by soaking in water or alkaline solution to break down protein and lipid components. The rice is then ground into fine particles and sieved to separate the starch. Centrifugation is used to further purify the starch. Alkaline steeping and enzymatic treatment can also be employed to enhance starch extraction. The quality of rice starch is influenced by factors such as rice variety and processing conditions, including temperature, pH, and enzyme concentration. The extracted starch has various applications in the food, pharmaceutical, and cosmetic industries.

Fig. 15: Preparation method of rice starch

Fig.16: Rice Starch

CORN STARCH

Fig. 17: Corn Starch

Drug Name: Corn Starch

Chemical Name: Polysaccharide (mainly amylose and amylopectin)

Description: Fine, white, tasteless, and odourless powder derived from maize; biocompatible and biodegradable

Application: Pharmaceutical excipient in transdermal patches Used as a film-forming agent, matrix polymer, and filler Provides structural integrity and controlled drug release.

Solubility: Insoluble in cold water, Swells and forms a gel or paste in hot water

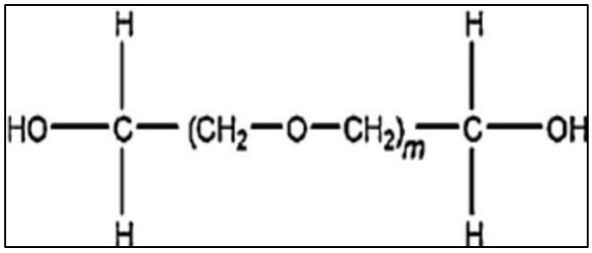
Storage: Store in a cool, dry place

Preparation method of corn starch

The corn kernels are first soaked in water to soften them. The kernels are then crushed to release the starch, and the resulting mixture is passed through a series of grinders and screens to separate the starch from other components like fibre, protein, and germ. The starch is then washed and centrifuged to remove impurities, resulting in a purified starch product. The starch is then dried to remove excess moisture, and the final product is packaged for use in various applications, including food, textiles, and pharmaceuticals.

- **PEG 400**

Structure:



Drug Name: Polyethylene Glycol (PEG)

Chemical Name: Poly(oxyethylene) or Polyethylene oxide (depending on molecular weight)

Description:

PEG is a synthetic polymer used as a solvent, plasticizer, and penetration enhancer in transdermal drug delivery systems. It enhances drug solubility, stabilizes the formulation, and improves skin permeability.

Application:

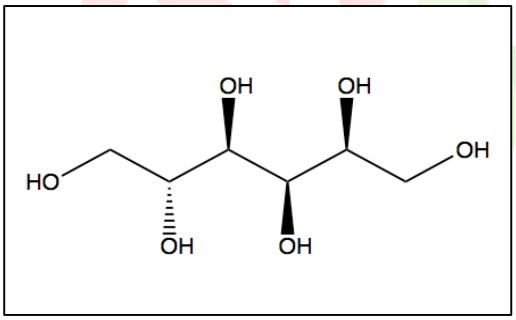
Solvent for active drugs

Plasticizer in polymeric films

Permeation enhancer to improve skin absorption

- **SORBITOL**

Structure:



Chemical Name :D-Sorbitol

Molecular Formula: $C_6H_{14}O_6$

Description:

Sorbitol is a sugar alcohol used as a humectant, stabilizer, and plasticizer in pharmaceutical formulations, including transdermal drug delivery systems.

Applications:

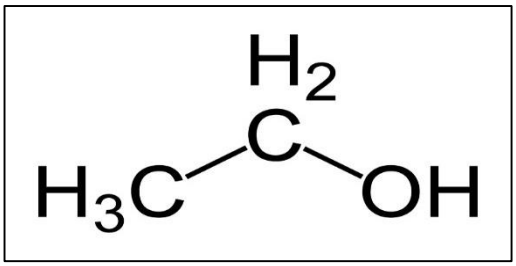
Pharmaceutical excipient: Used in various dosage forms.

Humectant: Helps retain moisture in formulations.

Plasticizer: Improves flexibility in polymeric films.

- **ETHANOL**

Structure:



Drug Name: Ethanol

Chemical Name: Ethyl alcohol

Description: A clear, colourless, volatile liquid with a characteristic alcoholic odor; commonly used as a solvent and permeation enhancer in transdermal formulations

Application:

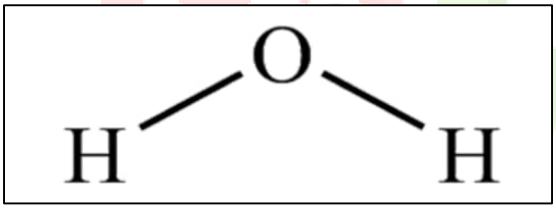
Solvent for drug and polymer dissolution

Permeation enhancer to increase drug absorption through the skin

Co-solvent in formulations to maintain drug stability

- **DISTILLED WATER (QS)**

Structure:



Drug Name: Distilled Water

Chemical Name: Purified Water (H_2O)

Molecular Formula: H_2O

Description: A clear, colourless, odourless, and tasteless liquid obtained by distillation to remove impurities and minerals; used as a universal solvent in pharmaceutical formulations

Application:

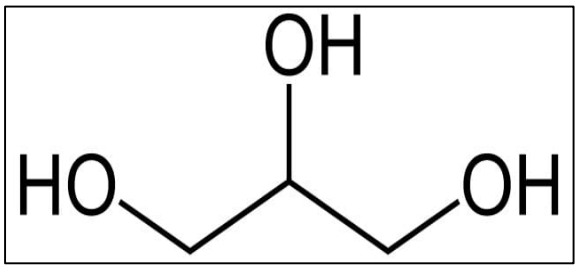
Used as a solvent in the preparation of drug-polymer solutions for transdermal patches

Helps in polymer swelling and gel formation

Assists in drug dispersion and mixing

- **GLYCERIN**

Structure:



Drug Name: Glycerin

Chemical Name: Propane-1,2,3-triol or Glycerol

Description: A humectant, solvent, and sweetener commonly used in pharmaceutical and cosmetic products.

Application: Used in transdermal patches, creams, lotions, and ointments for its moisturizing and humectant properties.

FORMULATION DEVELOMENT

Five different formulation was prepared with varying the concentration of all ingredients with named as F1, F2, F3, F4 and F5. and concentration of each ingredient was mentioned in table:

Sr. No	Ingredient	F1	F2	F3	F4	F5
1.	Cissus Quandragularis	2 ml	2 ml	2 ml	2 ml	2 ml
2.	Thespesia Populnea	2 ml	2 ml	2 ml	2 ml	2 ml
3.	Mentha Piperita	1 ml	1 ml	1 ml	1 ml	1 ml
4.	Rice Starch	5gm	2 gm	2 gm	2 gm	2gm
5.	Corn Starch	-	-	2 gm	2gm	2 gm
6.	PEG	0.5ml	0.5ml	0.5 ml	1 ml	1 ml
7.	Sorbitol	-	-	-	0.5ml	0.5ml
8.	Glycerine	1ml	1ml	1 ml	1 ml	1 ml
9.	Methyl Paraben	-	-	-	-	0.1 ml
9.	Water	Up to 25ml (QS)	Up to 25ml (QS)	Up to 25ml (QS)	Up to 25ml (QS)	Up to 25ml (QS)

In trial 5th we add in adequate quality of polymer, plasticizer, thickening agent,Humactant preservative, form the overall observation of 4 fail trial.

The patch become very stable and crack are not observed.

Fig.18: Transdermal patch

METHODOLOGY

INSTRUMENT:

Sr. No.	Name	Make	Model
1.	Weighing Balance	Mettler Toledo	Mettler Toledo XP205
2.	Moisture content Apparatus	Mettler Toledo	Mettler Toledo FS1
3.	Vernier Calliper	Starrett	Starrett 799

PROCEDURE

Step 1: Dispersion of Modified Rice Powder

To prepare a solution, accurately weigh the modified rice powder and corn starch and disperse it in distilled water. Gradually add water while stirring to ensure the powder dissolves evenly. Once fully dispersed, adjust the final volume to 25 mL with distilled water.

Step 2: Gel Formation

Heat the dispersion to 90°C for 2 hours, stirring gently to ensure even heating and prevent scorching. Continue stirring until a clear, homogenous liquid gel is obtained. Take care to avoid air bubble formation during the process, as this can affect the texture and quality of the final product.

Step 3: Addition of Additional Substances (Optional)

Add substances (e.g. drug/excipient) to the gel if desired.

Step 4: Film Casting/Drying

Pour exact portion of rice gel into a glass petri dish. and dry at 30°C for 2/3 days

Step 5: Film Removal and Evaluation

Carefully remove the cast films and observe their physical appearance visually, noting characteristics such as colour, clarity, texture, and uniformity. This visual inspection can provide valuable information about the film's quality and potential applications.

EVALUATION TEST OF TRANSDERMAL PATCH

1.Organoleptic Characteristics:

The organoleptic parameters include its nature, colour, odour, feel and consistency which were evaluated manually for its physical properties.

- **Appearance/Colour:**

Observe the colour (e.g., white, yellowish, brown, green, pale green).

Check for uniformity or discoloration.

- **Odour:**

Smell the patches and describe the aroma (e.g. characteristic,aromatic,Distinctive).

- **Texture/Feel:**

Rub a patch between fingers. Describe the texture ,some times simple microscope are also use (e.g. fine, gritty, coarse, sticky, smooth).

- **pH:**

Transdermal patches, dissolve or disperse the patch in 100 ml of distilled water, stir, and measure the pH using a calibrated pH meter or pH paper.

Table 9: Organoleptic characteristic of Patch.

Parameter	Result
Appearance	Smooth/Uniform
Colour	Pale Green
0dour	Distinctive
Texture	Sticky/ Smooth
pH	5-6

2. Thickness: Thickness of patches was measured using Vernier caliper in different places on the plaster and average thickness was calculated.

Table 10: Thickness of Patch

Trial	Result
1	0.19 mm
2	0.21 mm
3	0.18 mm

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

Table 11: Weight of Patch.

Trial	Result
1	0.08 gm
2	0.07 gm
3	0.08 gm

4. 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.

Table 12: Weight uniformity of Patch.

Trial	Result
1	0.08 gm
2	0.07 gm
3	0.08 gm

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

Moisture content = Ws-(W2-W1)/Ws x100

Where:

WS: Weight of sample

W1: Weight of dish

W2: Weight of dish after drying

CALCULATION OF MOISTURE CONTENT

Weight of dish=52.91

Weight of sample =0.08

Weight of dish after drying=52.98

Calculation-

Moisture Content = Ws-(W2-W1)/Ws x100

= 0.08- (52.98-52.91)/0.08 x100

= 0.08-0.07/0.08 x100

= 0.01/0.08 x100

= 0.125 x100

Moisture Content = **12. %**

MOISTURE ANALYZER

Table 13: Moisture content of Patch.

Trial	Result
1	11.4%
2	11%
3	10.2%

6. Folding endurance: A Particular area of the strip (1x1 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.

Table 14: Folding Endurance of Patch.

Trial	Result
1	10
2	12
3	11

7. 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 skin allergy and irritation at 15 minutes, 1 hour and 24 hours after the test patch was removed.

Table 15: Skin irritation test of Patch.

Sr. No.	Parameter	15 minute	1 hours	24 hours
1	Irritation	No	No	No
2	Redness	No	No	No
3	Swelling	No	No	No

8.Stability Studies: Stability testing of prepared formulation was conducted for formulation F5 by storing at different temperature conditions for the period of one month. The packed formulation stored at different temperature conditions viz. Room temperature, 20°C and 40°C and were evaluated for physical parameters like Colour, Odour, pH, Appearance Texture.

Table 16: Stability Testing

Parameter	25°C	20^{0C}	$40^{O}C$
Appearance	Smooth/Uniform	Smooth/Uniform	Slightly affected
Colour	Pale Green	Pale Green	Pale Green
0dour	No change	No change	No change
Texture	Sticky/ Smooth	Sticky/ Smooth	Slight variation
pH	5-6	5-6	5-6

PRECAUTIONS & BENEFITS

Precautions-

1. Monitor skin for irritation, redness, or rashes.

2. Be aware of potential allergic reactions.

3. Apply patches to clean, dry skin as instructed.

4. Avoid overlapping patches or applying to broken skin.

5. Follow dosage and usage guidelines.

6. Report side effects to your healthcare provider.

7. Consult your healthcare provider if pregnant, breastfeeding, or taking other medications.

Benefits-

Benefits of Transdermal Patches with Cissus Quadrangularis, Thespesia populnea Linn, and Mentha piperita

Cissus Quadrangularis

1. Pain relief: Cissus Quadrangularis has anti-inflammatory and analgesic properties.

2. Bone health: It's traditionally used to support bone health and fracture healing.

Thespesia populnea Linn

1. Anti-inflammatory: Thespesia populnea has anti-inflammatory properties.

2. Antioxidant: It has antioxidant effects.

Mentha Piperita

1. Pain relief: Menthol provides cooling sensation and pain relief.

2. Anti-inflammatory: Menthol has anti-inflammatory properties.

RESULT

The prepared transdermal patches were evaluated for physical parameters. The formulation exhibited a pale green colour and had a good, acceptable odour, which is desirable for pharmaceutical formulations. The texture of the patches was smooth, meeting the requirement. Additionally, the pH of all formulations was found to be near neutral, ranging between 5 and 6, which is suitable for transdermal applications. Also perform some another physiochemical test such as thickness, weight uniformity, moisture content, folding endurance. Which confirmed the patches' physical stability, mechanical integrity, and potential for effective transdermal delivery. And the results of irritancy test were shown in Table 10. Irritancy test showed negative results for irritancy, redness, swelling as the herbal in their natural form without addition of chemicals was found to be compatible with the skin proteins mild irritation because of presence of Cissus Quadrangularis. This formulation is safe to use for skin. Stability studies showed a different temperature over a period of one month revealed the insert nature of the Transdermal patch in the terms of colour, odour, texture, smoothness and pH in the between temperature 20^{o}C to 25 ^{o}C

Sr. No	Parameter	Result
1.	Appearance	Smooth/Uniform
2.	Colour	Pale Green
3.	0dour	Distinctive
4.	Texture	Sticky/ Smooth
5.	pH	5-6
6.	Thickness	0.19 mm
7.	Weight	0.08 mg
8.	Weight Uniformity	0.07 mg
9.	Moisture Content	10.86%
10.	Folding Endurance	11 Times
11.	Skin Irritation Test	Nil
12.	Stability Study	Stable

DISCUSSION

The present study was aimed at incorporating herbal drugs in novel drug delivery system i.e. transdermal patch for the treatment of inflammatory disease like rheumatoid arthritis (RA), Back pain, Joint pain, muscle pain. anti-inflammatory transdermal patches were formulated using there different Phyto - constituent steroid, kaempferol, and quercetin, menthol selection of Phyto constituent on the basis of their therapeutic efficacy means they suppress inflammation and proved time tested and safe drug. The dose of the phytopharmaceutical was selected based upon reported topical dose from the literature. As compare with the conventional dosage form, in transdermal drug delivery system, drug permeates directly into the blood stream without undergoing first pass metabolism.

In which we prepared 5 formations with different quantities of excipient such as, Rice starch, Corn starch as a Biopolymer, PEG as a permeation enhancer , sorbitol as a Humectant and plasticizer of active ingredient. Moisture content in formulation F1 is decreases with increasing in concentration of polymer. The F2 Formulation showed semisolid matrix. The result indicates that the hydrophilicity of the polymer directly proportional to % mc. F3 and F4 does not compare with standard. However, we choose another formulation, for further future studies i.e. F5 formulation are physical and chemical compatible with Standard. The physicochemical parameter of the optimized formulation was not significantly changed on storage. The result indicated that the formulation was stable on the required storage condition.

CONCLUSION

The present study successfully demonstrated the formulation and evaluation of herbal transdermal patches using extracts of **Cissus quadrangularis, Thespesia populnea Linn, and Mentha piperita Linn.** These patches were designed with the aim of delivering therapeutic agents through the skin, offering a sustained-release herbal dosage form with improved patient compliance and minimized side effects.

The formulation process included proper extraction techniques, solubility analysis, and phytochemical screening, ensuring the presence of bioactive constituents. Evaluation parameters such as thickness, weight variation, moisture content, folding endurance. confirmed the patches' physical stability, mechanical integrity, and potential for effective transdermal delivery.

Overall, the results indicate that herbal transdermal patches represent a promising alternative to conventional drug delivery systems. They offer several benefits including ease of application, avoidance of first-pass metabolism, and the ability to maintain steady-state drug levels over an extended period. This approach bridges the gap between traditional herbal remedies and modern pharmaceutical technology, paving the way for the development of effective and patient-friendly herbal therapies.

DIFFERENT FORMULATION

TABLET

Tablet Formulation Procedure

Weigh Cissus quadrangularis extract, Thespesia populnea extract, Mentha piperita oil, and excipients. Mix extracts and oil, then add excipients and granulate. Compress into tablets, coat with Opadry, and package in blister packs or bottles.

EVALUATION TEST

SR.NO.	PARAMETER	RESULT
1.	Colour	White
2.	Size	3 mm
3.	Shape	Round
4.	Hardness	6kg
5.	Weight Variation	-9%
6.	Thickness	2.12 mm

GEL

Gel Formulation Procedure

Weigh Cissus quadrangularis extract, Thespesia populnea extract, Mentha piperita oil, Glycerin, Carbopol, and TEA. Mix extracts and oil, then add Glycerin and water. Add Carbopol, stirring constantly, and neutralize with TEA to form a gel. Add preservative and mix until uniform. Fill and label containers with the gel.

EVALUATION TEST-

SR.NO.	PARAMETER	RESULT
1.	Colour	Creamy
2.	Odour	Distinctive
3.	pH	5-6
4.	Viscosity	2.6 P
5.	Spread-ability	Yes
6.	Skin Irritability	No
7.	Stability	Stable

POWDER

Herbal Powder Preparation Procedure

Dry Cissus quadrangularis leaves, Thespesia populnea leaves, and Mentha piperita leaves. Grind into fine powder and mix with Geru and Camphor. Blend thoroughly, sift to remove lumps, and fill into containers like capsules or sachets for packaging and use.

EVALUATION TEST

SR.NO.	PARAMETER	RESULT
1.	Colour	Brownish
2.	Odour	Characteristics
3.	Texture	Fine
4.	Appearance	Smooth
5.	Tapped density	0.92 g/mol
6.	Bulk density	0.83 g/mol
7.	Angle of repose	34.21
8.	Hausner’s ratio	1.12
9.	Carr’s index	11%
10.	pH	5-6

SPRAY

Spray Formulation Procedure

Mix Cissus Quadrangularis and Thespesia populnea extracts, then add menthol, ethanol, glycerin, water, and preservative, stirring well after each addition. Filter the mixture to remove impurities and fill into spray bottles for packaging and use.

EVALUATION TEST

SR.NO.	PARAMETER	RESULT
1.	Colour	Pale green
2.	Odour	Characteristics
3.	pH	5-6
4.	Stability testing	Stable
5.	Irritability	No

OIL

Herbal Oil Preparation Procedure

Dry Cissus quadrangularis stem, Thespesia populnea leaves, and Mentha piperita leaves. Grind into fine powder and mix with carrier oil. Heat gently for 2-3 hours, then strain and filter the oil. Bottle in a clean container and store in a cool, dark place.

EVALUATION TEST

SR.NO.	PARAMETER	RESULT
1.	Colour	Brownish
2.	Odour	Characteristics
3.	pH	5-6
4.	Stability testing	Stable
5.	Irritability	No

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