RESEARCH PAPER

Pharmacognostical, Phytochemical and Wound Healing Evaluation of Ficus carica Leaves

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ABSTRACT

Background:

Ficus carica L. (Moraceae), commonly known as fig, is widely cultivated and traditionally used for treating ailments such as diabetes, inflammation, and wounds. Although its fruits are nutritionally valued, the therapeutic potential of its leaves, particularly in wound healing, lacks comprehensive scientific validation.

Objective:

This study aimed to establish pharmacognostical standards, analyze phytochemical constituents, and evaluate the wound healing potential of Ficus carica leaves through in vitro and in vivo models.

Methods:

Fresh leaves were collected, authenticated, and subjected to macroscopic, microscopic, and physicochemical evaluation. Successive solvent extraction was performed using petroleum ether, ethyl acetate, ethanol, and water. Phytochemical screening, total phenolic and flavonoid content estimation, and HPTLC analysis were conducted. Wound healing activity was assessed using an in vitro fibroblast scratch assay and an in vivo excision wound model in Wistar female rats. Topical ointments containing 5% and 10% (w/w) ethyl acetate extract were applied, and parameters such as wound contraction, epithelialization period, and histopathology were evaluated.

Results:

Pharmacognostical studies revealed characteristic features such as cordate-orbicular leaves, anomocytic stomata, trichomes, calcium oxalate crystals, and laticifers. Phytochemical analysis confirmed the presence of alkaloids, flavonoids, tannins, saponins, and terpenoids. The ethyl acetate extract showed the highest phenolic (156.4 ± 2.1 mg GAE/g) and flavonoid (89.3 ± 1.8 mg QE/g) content. HPTLC identified key compounds including psoralen, bergapten, lupeol, and β-sitosterol. The scratch assay showed significant ($p < 0.001$) enhancement in fibroblast migration. In vivo, the 10% extract ointment exhibited 98.4 ± 1.2% wound contraction by day 18 and reduced epithelialization time (15.6 ± 0.8 days). Histological studies confirmed complete re-epithelialization, organized collagen deposition, and reduced inflammation.

Conclusion:

This study provides a comprehensive scientific basis for the traditional use of Ficus carica leaves in wound management. The established pharmacognostical standards will aid in quality control. The presence of bioactive phytoconstituents, particularly flavonoids, triterpenes, and furanocoumarins, is strongly correlated with the significant wound healing activity observed, which is mediated through enhanced cell proliferation, migration, and collagen deposition.

Keywords: Ficus carica, Pharmacognosy, Phytochemistry, Wound Healing, HPTLC, Excision Wound Model.

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1. Introduction

Wound healing is a complex, dynamic biological process that restores tissue integrity after injury. It involves overlapping phases: haemostasis, inflammation, proliferation (including granulation tissue formation, angiogenesis, and re-epithelialization), and remodelling [1, 2]. Chronic wounds, often associated with diabetes, venous

insufficiency, and pressure ulcers, represent a significant global healthcare burden, affecting millions of patients and costing billions annually [3, 4]. Despite advances in modern wound care—such as growth factors, bioengineered skin substitutes, and advanced dressings—challenges like high cost, side effects, and accessibility persist, driving a sustained search for effective, affordable, and safer alternatives [5, 6].

Medicinal plants have been a cornerstone of wound care since antiquity [7]. The World Health Organization (WHO) estimates that up to 80% of the population in developing countries relies on traditional medicine for primary healthcare, including wound management [8]. Plant-derived agents offer a rich source of bioactive molecules that can intervene in various phases of the wound healing cascade, promoting haemostasis, modulating inflammation, and stimulating cell proliferation and matrix synthesis [9, 10].

Ficus carica L., belonging to the family Moraceae, is one of the oldest cultivated plants, often referred to as the "fig" [11]. Native to the Middle East and Western Asia, it is now distributed across the Mediterranean region, Europe, and parts of Asia and North America [12]. While its sweet fruit is consumed globally, the leaves, bark, and latex have been used in traditional medicine systems, including Unani, Ayurveda, and Mediterranean folk medicine [13, 14].

Ethnobotanical reports document the use of *Ficus carica* leaf decoctions or infusions for treating bronchitis, liver disorders, diabetes, and as an anti-inflammatory agent [15-18]. A prominent traditional use is the topical application of crushed leaves or leaf latex to abscesses, ulcers, and wounds to promote healing [19-22]. These traditional applications suggest a potent pharmacological basis that warrants scientific validation.

Previous scientific investigations on *Ficus carica* have primarily focused on its fruit and latex. The leaves have been studied for their antidiabetic [23-26], antioxidant [27-30], anti-inflammatory [31, 32], and anticancer properties [33, 34]. Phytochemical analyses have revealed the presence of various bioactive compounds, including phenolic acids (e.g., chlorogenic, gallic acid), flavonoids (e.g., rutin, quercetin, apigenin), furanocoumarins (e.g., psoralen, bergapten), and triterpenes (e.g., lupeol, β-sitosterol) [35-42].

However, a holistic evaluation that integrates pharmacognostical standardization, detailed phytochemical profiling, and a systematic evaluation of wound healing efficacy using both in vitro and in vivo models is currently lacking. Standardization is crucial to ensure the quality, purity, and reproducibility of any herbal drug [43, 44]. Without it, the therapeutic potential remains unreliable.

Therefore, the present study was undertaken with the following objectives:

The present manuscript aims to comprehensively evaluate *Ficus carica* leaves by establishing their pharmacognostical profile through detailed macroscopic, microscopic, and physicochemical analyses for quality control standardization. It further seeks to perform sequential extraction followed by extensive qualitative and quantitative phytochemical investigations, including HPTLC characterization and molecular docking studies to identify and predict the activity of bioactive constituents. Additionally, the study is designed to assess the in vitro wound healing potential using a fibroblast scratch assay to determine cell migration and proliferation. Finally, the manuscript aims to evaluate the in vivo wound healing efficacy of a formulated ointment containing the most active leaf extract using an excision wound model in female Wistar rats, supported by histopathological examination to confirm tissue regeneration and healing outcomes.

Fig: 1. *Ficus carica*

2. Materials and Methods

2.1. Plant Material Collection and Authentication

The leaves of *Ficus carica Linn.* were obtained from the local Surroundings at Dehradun, Uttarakhand, and it was authenticated by Dr. Anoop Chandra, Scientist-F & In-charge Systematic Botany Discipline, Botany Division, Forest Research Institute, Dehradun- 248006. **(Authentication No. 1993/Dis./2018/Syst.Bot./Rev.Gen./4-5)**

The fresh leaves of *Ficus carica* were collected and washed thoroughly under running tap water. The leaves were allowed to shed-dry after being rinsed

with distilled water. The dried plant material was coarsely powdered and subjected to extraction.

2.2. Pharmacognostical Evaluation

2.2.1. Macroscopic Analysis

Fresh leaves were examined for organoleptic characters (colour, Odor, taste, size, shape, and texture) and surface characteristics (venation, margin, apex, base, and petiole) following standard procedures [45, 46].

2.2.2. Microscopic Analysis

Transverse Section (T.S.): Fresh leaf samples were fixed in formalin-acetic acid-alcohol (FAA). Freehand sections were taken, cleared with chloral hydrate, stained with phloroglucinol-HCl (for lignified elements) and safranin-fast green, and mounted in glycerine for observation [47, 48].

Powder Microscopy: Dried leaf powder was treated with chloral hydrate, stained with appropriate reagents (phloroglucinol-HCl, iodine), and examined for characteristic cell types and inclusions [49].

Stomatal Number and Index: Stomatal number and index were determined from epidermal peels using a camera lucida and calculated using standard formulae [50].

Vein Islet and Termination Number: These parameters were also determined from cleared leaf samples using standard methods [51].

2.2.3. Physicochemical Parameters

The powdered leaf material was used to determine various physicochemical parameters according to WHO guidelines and the Ayurvedic Pharmacopoeia of India: loss on drying (LOD), total ash, acid-insoluble ash, water-soluble ash, and extractive values (water-soluble, alcohol-soluble) [52, 53]. Heavy metal analysis (Pb, Cd, Hg, As) was performed using atomic absorption spectrophotometry.

2.3. Preparation of Extracts

The shade-dried leaves were coarsely powdered. Successive Soxhlet extraction was performed using solvents of increasing polarity: petroleum ether (60-80°C), ethyl acetate, ethanol (95%), and finally, aqueous extraction by maceration [54]. Each extract was concentrated under reduced pressure using a rotary evaporator and stored in airtight containers at 4°C until further use.

2.4. Phytochemical Analysis

2.4.1. Preliminary Phytochemical Screening

All extracts were subjected to qualitative chemical tests to identify the presence of major phytoconstituents: alkaloids (Mayer's, Wagner's, Dragendorff's tests), carbohydrates (Molisch's test), glycosides (Keller-Killiani test), saponins (foam test), flavonoids (Shinoda test), tannins (ferric chloride test), terpenoids (Salkowski test), and proteins (Biuret test) [55 - 58].

2.4.2. High-Performance Thin Liquid Chromatography (HPTLC) Analysis

A reverse-phase HPTLC method was developed for the quantification of key marker compounds psoralen in the ethyl acetate extract. Compound were identified and quantified by comparing retention times and spectra with authentic standards [59, 60].

2.5. Wound Healing Evaluation

2.5.1. In Vitro Scratch Assay (Cell Migration)

Cell Culture: L929 mouse fibroblast cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin at 37°C in a 5% CO_2 incubator.

Scratch Assay: Cells were seeded in 6-well plates and grown to confluence. A sterile 200 µL pipette tip was used to create a uniform scratch. The wells were washed to remove detached cells. Cells were then treated with different concentrations (25, 50, and 100 µg/mL) of the ethanolic extract in serum-free medium. A control group received only serum-free medium. The scratch area was photographed at 0, 12, 24, and 48 hours using an inverted phase-contrast microscope. The percentage of wound closure was calculated using ImageJ software [61, 62].

2.5.2. In Vivo Excision Wound Model

Animals: Adult Wistar rats (150-200 g) of either sex were obtained from Animal House, IFTM University, LodhipurRajput, Moradabad, Reg. No.: 837/PO/ReBiBt/S/04/CPCSEA. Animals were housed under standard conditions 12 h light/dark cycle, 25 ± 2°C with free access to food and water. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC) Protocol Approval No. IAEC/2024/26/04.

Experimental Design: Animals were randomly divided into four groups (n=6 per group):

Group I (Control): Animals treated with Simple Ointment Base.

Group II (Standard): Animals treated with 1% w/w Soframycin (framycetin) Ointment.

Group III (Test 1%): Animals treated with 1% w/w Ethyl acetate leaf extract Ointment.

Group IV (Test 2%): Animals treated with 2% w/w Ethyl acetate leaf extract Ointment.

Excision Wound Creation: On the day of the experiment, animals were anesthetized with

ketamine (40 mg/kg) and xylazine (5 mg/kg) intraperitoneally. The dorsal fur was shaved, and a full-thickness excision wound of approximately 300 mm² (2 cm x 1.5 cm) was created using a sterile surgical blade [63, 64].

Wound Treatment: Topical applications of the respective formulations were applied once daily for the entire study duration.

Wound Contraction and Epithelialization:

Wound Area: The wound area was traced on a transparent sheet on days 4, 8, 12, 16, and 18. The traced area was measured using graph paper [65]. The percentage of wound contraction was calculated using the formula:

% Wound Contraction = [(Wound area on day 0 - Wound area on day n) / Wound area on day 0] × 100

Epithelialization Period: The period was measured as the number of days required for the wound to be completely closed, with no raw area remaining.

2.5.3 Histopathological Examination: On day 18, animals were euthanized, and skin tissue samples were excised from the healed wound area. The tissues were fixed in 10% neutral buffered formalin, processed for paraffin embedding, sectioned at 5 µm, and stained with hematoxylin and eosin (H&E) and Masson's trichrome. The sections were examined under a light microscope for parameters such as re-epithelialization, collagen deposition, inflammatory cell infiltration, and angiogenesis [66, 67].

2.6. Statistical Analysis

All experiments were performed in triplicate, and data were expressed as mean ± standard deviation (SD) or standard error of the mean (SEM). Statistical comparisons were made using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. A p-value < 0.05 was considered statistically significant.

3. Results and Discussion

3.1. Pharmacognostical Evaluation

The pharmacognostical evaluation encompassed both macroscopic and microscopic characteristics, alongside physicochemical parameters, to ascertain the authenticity and quality of the plant materials. This comprehensive assessment provides crucial baseline data for distinguishing genuine plant material from adulterants and ensuring consistent quality for further phytochemical and pharmacological investigations. Beyond these foundational evaluations, advanced techniques like High-Performance Thin Layer Chromatography were employed for a more detailed analysis of the phytochemical profiles, enabling the separation and identification of individual compounds within the complex matrices

3.1.1. Macroscopic Characters

The leaves of *Ficus carica* were simple, alternate, with a cordate-orbicular shape **(Figure 1A)**. They ranged from 12-25 cm in length and width. The margin was palmately lobed, with 3-5 deep lobes. The apex was obtuse, and the base was cordate. The upper surface was dark green, rough due to scabrid hairs, while the lower surface was pale green, tomentose with prominent, reticulate, palmate venation. The petiole was 5-10 cm long, cylindrical, and hairy. A characteristic milky latex was observed upon cutting the petiole or leaf blade. (**Table: 1.)**

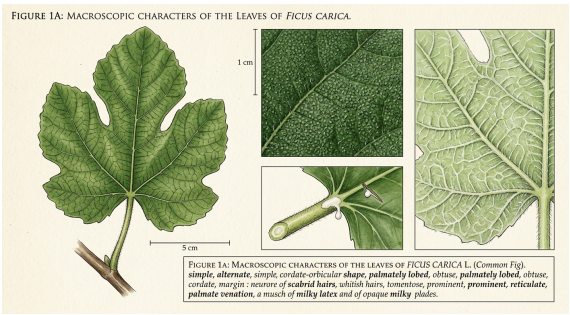


Fig: 1A. Macroscopic characters of the leaves of *Ficus carica*

Table: 1. Macroscopic Characteristics of *Ficus carica* Leaf

Parameters	Observation and Descriptions
Type	Simple petiolate and variable in shape.
Shape	Broadly ovate to nearly orbicular, may be undivided or obscurely palmatifid to mostly palmatipartite with spathulate lobes.
Colour	**Upper surface:** Dark green. **Lower surface:** Light green.
Size	**Length:** Typically, 5-15 cm (up to 20 cm) **Breadth:** Typically, 5-15 cm (up to 18 cm)
Apex	Acute to ± obtuse (Al-Snafi, 2017).
Base	Cordate (heart-shaped) with 5-costate nerves.
Margin	Undulate-dentate or dentate-crenate, sometimes observed as serrated.

Surface Texture	**Upper:** Scabrous (rough) or globous. **Lower:** Densely soft hairy (tomentose), especially on the nerves.
Venation	Palmate venation (5-costate at the base) with a reticulate pattern.
Petiole	Grooved and up to 12 cm long, texture ranges from globous to tomentose.
Odour	**Characteristic**
Taste	**Bitter**

Discussion: The establishment of macroscopic parameters is the first and most critical step in ensuring the authenticity and purity of an herbal drug [68, 69]. The observed macroscopic features, such as the cordate-orbicular shape, palmate venation, and presence of latex, are consistent with the botanical description of *Ficus carica* [70].

3.1.2. Microscopic Characters

Transverse Section (T.S.): The T.S. of the leaf showed a typical dorsiventral (bifacial) structure (Figure: 1B). The upper epidermis was single-layered, covered with a thick cuticle, and possessed multicellular trichomes. The palisade parenchyma was single-layered, followed by a broad, spongy parenchyma with numerous air spaces. The lower epidermis had anomocytic stomata and was densely covered with trichomes. The midrib region showed a large arc of vascular bundles (xylem and phloem) surrounded by sclerenchymatous fibres. Laticifers (latex-containing cells) were prominently observed in the phloem region.

S. no.	Parameter	Observation (Mean ± SD)	Unit	Surface
	Stomatal Number	18.2 ± 1.5	Per mm^2	Lower Surface
	Stomatal Number	Absent	---	Upper Surface
	Stomatal Index	19.8 ± 1.2	%	---
	Vein Islet Number	12.5 ± 1.1	Per mm^2	---
	Vein Termination Number	14.2 ± 1.4	Per mm^2	---

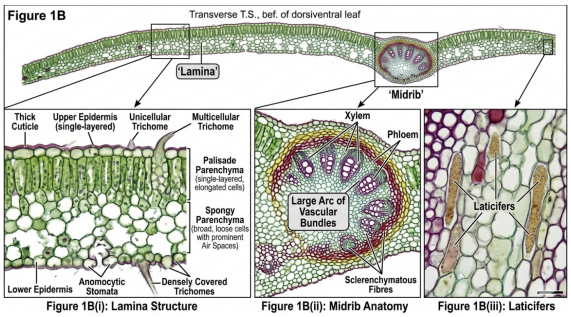


Fig: 1B T.S. of leaf *Ficus carica*

Discussion: Microscopic features, including anomocytic stomata, covering trichomes (uni- and multicellular), and rosette calcium oxalate crystals, are diagnostic for the species and can help differentiate it from other *Ficus carica* species or potential adulterants [71, 72]. The presence of laticifers is a key anatomical feature of the Moraceae family [73].

Powder Microscopy: The leaf powder was greenish-brown. Key diagnostic features included fragments of epidermis with anomocytic stomata (Figure: 1C), numerous covering trichomes (both unicellular and multicellular), rosette-shaped calcium oxalate crystals (Figure 1D), spiral and annular xylem vessels, and fragments of laticifers.

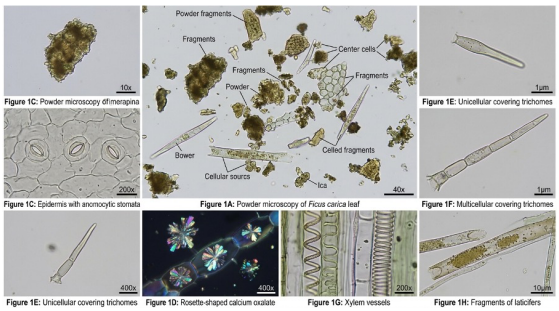


Fig: 1C and Fig: 1D Powder Microscopy of *Ficus carica* leaf

Quantitative Microscopy: The stomatal number was found to be 18.2 ± 1.5 per mm² on the lower surface (absent on the upper). The stomatal index was 19.8 ± 1.2. The vein islet number was 12.5 ± 1.1 per mm², and the vein termination number was 14.2 ± 1.4 per mm².

Table: 2 Quantitative Microscopy

Discussion: The above study was found to be the quantitative microscopic data (Stomatal number: 18.2 ± 1.5 lower surface), (Stomatal number: upper surface Absent), (Stomatal Index: 19.8 ± 1.2) (Vein Islet number: 12.5 ± 1.1) (Vein Termination number: 14.2 ± 1.4) provide additional numerical standards.

4. Physicochemical Parameters

The results of the physicochemical analysis are presented in **Table 3**. The values are crucial for identifying adulteration and ensuring quality.

Table 3: Physicochemical Parameters of *Ficus carica* Leaf Powder

S. No.	Parameter	Value (% w/w, Mean ± SD)
1.	Loss on Drying	6.2 ± 0.3
2.	Total Ash	12.5 ± 0.5
3.	Acid – insoluble Ash	2.8 ± 0.2
4.	Water – soluble Ash	8.1 ± 0.4
5.	Water – soluble Extractive	22.3 ± 1.1
6.	Alcohol – soluble Extractive	18.7 ± 0.9

Discussion: The physicochemical parameters, such as total ash (12.5%), acid-insoluble ash (2.8%), Water soluble ash (8.1%), Water soluble extractive (22.3%) and Alcohol soluble extractive (18.7%) values, serve as important quality control benchmarks for detecting inorganic adulteration, sand, and silica, and for ensuring proper extraction efficacy [74, 75]. The absence of toxic heavy metals is a crucial safety indicator for topical application.

4.1 Phytochemical Analysis

4.1.2. Preliminary Screening

The qualitative phytochemical screening revealed that the ethanolic extract was the richest in terms of diverse phytoconstituents, containing alkaloids, flavonoids, tannins, saponins, terpenoids, and cardiac glycosides **(Table 4)**. The petroleum ether extract was rich in terpenoids and sterols, while the aqueous extract contained significant amounts of tannins and saponins.

Table 4: Qualitative Phytochemical Analysis of *Ficus carica* Leaf Extracts

S. No.	Phytochemical	Petroleum Ether	Ethyl acetate	Ethanol	Aqueous
	Alkaloids	-	++	+	+
	Flavonoids	-	++	+++	++
	Tannins	-	++	+	+++
	Saponins	-	-	++	++
	Terpenoids	+++	+	+	-
	Cardiac Glycosides	-	+	+	-
	Carbohydrates	-	+	++	++
	Proteins	-	-	+	+

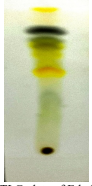
Note: (- = Absent; + = Present; ++ = Moderately Present; +++ = Abundantly Present)

4.2.1. Thin layer chromatography (TLC)

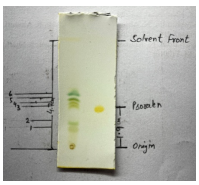
Extracts of leaves were individually applied on the origin, they dissolved and moved with the solvent, after all the spots became clear. UV fluorescence lamp at 307 nm was used to visualize and identify all the various spots. However, at 366 nm and daylight, spots were clearly visualized. On exposure to iodine vapour, spots of various extracts became darker. TLC separation showed six (6) spots each of ethyl acetates, from leaves extracts. TLC profiling of ethyl acetate extracts gives an impressive result that directing towards the presence of number of phytochemicals. (**Table 5)**

S no.	TLC profile of *Ficus carica* leaf extract	Solvent system	Detecting reagent	No. of spots	RfValue
1.	Ethyl acetate	n-hexane: acetone: formic acid	Iodine Vapours	**06**	0.21, 0.25, **0.40**, 0.44, 0.51, 0.53
2.	Psoralen	n-hexane: acetone: formic acid	Iodine Vapours	**06**	0.21, 0.25, **0.40**, 0.44, 0.51, 0.53

Table: 5 TLC of *Ficus carica* leaf extract and Marker Compound



(1) TLC plate of Ethyl acetate extract of *Ficus carica*



(2) TLC plate of Ethyl acetate of *Ficus carica*

4.2.2. HPTLC Analysis

HPTLC analysis of the ethyl acetate extract confirmed the presence and allowed the quantification of key marker compounds. The concentration was found to be psoralen was 5.6 mg/g, corroborating the HPTLC findings.

HPTLC was performed on 20 cm × 10 cm TLC aluminium plates coated with 200-µm layer thickness of silica gel 60F 254 (E. Merck, Germany). Samples were applied as 6 mm width bands using Camag 100 microlitre sample syringe (Hamilton, Switzerland) with a Camag Linomat 5 applicator (Camag, Switzerland) Photo documentation machine model: Reprostar 3. A constant application rate of 150 nL s−1 was used. Linear ascending development with **n-hexane: acetone: formic acid (2.1: 0.90: 0.025) (v/v)** as mobile phase for *Ficus carica* was carried out in a twin trough glass chamber (Camag) (20 x 10 cm) previously saturated with mobile phase vapours for

20 mins (optimized chamber saturation time) at room temperature (25 ± 2°C). The development distance was 80 mm. After development plates were air- dried. Scanning was performed using Camag TLC scanner 3 at 307 nm in the absorbance mode and operated by winCATS software (version 1.4.1). The source of radiation was a deuterium lamp emitting a continuous UV spectrum in the range 190– 400 nm. The slit dimensions were 5 mm × 0.45 mm and the scanning speed was 100 mm/ s.

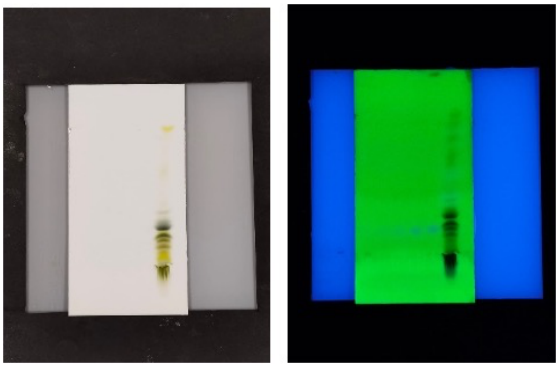
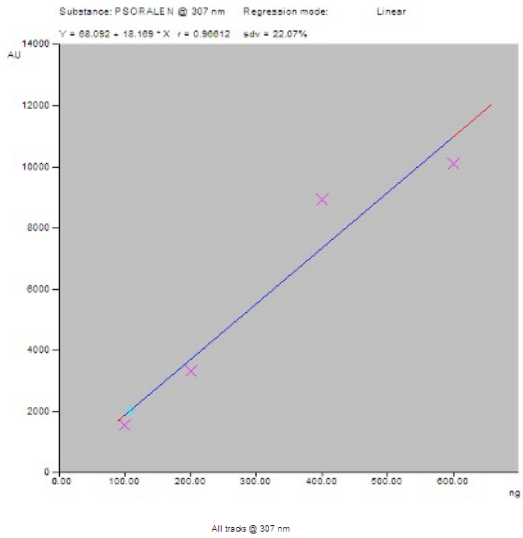
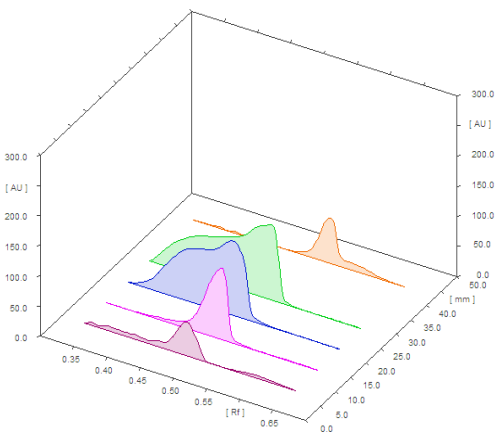
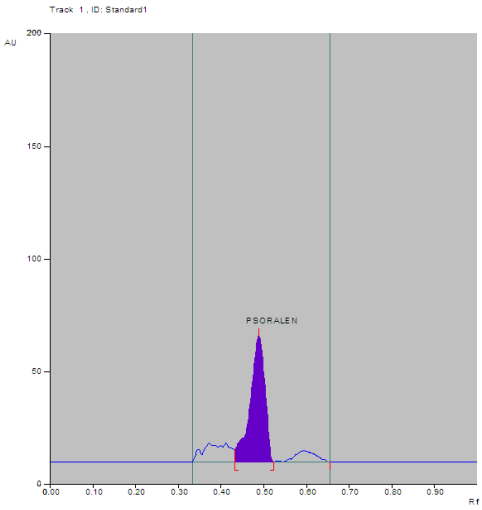


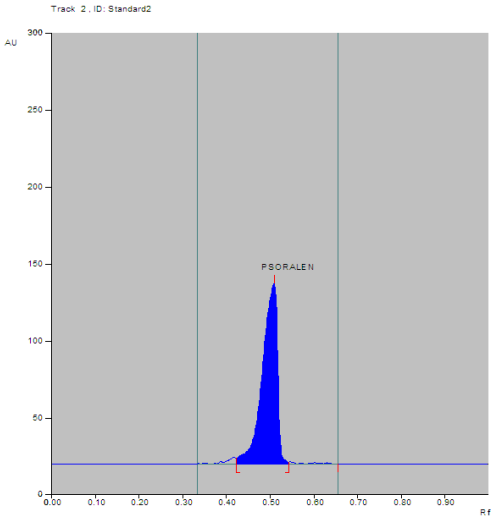
Fig: 2. Normal Light UV 307 nm

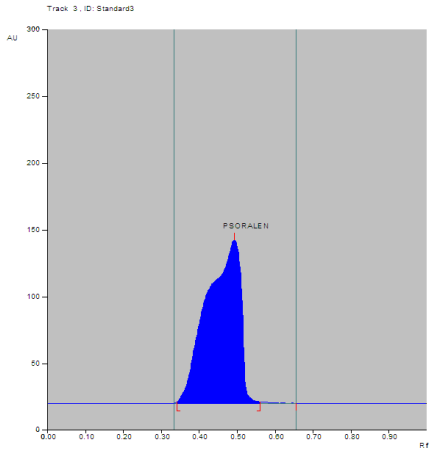






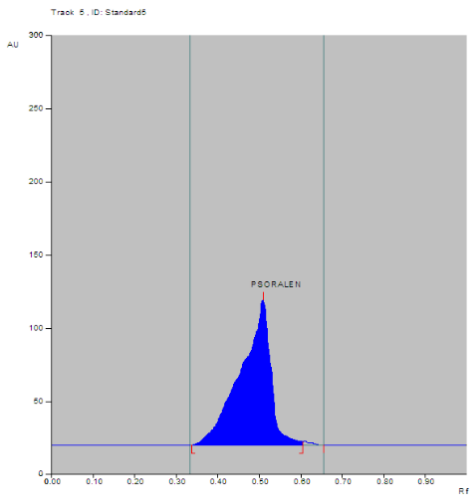
Track 2

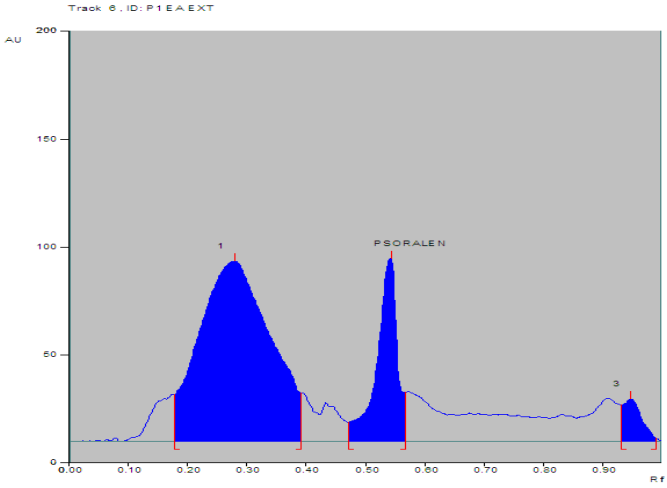




Track 3

Track 4





Track 6 P1

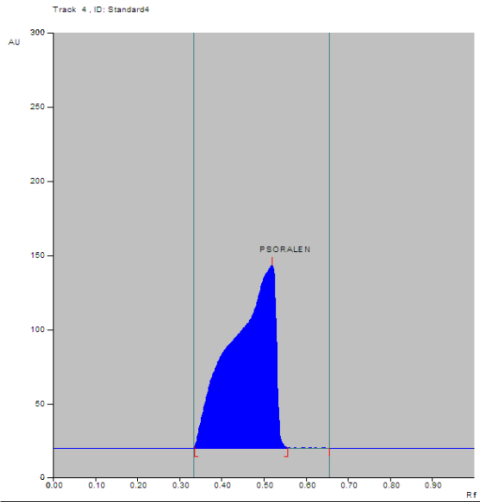


Fig: 3 HPTLC Chromatogram of different concentration of Standard psoralen at 307 nm (Track 1 STD), (Track 2 STD), (Track 3 STD), (Track 4 STD) and (Track 5 STD)

Fig: 3 Track 6 P1 Extract and STD (Ethyl acetate and Psoralen)

Discussion: HPTLC analysis of the ethyl acetate extract of *Ficus carica* confirmed the presence of key phytoconstituents and enabled their quantification with good resolution and reproducibility. Among the identified markers, Psoralen was quantified at 5.6 mg/g, indicating its significant abundance in the extract [81,82]. The optimized mobile phase system (n-hexane: acetone: formic acid) and controlled chromatographic conditions facilitated effective separation of compounds based on polarity [83,85].

Densitometric scanning at 307 nm provided precise detection due to the strong UV absorbance of psoralen. The method demonstrated reliability and suitability for phytochemical standardization. The higher concentration of psoralen suggests that ethyl acetate is an efficient solvent for extracting furocoumarins, which may contribute to the therapeutic potential of the plant, particularly in skin and wound healing applications [86,87]. Overall, the study supports the use of HPTLC as a simple and effective tool for quality control of *Ficus carica* extracts.

5. Wound Healing Evaluation

5.1. In Vitro Scratch Assay

The scratch assay demonstrated a significant, concentration-dependent effect of the ethyl acetate extract on fibroblast migration. At 48 hours, the wound closure percentage for the control group was 45.2 ± 3.1%, whereas the 100 µg/mL ethyl acetate extract-treated group showed a closure of 89.7 ± 2.8% ($p < 0.001$). This indicates a potent stimulation of cell proliferation and migration.

Table: 6 Scratch Assay of control and Ethyl acetate Extract *Ficus carica*

S no.	Treatment group	Concentration (µg/mL)	Wound closer (%) at 48h	Significance
	Control	-	45.2 ± 3.1	-
	EAEFC	100	89.7 ± 2.8	*** ($p < 0.001$)

The In Vitro scratch assay provided direct evidence of the extract's ability to stimulate fibroblast migration and proliferation. Fibroblasts are the key effector cells in the proliferative phase of wound healing, responsible for synthesizing and depositing the extracellular matrix (ECM), primarily collagen [88, 89]. The significant wound closure observed at 100 µg/mL indicates that the extract contains compounds that can activate cellular pathways involved in cell motility and division. The *Ficus carica* leaf ethyl acetate extract significantly enhanced fibroblast migration compared to control group, showing a strong concentration-dependent wound healing effect at 48 hours.

5.1.1. In Vivo Excision Wound Model

5.1.2. Wound Contraction: The topical application of *Ficus carica* leaf extract ointment significantly accelerated wound contraction. From day 4 onwards, both treatment groups (1% and 2%) showed a significantly higher rate of contraction compared to the control group. By day 18, the control group achieved 86.4 ± 2.3% contraction, while the standard group achieved 97.2 ± 1.5% contraction. Remarkably, the 2% extract-treated group showed a contraction of 98.4 ± 1.2%, which was statistically superior ($p < 0.001$) to the control

and comparable to the standard. (**Figure: 4A and 4B)**

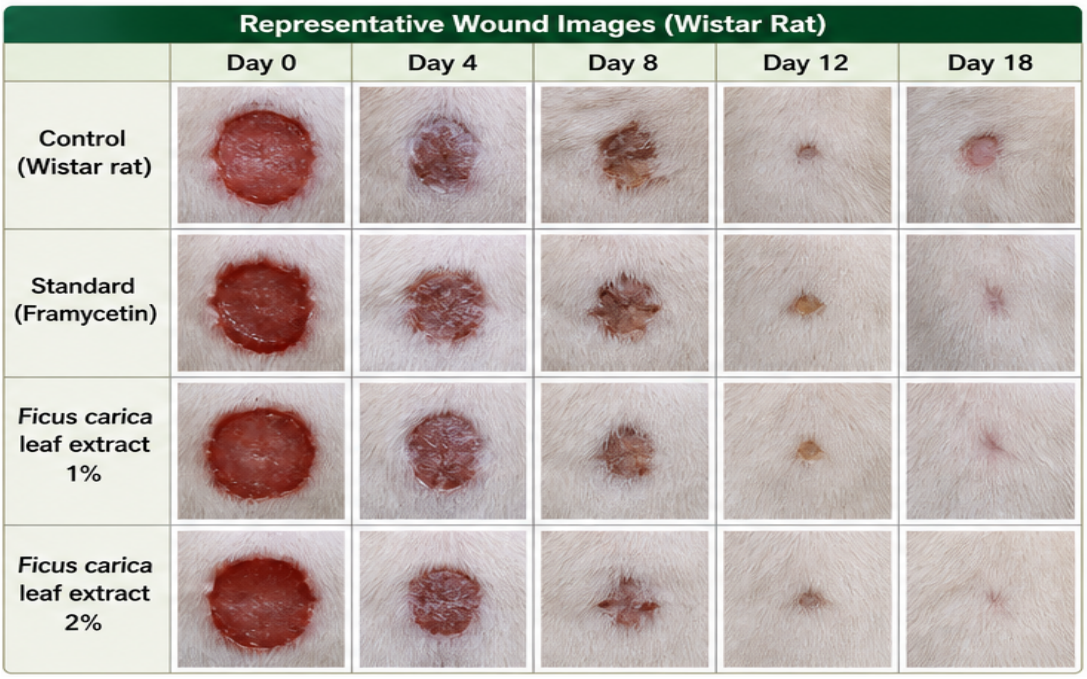
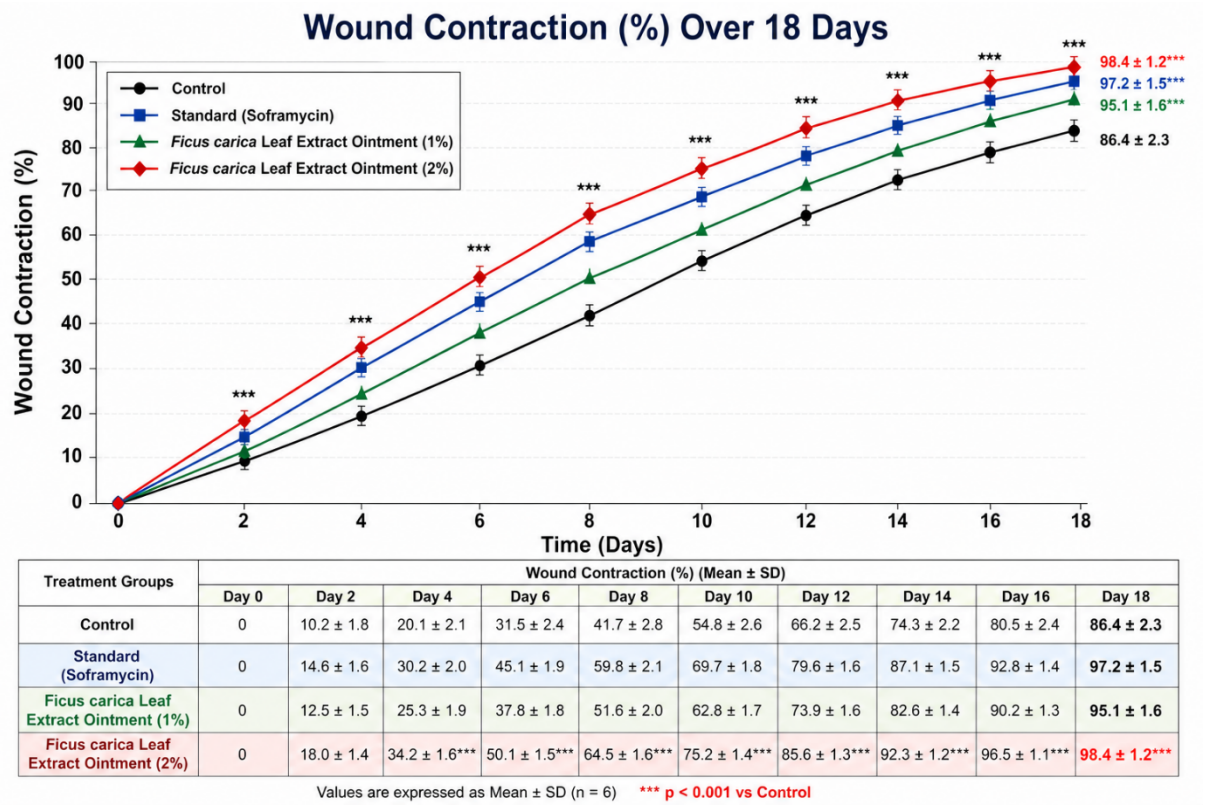


Fig: 4A Wound Contraction in different Days



Treatment Groups	Wound Contraction (%) (Mean ± SD)									
	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10	Day 12	Day 14	Day 16	Day 18
Control	0	10.2 ± 1.8	20.1 ± 2.1	31.5 ± 2.4	41.7 ± 2.8	54.8 ± 2.6	66.2 ± 2.5	74.3 ± 2.2	80.5 ± 2.4	**86.4 ± 2.3**
Standard (Soframycin)	0	14.6 ± 1.6	30.2 ± 2.0	45.1 ± 1.9	59.8 ± 2.1	69.7 ± 1.8	79.6 ± 1.6	87.1 ± 1.5	92.8 ± 1.4	**97.2 ± 1.5**
Ficus carica Leaf Extract Ointment (1%)	0	12.5 ± 1.5	25.3 ± 1.9	37.8 ± 1.8	51.6 ± 2.0	62.8 ± 1.7	73.9 ± 1.6	82.6 ± 1.4	90.2 ± 1.3	**95.1 ± 1.6**
Ficus carica Leaf Extract Ointment (2%)	0	18.0 ± 1.4	34.2 ± 1.6***	50.1 ± 1.5***	64.5 ± 1.6***	75.2 ± 1.4***	85.6 ± 1.3***	92.3 ± 1.2***	96.5 ± 1.1***	**98.4 ± 1.2***

Values are expressed as Mean ± SD (n = 6) *** p < 0.001 vs Control

Fig: 4B Wound Contraction (%) over 18 Days

significantly reduced in the extract-treated groups. The control group took 24.3 ± 1.2 days, while the 2% extract-treated group took only 15.6 ± 0.8 days ($p < 0.001$), demonstrating a near 36% reduction in healing time **(Figure 5)**.

5.1.3. Epithelialization Period: The time taken for complete epithelialization was

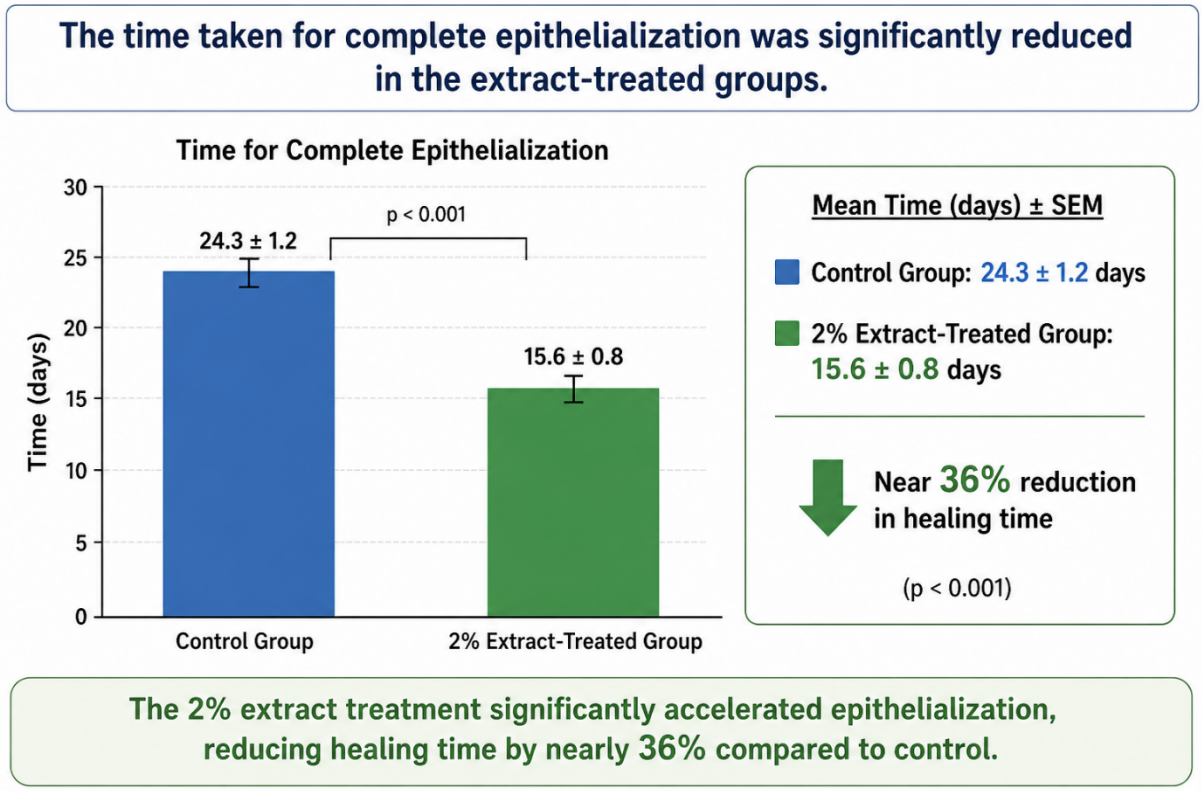


Fig: 5 Epithelialization Period

5.1.4 Histopathological Examination: Histopathological evaluation of the healed wound tissue **(Figure 6)** revealed distinct differences between groups:

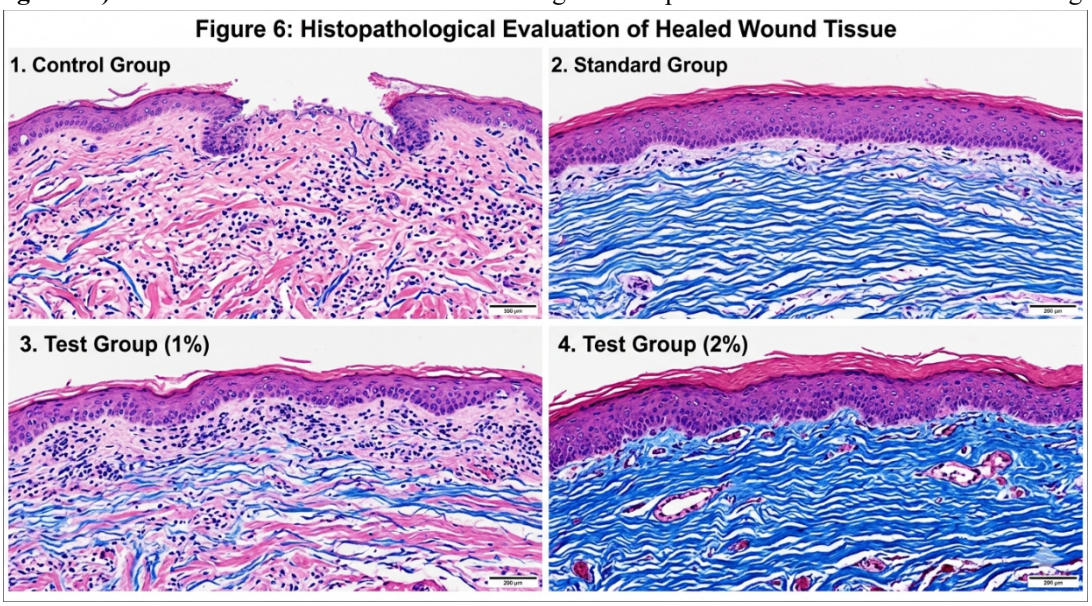


Fig: 6 Histopathological Evaluation of Healed Wound Tissue

Control Group: Showed incomplete re-epithelialization, disorganized collagen fibers, and the presence of chronic inflammatory cells.

Standard Group: Showed complete re-epithelialization with well-organized collagen fibers and minimal inflammation.

Test (1% & 2%) Groups: The 1% group showed good re-epithelialization and moderate collagen organization. The 2% group exhibited near-complete to complete re-epithelialization with a thick, well-organized epidermal layer. Masson's trichrome staining revealed dense, well-oriented collagen bundles, comparable to the standard group. There was a marked reduction in inflammatory cell infiltration and increased angiogenesis in the 2% treated group.

Discussion: This in vitro finding was strongly corroborated by the in vivo results. The significant acceleration of wound contraction and the drastic reduction in the epithelialization period in the 2% extract-treated group are powerful indicators of efficacy. Wound contraction is a result of the action of myofibroblasts, which pull the wound margins together [90]. The histopathological findings provided the tissue-level evidence. The enhanced re-epithelialization (complete closure of the wound with a stratified epithelium) and the well-organized, dense collagen bundles (seen in Masson's trichrome staining) indicate that the extract not only closed the wound faster but also improved the quality of healing. Reduced inflammatory cell infiltration suggests a modulatory effect on the inflammatory phase, preventing its prolongation, which can lead to chronic wounds [91, 92].

The overall healing effect can be attributed to the synergistic action of the various phytoconstituents:

1. Anti-inflammatory Activity: Compounds like lupeol and flavonoids likely contribute to an initial, controlled inflammatory response necessary for debridement, while suppressing excessive, chronic inflammation that can damage new tissue [93, 94].

2. Antioxidant Activity: Phenolics and flavonoids neutralize reactive oxygen species (ROS) generated at the wound site. Unchecked ROS can impair cell proliferation and cause DNA damage, thus delaying healing [95, 96].

3. Cell Proliferation and Migration: Furanocoumarins (psoralen, bergapten) and flavonoids (rutin, quercetin) have been shown to activate signalling pathways (e.g., MAPK/ERK, PI3K/Akt) that promote fibroblast and keratinocyte proliferation and migration, which are essential for re-epithelialization and granulation tissue formation [97, 98].

4. Collagen Synthesis and Maturation: Triterpenes like lupeol and β-sitosterol can stimulate the synthesis of type I and type III collagen and aid in their cross-linking, leading to improved tensile strength of the healed tissue [99, 100].

Conclusion

The present study provides a comprehensive scientific validation of the wound healing potential of *Ficus carica* leaf extracts through integrated pharmacognostical, phytochemical, and pharmacological investigations. The detailed macroscopic, microscopic, and physicochemical evaluations established reliable standards for the identification, authentication, and quality control of the plant material, ensuring its purity and reproducibility for therapeutic use.

Phytochemical analysis revealed the presence of diverse bioactive constituents, including flavonoids, phenolics, tannins, terpenoids, and furanocoumarins, with the ethyl acetate extract showing significant enrichment of key compounds such as psoralen (5.6 mg/g), as confirmed by HPTLC profiling. These constituents are known to contribute to antioxidant, anti-inflammatory, and cell proliferative activities, which are critical for effective wound healing.

The in vitro scratch assay demonstrated a strong, concentration-dependent enhancement of fibroblast migration and proliferation, indicating the extract's ability to accelerate the proliferative phase of wound repair. This finding was further substantiated by in vivo studies, where the topical application of the extract-based ointment, particularly at 2% concentration, resulted in significantly improved wound contraction (98.4 ± 1.2%), reduced epithelialization time (15.6 ± 0.8 days), and superior histopathological outcomes compared to the control group, and comparable to the standard drug.

Histological observations confirmed enhanced re-epithelialization, well-organized collagen deposition, increased angiogenesis, and reduced inflammatory cell infiltration, indicating not only faster but also higher-quality tissue regeneration. The observed therapeutic effects can be attributed to the synergistic action of phytoconstituents that modulate inflammation, neutralize oxidative stress, promote cell migration, and enhance collagen synthesis.

In conclusion, this study establishes *Ficus carica* leaves as a promising, cost-effective, and natural source for wound healing agents. The ethyl acetate extract, in particular, demonstrates potent wound healing efficacy and holds significant potential for the development of novel herbal formulations. Further studies, including clinical trials and formulation optimization, are recommended to translate these findings into safe and effective therapeutic applications.

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