

Formulation Development and Evaluation of Bio Adhesive Drug Delivery System Containing Selected Phytopharmaceuticals

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Abstract—Background: Rheumatoid arthritis (RA) and osteoarthritis are chronic inflammatory disorders demanding prolonged therapeutic management. Conventional oral treatments often suffer from low bioavailability due to hepatic first-pass metabolism and cause severe gastrointestinal distress. Transdermal drug delivery systems (TDDS) offer a non-invasive alternative to circumvent these limitations. Objective: This study aimed to formulate, evaluate, and compare novel matrix-type and reservoir-type transdermal patches incorporating time-tested anti-inflammatory phytopharmaceuticals boswellic acids and 18 β -glycyrrhetic acid for controlled systemic delivery.

Methods: Reservoir-type patches (F4) containing 18 β -glycyrrhetic acid in a Carbopol 934 gel base were prepared via heat-sealing, utilizing an ethylene-vinyl acetate (EVA) rate-controlling membrane. Matrix-type patches (F10) containing boswellic acids were fabricated using HPMC E50 and ethyl cellulose (EC) polymers via the solvent-casting technique. Both formulations incorporated menthol (5% w/v) as a penetration enhancer and piperine as a bioenhancer. Patches were characterized via FTIR, DSC, skin irritancy tests, *in-vitro* and *ex-vivo* (rat skin) permeation studies, and carrageenan-induced rat paw edema models to judge *in-vivo* anti-inflammatory efficacy. Results: FTIR and DSC thermograms confirmed no chemical incompatibility, revealing homogenous drug dispersion within the polymer matrices. Optimized reservoir (F4) and matrix (F10) patches exhibited exceptional drug content uniformity (99.33 \pm 0.014% and 99.34 \pm 0.015%, respectively). The incorporation of 0.5% piperine

significantly enhanced the *in-vitro* release of 18 β -glycyrrhetic acid to 95.55 \pm 0.03% at 10 hours compared to formulations without the bioenhancer (40.11%). Drug release profiles fitted zero-order kinetics followed by the Korsmeyer-Peppas model, confirming a non-Fickian diffusion mechanism. Both formulations were non-irritant (Primary Irritation Index, PII<2). In *in-vivo* studies, the matrix patch (F10) demonstrated a superior carrageenan-induced paw edema inhibition of 89.77% at 10 hours compared to the reservoir patch (87.5%), with both herbal formulations outperforming the standard commercial aceclofenac patch. Stability testing confirmed no significant physicochemical degradation upon storage. Conclusion: The findings demonstrate the successful feasibility of delivering therapeutic concentrations of phytoconstituents via transdermal routes. Comparative data indicates that the matrix-type system (F10) provides superior skin permeation and anti-inflammatory activity, presenting a promising, safer, and highly efficient therapeutic strategy for management of chronic inflammatory diseases.

Index Terms—Transdermal patch; Boswellic acids; 18 β -glycyrrhetic acid; Piperine; Anti-inflammatory; Rheumatoid arthritis.

I. INTRODUCTION:

The integration of traditional herbal medicines into modern pharmaceutical drug delivery systems is accelerating globally. The World Health Organization

(WHO) estimates that approximately 33.33% of the world's population relies on natural, plant-sourced formulations to treat a variety of illnesses.¹ According to the Department of AYUSH (Ministry of Health, India), this paradigm shift opens new horizons for integrated medicine fusing traditional remedies with state-of-the-art pharmaceutical technologies to optimize health promotion and chronic disease management.² Conventional pharmaceuticals often provide only symptomatic relief or fail to sustainably manage complex conditions like gout, chronic arthritis, tuberculosis, and respiratory illnesses.³ Plant-derived compounds are broadly trusted for long-term therapy due to generations of documented safe traditional use.⁴ Phytoconstituents target multi-pathway mechanisms, offering reliable treatment outcomes while minimizing the severe side effects typical of synthetic chemicals (e.g., gastrointestinal ulcers caused by oral NSAIDs).⁵ To design an effective transdermal system, the drug must overcome the skin's inherent biological barrier.⁶

The skin consists of four distinct anatomical layers:

- **Non-Viable Epidermis (Stratum Corneum):**
The absolute outermost layer consisting of 10-20 layers of flattened, dead keratinocytes arranged in a dense "brick-and-mortar" fashion. This is the primary physical and rate-limiting barrier to transdermal delivery.⁷
- **Viable Epidermis:**
Located directly beneath the stratum corneum 50-100µm thick. Physicochemically similar to other living tissues, it contains no blood vessels and is composed of roughly 90% water.
- **Viable Dermis:**
A thick structural layer 2000--3000µm made of loose connective tissue and fibrous fibrin proteins embedded in an amorphous ground substance. This layer contains the capillary networks that absorb drugs into systemic circulation.⁸
- **Subcutaneous Tissue (Hypodermis):**
Deep fat-rich layer that serves as a mechanical cushion and blood vessel pathway. If lipophilic drugs pass too deeply without immediate capillary absorption, this fatty tissue can become an unintentional depot/storehouse.⁹

Principles of Permeation & Transport Pathways
Transdermal drug delivery relies on passive diffusion driven by the concentration gradient between the high-density patch and the low-density cutaneous blood vessels.¹⁰

Routes of Penetration

- **Transcellular (Intracellular) Route:**
Direct passage through both the lipid matrix and the dense keratin bricks of the stratum corneum cells.
- **Intercellular Route:**
Tortuous diffusion strictly winding through the continuous lipid bi-layers between the cells. This is the primary pathway for most small-molecule transdermal drugs.
- **Transappendageal Route:**
Permeation via sweat glands, sebaceous glands, and hair follicles. Though these bypass the stratum corneum bricks, they occupy a negligible surface area and are considered minor pathways.¹¹

The Lipophilic-Hydrophilic Balance:
The optimal candidate drug for passive transdermal diffusion requires an even balance ideally 50% lipophilic and 50% hydrophilic. Purely lipid-soluble substances easily enter the intercellular lipid bi-layer but fail to exit into the aqueous viable epidermis. Conversely, purely water-soluble drugs are completely blocked by the hydrophobic lipid mortar of the stratum corneum.¹²

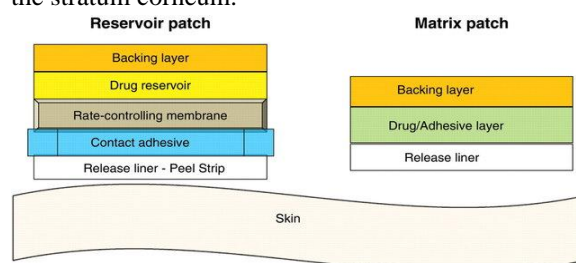


Fig. 1: Structural comparison of Reservoir vs. Matrix patch

Modern TDDS formulations are categorized into two primary engineering layouts, depending on how they control drug release over time:¹³

A. Reservoir Systems

The active pharmaceutical ingredient (API) is securely sandwiched as a gel, suspension, or solution between

an impermeable backing layer and a dedicated microporous rate-controlling membrane (such as Ethylene-Vinyl Acetate or silicone rubber). The drug must diffuse through this membrane before hitting the adhesive layer and entering the skin.¹⁴

B. Matrix Systems

Drug-in-Adhesive: The drug is directly dissolved or dispersed into a polymeric adhesive solution, which is then cast directly onto an impermeable backing layer. The single layer acts as both the active reservoir and the skin-contact adhesive.

Matrix Dispersion:

The drug is homogeneously blended throughout a separate hydrophilic or hydrophobic polymer disk (e.g., HPMC or Ethyl Cellulose). This medicated disk is glued to an occlusive base plate, with adhesive applied around its outer circumference.¹⁵

Micro-Reservoir:

A hybrid approach where the drug is dissolved in microscopic, liquid spheres of hydrophilic polymers, which are then uniformly suspended throughout a continuous lipophilic polymer matrix.¹⁶

Next-Gen Enhancements: Advanced TDDS Technologies

When passive patch diffusion is insufficient to achieve therapeutic plasma levels, modern pharmaceutical science utilizes active structural, electrical, or physical forces to create micro-pathways through the stratum corneum:

Micro-needles & Macroflux® Arrays:

Incorporate tiny silicon or titanium projections (< 200µm long). They pierce the non-viable epidermis to safely deliver large biological macromolecules (e.g., insulin, vaccines) without stimulating underlying dermal pain receptors.¹⁷

Iontophoresis:

Applies a continuous low-voltage electrical current (1e 0.5\ mA/cm²) to drive charged, ionized drug molecules directly across the skin barrier via electrostatic repulsion.

Electroporation:

Employs brief, high-voltage pulses (sim 100V) to induce temporary, reversible aqueous pores directly

through the lipid bi-layers, accommodating large molecules up to 39kDa.

Sonophoresis:

Utilizes the physical energy of ultrasound waves to break up or agitate intercellular lipids, fluidizing the skin matrix to accelerate topically applied creams, gels, or patches.¹⁸

Dermal Abrasion Devices (e.g., D3S System):

Gently remove or disrupt the dead stratum corneum layers using mechanical resurfacing techniques, yielding up to a 100-fold increase in the systemic absorption of difficult-to-formulate therapeutics.

II. AIM

The present study was aimed at incorporating herbal drugs in novel drug delivery system i.e., transdermal patch for the treatment of inflammatory diseases like rheumatoid arthritis (RA), osteoarthritis, etc.

III. OBJECTIVES

- **Develop and Compare Two System Architectures:** Fabricate and evaluate both reservoir-type patches (using 18 β-glycyrrhetic acid} in a Carbopol 934 gel core with an EVA membrane via heat-sealing) and matrix-type patches (using boswellic acids in HPMC E50 and Ethyl Cellulose polymers via solvent casting).
- **Optimize Permeation and Bioavailability:** Evaluate the synergistic effect of using menthol (5%) as a penetration enhancer to disrupt the stratum corneum lipid barrier, alongside piperine as a bioenhancer to increase skin absorption and slow down local drug clearance.
- **Determine Polymer Effects on Physical Metrics:** Study how varying ratios of hydrophilic polymers (HPMC E50) and hydrophobic polymers (EC) alter the Water Vapor Transmission Rate (WVTR), Percentage Moisture Content (%MC), and patch brittleness.¹⁹

3.1. DRUG PROFILE:

Phytoconstituents represent marker constituents present in plant drug which is responsible for its major therapeutic action.

For present formulations two phytoconstituents selected are boswellic acids obtained from oleogum

resin of *Boswellia serrata*, 18 β -glycyrrhetic acid obtained from roots and stolons of *Glycyrrhiza glabra* and bioenhancer piperine obtained from dried fruits of *Piper longum*.

Boswellia serrata

Botanical source

It consists of oleogum resin of *Boswellia serrata* Roxb.

Family: Burseraceae

Vernacular names Sanskrit: Sallaki, Kunduru

Hindi: Salai gugal

Gujarati: Saledo, Dhup, Gugali

English: Indian Olibanum tree Geographical source

Grows on dry hills of the Gujarat, Arvali hills of Rajasthan, Madhya Pradesh and Bihar

Morphology



Fig 2: Oleo gum resin of *Boswellia serrata*

Chemical constituents:

Resin (55%): Mixture of total organic acids like α boswellic acid, β boswellic acid, 11- keto- β boswellic acid, 3-O-acetyl β boswellic acid, 3-O-acetyl 11-keto- β boswellic acid.²⁰

Therapeutic use:

Anti-inflammatory, Anti hyperlipidemic

Liquorice

Botanical source:

It consists of dried peeled or unpeeled roots and stolons of *Glycyrrhiza glabra* Linn.

Family: Leguminosae.

Plant is cultivated in Punjab and Sub-Himalayan tracts.

Commercial varieties of the plant are *Glycyrrhiza glabra* var. *typica* (Spanish): purplish blue color

flower, grown in USA, England, France, and Germany. *Glycyrrhiza glabra* var. *glandulifera* (Russian): grown in central and southern Russia. *Glycyrrhiza glabra* var. *violacea* (Perssian): violate flower, collected from Iran and Iraq in the valleys of the Tigris²¹



Fig 3: Roots of liquorice

Chemical constituents Marker constituent

Triterpenoid saponin glycoside: glycyrrhizin (2-20%) is 50 times as sweet as sugar

Therapeutic use

Demulcent, anti-inflammatory, anti-ulcer

1.1.1 Pippali Botanical source

It consists of dried fruits of *Piper longum*. Family: Piperaceae.²²



Fig. 4: *Piper longum* fruits

Chemical constituents Marker constituent Alkaloid: piperine (4-5%)

Therapeutic use

Bioenhancer (1-30mg)

IV. METHODOLOGY:

Materials:

4.1. Identification of Phytoconstituents

4.1.1. Identification of 18 β -Glycyrrhetic Acid

18 β -Glycyrrhetic acid was procured from Yucca Enterprises, Mumbai-37. It was identified on the basis of physicochemical properties and by using the HPTLC method described in the literature.²³

Identification methods:

- By physicochemical properties^{1,2}
- By HPTLC method²

Standard:

18 β -Glycyrrhetic acid

Preparation of standard solution:

10 mg of the sample was dissolved in 10 mL of methanol.

Preparation of test solution:

1 g of powdered sample was refluxed with 20 mL of 5 M hydrochloric acid for 5 h and extracted with chloroform (3 \times 15 mL). The chloroform extract was concentrated, and the residue obtained was dissolved in 10 mL of chloroform.

Chromatographic conditions:

- Stationary phase: Silica gel 60 F254 plates (10 \times 5 cm), prewashed with methanol
- Mobile phase: Toluene: Ethyl acetate: Glacial acetic acid (12.5: 7.5: 0.5)
- Saturation time: 30 min
- Band width: 6 mm
- Space between bands: 5 mm
- Spotting rate of solute: 5 s/ μ L
- Solvent migration distance: 8 cm
- Spray reagent: Anisaldehyde–sulphuric acid
- Scanning wavelength: 254 nm

4.1.2. Identification of Boswellic Acids

Boswellic acids were procured from Natural Remedies, Bangalore. They were identified on the basis of physicochemical properties and by using the HPTLC method described in the literature.²⁴

Identification methods:

- By physicochemical properties^{1,2}
- By HPTLC method²

Standard:

Boswellia serrata dry extract (resin)

Preparation of standard solution:

5 mg of sample was dissolved in 5 mL of methanol.

Preparation of test solution:

To 1 g of powdered sample, 5 mL of petroleum ether was added and filtered. The residue was dried and extracted with 5 mL of methanol. The methanolic extract was concentrated and the residue obtained was dissolved in 1 mL of methanol.

Chromatographic conditions:

- Stationary phase: Silica gel 60 F254 plates (10 \times 5 cm), prewashed with methanol
- Mobile phase: Hexane: Ethyl acetate (7: 3)
- Saturation time: 30 min
- Band width: 6 mm
- Space between bands: 5 mm
- Spotting rate of solute: 5 s/ μ L
- Solvent migration distance: 8 cm
- Spray reagent: 10% sulphuric acid
- Scanning wavelength: 254 nm²

4.2. Preformulation Study

Investigation of the physicochemical compatibility between drug and polymer/drug-excipient combinations plays a vital role in formulation development, particularly with respect to drug release from the formulation and overall stability. Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) techniques were employed to study the physical and chemical interactions between drugs and excipients.

For the reservoir-type transdermal patch, 18 β -glycyrrhetic acid was selected as the drug and Carbopol 934 as the polymer.²⁵

4.2.1. Preformulation Study of 18 β -Glycyrrhetic Acid

By Fourier Transform Infrared Spectroscopy (FTIR) Infrared spectra were recorded using FTIR equipment by the potassium bromide (KBr) disc method over a

wavelength range of 4000–400 cm^{-1} . The spectra of the drug, polymer, and physical mixtures of drug and polymer were compared to investigate any possible interactions between them^{3,4}.

By Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) is a thermoanalytical technique in which the difference in the amount of heat required to increase the temperature of a sample and a reference is measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature throughout the experiment.²⁶

A 2 mg sample (drug, polymer, or drug-excipient mixture) was individually sealed in an aluminum pan with a pierced lid and analyzed using a NETZSCH DSC 204 F1 Phoenix (240-12-0239-L). The instrument was operated under the following conditions:

Experimental conditions:

- Atmosphere: Nitrogen
- Heating rate: 10°C/min
- Gas flow rate: 20 mL/min
- Temperature range: 10–600°C
- Sample size: 2 mg^{5,6}

For the matrix-type transdermal patch, Boswellic acid was selected as the drug and HPMC E50 and ethyl cellulose were selected as polymers.

4.2.2. Preformulation Study of Boswellic Acid

By Fourier Transform Infrared Spectroscopy (FTIR) Infrared spectra were recorded using FTIR equipment by the potassium bromide (KBr) disc method over a wavelength range of 4000–400 cm^{-1} . The spectra of the drug, polymers, and physical mixtures of drug and polymers were compared to identify any possible interactions^{3,4,27}

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Experimental conditions:

- Atmosphere: Nitrogen
- Heating rate: 10°C/min
- Gas flow rate: 20 mL/min
- Temperature range: 10–600°C
- Sample size: 2 mg^{5,6}

4.3. Preparation of Reservoir-Type Patch

4.3.1. Calculation of Dose

According to the literature review, a liposomal gel containing 18 β -glycyrrhetic acid at a concentration of 0.9% w/w (9 mg in 1 g of gel base) exhibited stronger anti-inflammatory activity. Therefore, a dose of 9 mg per gram of gel base was selected for the present study⁷. A 2³ factorial design was employed to evaluate the effect of independent variables on the formulation characteristics. The independent variables included gel base, penetration enhancer, and rate-controlling membrane, while the dependent variable was percentage drug release (% drug release)⁸.

4.4. Preparation of Transdermal Patch (Matrix Type)

4.4.1. Calculation of Dose

According to the literature review, topical formulations used for the symptomatic treatment of musculoskeletal disorders containing *Boswellia* extract in concentrations ranging from 0.001% to 5% have demonstrated significant anti-inflammatory activity. From this concentration range, a dose of 2% w/w boswellic acid was selected for the present study. Thus, 20 mg of boswellic acid was incorporated per gram of formulation base⁹. Accordingly, for the preparation of the matrix-type transdermal patch, 20 mg of boswellic acid was incorporated into a patch with a surface area of 4 cm^2 .

4.4.2. Selection of Batches

Batches were selected on the basis of drug-to-polymer ratios of 1:1 and 1:2 to evaluate the effect of independent variables such as polymer type and penetration enhancer on the dependent variable, namely percentage drug release. Two different polymers, namely ethyl cellulose (hydrophobic polymer) and hydroxypropyl methylcellulose (HPMC

E50; hydrophilic polymer), were used in the formulation. Menthol was incorporated as a penetration enhancer¹⁰ and glycerine was used as a plasticizer. Since phytopharmaceutical formulations generally require a higher amount of plasticizer to improve flexibility and enhance the flow properties of formulation components, glycerine was incorporated at 30% of the total polymer concentration^{11,29}.

4.5. Simultaneous UV Method Development for 18 β -Glycyrrhetic Acid and Piperine

Instrumentation

A UV–Visible double-beam spectrophotometer, Shimadzu Corporation (Japan), Model UV-1800, with a bandwidth of 0.5 nm and matched quartz cells of 1 cm path length was used for the analysis. An analytical balance (Denver Instruments, Germany) and a sonicator (Electro Quip Ultra Sonicator, Texas) were also used during the study. Calibrated glassware was used throughout the experimental work.

Chemicals

The drugs used were 18 β -glycyrrhetic acid and piperine procured from Yucca Enterprises, Mumbai. Methanol (AR grade, Chemdyes Co., Ahmedabad) and distilled water were used as solvents and reagents.

Method

Preparation of Standard Stock Solution

Accurately weighed quantities of 10 mg each of 18 β -glycyrrhetic acid and piperine were transferred separately into two 100 mL volumetric flasks and dissolved in methanol. The solutions were shaken thoroughly and the final volume was adjusted with methanol to obtain stock solutions with concentrations of 100 μ g/mL of each drug.³⁰

Methodology

Working standard solutions of 18 β -glycyrrhetic acid and piperine were prepared separately by suitable dilution of stock solutions with methanol to obtain concentrations of 10 μ g/mL. These solutions were scanned in the wavelength range of 200–400 nm against methanol as a blank.

The maximum absorption wavelengths (λ_{max}) of the drugs were found to be 250 nm (λ_1) for 18 β -glycyrrhetic acid and 343.17 nm (λ_2) for piperine.³¹

Simultaneous Equation Method

Two wavelengths selected for the analysis were 250 nm and 343.17 nm, corresponding to the absorption maxima of 18 β -glycyrrhetic acid and piperine, respectively.

The stock solutions of both drugs were further diluted with methanol to obtain standard solutions of:

- 18 β -glycyrrhetic acid: 5–15 μ g/mL
- Piperine: 4–20 μ g/mL

The absorbance values were measured at both selected wavelengths, and absorptivity coefficients (ϵ) for both drugs at each wavelength were determined as the mean of five independent determinations.

4.6. Evaluation Parameters of Reservoir-Type Patch

4.6.1. Drug Content Uniformity^{16,17}

A 2 \times 2 cm² patch was placed in 100 mL phosphate buffer (pH 7.4) and stirred at 50 rpm for 24 h. The solution was filtered through Whatman filter paper and 0.5 mL filtrate was extracted with 5 mL chloroform. The chloroform layer was evaporated, and the residue was reconstituted in 5 mL methanol. Drug content of 18 β -glycyrrhetic acid and piperine was analyzed at 250 nm and 343.17 nm using the simultaneous UV method against placebo patch solution.³²

4.6.2. In-vitro Permeation Study^{16,17,18}

The formulated patch (2 \times 2 cm²) was mounted on a cellulose acetate membrane treated with 0.1 N sodium hydroxide and soaked overnight in phosphate buffer pH 7.4. The membrane was placed in a Franz diffusion cell with the drug-releasing surface facing the receptor compartment containing 50 mL phosphate buffer (pH 7.4) at 37 \pm 0.5 $^{\circ}$ C. The receptor medium was stirred at 50 rpm. Samples (5 mL) were withdrawn at predetermined intervals and replaced with fresh medium. Samples were extracted with chloroform, evaporated, reconstituted in methanol, and analyzed at 250 nm and 343.17 nm.³⁵

4.6.3. Ex-vivo Permeation Study (F4 Formulation)^{18,19}

Full-thickness abdominal skin from Wistar rats (200–210 g) was excised, cleaned, and mounted on a Franz diffusion cell with the stratum corneum facing the donor compartment. The receptor compartment contained phosphate buffer pH 7.4. Samples were collected at predetermined intervals, replaced with

fresh medium, and analyzed for drug content by the simultaneous UV method.³⁶

4.6.1.1. Kinetic Modeling of Drug Release³⁷

Drug release data were fitted to Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models to determine release kinetics and mechanism.³⁸

4.6.4. Skin Irritancy Test (F4 Formulation)³⁹

Skin irritancy was evaluated in Wistar rats (200–210 g) according to the Draize method. Animals were divided into control, disease control, and test groups (n=6). The F4 patch was applied for three consecutive days. Erythema and edema were assessed after 24 h and 72 h using a visual scoring scale (0–4). Primary Irritation Index (PII) values were calculated and formulations classified accordingly.⁴⁰

4.6.5. In-vivo Anti-inflammatory Activity^{41,42}

Anti-inflammatory activity was evaluated using the carrageenan-induced rat hind paw edema model. Animals were divided into control, standard, and test groups (n=6). Paw edema was induced by subplantar injection of 0.1 mL of 1% w/v carrageenan suspension. Paw volume was measured at specified intervals using a plethysmometer.⁴⁴

Percentage inhibition of edema was calculated using:

$$\% \text{ Inhibition of edema} = (1 - V_t/V_c) \times 100$$

Where:

V_t =edema volume of test group

V_c = edema volume of control group

V. RESULTS AND DISCUSSION

5.1. Identification of phytoconstituents

5.1.1 18 β -glycyrrhetic acid⁴⁵

By Physicochemical properties White colour powder, tasteless, odourless. It is freely soluble in ethanol, chloroform. Melting point: 294°C.

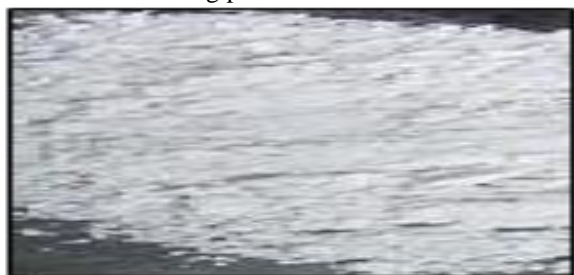


Fig 5.1: Powder of 18 β -glycyrrhetic acid

By HPTLC method

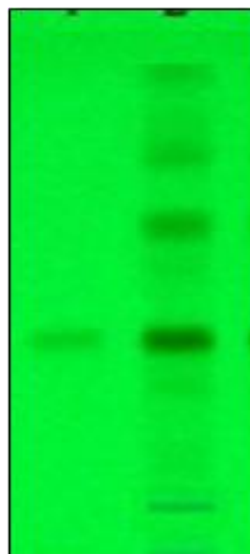


Fig 5.2: HPTLC of 18 β -glycyrrhetic acid (R_f 0.4)

5.1.1 Boswellic acids

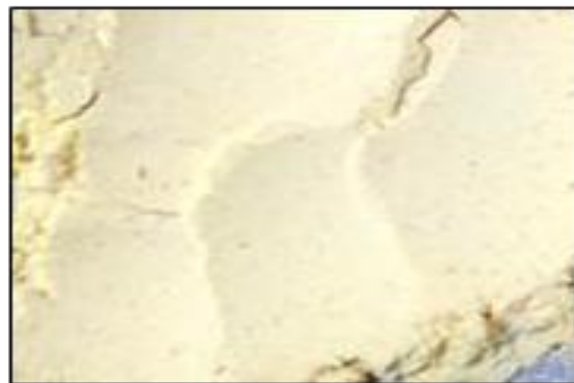


Fig 5.3: Powder of *Boswellia serrata* dry extract (resin)

By HPTLC method



Fig 5.4: HPTLC of Boswellic acids

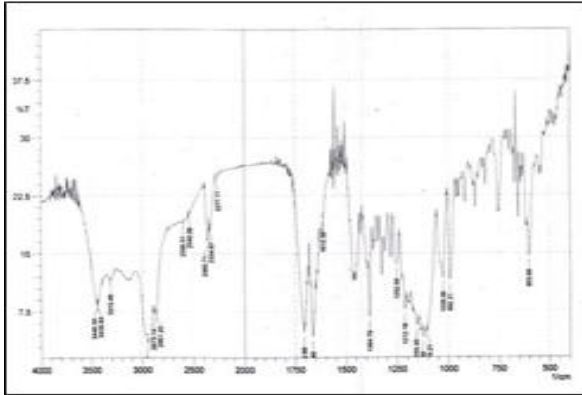


Fig 5.5: FTIR of 18 β -glycyrrhetic acid

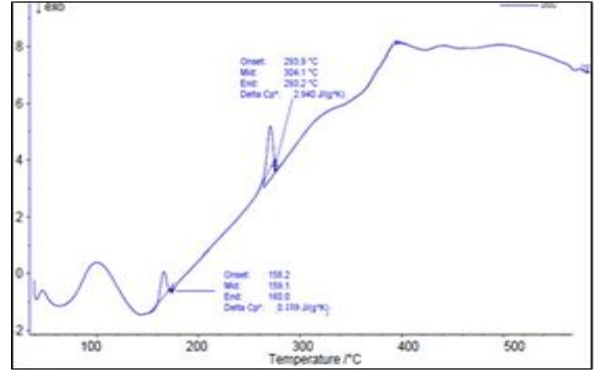


Fig 5.9: DSC of 18 β -glycyrrhetic acid and excipients of carbopol 934 gel formulation

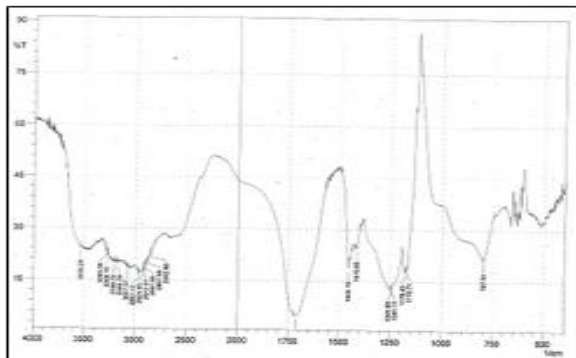


Fig 5.6: FTIR of carbopol 934

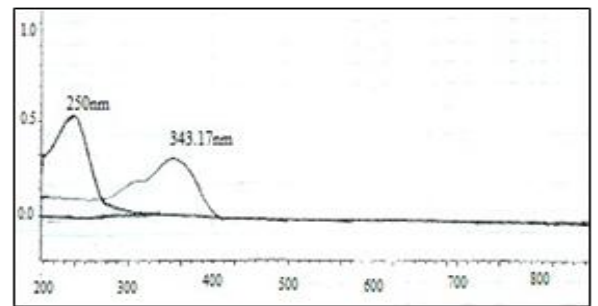


Fig 5.10: Overlay spectra of 18 β -glycyrrhetic acid (15 μ g/ml) and piperine (8 μ g/ml)

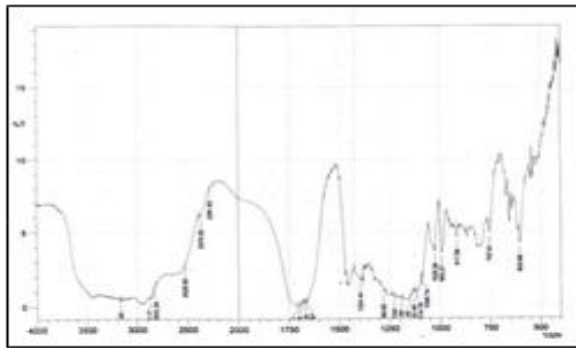


Fig 5.7: FTIR of 18 β -glycyrrhetic acid and excipients of carbopol 934 gel formulation

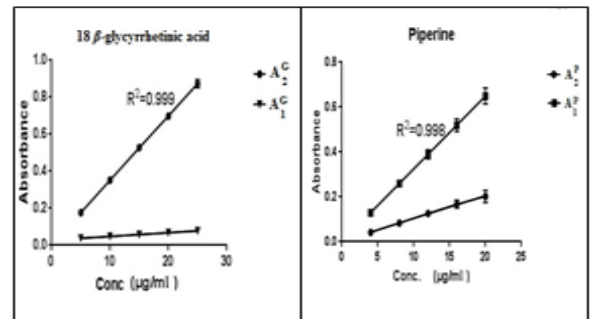


Fig 5.11: Calibration curve of 18 β -glycyrrhetic acid and piperine

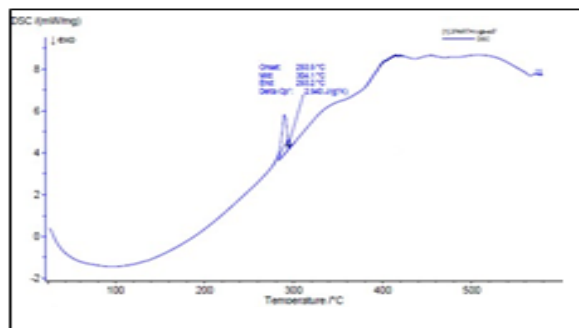


Fig 5.8: DSC of 18 β -glycyrrhetic acid

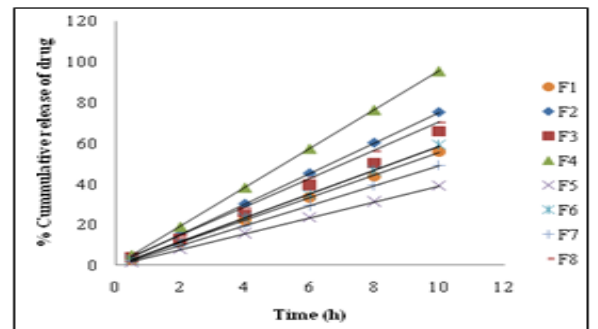


Fig 5.12: % Cumulative drug release of 18 β -glycyrrhetic acid patches

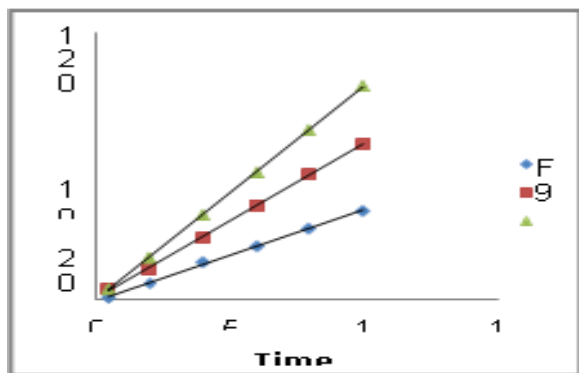


Fig 5.13: % Cumulative drug release of 18β-glycyrrhetic acid patch showing bioenhancer property of piperine

Tab 1: Anti-inflammatory effect of reservoir patches

Time (h)	% Inhibition of edema		
	Standard group	Test group-1	Test group-2
0	0	0	0
1	46.55	51.72	29.31
2	54.05	63.06	31.53
4	72.30	74.32	35.14
6	79.71	81.16	34.78
8	81.25	86.72	36.72
10	85.23	87.5	37.50
12	85.06	87.36	36.78

The present study aimed to develop herbal transdermal patches for the treatment of inflammatory disorders such as rheumatoid arthritis and osteoarthritis using 18β-glycyrrhetic acid and boswellic acids due to their proven anti-inflammatory activity and safety profile.

Two types of patches were developed: a reservoir-type patch containing 18β-glycyrrhetic acid with Carbopol 934 and a matrix-type patch containing boswellic acid with HPMC E50 and ethyl cellulose. Menthol was used as a penetration enhancer and piperine as a bioavailability enhancer.⁴⁶

FTIR and DSC studies confirmed compatibility between drugs and polymers with no significant interactions observed. Drug content uniformity was within 98–99%, indicating homogeneous drug distribution. Hydrophilic polymers showed higher moisture content and drug release compared to hydrophobic polymers.

Drug release from reservoir patches was influenced by Carbopol concentration, menthol concentration, EVA

membrane composition, and piperine content. Increased menthol and piperine enhanced permeation, while higher Carbopol concentration reduced release. Matrix patches containing HPMC E50 showed greater drug release than ethyl cellulose formulations.⁴⁷ Optimized formulations F4 and F10 demonstrated enhanced ex-vivo permeation, non-irritant behavior (PII <2), and significant anti-inflammatory activity in carrageenan-induced rat paw edema studies compared with the standard aceclofenac patch. Release kinetics followed zero-order and Korsmeyer–Peppas models, indicating diffusion-controlled and non-Fickian release mechanisms. Stability studies confirmed that the optimized formulations remained stable during storage.

Overall, the study demonstrated that transdermal delivery of phytopharmaceuticals with piperine improved drug bioavailability and therapeutic efficacy.

VI. CONCLUSION:

Through the present study, it was found that herbal drugs can be incorporated into modern dosage forms. Here herbal transdermal patches were prepared and evaluated. Reservoir type F4 patch formulated using 5% menthol, 42% ethanol, 50g carbopol934 gel base with 0.5% piperine as bioenhancer while the matrix type F10 patch formulated using 200mg polymer (HPMC E50), 5% menthol, 30% glycerine (plasticiser) and 25% piperine. Looking to reservoir and matrix system, all the evaluation parameters comparatively show the matrix system is better in anti-inflammatory activity. The present study was one of the few attempts to incorporate phytconstituents in transdermal system and it needs to be further optimized and characterised. These types of herbal formulations possess tremendous potential for the treatment of some of the disease.

Disclosure statement

The authors declare no potential conflicts of interest.

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