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Original Research Article

Anti-Proliferative, Anti-Inflammatory, *In Vitro* Wound Healing Potentials and Phenolic Content of *Phlomis Crinita* Cav. Extracts

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ABSTRACT

Phlomis crinita Cav. (*P. crinita*), a medicinal plant from the Lamiaceae family, is widely used as a natural remedy in traditional North African and Southern European folk medicine to treat lesions and burns through the application of its leaves This study aimed to investigate its biological activities, including antiproliferative, anti-inflammatory, and wound-healing properties. Hydromethanolic extracts were prepared from the leaves, flowers, and rhizomes. Phytochemical analysis determined total phenolic content (TPC) and flavonoid content (FC). Antiproliferative activity was evaluated using the sulforhodamine B (SRB) assay against five human tumor cell lines (AGS, Caco-2, HeLa, MCF-7, and NCI-H460), each derived from a carcinoma of a distinct organ. Anti-inflammatory activity was assessed by measuring nitric oxide production in LPS-stimulated RAW 264.7 macrophages. The wound-healing potential was evaluated using the scratch assay. Phytochemical analysis revealed significant variations in TPC and FC among the extracts, with the rhizome extract exhibiting the highest levels: TPC: 128.15 µg GAE/mg DW and FC: 46.91 µg QE/mg DW. All extracts demonstrated antiproliferative activity against the tumor cell lines, with the rhizome extract showing the most potent growth inhibition (GI_{50}: 178.11 ± 4.10 µg/mL against AGS). The rhizome extract also exhibited the most potent inhibition of nitric oxide production (IC_{50}: 152.42 ± 10.88 µg/mL) compared to the other extracts tested. In the wound-healing assay, leaf extract demonstrated comparable healing effects to Allantoin, a known wound-healing agent. Our findings support the notion that *P. crinita* can be considered a promising source of therapeutic bioactive compounds.

Keywords: *Phlomis crinita*, Herbal medicine, Cancer cell line, Anti-inflammatory potential, Wound healing potential, Phenolic compounds.

Introduction

Despite the growing influence of modern healthcare, medicinal plants continue to play a crucial role. Of the estimated 250 000 higher plant species on Earth, over 80 000 are documented to possess at least some medicinal properties.[1] Natural compounds derived from medicinal and aromatic plants (MAPs) remain important sources of therapeutic agents and provide models for the design, semi-synthesis, and synthesis of drugs to treat both human and animal diseases.[2] A notable example is paclitaxel, extracted from *Taxus brevifolia*, a widely used chemotherapeutic agent for human cancers.[3] The *Phlomis* genus, comprising over 100 species within the Lamiaceae family, is predominantly distributed around the 40°N latitude, spanning regions of North Africa, Europe, and Asia.[4]

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Extracts from *Phlomis* species have shown considerable potencial in treating various ailments, including wounds, inflammation, gastric ulcers, diabetes, and hemorrhoids. This effectiveness is linked to their diverse bioactive properties, such as anti-inflammatory, immunomodulatory, antioxidant, antimicrobial, antimutagenic, and anti-ulcer activities. Additionally, these plants exhibit antiplasmodial and anticancer effects.[5,6,7] Research also indicates that the *Phlomis* genus is rich in secondary metabolites, leading to the production of numerous bioactive molecules, primarily including flavonoids, phenolic acids, iridoids, phenylethylalcohol glycosides, benzyl glycosides, and phenylethanoids.[4,8,9]

Phlomis crinita Cav. (syn.: *P. biloba*), one of four *Phlomis* species native to Algeria, is commonly referred to as "Khayat el-djerah" (syn.: wound healer) due to its traditional use in treating burns and lesions.[8,10] Previous research on extracts from this species has revealed promising antioxidant,[11] *in vivo* and *in vitro* anti-inflammatory (via protein denaturation and membrane stabilization assays),[10,12] antibacterial and anti-ulcerogenic properties.[13] Additionally, *in vitro* studies have shown immunomodulating,[14] antimutagenic (through antioxidant activity),[14] and *in vivo* wound-healing effects.[6] However, notably, the antiproliferative and *in vitro* wound-healing activities of *P. crinita* extracts remain unexplored, representing a significant gap in the existing literature and the primary focus of this study. In this study, we aimed to evaluate the antiproliferative, anti-inflammatory, and *in vitro* wound-healing properties of hydromethanolic extracts from the leaves (LME), flowers (FME), and rhizome (RME) of *P. crinita*. To accomplish this, we performed the following: (1) spectrophotometric quantification of total phenolic compounds and flavonoids in the

extracts; (2) assessment of antiproliferative (cytotoxic) effects on five human tumor cell lines— gastric adenocarcinoma (AGS), colorectal adenocarcinoma (Caco-2), cervical carcinoma (HeLa), breast adenocarcinoma (MCF-7), lung carcinoma (NCI-H460)—and a non-tumor cell line, African green monkey kidney (Vero); (3) evaluation of anti-inflammatory potential by measuring nitric oxide (NO) inhibition in LPS-stimulated RAW 264.7 macrophages; and (4) investigation of *in vitro* wound-healing activity using the scratch (cell migration) assay. In addition to antiproliferative and *in vitro* wound healing effects, this study also represents the first cell-based assessment of the anti-inflammatory potential of *P. crinita* extracts using the nitric oxide (NO) inhibition method in LPS-stimulated macrophages.

Materials and Methods

Selection and collection of plant material

Following botanical identification by Professor Abdelkader Saadi (Faculty of Natural and Life Sciences, University of Chlef), *Phlomis crinita* Cav. was collected in June 2023 from El-abadia, a locality within the Ain-defla province in the northern central region of Algeria (latitude: 36°11'10.3 'N, longitude: 1°18'18.2 "E). After harvesting, the plants were air-dried in the shade for 15 days. Subsequently, leaves and flowers were ground into a fine powder using a blender, while rhizomes were ground using a mortar and pestle. All powdered plant material was stored in opaque containers at room temperature (25°C) until further use.

Preparation of extracts

Extraction was carried out according to the method described by Merouane *et al.*, with a few modifications.[11] (10 g) of fine powder from each sample (leaves, flowers and rhizomes) were macerated in 200 mL of 80% methanol at room temperature and the mixture was stirred continuously for 24 hours using a WIS-10 shaker (Daihan Scientific Co. Ltd., Korea). After maceration, the mixtures were filtered through Whatman No. 1 filter paper. The residues were then rinsed twice with 20 mL aliquots of 80% methanol. The filtrates obtained were then concentrated using a Büchi rotary evaporator (Flawil, Switzerland) at a temperature below 48°C. After concentration, the extracts were dried at 35°C for 48 hours to remove all traces of water. Once dried, each crude extract was weighed and its yield calculated. Finally, the extracts were stored in a refrigerator at 4°C until further use for analysis.

Evaluation of extraction yield

The yield (%) of soluble constituents obtained by the hydro-methanolic extraction was quantified using the following equation 1 to assess the extraction efficiency:

$$\text{Rdt}\ (\%) = \frac{\text{Mass of dry extract\_mg}}{\text{Initial mass of sample\_mg}} \times 100 \quad \textbf{(Eq. 1)}$$

Quantification of total phenolic compounds (TPC)

TPCs of the extracts (LME, FME and RME) were quantified using the Folin-Ciocalteu method.[15] After mixing 125 µL of each extract (1 mg/mL) with 500 µL distilled water and 125 µL Folin-Ciocalteu reagent (10%), the mixture was left to stand for 5 minutes. Next, 1250 µL of 7% sodium carbonate and 1000 µL of distilled water were added. After 90 minutes of incubation in the dark at room temperature, the absorbance of each solution was measured at 765 nm using a Uv-Vis spectrophotometer (Optizen 2120, Mecasys Co. Ltd., Korea). A calibration curve was established using a series of gallic acid solutions of known concentrations to determine the concentration of total phenolic compounds, expressed as mg gallic acid equivalent per gram of crude extract (µg GAE/mg DW (Dry Weight)).

Quantification of total flavonoids (TF)

TFs of the extracts (LME, FME and RME) were quantified using Aluminum chloride method.[16] After mixing 1mL of each extract (1 mg/mL) with 1mL of 2% aluminum chloride, the mixture was incubated in the dark for 10 minutes. Absorbance was then measured at 430 nm using a Uv-Vis spectrophotometer (Optizen 2120, Mecasys Co. Ltd., Korea). A calibration curve with quercetin was used to determine total flavonoid concentration, expressed as mg quercetin equivalent per gram of crude extract (µg QE/mg DW (Dry Weight)).

Antiproliferative activity

The antiproliferative activity of each extract (LME, FME, and RME) was evaluated by a sulphorhodamine B (SRB) assay.[17] The extracts were re-dissolved in water to obtain stock solution of 8 mg/mL, which was further diluted to obtain a final range of concentrations tested being 6.25 - 400 µg/mL (in mixture). The human tumor cell lines used in this study included Caco-2 (colorectal adenocarcinoma), AGS (gastric adenocarcinoma), NCI-H460 (non-small cell lung carcinoma), HeLa (cervical carcinoma), and MCF-7 (breast adenocarcinoma). Additionally, the non-tumor cell line Vero, derived from the kidney of the African green monkey, was also used. The results were expressed in growth inhibition GI_{50} values (µg/mL), which correspond to the sample concentration providing 50% of inhibition of cell growth.

Anti-inflammatory activity

To assess the anti-inflammatory potential of each extract (LME, FME, and RME), we measured their ability to inhibit nitric oxide (NO) production in murine macrophage-like RAW 264.7 cells according to the method of Dridi *et al.*[18] These cells were stimulated with LPS to induce NO production. Different concentrations of extracts (6.25 to 400 µg/mL) were then added. The amount of NO produced was determined using Griess' reagent and expressed as IC_{50}, i.e. the concentration required to inhibit NO production by 50%. Dexamethasone, a known anti-inflammatory agent, served as a positive control, while cells untreated with LPS constituted the negative control.

Wound healing assay

To assess the potential wound-healing properties of *P. crinita* each extract (LME, FME, and RME), it is crucial to first evaluate their cytotoxicity on human fibroblast cells (HFF1).

Cytotoxicity assessment of extracts on fibroblast cells

Since fibroblast proliferation is a critical step in the wound healing process,[19] it is important to evaluate the ability of these cells to survive and proliferate in the presence of the extracts to determine non-toxic concentrations of the extracts. For this cytotoxicity test, the human fibroblast cell line (HFF1) was used. The same SRB method described in the antiproliferative (cytotoxicity) assay we conducted was also used on HFF1.[17]

Wound healing assay

The cell migration assay was conducted following established protocols from previous studies.[20,21] Initially, HFF1 cells were cultured until they reached confluence in a 48-well plate. Once confluence was achieved, the DMEM medium was removed, and a scratch was made in the cell monolayer using a plastic pipette tip (200 µL). The cells were then rinsed with HBSS to eliminate any detached cells, after which the culture medium containing the extracts (LME, FME, and RME) was added. The concentration tested (400 µg/mL) was chosen based on the results of the SRB assay, which assessed the cytotoxic effects of the plant extracts on fibroblasts. Prior to addition to the cell culture medium, the extracts were dissolved in distilled water. The extract solution was filtered through a nylon filter. The culture medium was used as a negative control and allantoin (10 mg/mL), already proven as a healing agent, was used as a positive control. The injured area was photographed at t = 0, 2, and 4 days with a phase contrast microscope (Nikon Eclipse TS100) coupled to a digital camera (Carl Zeiss Studio Co., Ltd. Axiocam 208 Color, Zeiss). The images were analyzed, and the wound area was determined over time.

Statistical analysis

Statistical analyses were conducted using SPSS Statistics 27.0.1. Data are presented as mean ± standard deviation. One-way ANOVA (α = 0.05) with Tukey's post-hoc test was used to compare three or more groups. Student's t-test was used for pairwise comparisons between the two groups. TPC and FC assays were performed in triplicate, while antiproliferative and anti-inflammatory assays were performed in duplicate per extract concentration.

Results and Discussion

Extraction yield

P. crinita hydromethanolic extracts (LME, FME, and RME) showed extraction yields of 22.5%, 19.2%, and 6.1%, respectively (Table 1). A previous study by Merouane *et al.*[11] on *P. crinita* demonstrated that the extraction yields of hydromethanolic extracts from the plant's leaves and floral parts were comparable to our results, with values of approximately 21.66% and 22.26%, respectively.

Total phenolic content (TPC)

The results of TPC in extracts presented in Table 1, reveal a significant difference ($p<0.05$) between the organs studied. TPC was 128.15 ± 6.33 µg GAE/mg DW in RME, compared to 113.66 ± 4.60 in LME and 92.79 ± 5.18 in FME. Variations in TPC of *P. crinita* may be attributed to factors such as cultivation time, geography, extraction techniques, or others.[22] Some studies have focused on the TPC of this plant species. For instance, Merouane et *al.*,[11] found a similar TPC value of 117.96 ± 1.70 µg GAE/mg DW in the hydromethanolic extract of leaves.

Table 1: Yield of extraction and bioactive content of hydroethanolic extracts from organs of *Phlomis crinita.*

Extract	Yield (% w/w)	Total Phenolics (µg GAE/mg DW)	Flavonoids (µg QE/mg DW)
Leaves (LME)	22.5	113.66 ± 4.60[a]	41.27 ± 1.93[a]
Flowers (FME)	19.2	92.79 ± 5.18[b]	35.32 ± 1.58[b]
Rhizome (RME)	6.1	128.15 ± 6.33[c]	46.91 ± 1.78[c]

Note: w/w: mg extract mass per mg sample mass; µg GAE/mg DW: expressed as µg gallic acid equivalents per mg of extract's dry weight; µg QE/mg: expressed as µg quercetin equivalents (QE) per mg of extract's dry weight; values are means ± standard deviation (n=3); a–c: indicates that values with different letters in the same column are significantly different ($p<0.05$).

Flavonoid content (FC)

The results in Table 1 show a significant difference ($p<0.05$) in FC between organs. RME showed an FC of 46.91 ± 1.78 µg QE/mg DW, while LME and FME showed 41.27 ± 1.93 and 35.32 ± 1.58, respectively. Supporting our findings, Merouane *et al.*,[11] previously documented a significant FT content of 42.72 ± 0.53 µg QE/mg DM in the methanolic extract of *P. crinita* leaves. These results, in conjunction with our own, reinforce the notion that *P. crinita* is a rich source of flavonoids. Flavonoids, a class of compounds renowned for their diverse biological activities, have been shown to exhibit anti-inflammatory, anti-mutagenic, anti-carcinogenic, and antioxidant properties. Additionally, they play a crucial role in regulating the function of key cellular enzymes.[13]

Anti-proliferative potential

Cancer, with millions of new patients diagnosed each year, is one of the leading causes of death worldwide.[35] Therefore, chemoprevention, the use of natural, synthetic, or biological substances to prevent or delay cancer development, offers a promising avenue in the fight against this major global health concern.[24] Moreover, several plant secondary metabolites have been implicated in the management of cancer in both humans and animals.[36] The cytotoxic potential of the hydromethanolic extracts from different parts of *P. crinita* was assessed using five human tumor cell lines and one non-tumor cell line (Table 2). The extracts demonstrated antiproliferative activity with GI_{50} values ranging from 178 to 338 µg/mL in tumor cells. Among the extracts, RME showed the lowest GI_{50} value (178.11 ± 4.10 µg/mL), indicating the most potent antiproliferative effect. According to the American National Cancer Institute, activity <30 µg/mL is considered significant,[7] while others are moderate to weak.

In terms of sensitivity, the AGS cell line was the most responsive, followed closely by the Caco-2, MCF-7, and NCI-H460 cell lines. In contrast, the HeLa cell line showed resistance to the tested concentrations, with GI_{50} values exceeding 400 µg/mL (Table 2), indicating that none of the extracts displayed cytotoxicity against this cell line. Additionally, only the LME and RME extracts were able to inhibit Caco-2 cell proliferation, although the difference between them was not statistically significant ($p>0.05$). Of the extracts tested, LME was the only one that failed to inhibit the proliferation of the NCI-H460 cell line, while the other two extracts demonstrated significant differences ($p<0.05$), with RME exhibiting the lowest GI_{50} value (259.93 ± 22.11 µg/mL). Furthermore, the AGS and MCF-7 cell lines were inhibited exclusively by RME. Notably, none of the extracts showed antiproliferative potential against the HeLa cell line at the tested concentrations. Importantly, all extracts were non-toxic to the non-tumor Vero cell line (GI_{50}>400 µg/mL), indicating a favorable safety profile. The reported bioactivity is most probably correlated with the phenolic content of the extracts. Indeed, RME with higher phenolic content was the one with higher cytotoxicity. Several mechanisms have been elucidated to describe the interaction between phenolic compounds and tumor cells. These include the induction of apoptosis, cell cycle arrest, and the prevention of metastasis and invasion.[25]

Previous studies have primarily focused on the cytotoxic effects of extracts from various *Phlomis* species, particularly those derived from aerial parts such as flowers and leaves.[7] While these studies have demonstrated varying degrees of cytotoxicity against human cancer cell lines, our investigation represents the first to explore the antiproliferative effects of *P. crinita*, specifically focusing on its rhizome extract (HRE). Stojković *et al.*,[33] reported a weak anti-proliferative effect of *P. fruticosa* methanolic extract against the MCF-7 cell line (GI_{50} = 454 µg/mL), our *P. crinita* HRE exhibited more potent activity against this cell line with a lower GI_{50} value of 255.93 µg/mL. Furthermore, this study is the first to report the antiproliferative effects of a *Phlomis* species against NCI-H460 and AGS cell lines. Despite the observed antiproliferative activity, future research should aim to enhance the potency of *P. crinita* hydromethanolic extracts. This could be achieved through rigorous fractionation and isolation of the bioactive compounds responsible for the observed effects.

The anti-inflammatory activity

Inflammation typically arises from various stimuli, including trauma, infectious agents, and chemicals. Macrophages play essential roles in the inflammatory response by producing a range of signaling molecules. Upon activation, these macrophages respond to pathogen invasion by secreting pro-inflammatory cytokines and inflammatory mediators, including nitric oxide. However, excessive nitric oxide production can trigger the inflammatory cascade, potentially leading to systemic inflammatory response syndrome (SIRS).[26,27] Therefore, compounds that can scavenge nitric oxide or inhibit its production are of great interest due to nitric oxide's role in promoting lipid peroxidation and chronic inflammation. Inhibiting nitric oxide offers potential therapeutic advantages.[28]

Table 2 - Anti-proliferative activity of *Phlomis crinita* hydromethanolic extracts against human tumor cell lines and non-tumor cells

Cell line	RME (GI_{50} µg/mL)	FME (GI_{50} µg/mL)	LME (GI_{50} µg/mL)
Tumor cell			
HeLa	>400	>400	>400
MCF7	255.93 ± 22.11	>400	>400
Caco-2	226.37 ± 2.58 [a]	>400	246.07 ± 19.82 [a]
NCI-H460	259.93 ± 22.11[a]	338.34 ± 8.99 [b]	>400
AGS	178.11 ± 4.10	>400	>400
Non-tumor cell			
Vero	>400	>400	>400

Note: values expressed as arithmetic mean ± standard deviation (n = 2). According to Student's t-test, means followed by the same letter on the same line are not statistically different ($p< 0.05$). GI_{50}: extract concentration corresponding to 50% growth inhibition activity. RME: rhizome, FME: flowers, LME: leaves. MCF-7: breast adenocarcinoma, NCI-H460: lung carcinoma, HeLa: cervical carcinoma, AGS: gastric adenocarcinoma, Caco-2: colorectal adenocarcinoma, and Vero: primary cell culture obtained from African green monkey kidney. Elipticine values in µg/mL - HeLa: 1.01 ± 0.03; MCF-7: 1.02 ± 0.02; Caco-2: 1.21 ± 0.02; AGS: 1.23 ± 0.03; NCI-H460: 1.01 ± 0.01; VERO: 1.41 ± 0.06.

In this context, the anti-inflammatory activity of the extracts (LME, FME, and RME) was assessed by evaluating their ability to inhibit nitric oxide (NO) production induced by LPS in murine macrophage-like RAW 264.7 cells. All extracts demonstrated anti-inflammatory activity, with IC_{50} values ranging from 152 to 386 µg/mL. The highest activity was observed in RME (152.42 ± 10.88 µg/mL), which contains a greater quantity of phenolic compounds, followed by LME (209.85 ± 7.74 µg/mL) and FME (386.95 ± 2.68 µg/mL). Notably, the differences in IC_{50} values among the extracts were statistically significant ($p< 0.05$). This is the first study to evaluate the ability of *P. crinita* extract to modulate NO synthesis and release in LPS-stimulated RAW cells. However, in other *Phlomis* genus species, a remarkable anti-inflammatory activity of *P. rigida* extracts was observed in their ability to modulate NO synthesis and release in LPS-stimulated RAW cells.[26] Previous studies have shown that the methanol extract of *P. crinita* demonstrated significant anti-inflammatory activity by preventing protein denaturation and stabilizing human red blood cell membranes.[10]

The observed inhibition of NO production may be attributed to the presence of phenols, as numerous studies have shown that phenols serve as effective anti-inflammatory agents and play a crucial role in modulating oxidative stress and inflammation.[29,30] Furthermore, extracts may function by inhibiting inducible nitric oxide synthase (iNOS) or through their antioxidant properties.[28]

Evaluation of Wound Healing in Vitro

Cytotoxicity Assessment of Extracts on Fibroblast Cells

To assess the wound-healing potential of the extracts, it was first necessary to evaluate their cytotoxicity on human fibroblast cells (HFF1). Treatment with the extracts (LME, FME, RME) showed toxicity to fibroblast cells, as confirmed by the SRB method. A decrease in color intensity with increasing extract concentration indicated a significant reduction in cell proliferation. The GI_{50} value, representing the concentration of extract responsible for 50% growth inhibition, was calculated to be >400 µg/mL for all extracts. This concentration (400 µg/mL) was used to assess the toxic effects of the plant extracts on fibroblasts.

Wound healing assay

The physiological wound-healing process takes place in four successive but interrelated stages: homeostasis, inflammation, proliferation, and remodeling, culminating in the formation of scar tissue.[19] The migration of fibroblasts to the wound site is essential for successful wound healing. To study this migration process, we analyzed the closure of an open wound zone, created in a monolayer of cells (scratch assay).[31] Results, presented in Figure 1, demonstrate that extracts from leaves (LME) and flowers (FME) enhanced fibroblast migration. LME exhibited effects comparable to the positive control (allantoin), while RME (rhizome) showed practically no cell migration.

To support these findings, the scratch assay is widely used to investigate the *in vitro* wound-healing potential of plant-derived compounds. Study by Okur *et al.*,[37] have shown that wound closure was enhanced when L929 fibroblast cell lines were treated with *Phlomis pungens* extract. While our study provides compelling evidence for the *in vitro* wound-healing potential of *P. crinita* extracts, *in vivo* validation is crucial. Previous research by Baali *et al.*,[6] has demonstrated both the safety and efficacy of *P. crinita* methanolic extract in animal models. Their findings indicate that this extract significantly accelerated wound healing in animal models, even outperforming the reference drug in certain cases. Moreover, it is hypothesized that the antioxidant and anti-inflammatory activities of the extracts also contribute to the wound-healing effect.[34] In fact, the wound-healing effects of *P. crinita* extracts may be attributed to their antioxidant and anti-inflammatory activities.[10,11,12] These findings strongly suggest that *P. crinita* extracts possess promising wound-healing properties and warrant further investigation for potential therapeutic applications. This also confirms the use of *P. crinita* leaves in traditional medicine to heal wounds. Medicinal plants have long been valued for their wound-healing properties, largely due to the bioactive compounds they contain, which work through multiple mechanisms. Among these compounds, polyphenols play a particularly important role in promoting wound healing. Some polyphenols demonstrate antimicrobial activity against bacteria commonly associated with chronic wound infections. The combination of polyphenols' strong antimicrobial, anti-inflammatory, and antioxidant properties has spurred researchers to investigate their effects on wound healing.[3]

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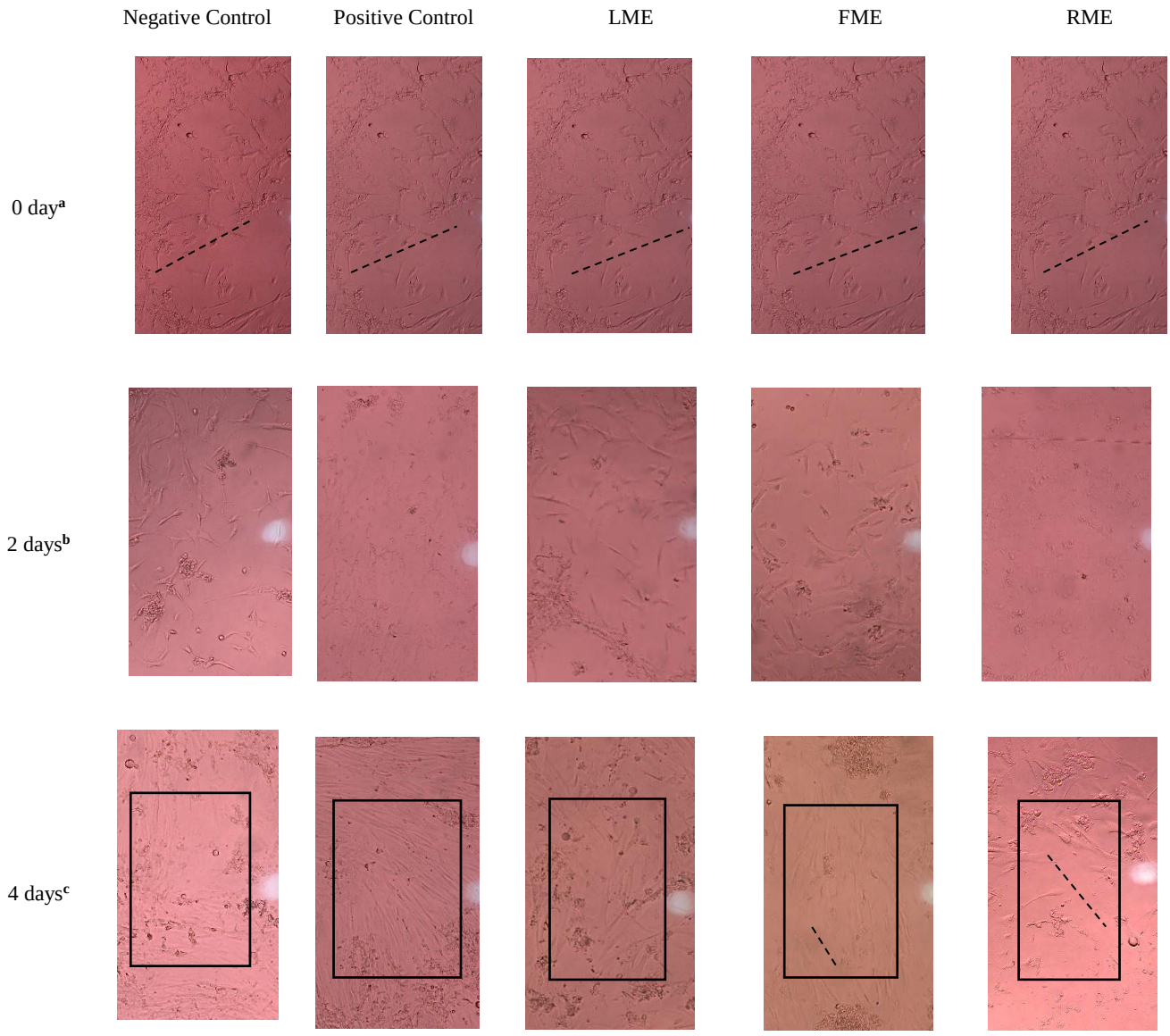

Figure 1: *In vitro* scratch assay assessing HFF1 fibroblast cell migration over 4 days. A confluent monolayer was scratched, and cells were treated with *P. crinita* extracts (LME : leaves, FME: flowers, RME: rhizome) at 400 µg/mL, allantoin at 10 mg/mL (positive control), or left untreated (negative control). Images were captured at 0, 2, and 4 days post-scratch. (a) Establishing a clear wound area. (b) No significant changes in wound closure were observed across treatments. (c) By day 4, the positive control exhibited complete wound closure with strong cell migration, and LME treatment achieved complete wound closure, though cell migration was less pronounced. FME treatment resulted in partial closure; on the other hand, in the treatment with RME, the wound remained visible, and there was practically no cell migration.

Conclusion

Despite the advancements in modern healthcare, medicinal plants continue to serve as valuable therapeutic options. When produced with high standards of quality, safety, and efficacy, plant-based medications offer viable alternatives. In this study, extracts from *Phlomis crinita* demonstrated potential bioactivity, including antiproliferative, anti-inflammatory, and wound-healing properties. Among the extracts tested, the hydromethanolic extract from the rhizome exhibited the strongest antiproliferative and anti-inflammatory effects, while the leaf extract demonstrated the greatest wound-healing potential, comparable to a commercial wound-healing agent. These therapeutic effects are likely attributable to the bioactive compounds present in *P. crinita*, particularly phenolic compounds and flavonoids. Moreover, the observed wound healing in some extracts aligns with the traditional use of the leaves of this plant to treat wounds. Furthermore, although all extracts showed some degree of antiproliferative and anti-inflammatory activity, the effects observed were modest, suggesting the need for further research and optimization to fully exploit their potential for anti-cancer and anti-inflammatory applications. Ultimately, the findings suggest that *P. crinita* could be a promising source for the development of novel pharmaceutical agents.

Conflicts of Interest

The authors declare no conflict of interest

Authors' Declaration

The authors hereby declare that the works presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

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