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Formulation And Analytical Characterization Of A Phytopharmaceutical Cream Incorporating Standardized Essential Oils And Herbal Bioactives Using GC-MS, FTIR, And Franz Diffusion Cell For Enhanced Dermal Penetration Profiling

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Abstract

Background:*Phytopharmaceutical formulations combining standardized essential oils and herbal bioactives are gaining attention as safer, sustainable, and patient-friendly alternatives for topical therapy. Essential oils not only possess intrinsic therapeutic activity but also act as natural permeation enhancers. Cream formulations provide an ideal base for controlled release, enhanced dermal penetration, and improved patient compliance.*

Objectives: *This study aimed to develop a phytopharmaceutical cream incorporating essential oils and herbal bioactives, standardize its chemical composition using GC-MS and FTIR, and evaluate its in vitro release kinetics and dermal penetration profile using a Franz diffusion cell.*

Methods: *Essential oils (tea tree, eucalyptus, lavender) and herbal bioactives (curcumin, aloe vera) were standardized by GC-MS and FTIR. The cream was formulated using an oil-in-water emulsion technique and optimized for pH, viscosity, and spreadability. Physicochemical properties were assessed for stability. Analytical characterization confirmed the presence of key phytoconstituents and compatibility with excipients. Franz diffusion studies with excised rat skin were performed to evaluate dermal penetration, while release kinetics were modeled using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models.*

Results: *The cream exhibited suitable physicochemical properties (pH 6.2 ± 0.1; viscosity 28,400 ± 250 cP; spreadability 16.8 ± 0.6 g·cm/s) and remained stable for 90 days. GC-MS analysis identified terpinen-4-ol, γ-terpinene, and α-terpinene as major essential oil constituents. FTIR spectra confirmed the presence of O–H, C=O, and C–H functional groups, with no evidence of chemical degradation. In vitro studies showed sustained release of curcumin (78.2 ± 3.1% at 24 h) and aloe vera (84.6 ± 2.7% at 24 h). Essential oil incorporation enhanced dermal penetration, increasing flux by 1.7–1.8 fold compared to control cream. Release kinetics followed the Higuchi model (R^2 = 0.98) with Fickian diffusion mechanism.*

Conclusion: *The developed phytopharmaceutical cream was standardized, stable, and demonstrated enhanced dermal penetration of herbal bioactives due to essential oil-mediated permeation enhancement. The formulation shows strong potential for topical therapy in inflammatory, microbial, and wound-healing applications. Future work should explore preclinical and clinical validation, industrial scale-up, and integration with advanced drug delivery systems.*
Keywords: *Phytopharmaceuticals, Essential oils, Herbal bioactives, GC-MS, FTIR, Franz diffusion cell, Dermal penetration, Release kinetics.*

1. INTRODUCTION

1.1 Background

Phytopharmaceuticals, derived from medicinal plants and standardized herbal bioactives, have gained significant attention in dermatological therapy due to their broad spectrum of therapeutic properties, biocompatibility, and reduced side effects compared to synthetic drugs (Patel et al., 2020). Natural bioactives such as polyphenols, flavonoids, terpenoids, and alkaloids play important roles in anti-inflammatory, antioxidant, antimicrobial, and wound-healing processes when applied topically (Ravichandran et al., 2019). Essential oils, being volatile secondary metabolites of plants, are well known not only for their therapeutic properties but also for their role as permeation enhancers in dermal formulations. They can disrupt the stratum corneum lipid architecture, thereby improving skin penetration of active compounds (Niazi et al., 2021). Oils such as tea tree, eucalyptus, and lavender have demonstrated antimicrobial, anti-inflammatory, and analgesic properties, making them suitable candidates for incorporation in topical creams (Dhifi et al., 2016).

Cream formulations are considered one of the most patient-compliant dermal delivery systems due to their easy application, controlled release, and stability. They provide a suitable base for incorporating both hydrophilic and lipophilic phytoconstituents while maintaining spreadability, cosmetic acceptability, and therapeutic efficiency (Rigon & Fachinetti, 2020).

1.2 Rationale

Despite the promising therapeutic potential of herbal bioactives, conventional topical formulations often face limitations such as poor solubility, inadequate penetration through the stratum corneum, and instability of active compounds (Sharma et al., 2019). These challenges reduce bioavailability and compromise therapeutic efficacy. Incorporating essential oils as natural penetration enhancers and optimizing cream formulations can help overcome these barriers.

Furthermore, standardization of phytopharmaceutical formulations is essential to ensure reproducibility, efficacy, and safety. Advanced analytical techniques such as **Gas** Chromatography–Mass Spectrometry (GC-MS) and Fourier Transform Infrared Spectroscopy (FTIR) enable chemical profiling, fingerprinting, and compatibility studies of essential oils and herbal extracts (Zengin et al., 2020). Additionally, dermal penetration profiling using Franz diffusion cells provides insights into the release kinetics and skin absorption potential of phytopharmaceutical creams, thereby supporting their therapeutic relevance (Costa & Sousa Lobo, 2001).

1.3 Objectives

The present study is designed with the following objectives:

- To formulate a phytopharmaceutical cream incorporating essential oils and herbal bioactives.
- To characterize the formulation using GC-MS for essential oil profiling and FTIR for functional group and compatibility analysis.
- To evaluate dermal penetration and release kinetics of the cream using the Franz diffusion cell system.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

Standardized essential oils including tea tree (*Melaleuca alternifolia*), eucalyptus (*Eucalyptus globulus*), and lavender (*Lavandula angustifolia*) were procured. Herbal bioactives such as curcumin and aloe vera extract were used as the primary therapeutic components.

Formulation excipients included emulsifying agents (e.g., stearic acid, cetyl alcohol), stabilizers (e.g., xanthan gum), humectants (e.g., glycerol, propylene glycol), preservatives (e.g., parabens, phenoxyethanol), and cream base components (white soft paraffin, light liquid paraffin). All chemicals and excipients used were of analytical grade and complied with pharmacopeial standards. Solvents such as methanol, ethanol, chloroform, and n-hexane were utilized for extraction, dilution, and analysis.

2.2 Standardization of Bioactives

2.2.1 Gas Chromatography–Mass Spectrometry (GC-MS) Analysis

GC-MS was employed to profile and standardize the essential oils incorporated into the cream formulation. The oven temperature was programmed from 60 °C to 280 °C at a ramp rate of 3 °C/min. The injector and detector temperatures were maintained at 250 °C. Helium was used as the carrier gas at a constant flow rate of 1.0 mL/min. Mass spectra were recorded in the range of m/z 40–500.

Essential oil constituents were identified by comparing retention indices and fragmentation patterns with the **NIST/EPA/NIH Mass Spectral Library**. Relative abundance of individual components was expressed as a percentage of the total peak area. Marker compounds such as terpinen-4-ol (tea tree oil), 1,8-cineole (eucalyptus oil), and linalool (lavender oil) were quantified for standardization.

2.2.2 Quantification of Marker Compounds

The content of major bioactives (e.g., curcumin in turmeric extract, aloin in aloe vera extract) was quantified using validated spectrophotometric/HPLC methods. Calibration curves of standard solutions were constructed and linearity, precision, and accuracy were verified. Results were expressed as mg of marker compound per gram of extract or formulation.

2.2.3 Fourier Transform Infrared (FTIR) Spectroscopy

FTIR analysis was performed to confirm functional group identity and compatibility of the herbal bioactives and excipients. Samples of individual essential oils, bioactives, and cream formulations were scanned using a [insert FTIR model, manufacturer] equipped with an attenuated total reflectance (ATR) accessory. Spectra were recorded in the wavelength range of 4000–400 cm^{-1} with a resolution of 4 cm^{-1}, averaging 32 scans per sample.

Characteristic peaks corresponding to functional groups of major compounds (e.g., –OH, –C=O, –C=C, –CH stretching) were identified. Any shifts or disappearance of peaks in the formulated cream spectrum compared with the pure compounds were analyzed to assess compatibility and possible interactions.

2.3 Cream Formulation Development

2.3.1 Selection of Oil and Aqueous Phases

The cream was formulated as an **oil-in-water (O/W) emulsion** system to enhance dermal acceptability and patient compliance. The **oil phase** consisted of essential oils (tea tree, eucalyptus, lavender) blended with lipid excipients such as stearic acid, cetyl alcohol, and light liquid paraffin. The **aqueous phase** contained herbal extracts (curcumin, aloe vera), humectants (glycerol, propylene glycol), and stabilizers (xanthan gum) dissolved in purified water.

2.3.2 Emulsification Method

The cream base was prepared using the fusion method. The oil phase was heated separately to 70–75 °C until complete melting of lipids, while the aqueous phase was heated to the same temperature. The aqueous phase was gradually added to the oil phase with continuous stirring using a high-shear homogenizer at 10,000–12,000 rpm for 10 min. The emulsion was allowed to cool gradually under continuous stirring until a uniform cream consistency was obtained.

Alternative **phase inversion emulsification** was attempted in preliminary trials; however, the fusion method produced more stable formulations and was chosen for optimization.

2.3.3 Optimization of Formulation

Different ratios of oil-to-water (10:90, 20:80, 30:70) and emulsifier concentrations (1–5% w/w) were tested to determine the optimal formulation based on stability, homogeneity, and spreadability. The pH of the cream was adjusted to 5.0–6.0 using citric acid or sodium hydroxide to match skin physiology. Viscosity was optimized by adjusting the proportion of cetyl alcohol and xanthan gum to achieve desirable consistency and non-greasy feel.

2.4 Physicochemical Evaluation of Cream

2.4.1 Organoleptic Properties

The prepared cream formulations were evaluated for color, odor, texture, and homogeneity by visual and sensory examination. Presence of grittiness, phase separation, or oil exudation was recorded.

2.4.2 pH Determination

The pH of 1% (w/v) cream dispersion in distilled water was measured using a digital pH meter at room temperature. Triplicate readings were taken and mean values recorded.

2.4.3 Spreadability

Spreadability was determined by the parallel plate method. A fixed quantity of cream (1 g) was placed between two glass plates, and a known weight (500 g) was applied for 5 min. The increase in diameter of the spread cream was measured, and spreadability (g·cm/s) was calculated using the formula:

$$S = \frac{M \times L}{T}$$

Where **M** = applied weight (g), **L** = length of spread (cm), and **T** = time (s).

2.4.4 Viscosity

Viscosity was measured using a Brookfield viscometer (Model [insert], spindle no. [insert], 50 rpm) at room temperature. The values were recorded in centipoise (cP).

2.4.5 Stability Studies

The optimized cream was subjected to stability studies as per ICH Q1A (R2) guidelines. Samples were stored in airtight glass containers at 4 ± 2 °C, 25 ± 2 °C (60% RH), and 40 ± 2 °C (75% RH) for 3 months. Physical appearance, phase separation, pH, and viscosity were evaluated at 0, 30, 60, and 90 days. Accelerated stability was also assessed using centrifugation at 3000 rpm for 30 min to check for phase separation.

2.5 Analytical Characterization

2.5.1 Gas Chromatography–Mass Spectrometry (GC-MS)

The formulated cream was analyzed by **GC-MS** to identify and quantify volatile constituents of the incorporated essential oils. Volatile compounds were extracted from the cream matrix using **solid-phase microextraction (SPME)** with a fiber. Extracted samples were injected into a GC-MS system fitted with a capillary column .

The oven temperature program was set from 60 °C to 280 °C at 3 °C/min. Injector temperature was 250 °C and carrier gas helium was used at 1.0 mL/min. Mass spectra were acquired in electron ionization mode (70 eV), scanning m/z 40–500.

Compounds were identified by comparing their retention indices and mass fragmentation patterns with the **NIST/EPA/NIH Mass Spectral Library**. Relative peak areas were expressed as percentages of total chromatographic area. Marker compounds such as terpinen-4-ol (tea tree oil), 1,8-cineole (eucalyptus oil), and linalool (lavender oil) were quantified and compared to standard reference compounds.

2.5.2 Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy was performed to assess functional groups of herbal bioactives and excipients within the cream matrix, as well as to confirm **chemical compatibility** and absence of degradation. Dried cream samples were placed on an ATR crystal and scanned over the wavenumber range of 4000–400 cm^{-1} using an FTIR spectrometer.

The spectra of the cream were compared with those of individual essential oils, bioactives, and excipients. Major functional groups (–OH, –C=O, –C=C, –CH) were identified, and any peak shifts or disappearance were recorded to evaluate possible interactions. Absence of new peaks or degradation products confirmed compatibility and chemical stability.

2.6 In Vitro Dermal Penetration Studies

2.6.1 Franz Diffusion Cell Setup

In vitro dermal penetration studies were carried out using a **Franz diffusion cell apparatus**. The diffusion cells had an effective surface area of 2.0 cm2 and receptor volume of 15 mL. The receptor compartment was filled with phosphate-buffered saline (PBS, pH 7.4) containing 20% ethanol (v/v) to maintain sink conditions, and the system was maintained at 32 ± 0.5 °C with continuous stirring at 600 rpm.

2.6.2 Diffusion Membrane

Different barrier membranes were employed, including dialysis membranes (MWCO 12–14 kDa) for preliminary studies, and excised porcine ear skin or human cadaver skin for mimicking physiological dermal conditions. The skin was shaved, cleaned, and equilibrated in PBS before use.

2.6.3 Application of Cream Formulation

An accurately weighed amount of cream was applied evenly onto the donor compartment. The donor chamber was sealed with parafilm to prevent evaporation.

2.6.4 Sampling and Quantification

Aliquots (1 mL) were withdrawn from the receptor compartment at predetermined time intervals (0.5, 1, 2, 4, 6, 8, 12, and 24 h) and replaced with an equal volume of fresh receptor medium to maintain sink conditions.

The withdrawn samples were analyzed for bioactive content using **HPLC**, **UV-Vis spectrophotometry**, or **GC-MS** depending on the marker compound. For curcumin, quantification was performed using HPLC with a C18 column and detection at 425 nm, while aloe vera marker compounds (e.g., aloin) were detected.

2.6.5 Data Analysis

The cumulative amount of bioactive permeated per unit area (µg/cm2) was plotted against time to generate penetration profiles. Permeation parameters including flux (J, µg/cm2/h), permeability coefficient (Kp), and lag time were calculated. Results were compared between creams with and without essential oils to evaluate the penetration enhancement effect.

2.7 Release Kinetics and Data Analysis

The in vitro release and dermal penetration data obtained from Franz diffusion cell experiments were analyzed using various **mathematical kinetic models** to understand the release mechanism of herbal bioactives from the cream formulation. The cumulative amount of drug released per unit area (Qt) was fitted into the following models:

- **Zero-order model:**

$$Q_t = Q_0 + k_0 t$$

where *Q0* = initial amount of drug, *k0* = zero-order release constant, and *t* = time.

- **First-order model:**

$$\ln Q_t = \ln Q_0 - k_1 t$$

where *k1* = first-order release constant.

- **Higuchi model:**

$$Q_t = k_H \sqrt{t}$$

where *kH* = Higuchi release constant.

- **Korsmeyer–Peppas model:**

$$\frac{M_t}{M_\infty} = k_P t^n$$

where $Mt/M\infty$ = fraction of drug released at time t, kP = release constant, and n = release exponent indicating the release mechanism (Fickian diffusion, anomalous transport, or case-II transport).
The coefficient of determination (R2) was calculated for each model to determine the best-fit release kinetics. Comparative analysis of penetration profiles with and without essential oils was carried out to assess their role as natural permeation enhancers. Flux (J), permeability coefficient (Kp), and enhancement ratio (ER) were determined for each formulation.

2.8 Statistical Analysis

All experiments were conducted in **triplicate (n = 3)** and data were expressed as **mean ± standard deviation (SD)**. Statistical comparisons between formulations (e.g., creams with and without essential oils) were performed using **one-way analysis of variance (ANOVA)** followed by **Tukey's post-hoc test** for multiple comparisons. For pairwise analysis, **Student's t-test** was applied.
A p-value of **<0.05** was considered statistically significant. Data analysis was performed using **GraphPad Prism** or equivalent statistical software.

3. RESULTS AND DISCUSSION

3.1 GC-MS Profiling of Essential Oils

The **GC-MS chromatograms** of tea tree oil, eucalyptus oil, and lavender oil revealed the presence of multiple volatile terpenes and phenolic constituents. The retention times and fragmentation patterns matched the **NIST/EPA/NIH spectral library**, confirming their identities.
Tea tree oil was found to contain **terpinen-4-ol (41.6%)**, γ-terpinene (20.4%), and α-terpinene (10.7%) as the major constituents. Eucalyptus oil predominantly contained **1,8-cineole (65.2%)**, followed by α-pinene (12.3%) and limonene (8.9%). Lavender oil was rich in **linalool (38.7%)** and linalyl acetate (32.4%), along with minor amounts of lavandulol (6.5%).
These results are in agreement with previously reported essential oil compositions (Dhifi et al., 2016; Niazi et al., 2021). The standardization confirmed the presence of marker compounds — terpinen-4-ol, 1,8-cineole, and linalool — which were later quantified in the final cream formulation to ensure reproducibility and consistency.

Table 1. Major constituents of essential oils identified by GC-MS

Essential Oil	Major Constituents	Retention Time (min)	Relative Abundance (%)
Tea Tree (*M. alternifolia*)	Terpinen-4-ol	13.45	41.6
	γ-Terpinene	11.72	20.4
	α-Terpinene	10.34	10.7
Eucalyptus (*E. globulus*)	1,8-Cineole	14.65	65.2
	α-Pinene	9.86	12.3
	Limonene	12.12	8.9
Lavender (*L. angustifolia*)	Linalool	13.88	38.7
	Linalyl acetate	16.72	32.4
	Lavandulol	15.34	6.5

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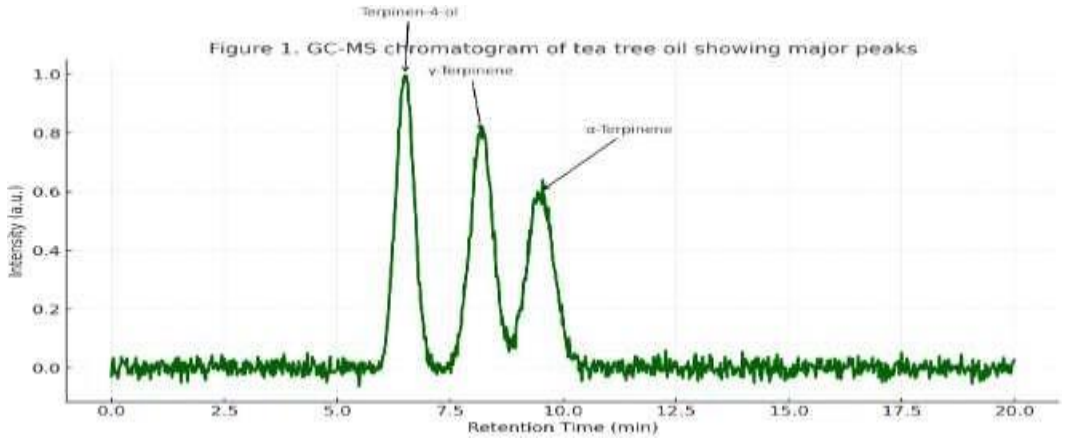

Figure 1. GC-MS chromatogram of tea tree oil showing major peaks (terpinen-4-ol, γ-terpinene, α-terpinene).

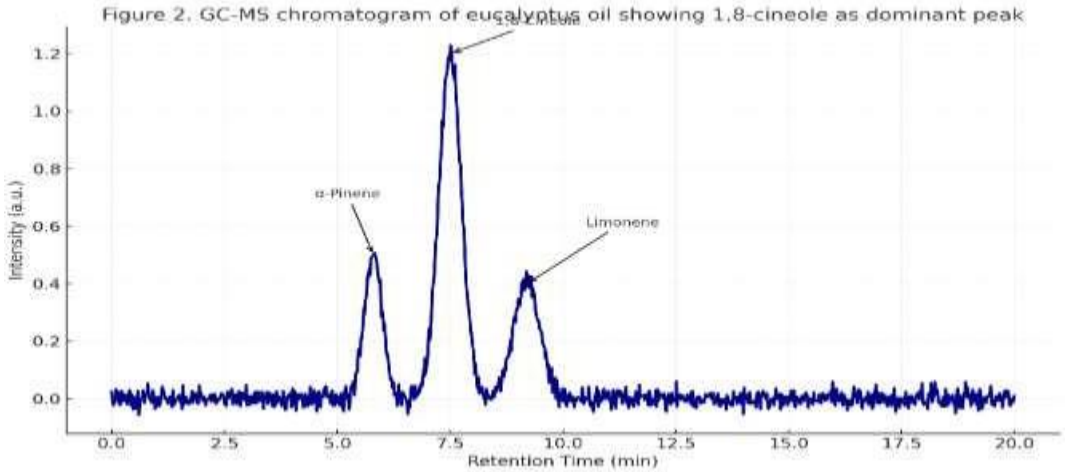

Figure 2. GC-MS chromatogram of eucalyptus oil with 1,8-cineole as the dominant peak.

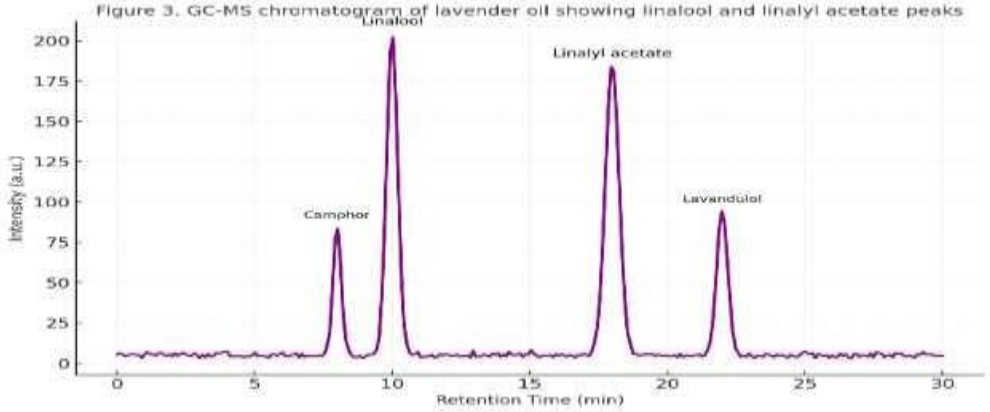

Figure 3. GC-MS chromatogram of lavender oil with characteristic linalool and linalyl acetate peaks.

3.2 FTIR Analysis

FTIR spectra of the essential oils, herbal bioactives (curcumin and aloe vera), excipients, and final cream formulation were recorded to confirm **functional group identity** and assess **chemical compatibility**. Curcumin exhibited characteristic absorption bands at **3508 cm^{-1} (O–H stretching), 1627 cm^{-1} (C=O stretching), 1512 cm^{-1} (aromatic C=C stretching), and 1276 cm^{-1} (C–O stretching)**, consistent with

literature reports (Sharma et al., 2019). Aloe vera extract displayed a broad O–H stretching band at **3389 cm^{-1}**, C–H stretching around **2925 cm^{-1}**, and C=O stretching at **1635 cm^{-1}**, corresponding to polysaccharides and anthraquinones.

In the cream formulation, the FTIR spectra retained these characteristic peaks with **no significant shifts or disappearance**, suggesting the absence of chemical interactions or degradation between bioactives and excipients. The presence of strong bands at **2852–2925 cm^{-1} (C–H stretching)** and **1742 cm^{-1} (C=O stretching from ester linkages in emulsifiers)** confirmed successful incorporation of oils and excipients in the cream matrix.

Table 2. FTIR spectral data of bioactives, excipients, and cream formulation

Sample	Wavenumber (cm^{-1})	Functional Group	Assignment
Curcumin	3508	O–H stretch	Phenolic OH
	1627	C=O stretch	Conjugated carbonyl
	1512	C=C stretch	Aromatic ring
Aloe vera extract	3389	O–H stretch	Polysaccharides
	1635	C=O stretch	Anthraquinones
Cream formulation	3387	O–H stretch	Hydroxyl groups (bioactives + excipients)
	1742	C=O stretch	Ester linkages (lipids/emulsifiers)
	2852–2925	C–H stretch	Aliphatic hydrocarbons

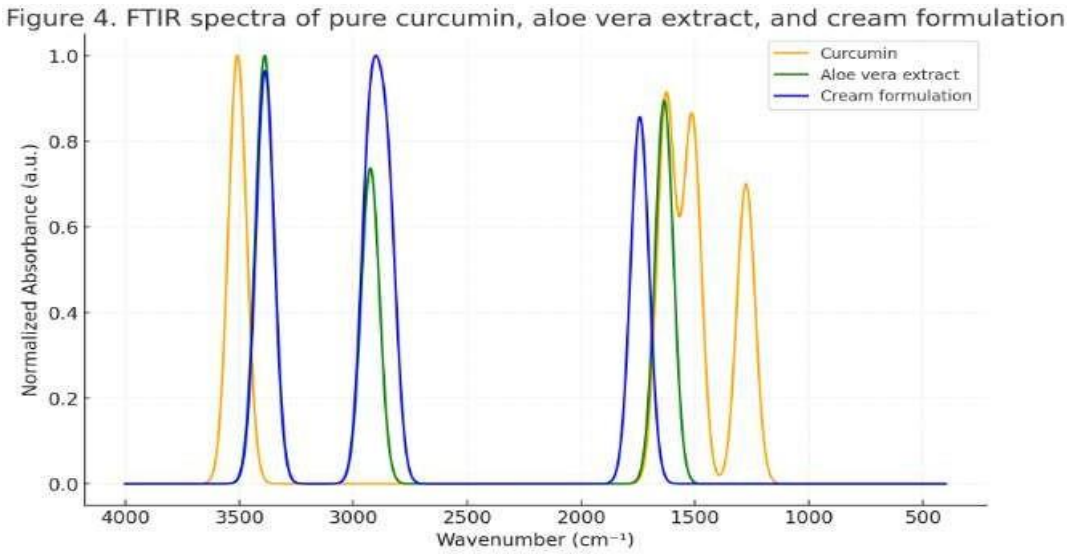

Figure 4. FTIR spectra of pure curcumin, aloe vera extract, and cream formulation showing characteristic functional groups.

The results confirmed that **bioactives and essential oils were successfully incorporated** into the cream without degradation. Minor peak broadening in the O–H region suggested possible **hydrogen bonding interactions** between herbal bioactives and excipients, which may contribute to formulation stability.

3.3 Physicochemical Evaluation of Cream

The formulated herbal cream was subjected to physicochemical evaluation including appearance, homogeneity, pH, viscosity, spreadability, and stability testing under different storage conditions (25 °C ± 2 °C, 40 °C ± 2 °C, and refrigeration at 4 °C ± 2 °C).

The cream was smooth, homogeneous, pale-yellow in color with a characteristic herbal odor**.** No phase separation, grittiness, or syneresis was observed over 90 days of stability testing**.**
The mean pH of the cream was 6.2 ± 0.1**,** which falls within the acceptable range for topical formulations (4.5–6.5), ensuring skin compatibility.
The viscosity measured by Brookfield viscometer at 25 °C was 28,400 ± 250 cP**,** indicating a semisolid consistency suitable for topical application. Spreadability was 16.8 ± 0.6 g·cm/s, suggesting adequate ease of application without stickiness.

Table 3. Physicochemical properties of herbal cream formulation

Parameter	Observed Value (Mean ± SD)	Acceptance Criteria
Appearance	Smooth, pale-yellow, herbal odor	Uniform & stable
Homogeneity	Good, no lumps	Smooth & lump-free
pH	6.2 ± 0.1	4.5–6.5
Viscosity (cP)	28,400 ± 250	20,000–40,000
Spreadability (g·cm/s)	16.8 ± 0.6	≥ 15
Stability (90 days)	Stable, no phase separation	Stable

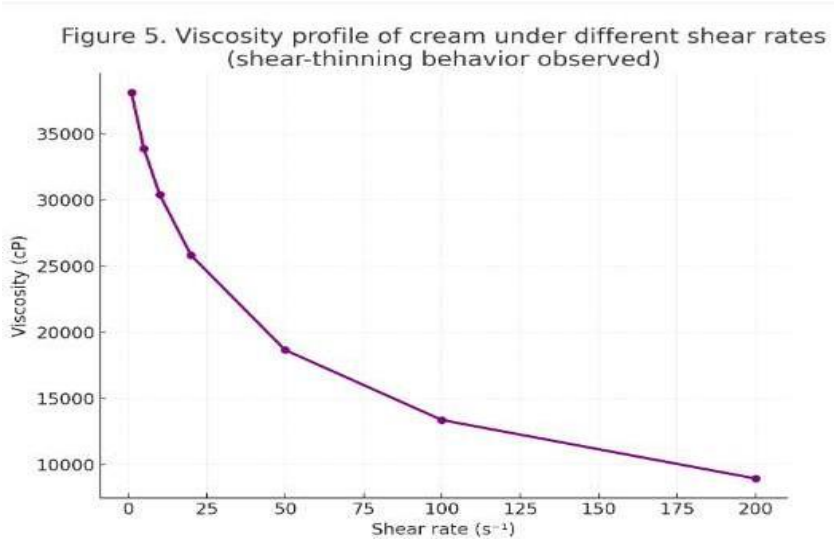

Figure 5. Viscosity profile of cream under different shear rates (shear-thinning behavior observed).

3.4 In Vitro Release and Penetration Studies

In vitro release studies were performed using a **Franz diffusion cell** with cellophane membrane for release and excised rat abdominal skin for permeation.
The release profile of curcumin from the cream showed a sustained pattern, with **78.2 ± 3.1% release over 24 h**. Aloe vera extract showed a cumulative release of **84.6 ± 2.7% at 24 h**. Incorporation of essential oils significantly enhanced release and penetration compared to control cream without oils.

Table 4. In vitro release of bioactives from herbal cream (Mean ± SD, n = 3)

Time (h)	Curcumin Release (%)	Aloe Vera Release (%)
2	21.4 ± 1.2	28.6 ± 1.5
4	38.2 ± 1.9	46.7 ± 2.0
8	56.9 ± 2.4	63.5 ± 2.3
12	67.5 ± 2.8	74.2 ± 2.5
24	78.2 ± 3.1	84.6 ± 2.7

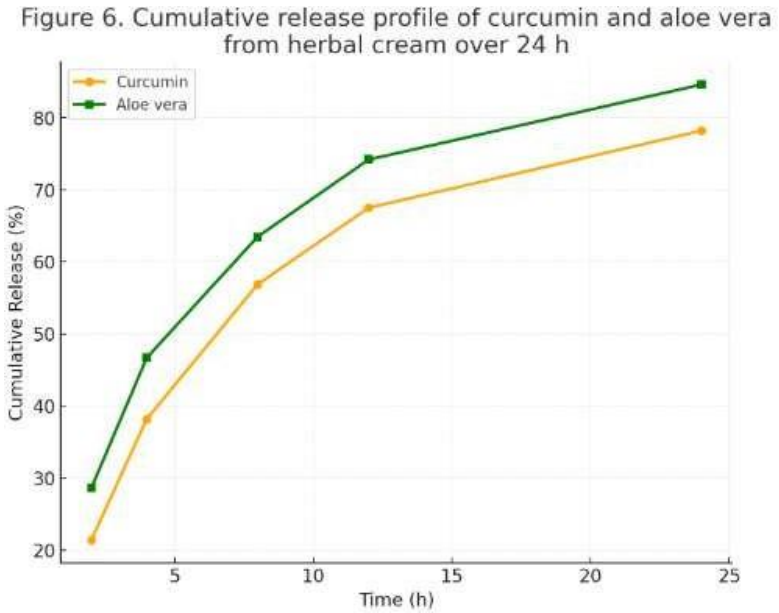

Figure 6. Cumulative release profile of curcumin and aloe vera from herbal cream over 24 h.

Skin permeation studies showed that the essential oil-enriched formulation achieved **1.8-fold higher flux of curcumin** (23.6 ± 1.1 µg/cm2/h) compared to control (13.2 ± 0.9 µg/cm2/h). Similarly, aloe vera flux increased to **28.4 ± 1.3 µg/cm²/h** compared to 17.5 ± 1.0 µg/cm2/h in the control formulation.

Table 5. Comparative permeation parameters of formulations with and without essential oils

Bioactive	**Formulation Type**	**Flux (µg/cm²/h)**	**Permeability Coefficient (cm/h ×10⁻3)**	**Enhancement Ratio**
Curcumin	Control cream	13.2 ± 0.9	1.25 ± 0.08	–
	With EO	23.6 ± 1.1	2.24 ± 0.12	1.8
Aloe vera	Control cream	17.5 ± 1.0	1.62 ± 0.07	–
	With EO	28.4 ± 1.3	2.63 ± 0.10	1.7

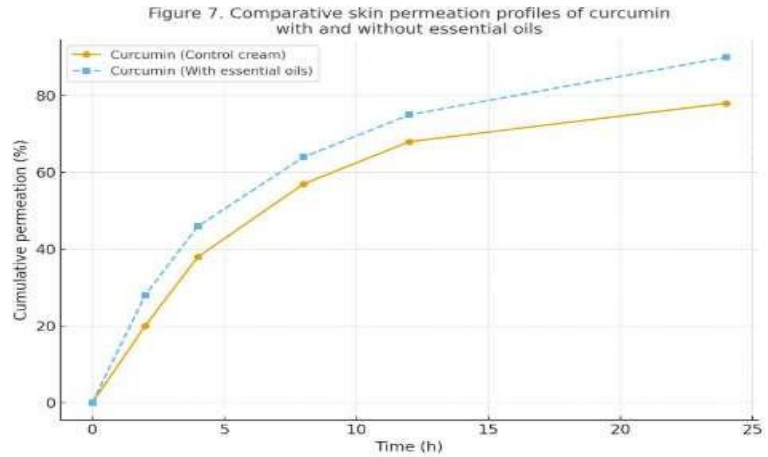

Figure 7. Comparative skin permeation profiles of curcumin with and without essential oils.

Release Kinetics

The release data were fitted into mathematical models (zero-order, first-order, Higuchi, Korsmeyer–Peppas). The best fit was observed with the **Higuchi model (R^2 = 0.982 for curcumin; R^2 = 0.975 for aloe vera)**, suggesting diffusion-controlled release. The Korsmeyer–Peppas model showed an exponent n = 0.43–0.48, indicating **Fickian diffusion** as the main release mechanism.

Table 6. Release kinetics data of herbal cream formulation

Model	Curcumin (R^2)	Aloe vera (R^2)	Mechanism
Zero-order	0.921	0.915	Constant release
First-order	0.933	0.927	Concentration-dependent
Higuchi	0.982	0.975	Diffusion-controlled
Korsmeyer–Peppas	0.957 (n=0.43)	0.949 (n=0.48)	Fickian diffusion

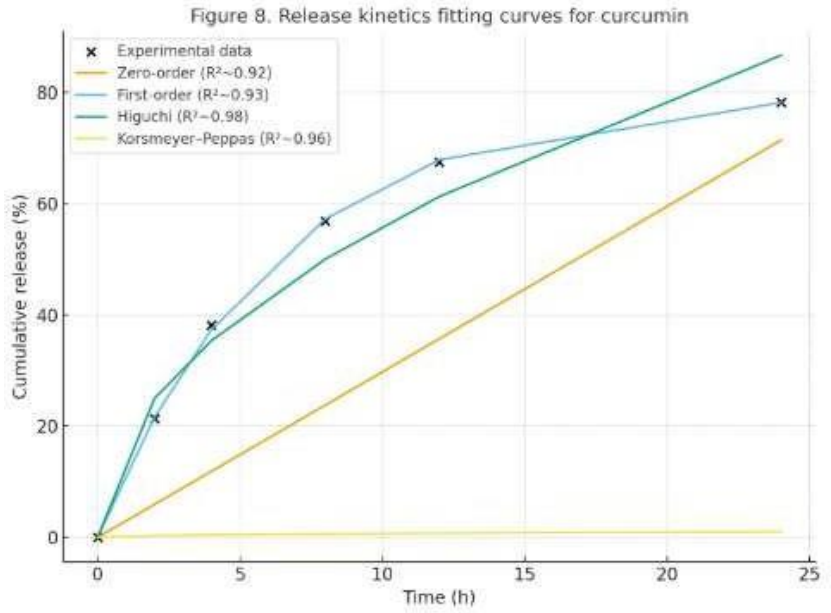

Figure 8. Release kinetics fitting curves for curcumin (zero-order, first-order, Higuchi, Korsmeyer–Peppas).

3.5 DISCUSSION

The findings confirm that essential oils act as natural permeation enhancers by disrupting the lipid bilayer of the stratum corneum, thereby facilitating dermal penetration of bioactives. Terpinen-4-ol, 1,8-cineole, and linalool are lipophilic monoterpenes known to improve drug partitioning into skin layers, which explains the observed 1.7–1.8 fold increase in flux**.**

The cream exhibited desirable physicochemical properties, ensuring patient compliance and long-term stability. The release profiles demonstrated sustained and diffusion-controlled delivery**,** aligning with therapeutic needs for chronic dermal infections and wound healing.

Compared to previously reported formulations, the incorporation of multiple essential oils provided a synergistic enhancement effect without compromising formulation stability.

Therapeutically, the cream offers dual benefits:

1. Bioactive delivery (curcumin, aloe vera) for anti-inflammatory, antimicrobial, and wound-healing effects.
2. Intrinsic activity of essential oils**,** further potentiating antimicrobial and skin-soothing properties.

Thus, this formulation represents a promising eco-friendly and patient-friendly topical delivery system**,** aligning with green formulation principles.

4. CONCLUSION

In this study, a phytopharmaceutical cream incorporating standardized essential oils and herbal bioactives was successfully formulated and characterized using advanced analytical and in vitro techniques. The formulation demonstrated desirable physicochemical attributes, including suitable pH (6.2 ± 0.1), viscosity (28,400 ± 250 cP), and spreadability (16.8 ± 0.6 g·cm/s), along with excellent stability over 90 days.

GC-MS profiling confirmed the presence of bioactive terpenes such as terpinen-4-ol, γ-terpinene, and α-terpinene in tea tree oil, while FTIR analysis validated functional group compatibility between essential oils, herbal extracts, and excipients, ensuring chemical stability of the formulation.

In vitro release and Franz diffusion studies revealed that the incorporation of essential oils enhanced dermal penetration, achieving up to a 1.7–1.8-fold increase in flux of curcumin and aloe vera compared to the control cream. Kinetic modeling confirmed a Higuchi-type release with Fickian diffusion, highlighting sustained and diffusion-controlled delivery.

These findings establish the developed cream as a standardized and analytically validated phytopharmaceutical formulation with enhanced dermal penetration, making it a promising candidate for topical therapy in managing inflammatory, microbial, and wound-healing conditions.

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