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Research article

# Enhancement of wound healing potential of *Fagonia cretica* and curcumin-loaded phytosomal gel: Characterization and in-vivo evaluation

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ABSTRACT

Fagonia cretica L. is a medicinal plant rich in flavonoids, phenolics, saponins, and other bioactive compounds with significant therapeutic potential. The present study aimed to develop and characterize phytosomes of Fagonia cretica extract and curcumin to enhance the stability, bioavailability, and therapeutic efficacy of their bioactive constituents. Phytosomes were prepared using the thin-film hydration method with soya lecithin as a phospholipid carrier and characterized for particle size, zeta potential, and entrapment efficiency. The phytosomal formulations were incorporated into a topical gel and evaluated for physicochemical properties and in vitro drug-release behavior. The wound-healing potential of the developed gel was assessed using an excision wound model in Wistar rats. The phytosomal gel exhibited good stability, uniform particle distribution, and sustained-release characteristics. Furthermore, it demonstrated enhanced wound contraction, shortened epithelialization period, and improved tissue regeneration compared with the conventional extract gel. The findings suggest that phytosomal delivery of Fagonia cretica extract and curcumin represent a promising strategy for improving their therapeutic performance and pharmaceutical applications in wound management.

## 1. Introduction

*Fagonia cretica* L. is a small spiny perennial herb belonging to the family Zygophyllaceae [1]. The plant is widely distributed in arid and semi-arid regions of Asia, Africa and Mediterranean countries [2]. The plant has been extensively used in traditional system of medicine for the treatment of wounds, ulcers, skin diseases, tumors, fever, dropsy, inflammation, diabetes and any disorder which arises from poisoning [1].

*Fagonia cretica* contains several bioactive phytoconstituents, including flavonoids, saponins, phenolic compounds, alkaloids and terpenoids [3]. These compounds exhibit a wide range of pharmacological activities such as antioxidant, anti-inflammatory, anti-microbial, tissue-protective, anti-allergic and neuroprotective effect. The presence of these biologically active constituents contributes significantly to the therapeutic potential of *Fagonia cretica* and supports its traditional use in the treatment of wounds and various inflammatory disorders. [4] However, the therapeutic effectiveness of these phytoconstituents may be limited due to poor stability, low permeability and inadequate bioavailability.

Poor bioavailability is a major challenge in the development of phytochemicals as therapeutic agents. Several naturally occurring compounds demonstrate promising pharmacological activities but their clinical and therapeutic utilization is restricted by poor solubility, limited absorption, rapid metabolism and low systemic or tissue availability. Therefore, various bio enhancement approaches, including nanocarrier-based drug delivery systems, have been investigated to improve the solubility, stability, permeability and bioavailability of poorly bioavailable phytochemicals. In particular, nanocarrier systems have demonstrated considerable potential for improving the delivery of phytochemicals such as curcumin, quercetin and resveratrol [5]. Curcumin is a well-known example of a poorly bioavailable phytochemical, despite possessing significant antioxidant, anti-inflammatory and wound-healing properties. Its therapeutic application is restricted mainly because of its poor aqueous solubility, low absorption, and rapid metabolism [6].

Therefore, the development of advanced drug delivery systems is essential to enhance the utilization of these bioactive compounds. Phytosome technology has emerged as an effective phospholipid-based approach for improving the delivery of plant-derived constituents. Phytosomes are molecular complexes in which phytoconstituents are associated with phospholipids, resulting in improved lipid affinity,

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stability, membrane interaction, absorption, and bioavailability [7]. The phytosomal approach is particularly useful for phytochemicals having poor solubility and permeability and may overcome some of the limitations associated with conventional delivery systems.

In the present study, Fagonia cretica extract and Curcumin are incorporated into the phytosomal delivery system with the objective of enhancing the stability, delivery, and therapeutic availability of their bioactive constituents. Fagonia cretica provides a complex combination of flavonoids, phenolics, saponins and other phytoconstituents possessing antioxidant, anti-inflammatory and tissue-protective activities, whereas Curcumin is a well-characterized bioactive compound with potent antioxidant and anti-inflammatory properties relevant to wound healing [3,4,6]. The combination of these two natural bioactive sources is therefore expected to provide complementary pharmacological effects and potentially a greater wound-healing response than either component alone. The phytosomal system is expected to improve the delivery of these poorly bioavailable constituents and increase their availability at the target site.

The phytosomes of Fagonia cretica extract and Curcumin are prepared separately and subsequently incorporated together into the topical gel to allow appropriate optimization of the delivery characteristics of each bioactive component according to its individual physicochemical properties. Fagonia cretica is a chemically complex plant extract containing numerous phytoconstituents, whereas Curcumin is a defined, highly lipophilic compound with different physicochemical and complexation characteristics. Separate phytosomal preparation therefore provides better control over the formulation and optimization of each component before their incorporation into the final combined formulation. The subsequent combination of the optimized phytosomes is expected to provide complementary antioxidant and anti-inflammatory effects while improving the delivery of both bioactive components.

Furthermore, incorporation of the phytosomal formulation into a topical gel may provide prolonged retention at the wound site, improved skin interaction and sustained release of the active compounds [8]. The combined action of Fagonia cretica phytoconstituents and Curcumin may accelerate wound contraction, promote collagen synthesis and deposition, enhance epithelialization, reduce excessive inflammation and oxidative stress, and facilitate overall tissue regeneration. Thus, the proposed formulation combines phytochemical bioenhancement through phytosomal technology with localized topical delivery, providing a rational approach for improving the therapeutic potential of poorly bioavailable natural compounds in wound management.

The aim of the study is to improve the stability and delivery of Fagonia cretica extract and Curcumin by entrapping them into phytosomal systems and subsequently incorporating the optimized phytosomes into a topical gel formulation. The study further involves characterization of the phytosomes, evaluation of their physicochemical properties and assessment of the wound-healing activity of the developed formulation using an excision wound model.

## 2. Materials and method

### 2.1. Materials

All chemicals and reagents used in the study were of analytical reagent (AR) grade. Curcumin was procured from Orgonexus Biochemira Pvt. Ltd., Satara, India, while soya lecithin was obtained from Urban Platter, Mumbai, India. Tocopherol was procured from Hollywood Secrets, Panaji, Goa, India. The solvents used, including ethanol and methanol, were of AR grade and were utilized without further purification.

### 2.2. Plant material

The aerial parts of Fagonia cretica were collected from the Devrai (Botanical Garden) of Amolak College, Kada, Tal. Ashti, Dist. Beed, Maharashtra, India. The collected plant material was identified and authenticated by **Dr. S. S. Patale**, Department of Botany, Amolak College, Kada, Maharashtra, India. A voucher specimen was deposited for future reference. (Voucher specimen No.: GC/2026/04)

### 2.3. Pharmacognostic evaluation of Fagonia cretica

The powdered aerial parts of Fagonia cretica were evaluated for organoleptic characteristics including color, odor, taste, texture, and appearance. Physicochemical parameters such as total ash, acid-insoluble ash, water-soluble ash, alcohol-soluble extractive value, water-soluble extractive value, and loss on drying were determined according to standard pharmacognostic and pharmacopoeial procedures


**Fig. 1.** Parts of Fagonia.

[8,9].

### 2.4. Characterization of curcumin

Curcumin was characterized by UV–Visible spectroscopy, Fourier Transform Infrared (FTIR) spectroscopy, and melting point determination. The UV spectrum was recorded using a UV–Visible spectrophotometer (Shimadzu UV-1900i) in methanol, and the maximum absorption wavelength (λmax) was observed at 420–425 nm. FTIR analysis was performed using an FTIR spectrophotometer (Shimadzu 8400S) to identify characteristic functional groups. The melting point of curcumin was determined using a digital melting point apparatus to assess its purity and identity [10].

### 2.5. Preparation of hydroalcoholic extract of Fagonia cretica

The aerial parts of Fagonia cretica were washed, shade-dried, powdered, and passed through sieve No. 40. The powdered material (100 g) was defatted with petroleum ether and dried at room temperature. The defatted powder was subjected to maceration using a hydroalcoholic solvent (Ethanol: Water, 70:30 v/v) for 72 h at room temperature with intermittent shaking. The extract was filtered through Whatman filter paper and concentrated at 40°C to obtain a dry extract. The dried extract was weighed, and the percentage yield was calculated. The obtained extract was stored in an airtight amber-coloured container at 4°C until further use [11].

### 2.6. Preliminary phytochemical screening

The hydroalcoholic extract of Fagonia cretica was subjected to preliminary phytochemical screening using standard qualitative methods to identify the presence of major secondary metabolites, including alkaloids, flavonoids, tannins, saponins, and phenolic compounds. Alkaloids were detected using Dragendorff's, Wagner's, Mayer's, and Hager's tests; flavonoids by Shinoda and alkaline reagent tests; tannins by ferric chloride and gelatin tests; saponins by the foam test; and phenolic compounds by ferric chloride and lead acetate tests. The results were interpreted based on characteristic color changes or precipitate formation as described in standard phytochemical screening procedures [12].

### 2.7. Preparation and optimization of phytosomes

Phytosomes of *Fagonia cretica* extract and curcumin were prepared separately by the thin-film hydration method using soya lecithin as a phospholipid carrier and tocopherol as an antioxidant. Briefly, soya lecithin and tocopherol were dissolved in ethanol, while *Fagonia cretica* extract or curcumin was dissolved separately in ethanol. The respective solutions were mixed and stirred at 40–45°C to facilitate phytoconstituent–phospholipid complex formation. The organic solvent was evaporated to form a thin lipid film, which was subsequently dried and desiccated to remove residual solvent. The resulting film was hydrated with phosphate buffer (pH 7.4) under continuous stirring at 40°C to obtain phytosomal suspensions. Various formulation batches were prepared by varying the concentration of soya lecithin. The prepared phytosomes were characterized for particle size, zeta potential, and entrapment efficiency. Based on the evaluation results, the optimized *Fagonia* phytosome and curcumin phytosome formulations were selected for incorporation into the topical gel formulation for wound-healing studies [13–16].

### 2.8. Characterization of phytosomes

The prepared Fagonia and curcumin phytosomes were characterized for particle size, polydispersity index (PDI), zeta potential, and entrapment efficiency.

Particle size, PDI, and zeta potential were determined using a dynamic light scattering (DLS)-based nanoparticle analyzer (Microtrac, AICTE-MODROB). Measurements were performed at room temperature in triplicate, and the results were expressed as mean ± SD. Particle size analysis was carried out to determine the average vesicle diameter, while PDI was used to assess the uniformity of particle size distribution. Zeta potential was measured to evaluate the surface charge and physical stability of the phytosomal vesicles. [17]

Entrapment efficiency (EE) was determined by the centrifugation method. Briefly, the phytosomal dispersion was centrifuged at 15,000 rpm for 30 min to separate the unentrapped drug. The concentration of free drug present in the supernatant was quantified using a UV–Visible spectrophotometer at the respective λmax. [18] The entrapment efficiency was calculated using the following equation:

$$\%EE = \frac{Total\ \ Drug - DRUG}{Total\ \ TOtal} \times 100$$

The optimized phytosomal formulations were selected based on particle size, PDI, zeta potential, and entrapment efficiency values.

### 2.9. Formulation of Fagonia–Curcumin phytosomal gel (FCPG)

The Fagonia–Curcumin phytosomal gel (FCPG) was prepared by incorporating the optimized batches of *Fagonia cretica* phytosomes and curcumin phytosomes into a Carbopol 934 gel base for topical wound-healing application.

**Table 1**
Formulation table of *Fagonia cretica* Phytosomes.

| Sr.no. | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| **Curcumin and soya lecitin Ratio** | 1:0.5 | 1:1 | 1:1.5 | 1:2 | 1:2.5 |
| **Curcumin** | 300 mg | 300 mg | 300 mg | 300 mg | 300 mg |
| **Soya lecitin** | 150 mg | 300 mg | 450 mg | 600 mg | 750 mg |
| **Tocopherol** | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |


**Fig. 2.** Preparation of fagonia extract.

**Table 2**
Formulation table of curcumin phytosomes.

| Sr.no. | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| ***Fagonia cretica* extract and soya lecitin ratio** | 1:0.5 | 1:1 | 1:1.5 | 1:2 | 1:2.5 |
| **Fagonia cretica extract** | 1 g | 1 g | 1 g | 1 g | 1 g |
| **Soya lecitin** | 0.5 g | 1 g | 1.5 g | 2 g | 2.5 g |
| **Tocopherol** | 20 mg | 20 mg | 20 mg | 20 mg | 20 mg |

#### 2.9.1. Preparation procedure

- Carbopol 934 was dispersed in distilled water under continuous stirring and allowed to hydrate completely to form a clear gel base.
- Methyl paraben and propyl paraben were dissolved in propylene glycol and incorporated into the gel base with continuous stirring.
- The optimized Fagonia cretica phytosomes and curcumin phytosomes were uniformly mixed and gradually added to the prepared gel base.
- Propylene glycol was added to improve the consistency and skin penetration characteristics of the formulation.
- The pH of the gel was adjusted using triethanolamine until a smooth and homogeneous gel was obtained.
- The prepared FCPG was transferred into suitable containers and stored for further evaluation studies. [19]

### 2.10. Evaluation of Fagonia–Curcumin phytosomal gel (FCPG)

- Appearance
  The prepared gel was visually examined for color, homogeneity, consistency, smooth texture, and absence of grittiness or phase separation.
- **PH**
  The pH was measured using a digital pH meter to ensure compatibility with normal skin pH [20].
- Viscosity
  The viscosity was determined using a Brookfield Viscometer to evaluate the consistency and ease of application of the gel [21, 22].
- **Spreadability** [23]
  Spreadability was evaluated by the glass slide method, and the ease of spreading was calculated using the formula:
  Where:
  **S** = Spreadability
  **M** = Weight applied
  **L** = Distance moved by the glass slide
  **T** = Time taken by the upper slide to move
- In Vitro Drug Release Study
  The in-vitro release of curcumin from the phytosomal gel was evaluated using a Franz diffusion cell equipped with a dialysis membrane (12–14 kDa molecular-weight cut-off) having an effective diffusion area of approximately 1.77 $cm^2$. The receptor compartment, containing 12 mL of phosphate buffer (pH 7.4), was maintained at 37 ± 0.5 °C and continuously stirred at 50 rpm. A predetermined quantity of phytosomal gel was uniformly placed in the donor compartment over the pre-soaked dialysis membrane. At predetermined intervals (1, 2, 4, 6, 8, 10 and 12 h), 1 mL of receptor medium was withdrawn and immediately replaced with an equal volume of fresh phosphate buffer to maintain a constant receptor volume and sink conditions. The samples were suitably diluted and analyzed using a UV–Visible spectrophotometer at the experimentally determined λmax of curcumin. The concentration of curcumin was determined using a previously established calibration curve. The cumulative amount and cumulative percentage of curcumin released were calculated after correcting for the withdrawn and replaced receptor medium and plotted against time [24].
- Rheological Study

**Table 3**
Formulation table of Fagonia - Curcumin Phytosomal Gel.

| Sr. No. | Ingredients | Quantity for 50 g of gel | Function |
|---|---|---|---|
| 1 | Optimized Fagonia phytosomes | 3 g | Active |
| 2 | Optimized Curcumin phytosomes | 1 g | Active |
| 3 | Carbopol 934 | 1 g | Gelling agent |
| 4 | Propylene glycol | 5 g | Penetration enhancer |
| 5 | Methyl paraben | 0.1 g | Preservative |
| 6 | Propyl paraben | 0.01 g | Preservative |
| 7 | Triethanolamine | q.s. | pH adjustment |
| 8 | Distilled water | q.s. | Vehicle |

The rheological properties of the FCPG were evaluated using a rotational viscometer at 25 ± 1°C. Viscosity was measured at different shear rates to determine the flow behavior of the gel. The study was performed to evaluate the consistency, stability, spreadability, and ease of topical application of the formulation.

### 2.11. Assessment of wound healing activity [25,26]

To evaluate the wound healing activity of the prepared formulation, the excision wound model was selected for the present study. The excision wound model is one of the most commonly used experimental methods for assessing wound healing because it allows easy measurement of wound contraction and epithelialization period. In this model, a circular or rectangular portion of the skin is surgically removed under aseptic conditions to create a full-thickness wound. The rate of wound closure is then monitored periodically until complete healing occurs.

The excision wound model was preferred because it provides reliable and reproducible results regarding wound contraction, tissue regeneration, and re-epithelialization. It is especially useful for evaluating topical formulations such as gels and creams, as the healing progress can be visually observed and measured accurately over time.

To evaluate the wound healing efficacy of FCPG containing curcumin and Fagonia extract using the excision wound model and compare it with a Fagonia-curcumin extract gel (FCEG) containing curcumin and Fagonia extract without phytosomal incorporation.

#### 2.11.1. Test system and management

*2.11.1.1. Animal welfare.* All procedures such as Housing, dosing, Sacrifice, rehabilitation was done in accordance with the standard operating procedures and the guidelines provided by the Committee for the Control and Supervision of Experiments on Animals (CCSEA) as published in The Gazette of India, December 15, 1998 and Biological evaluation of medical devices- Part 2: Animal welfare requirements. Study has been approved in Institutional Animal Ethics Committee meeting of Invitox R & D Institute.

**Table 4**
Experimental grouping of Animals.

| Group | Type of Group | Treatment |
|---|---|---|
| Group I | Control | No treatment |
| Group II | Negative Control | Gel base (placebo) |
| Group III | Standard | Standard drug (e.g., Povidone iodine) |
| Group IV | Sample 1 | FCEG |
| Group V | Sample 2 | FCPG |

**Table 5**
Test System.

| Parameter | Details |
|---|---|
| Species | Albino Wister rats. |
| Source | Crystal Biological Solutions, Pune |
| Sex | Male |
| Weight Range | 180–220 g |
| Number of Animals | 30 |
| Housing | Polycarbonate cages, standard laboratory conditions |
| Acclimatization | Minimum 5 days before dosing |
| Ethics Approval | IRDA/IAEC/M05/ 96/2025–26 |

**Table 6**
Environmental conditions.

| | |
|---|---|
| **Room temperature** | 22–23 °C |
| **Accommodation** | Six Rats in single cage |
| **Diet** | Pelleted feed supplied by Nutrivet Pvt. Ltd. ad libitum during the study. |
| **Water** | RO filtered water was provided ad libitum |

**Table 7**
Animal Husbandry.

| | |
|---|---|
| **Environmental conditions** | Temperature of experimental area maintained between 22 ± 2 °C, relative humidity 55 ± 5% and illumination cycle set to 12 h light and 12 h dark |
| **Accommodation** | Six animal per cage housed in polypropylene cage and Stainless-steel cage top with facilities for food and water bottle, and bedding of clean paddy husk. |
| **Diet** | Commercial Pelleted food supplied by Nutrivet Pvt. Ltd., Pune, was provided *ad libitum* during acclimatization and during the study. |
| **Water** | Potable water passed through 'RO Unit' provided *ad libitum* in Polypropylene bottles with stainless steel sipper tubes. |

*2.11.1.2. Animal acclimatization.* 30 Albino Rats were selected and allowed to acclimatize for period of 07 days prior to dosing. During this period, animals were observed daily for clinical signs. All animal met the health and weight criteria.

*2.11.1.3. Study design.* A total of 30 Wistar albino rats were used in the study and divided into four groups (n = 6 per group). Animals were maintained under standard laboratory conditions.

The study was designed to evaluate the wound healing potential of the prepared gel formulation using an excision wound model. Initially, animals were acclimatized and the dorsal fur was removed under light anaesthesia. A full-thickness circular excision wound was created on the dorsal region of each animal using sterile surgical instruments.

After wound induction, animals were treated as per their respective groups, including normal control, gel base (negative control), standard treatment (e.g., povidone iodine/silver sulfadiazine), and test formulation. The formulations were applied topically once daily throughout the experimental period.

At the end of the study, wound healing was assessed based on parameters such as percentage wound contraction, epithelialization period, and histopathological observations. The results were recorded and compared among different groups to evaluate the effectiveness of the test formulation.

*2.11.1.4. Experimental animals.* Healthy adult Albino Wister rats (either sex), weighing between 180–200 g, were used for the study. The animals were housed in clean polypropylene cages with standard laboratory conditions of 12-hour light/dark cycle, room temperature (22 ± 2°C), and relative humidity (55 ± 5%). They were allowed free access to a standard pellet diet and clean water ad libitum. The study was conducted as per guidelines of the OECD and approved by the Institutional Animal Ethics Committee (IAEC).

*2.11.2. Determination of epithelialization period*

The epithelialization period was determined in the excision wound model by observing the wound area daily after topical application of the respective treatments. The wounds were carefully examined for the formation and subsequent falling of the scab (eschar).

The number of days required for complete covering of the wound surface with new epithelial tissue, without any residual raw wound, was recorded as the epithelialization period. Shorter epithelialization time was considered indicative of better wound healing activity of the test formulation.

*2.11.3. Hydroxyproline estimation*

Hydroxyproline estimation is an important biochemical parameter used in the assessment of wound healing activity because hydroxyproline is a major constituent of collagen. Increased hydroxyproline content indicates enhanced collagen synthesis, which reflects improved tissue repair and wound healing.

*2.11.3.1. Procedure for estimation of hydroxyproline.* Granulation tissue collected from the experimental animals was dried in a hot air oven at 60 °C until a constant weight was obtained. The dried tissue was accurately weighed and hydrolysed with 6 N hydrochloric acid (HCl) in sealed tubes at 110 °C for 24 h.

After hydrolysis, the samples were cooled to room temperature and filtered. The filtrate was neutralized to pH 7.0 using sodium hydroxide solution and diluted with distilled water to obtain the required concentration.

An aliquot of the sample solution was transferred into a test tube, followed by the addition of chloramine-T reagent. The mixture was allowed to stand for 20 min at room temperature for oxidation. Subsequently, Ehrlich's reagent was added, and the tubes were incubated in a water bath at 60 °C for 15–20 min for color development.

After cooling, the absorbance was measured at 557 nm using a UV-Visible spectrophotometer against a reagent blank. The hydroxyproline concentration was determined from the standard calibration curve prepared using standard hydroxyproline solution.

The hydroxyproline content was expressed as mg/g of dry tissue

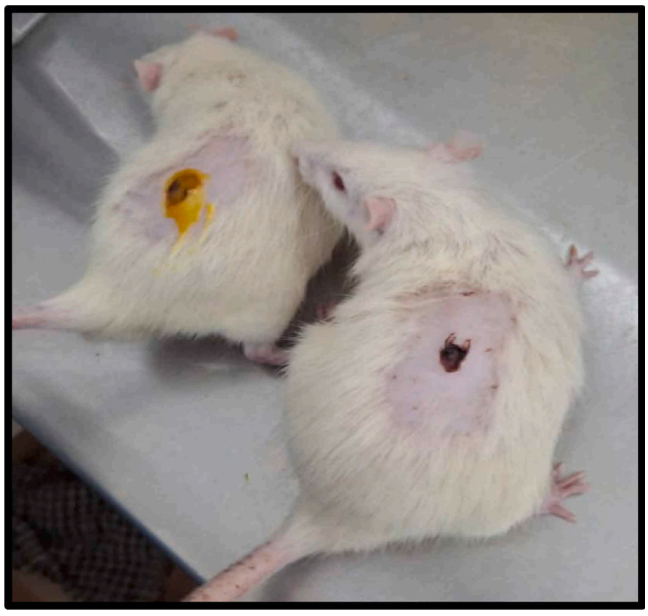


**Fig. 8.11.** Before and after application of gel on wound on animal.

weight, and increased hydroxyproline levels were considered indicative of enhanced collagen formation and improved wound healing activity.

## 3. Statistical analysis

All data were expressed as mean ± standard deviation (SD) for each group (n = 6). Wound-contraction data measured at different time points were analyzed using two-way repeated-measures ANOVA followed by Tukey's multiple-comparison test. Data were checked for normality and homogeneity of variance before analysis. Exact p values were reported where applicable, and $p < 0.05$ was considered statistically significant.

## 4. Result

### 4.1. Pharmacognostic and physicochemical evaluation of Fagonia cretica

The organoleptic characteristics of Fagonia cretica powder are presented in Table 8. The powder exhibited a greenish-brown color, characteristic odor, bitter-astringent taste, and a fine fibrous texture.

The physicochemical parameters of Fagonia cretica were determined to assess the quality and purity of the plant material. The obtained values were within acceptable limits, indicating suitability of the crude drug for further formulation studies (Table 9).

### 4.2. Characterization of Curcumin

#### 4.2.1. UV–visible spectroscopy

Curcumin exhibited a characteristic absorption maximum (λmax) at 420 nm. The calibration curve showed good linearity within the concentration range of 5–25 μg/mL, with a correlation coefficient ($R^2$) of 0.999, indicating compliance with Beer–Lambert's law and suitability of the method for quantitative analysis.

#### 4.2.2. FTIR analysis

FTIR analysis confirmed the characteristic functional groups of curcumin, including aromatic C═C, phenolic C–O, ether C–O–C, and conjugated alkene groups. The observed absorption bands were consistent with reported spectra of pure curcumin, confirming its identity and purity.

#### 4.2.3. Melting point

The melting point of curcumin was found to be **182 ± 1°C**

### 4.3. Extraction yield

The hydroalcoholic extraction of Fagonia cretica was carried out by the maceration method. The percentage yield of the dried extract was found to be 6.07% w/w

### 4.4. Preliminary phytochemical screening

Preliminary phytochemical screening of the hydroalcoholic extract of Fagonia cretica revealed the presence of various bioactive constituents, including alkaloids, flavonoids, tannins, saponins, and phenolic compounds (Table 12).

**Table 8**
Organoleptic characteristics of **Fagonia cretica** powder.

| Parameter | Observation |
|---|---|
| Colour | Greenish-brown to brown |
| Odour | Characteristic, slightly aromatic |
| Taste | Bitter and slightly astringent |
| Texture | Fine and slightly rough powder |
| Appearance | Dry, free-flowing fibrous powder |

**Table 9**
Physicochemical parameters of Fagonia cretica.

| Parameter | Value (%) |
|---|---|
| Total ash | 2.40 |
| Acid-insoluble ash | 1.24 |
| Water-soluble ash | 1.20 |
| Alcohol-soluble extractive value | 10.62 |
| Water-soluble extractive value | 14.38 |
| Loss on drying | 0.52 |

**Table 10**
Calibration curve parameters of curcumin.

| Parameter | Value |
|---|---|
| Slope | 0.0479 |
| Intercept | 0.0321 |
| Correlation coefficient ($R^2$) | 0.999 |

**Table 11**
Characteristic FTIR peaks of curcumin.

| Peak ($cm^{-1}$) | Assignment |
|---|---|
| 1499.42 | Aromatic C═C stretching |
| 1270.55 | Phenolic C–O stretching |
| 1148.26 | Ether C–O–C stretching |
| 1021.98 | C–O stretching vibration |
| 961.22 | =C–H bending |
| 808.72 | Aromatic C–H bending |

The results confirmed the presence of important secondary metabolites in the hydroalcoholic extract of Fagonia cretica. These phytoconstituents are known to possess antioxidant, anti-inflammatory, and wound-healing properties, supporting the selection of the extract for phytosomal formulation and subsequent wound-healing studies.

### 4.5. Preparation of phytosomes

Phytosomes of Fagonia cretica extract and curcumin were successfully prepared by the thin-film hydration method using soya lecithin as the phospholipid carrier. Five formulation batches (F1–F5) were prepared by varying the drug-to-phospholipid ratio to obtain optimized phytosomal systems.

The prepared phytosomes appeared as fine, free-flowing yellowish-brown complexes with good dispersibility and uniform consistency. All formulations were evaluated for particle size, polydispersity index (PDI), zeta potential, and entrapment efficiency to identify the optimized batch.

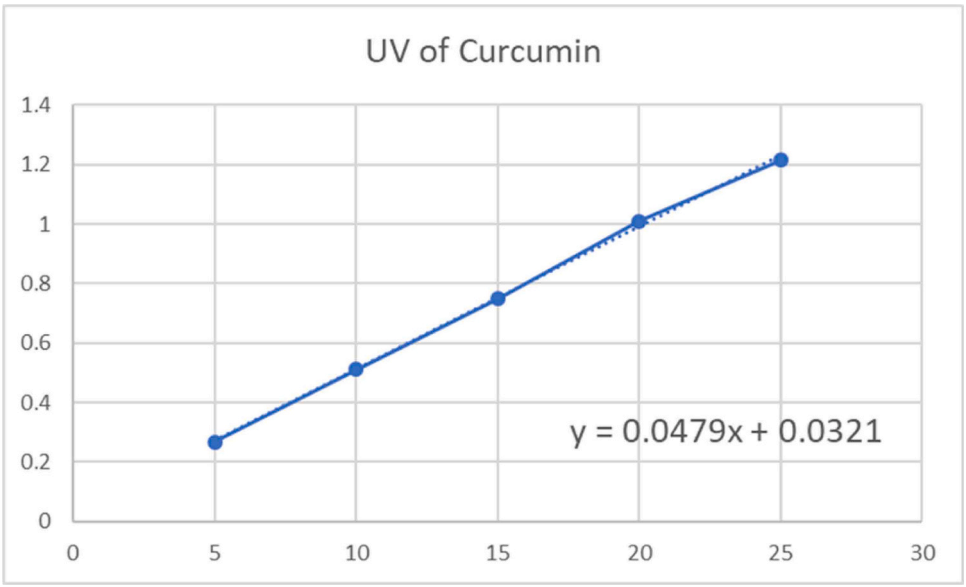
### 4.6. Characterization of phytosomes

Tables 13 and 14

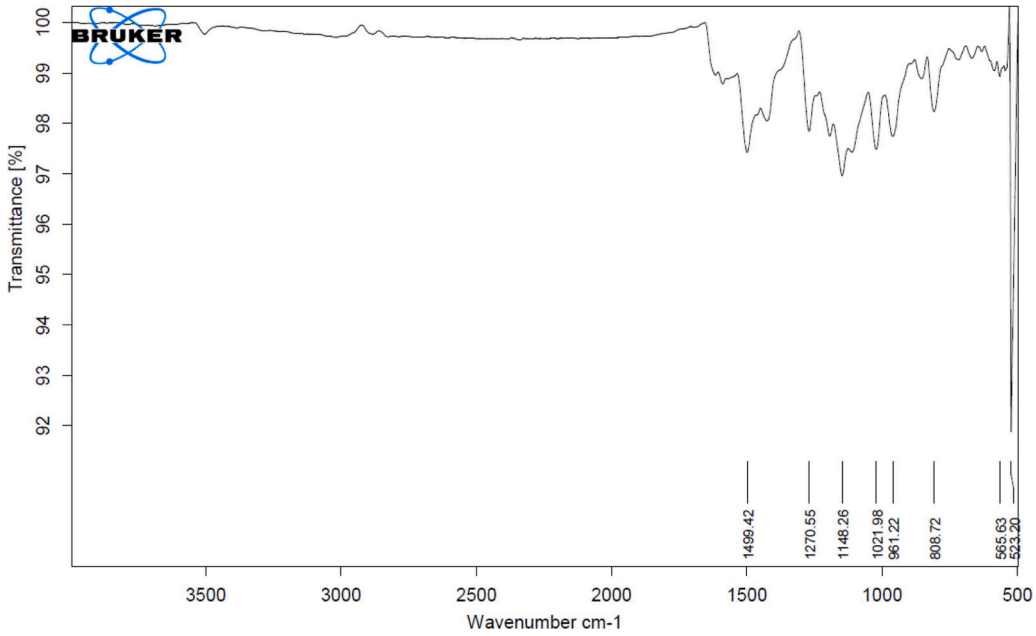
### 4.7. Optimized formulation

Formulation F4 (drug:soya lecithin = 1:2) was selected as the optimized phytosome formulation for both Fagonia extract and curcumin because it showed the most desirable physicochemical characteristics. Phytosome formation involves interaction of the phytoconstituents with phospholipids, which can improve lipid compatibility, membrane permeability and stability of plant-derived compounds [27].

For Fagonia phytosome, F4 exhibited a particle size of 583.0 ± 3.0 nm, PDI of 0.1626 ± 0.003, zeta potential of +26.7 ± 0.5 mV, and entrapment efficiency of 82.64 ± 0.87%. For curcumin phytosome, F4 showed a smaller particle size of 257.2 ± 3.2 nm, PDI of 0.2524 ± 0.004, zeta potential of +28.3 ± 0.4 mV, and the highest entrapment




**Graph 1.** Calibration curve for Curcumin.




**Graph 2.** FTIR spectrum of Curcumin.

**Table 12**
Preliminary phytochemical screening of hydroalcoholic extract of **Fagonia cretica**.

| Phytoconstituent | Result |
|---|---|
| Alkaloids | + |
| Flavonoids | + |
| Tannins | + |
| Saponins | + |
| Phenolic compounds | + |

(+ = Present; − = Absent)

efficiency of 86.87 ± 0.76%**.** The lower PDI indicates a comparatively uniform particle-size distribution, while the positive zeta potential suggests good electrostatic stabilization of the dispersion.

The increase in lecithin concentration from 1:0.5–1:2 improved

**Table 13**
*Fagonia cretica* extract Phytosome characterization of all formulations (F1-F5).

| Formulation | Extract: Soya lecithin | Particle size (nm), Mean ± SD | PDI, Mean ± SD | Zeta potential (mV), Mean ± SD | Entrapment efficiency (%), Mean ± SD |
|---|---|---|---|---|---|
| F1 | 1:0.5 | 812.4 ± 8.7 | 0.421 ± 0.012 | +18.6 ± 0.8 | 62.34 ± 1.21 |
| F2 | 1:1 | 704.6 ± 7.9 | 0.338 ± 0.010 | +21.4 ± 0.7 | 69.82 ± 1.08 |
| F3 | 1:1.5 | 641.8 ± 6.5 | 0.241 ± 0.009 | +24.8 ± 0.6 | 76.45 ± 0.94 |
| **F4** | **1:2** | **583.0 ± 3.0** | **0.1626 ± 0.003** | **+26.7 ± 0.5** | **82.64 ± 0.87** |
| F5 | 1:2.5 | 598.7 ± 5.8 | 0.198 ± 0.007 | +25.9 ± 0.6 | 80.17 ± 1.02 |

**Table 14**
Curcumin Phytosome characterization of all formulations (F1-F5).

| Formulation | Curcumin:Soya lecithin | Particle size (nm), Mean ± SD | PDI, Mean ± SD | Zeta potential (mV), Mean ± SD | Entrapment efficiency (%), Mean ± SD |
|---|---|---|---|---|---|
| F1 | 1:0.5 | 421.6 ± 7.2 | 0.386 ± 0.011 | +19.8 ± 0.7 | 65.42 ± 1.15 |
| F2 | 1:1 | 342.8 ± 6.1 | 0.321 ± 0.009 | +22.7 ± 0.6 | 73.65 ± 1.03 |
| F3 | 1:1.5 | 289.4 ± 5.3 | 0.278 ± 0.008 | +25.4 ± 0.5 | 81.26 ± 0.89 |
| **F4** | **1:2** | **257.2 ± 3.2** | **0.2524 ± 0.004** | **+28.3 ± 0.4** | **86.87 ± 0.76** |
| F5 | 1:2.5 | 268.9 ± 4.6 | 0.269 ± 0.006 | +27.1 ± 0.5 | 84.13 ± 0.91 |

drug–phospholipid interaction and entrapment, resulting in smaller and more uniform particles. However, at 1:2.5 (F5), particle size and PDI increased slightly and entrapment efficiency decreased, indicating that further increase in lecithin did not provide additional benefit. Thus, 1:2 was considered the optimum ratio. Similar studies report that phospholipid complexes can improve the physicochemical and biopharmaceutical properties of phytoconstituents, including curcumin [28].

Therefore, F4 was selected for incorporation into Carbopol gel to prepare Fagonia–Curcumin Phytosomal Gel (FCPG) for subsequent wound-healing studies.

### 4.8. Formulation of Fagonia–Curcumin phytosomal gel (FCPG)

The Fagonia–Curcumin phytosomal gel (FCPG) was successfully formulated by incorporating the optimized Fagonia phytosome (F4) and curcumin phytosome (F4) into a Carbopol 934 gel base. The prepared gel exhibited good homogeneity, smooth texture, satisfactory consistency, and no visible phase separation, indicating its suitability for topical application.

### 4.9. Evaluation of Fagonia–Curcumin phytosomal gel

#### 4.9.1. Physicochemical properties

The prepared FCPG was yellowish-brown in color with a characteristic odor and smooth, homogeneous texture. No signs of grittiness, lump formation, or phase separation were observed. The pH of the formulation was found to be 5.88, which is within the physiological skin pH range and indicates suitability for topical application. The viscosity of the gel was 1098 cP, reflecting adequate consistency for easy application and retention at the site of administration. The spreadability of the formulation was 6.21 g·cm/s, indicating good spreadability and uniform distribution over the skin surface.

#### 4.9.2. In vitro drug release

The in-vitro release profile of curcumin from FCPG was evaluated over 360 min using a Franz diffusion cell. The cumulative percentage release refers specifically to the amount of curcumin, which was used as the marker compound for quantification of drug release. The cumulative release of curcumin increased progressively from 8.18 ± 0.0030% at 30 min to 83.03 ± 0.0020% at 360 min, indicating a sustained-release pattern. The observed sustained release may be attributed to the combined effect of the phospholipid-based phytosomal system and Carbopol gel matrix, which may retard diffusion of curcumin from the formulation.

**Table 15**
Physicochemical evaluation of FCPG.

| Parameter | Result |
|---|---|
| Appearance | Smooth, homogeneous gel |
| Color | Yellowish-brown |
| pH | 5.88 |
| Viscosity (cP) | 1098 |
| Spreadability (g·cm/s) | 6.21 |

**Table 16**
In vitro drug release profile of FCPG.

| Time (min) | Cumulative curcumin release (%) |
|---|---|
| 0 | 0 |
| 30 | 8.18 ± 0.0030 |
| 60 | 20.25 ± 0.0012 |
| 90 | 32.84 ± 0.0014 |
| 120 | 43.52 ± 0.0006 |
| 150 | 50.14 ± 0.0035 |
| 180 | 51.16 ± 0.0017 |
| 240 | 68.10 ± 0.0026 |
| 300 | 78.43 ± 0.0012 |
| 360 | 83.03 ± 0.0020 |

#### 4.9.3. Rheological study

The rheological evaluation revealed a decrease in viscosity with increasing shear rate, indicating pseudoplastic (shear-thinning) behaviour of the gel. The viscosity decreased from 4850 cP at 10 rpm to 2650 cP at 100 rpm. This non-Newtonian flow behaviour is desirable for topical formulations, as it provides adequate consistency during storage while facilitating easy spreading upon application.

The rheological findings confirmed that the developed FCPG possessed suitable flow characteristics, spreadability, and stability for topical wound-healing applications.

### 4.10. Assessment of wound-healing activity

#### 4.10.1. Wound contraction

The effect of different treatments on wound contraction is presented in Table 11. The FCPG-treated group exhibited significantly greater wound contraction compared with the untreated control, placebo gel, and FCEG groups throughout the study period. On day 14, the FCPG achieved 91.8 ± 2.4% wound contraction, which was comparable to the standard treatment (96.5 ± 2.2%) and markedly higher than FCEG (77.3 ± 2.3%). These findings suggest that phytosomal incorporation enhanced the wound-healing efficacy of Fagonia cretica extract and curcumin.

#### 4.10.2. Epithelialization period

The epithelialization period was significantly shortened in the treatment groups compared with the control groups (Table 17). The standard treatment showed the shortest epithelialization period (12.2 ± 0.8 days), followed by FCPG (13.6 ± 0.9 days). The FCPG-treated group demonstrated faster epithelial regeneration than the FCEG-

**Table 17**
Rheological properties of FCPG.

| Shear Rate (rpm) | Viscosity (cP) |
|---|---|
| 10 | 4850 |
| 20 | 4320 |
| 30 | 3980 |
| 50 | 3520 |
| 60 | 3310 |
| 80 | 2980 |
| 100 | 2650 |

treated group (16.5 ± 0.8 days), indicating improved wound-healing performance.

#### 4.10.3. Hydroxyproline content

Hydroxyproline estimation was performed as an indicator of collagen synthesis and extracellular matrix formation. The FCPG-treated group showed higher hydroxyproline content (55.4 ± 2.3 μg/mg tissue) than the FCEG (49.7 ± 2.8 μg/mg tissue) and placebo gel (34.2 ± 2.1 μg/mg tissue) groups. The increased hydroxyproline content suggests enhanced collagen deposition and improved tissue remodeling in the phytosomal gel-treated animals.

#### 4.10.4. Overall wound-healing performance

The FCPG demonstrated superior wound-healing activity compared with the non-phytosomal FCEG formulation, as evidenced by greater wound contraction, shorter epithelialization period, and higher hydroxyproline content. The enhanced therapeutic effect may be attributed to improved delivery of Fagonia cretica phytoconstituents and curcumin through phytosomal encapsulation, resulting in enhanced bioavailability at the wound site. Overall, the FCPG exhibited wound-healing activity comparable to the standard treatment and represents a promising topical formulation for wound management.

## 5. Conclusion

The present study successfully developed and evaluated a Fagonia–Curcumin Phytosomal Gel (FCPG) for topical wound-healing application. Phytosomes of Fagonia cretica extract and curcumin were successfully prepared and optimized, exhibiting favorable particle size, zeta potential, and entrapment efficiency. The optimized phytosomes were incorporated into a Carbopol-based gel, which demonstrated acceptable physicochemical properties, including suitable pH, viscosity, spreadability, homogeneity, and sustained drug-release characteristics.

In the excision wound model, FCPG showed significantly enhanced wound-healing activity compared with the non-phytosomal Fagonia–Curcumin Extract Gel (FCEG). The phytosomal formulation accelerated wound contraction, reduced the epithelialization period, and increased hydroxyproline content, indicating improved collagen synthesis and tissue regeneration. The enhanced therapeutic performance of FCPG may be attributed to improved solubility, skin permeation, and bioavailability of the phytoconstituents achieved through phytosomal encapsulation.

Overall, the findings suggest that phytosomal delivery of Fagonia cretica extract and curcumin represents a promising strategy for improving topical wound-healing therapy. The developed FCPG demonstrated superior efficacy over the conventional extract gel and may serve as a potential herbal nanocarrier-based formulation for wound management. Further studies focusing on long-term stability, detailed mechanistic investigations, and clinical evaluation are warranted to establish its therapeutic applicability.

## CRediT authorship contribution statement

**Samruddhi Bhandari:** Methodology, Investigation.

## Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (OpenAI) for language editing, grammar correction, and improvement of manuscript readability. The authors carefully reviewed and edited the generated content as necessary and take full responsibility for the content of the published article.

**Table 18**
Effect of treatments on wound contraction (%).

| Day | Control | Placebo Gel | Standard | FCEG | FCPG |
|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 |
| 3 | 12.5 ± 1.2 | 18.3 ± 1.5 | 32.6 ± 2.1*** | 24.7 ± 1.2** | 28.4 ± 1.8*** |
| 7 | 28.6 ± 2.0 | 36.2 ± 2.3 | 65.8 ± 2.7*** | 42.5 ± 2.2** | 58.3 ± 2.5*** |
| 10 | 45.2 ± 2.4 | 52.6 ± 2.6 | 82.4 ± 3.0*** | 61.9 ± 2.5** | 75.6 ± 2.8*** |
| 14 | 62.3 ± 2.8 | 70.1 ± 3.1 | 96.5 ± 2.2*** | 77.3 ± 2.3** | 91.8 ± 2.4*** |

Values are expressed as Mean ± SEM (n = 6); **p < 0.05, ***p < 0.01 versus placebo gel group.

**Table 19**
Epithelialization period.

| Group | Epithelialization Period (Days) |
|---|---|
| Control | 20.4 ± 1.2 |
| Placebo Gel | 18.6 ± 1.0 |
| Standard | 12.2 ± 0.8 |
| FCEG | 16.5 ± 0.8 |
| FCPG | 13.6 ± 0.9 |

**Table 20**
Hydroxyproline content of wound tissue.

| Group | Hydroxyproline Content (μg/mg tissue) |
|---|---|
| Control | 68.6 ± 1.8 |
| Placebo Gel | 34.2 ± 2.1 |
| Standard | 62.8 ± 2.5 |
| FCEG | 49.7 ± 2.8 |
| FCPG | 55.4 ± 2.3 |

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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