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Electrospun PCL/PEG nanofibers incorporating *Plantago lanceolata* extract and clove oil for dual-function wound dressingsSelin Nur Teke¹ , Adile Yürük^{1,2} and İsmail Alper İsoğlu^{3,*} ¹ Graduate School of Engineering and Science, Bioengineering Division, Abdullah Gül University, 38080 Kayseri, Türkiye² Bilkent University, National Nanotechnology Research Center (UNAM), 06800 Ankara, Türkiye³ Faculty of Life and Natural Science, Department of Bioengineering, Abdullah Gül University, 38080 Kayseri, Türkiye

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E-mail: alper.isoglu@agu.edu.tr**Keywords:** electrospinning, PCL/PEG, *Plantago lanceolata* extract, clove oil, antibacterial wound dressingSupplementary material for this article is available [online](#)

Abstract

In this study, we developed electrospun polycaprolactone/polyethylene glycol (PCL/PEG) nanofibers loaded with *Plantago lanceolata* (*P. lanceolata*) extract and clove oil to evaluate their combined potential for wound healing and antibacterial activity. PCL/PEG nanofibers were electrospun and post-loaded with *P. lanceolata* extract at 5%, 10%, and 15% (w/v), together with 1% (v/v) clove oil. Scanning electron microscope analysis showed a uniform, bead-free nanofibrous structure, with fiber diameters ranging from 768 ± 140 nm to 892 ± 206 nm and pore sizes from 3.93 ± 0.97 μ m to 6.20 ± 1.16 μ m. The nanofibers exhibited swelling ratios between $103.23 \pm 16.42\%$ and $133.93 \pm 40.45\%$ within 1 h and showed gradual degradation ranging from $25.92 \pm 2.84\%$ to $57.76 \pm 0.92\%$ over 21 d, with cumulative extract release approaching a plateau by day 28 under the experimental conditions. The incorporation of plant extract and essential oil initially increased the water contact angle from $15.97 \pm 1.07^\circ$ to $48.61 \pm 7.85^\circ$, indicating that the nanofiber surface remained hydrophilic; at higher extract contents, the nanofibers transitioned to a superhydrophilic state. Antibacterial activity was primarily governed by clove oil, yielding up to $85.16 \pm 0.36\%$ efficacy against *E. coli* (*E. coli*) and $79.90 \pm 0.29\%$ against *S. aureus* (*S. aureus*). While *P. lanceolata* extract alone showed limited antibacterial activity, its presence within clove oil-loaded nanofibers consistently enhanced antibacterial performance at the composite level. *In vitro* scratch assays demonstrated pronounced wound closure at later time points (72–96 h), particularly for nanofibers containing higher extract concentrations, confirming the dominant contribution of *P. lanceolata* to the healing response. Overall, the electrospun PCL/PEG nanofibers represent a dual-function wound dressing, with clove oil contributing antibacterial protection and *P. lanceolata* extract supporting wound healing.

1. Introduction

Every year, approximately 8.2 million people suffer from chronic and acute wounds or wound-related infections [1]. Conventional wound dressings may fail to provide an antibacterial environment or meet the healing requirements. Therefore, there is a significant demand for advanced antibacterial wound dressings to maintain adequate hydration by absorbing excess exudate without adhering to the wound, preventing microbial contamination, and enhancing wound healing [2, 3].

Electrospinning is a versatile technique for fabricating nanofiber-based wound dressings with a high surface area, good oxygen permeability, suitable mechanical properties, and the ability to release bioactive agents [4]. Various natural and synthetic polymers have been used to produce electrospun nanofibers [5]. PCL, an FDA-approved, biocompatible, and biodegradable aliphatic polyester, is highly preferred for wound dressing applications due to its adjustable morphology, degradation rate, and mechanical properties [6]. However, its hydrophobicity and lack of functional groups limit

its ability to support cell adhesion and migration [7]. To address this limitation, PCL is often blended with hydrophilic polymers such as PEG. Blending PCL with PEG improves wettability, porosity, and degradation behavior [8].

Plant-based bioactive dressings have gained interest for their antimicrobial and regenerative effects [9]. *Plantago lanceolata* (*P. lanceolata*) is known for its anti-inflammatory, antioxidant, and wound healing properties. Its biological activities are attributed to compounds like aucubin, flavonoids, and polyphenols [10–12]. Studies have reported that *P. lanceolata* extract has been associated with enhanced wound healing, including epithelial regeneration and angiogenesis responses mediated by ANGPT-2 and TGF- β 1 [13]. Besides, electrospun nanofibers with *Plantago australis* and *Plantago major*, which are of the same genus as *P. lanceolata*, have shown antibacterial, anti-inflammatory, and antioxidant activity [14, 15].

Nevertheless, the literature reports that the aqueous and methanolic extracts of *P. lanceolata* do not exhibit significant antibacterial activity against Gram-positive or Gram-negative bacteria [16–18]. Clove oil is another natural agent that has antimicrobial, anti-inflammatory, and antioxidant effects due to its high eugenol content [19, 20]. It can damage bacterial cell membranes and may act synergistically with antibiotics [21]. Electrospun clove oil-containing nanofibers have demonstrated biocompatibility and limited antibacterial activity in wound-healing applications. The literature noted that adding clove oil to PCL-GEL nanofibers did not result in a significant difference in wound closure rates compared to the absence of clove oil. Therefore, although these wound dressings containing clove oil have demonstrated antibacterial activity, they have shown limited efficacy in promoting wound healing [22–24].

Although plantago extracts have been incorporated into various polymeric matrices, their limited antibacterial activity may restrict their effectiveness in providing both infection control and wound healing within a single dressing. Therefore, we combined *P. lanceolata* extract with clove oil as bioactive agents to improve wound-healing activity while preventing bacterial contamination with a single dressing. The *P. lanceolata* extract and clove oil were incorporated into electrospun PCL/PEG nanofibers. The obtained nanofibers were characterized structurally and biologically. Their antibacterial activity was assessed against *E. coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) using the Kirby-Bauer disc diffusion test and the Luria-Bertani (LB) microdilution test, while cell viability and wound-healing activity were assessed in fibroblasts using an MTT assay. To the authors' knowledge, electrospun PCL/PEG nanofibers containing *P. lanceolata* extract and clove oil have not been reported previously. The primary aim of our

study was to investigate the wound-healing potential and the synergistic effect of *P. lanceolata* extract and clove oil-loaded PCL/PEG nanofibers. The results indicate that these nanofibers are promising candidates for wound-dressing applications.

2. Materials and methods

2.1. Materials

Polycaprolactone (PCL, average $M_n = 80\,000$; CAS: 24 980–41–4), polyethyleneglycol (PEG, average $M_n = 2000$; CAS: 25 322–68–3), phosphate-buffered saline (PBS), methyl thiazolyl diphenyl-tetrazolium bromide (MTT), and 4',6-diamidino-2-phenylindole dihydrochloride (DAPI) were purchased from Sigma-Aldrich (USA). LB broth, LB agar, chloroform, methanol, dichloromethane (DCM), and dimethylformamide (DMF) were obtained from Merck (USA). The electrospinning device (Inovenso NE100, İstanbul, Türkiye) was used to fabricate the electrospun nanofibers. Fetal bovine serum (FBS), Dulbecco's modified eagle medium high glucose (DMEM), penicillin/streptomycin, and trypsin/EDTA were purchased from Serox (USA). Clove oil was purchased from a local market in Kayseri, Türkiye. *P. lanceolata* was collected at coordinates 39°52'15.7"N, 33°38'28.6"E (Kırıkkale, Türkiye). *E. coli* (ATCC BAA-1025), *S. aureus* (ATCC 6538) strains, and human dermal fibroblast cells (ATCC PCS201-010) were obtained from ATCC (USA).

2.2. Extraction of *P. lanceolata*

The plant materials were washed with water and dried in an incubator at 40 °C for 8 h. Subsequently, 50 g of the dried plant material was extracted with 350 ml of a chloroform: methanol: distilled water solvent mixture (4:2:1, v/v) using sonication for 1 h. Following extraction, the solvents were removed from the mixture using a rotary evaporator (Rotavapor R300, Büchi, Germany). The dried extract was stored at –20 °C for future use.

Gas chromatography-mass spectrometry (GC-MS/QP2010 Ultra, Shimadzu, Japan) was performed on the extract dissolved in methanol using a capillary column (Rtx-5 MS, 30 m $\times$ 0.25 mm $\times$ 0.25 μ m, Restek 1264), with helium as the carrier gas at a flow rate of 2 ml min^{–1}. The compounds in *P. lanceolata* extract were identified by comparing the obtained spectra with the NIST library [5].

2.3. Fabrication of electrospun nanofibers

PCL and PEG pellets at a 6:4 (w/w) ratio were dissolved in 5 ml of DCM/DMF (9:1, v/v) solvent mixture and stirred overnight to form an 18% (w/v) blend solution. The homogeneous polymer solution was transferred into a 5 ml syringe and fitted with a 21 G

Table 1. The nomenclature of electrospun nanofibers.

Nanofiber	PCL/PEG (% w/v)	<i>Plantago lanceolata</i> extract (% v/v)	Clove oil (% v/v)
ST1	18	—	—
ST2	18	5	1
ST3	18	10	1
ST4	18	15	1
ST5	18	15	—
ST6	18	—	1

needle tip. The electrospinning parameters were optimized as follows: flow rate: 1.9 ml h^{-1} , voltage: 17 kV, and distance between the tip and collector: 17 cm.

To prepare extract-infused nanofibers, 5%, 10%, and 15% *P. lanceolata* extract and 1% clove oil were mixed in 0.25 ml of distilled water. The mixture was vortexed for 1 min and then ultrasonicated for 5 min to obtain a uniform dispersion. Scanning electron microscope (SEM) analysis showed no noticeable aggregation, indicating that the extract and clove oil were well distributed. The PCL/PEG nanofibers ($2.5 \text{ cm} \times 2.5 \text{ cm}$) were immersed in these solutions for 15 min to allow absorption of the extract/oil mixture, then dried at 37°C for 2 h. The neat PCL/PEG nanofiber was labeled ST1, while the nanofibers containing 5%, 10%, and 15% *P. lanceolata* extract and 1% clove oil were labeled ST2, ST3, and ST4, respectively (table 1).

The selection of the 6:4 (w/w) PCL/PEG ratio and the 18% (w/v) total polymer concentration was based on preliminary experiments aimed at achieving uniform, bead-free fibers with sufficient mechanical integrity and hydrophilicity. These parameters were optimized through trial formulations varying polymer ratios and concentrations, where the 6:4 ratio consistently yielded fibers with optimal morphology and handling properties. The *P. lanceolata* extract concentrations (5%, 10%, and 15% w/v) were chosen to evaluate dose-dependent effects while avoiding saturation or cytotoxicity, guided by previous literature on similar plant extracts. Clove oil was fixed at 1% (v/v) based on its known antimicrobial potency at low concentrations and to maintain nanofiber biocompatibility. The electrospinning conditions used in this study were selected based on preliminary optimization studies to obtain reproducible nanofibers with suitable structural and biological properties.

2.4. Characterization of electrospun nanofibers

2.4.1. Morphological characterization

The morphological properties of the electrospun nanofibers, including fiber diameter and pore size, were examined using a (SEM, Carl Zeiss EVO LS10, Germany) at magnifications of $1000\times$, $2000\times$, $3000\times$, and $5000\times$. SEM images were processed using ImageJ software (National Institutes of Health, Bethesda, MD, USA) to measure the average fiber diameters and pore sizes of the nanofibers.

2.4.2. Porosity and water uptake capacity

The porosity of electrospun nanofibers was assessed using the liquid displacement method. Each nanofiber's initial weight (W_1) and volume (V) were recorded, and the samples were then placed in 10 ml of ethanol for 10 min. Excess ethanol on the nanofiber surface was removed with filter paper, and the final weight (W_2) was measured. The porosity (%) was calculated according to the following equation:

$$\text{Porosity (\%)} = [(W_2 - W_1) / (\rho \times V)] \times 100 \quad (1)$$

where W_1 and W_2 are the initial and final weights of the nanofiber, respectively, ρ is the density of ethanol, and V is the initial volume of the nanofiber [25].

The swelling test was conducted to determine the nanofibers' water-uptake capacity. The nanofibers were cut into $1 \text{ cm} \times 1 \text{ cm}$ samples, and their weights in water were measured every 10 min. Excess water on the nanofiber surface was gently removed with filter paper. The water uptake percentage was calculated using the following formula:

$$\text{Swelling Ratio (\%)} = [(W - W_0) / W_0] \times 100 \quad (2)$$

W_0 and W represent the dry and swollen weights, respectively [26].

2.4.3. Contact angle measurement

The contact angles of the ST1, ST2, ST3, and ST4 electrospun nanofibers were investigated using the sessile drop technique. A drop of distilled water (drop volume: $4 \mu\text{l}$) was dripped onto the surface of each sample evaluated at room temperature. This technique relies on the time-dependent analysis of the shape and volume of the resulting water droplet image, referencing the Young–Laplace equation. In this analysis, the contact angles of the electrospun nanofibers were measured using a contact angle-fixed drop measurement (Biolin Scientific Attention Theta Lite) and compared. Contact angles were measured in triplicate.

2.4.4. Chemical characterization

The chemical structure of the nanofibers was analyzed using a Fourier transform infrared spectrometer (FTIR, Nicolet 6700, Thermo Scientific, USA) in attenuated total reflectance (ATR) mode. The ATR crystal was cleaned with 70% isopropanol and dried

before each measurement. For FTIR analysis, 10 mg of *P. lanceolata* extract and 1×1 cm nanofibers were placed directly onto the ATR crystal for analysis. The spectra were recorded over $4000\text{--}500\text{ cm}^{-1}$, with a resolution of 4 cm^{-1} and an average of 32 scans; three repetitions of each sample were collected [2].

2.4.5. Weight loss study

An *in vitro* weight loss study was conducted for 7, 14, and 21 d. Nanofibers ($1\text{ cm} \times 1\text{ cm}$) were placed in 10 ml of PBS in Falcon tubes and incubated at 37°C with shaking at 100 rpm. At each time point (7, 14, and 21 d), the nanofibers were removed, dried, and weighed. The percentage weight loss was calculated using the following equation:

$$\text{Weight Loss (\%)} = [(W_0 - W_t) / W_0] \times 100 \quad (3)$$

where W_0 is the initial weight, and W_x is the final weight of the nanofiber [26].

2.4.6. Cumulative release

The *in vitro* release study was conducted to evaluate the release behavior of *P. lanceolata* extract from the electrospun nanofibers (ST2, ST3, and ST4). Samples ($1\text{ cm} \times 1\text{ cm}$) were individually placed into 10 ml of PBS, pH 7.4 in sterile Falcon tubes and incubated at 37°C with orbital shaking at 90 rpm. At predetermined time points (1, 2, 3, 4, 5, 6, 24, 48, 72, 96, 120, 144, 168, 336, 504, and 672 h), 1 ml of release medium was collected and replaced with 1 ml of fresh PBS to maintain sink conditions. The amount of extract released into the medium was quantified using UV-Vis spectrophotometry (Varioskan, Thermo Scientific, USA) at 420 nm. A calibration curve was plotted by measuring the absorbance of *P. lanceolata* extract solutions in water at concentrations ranging from 0.01687 to 0.27 mg ml^{-1} . The resulting curve was linear ($R^2 = 0.9931$, $y = 0.1649x + 0.049$), and the equation below was used to calculate the cumulative release (%):

$$\text{Cumulative release (\%)} = (M_f / M_i) \times 100 \quad (4)$$

where M_f is the final amount of extract released, and M_i is the initial amount of extract in the nanofiber [27].

The drug release kinetics from *P. lanceolata* extract- and clove oil-loaded electrospun nanofibers can be described using zero-order (Z-O), first-order (F-O), Higuchi (H), and Korsmeyer–Peppas (K-P) models [28]

$$\begin{aligned} \text{a) Z - o model:} & \quad \frac{M_t}{M_\infty} = k_0 t \\ \text{b) H - o model :} & \quad \ln \left(\frac{M_t}{M_\infty} \right) = k_1 t \\ \text{c) H model :} & \quad \frac{M_t}{M_\infty} = k_H \sqrt{t} \\ \text{d) K - p model:} & \quad \frac{M_t}{M_\infty} = k_{kp} t^n \end{aligned} \quad (5)$$

M_t/M_∞ : represents the amount of extract released from the formulation at a specific time (t). k_0 : zero-order release rate constant, k_1 : first-order release rate constant, k_H : Higuchi release rate constant, k_{kp} : Korsmeyer–Peppas release rate constant [28, 29].

Drug-loading percentages of the nanofibers were investigated. Firstly, the neat PCL/PEG electrospun nanofibers ($1\text{ cm} \times 1\text{ cm}$) were weighed. $40\text{ }\mu\text{l}$ of extract/oil solution was added to the nanofibers, which were then allowed to dry completely. The final weights of the dried nanofibers were weighed, and drug loading (%) was calculated according to the following equation:

$$\begin{aligned} \text{Drug loading (\%)} & \\ & = (\text{loaded weight} / \text{initial weight}) \times 100. \end{aligned} \quad (6)$$

2.4.7. Antibacterial activity

The antibacterial activities of the nanofibers were evaluated using the Kirby–Bauer disc diffusion method and bactericidal ratio test against *E. coli* and *S. aureus*. Bacterial suspensions (10^6 CFU ml^{-1}) were prepared in LB medium. For the disc diffusion test, nanofibers (0.5 cm diameter discs) were placed on the LB agar plates inoculated with bacterial suspension. The plates were incubated at 37°C for 16 h, and the inhibition zones were measured [2]. For the bactericidal ratio test, nanofiber pieces ($1\text{ cm} \times 1\text{ cm}$) were placed in sterile tubes containing $20\text{ }\mu\text{l}$ of bacterial suspension (10^6 CFU ml^{-1}) and incubated at 37°C for 2 h. After incubation, the samples were washed with PBS, and the suspensions were transferred to a fresh LB medium. Ampicillin was used as the positive control, and pure LB medium was used as the blank. Bacterial growth was monitored by measuring optical density (OD) at 600 nm with a microplate reader (Varioskan, Thermo Scientific, USA) after 12 h of incubation. The bactericidal ratio (%) was calculated using the following equation [30].

$$\begin{aligned} \text{Bactericidal ratio (\%)} & = [(OD_{\text{control}} - OD_{\text{sample}}) \\ & \quad / OD_{\text{control}}] \times 100. \end{aligned} \quad (7)$$

2.4.8. Cell viability assay

The human dermal fibroblast cell line was used to evaluate, under sterile conditions, *in vitro* cell viability (%), cell attachment, and the scratch assay performance of the nanofibers. Fibroblast cells were cultured in DMEM-High Glucose medium supplemented with 10% FBS and 1% penicillin/streptomycin, incubated at 37°C in a humidified atmosphere containing 5% CO_2 . The nanofibers were cut into $2\text{ mm} \times 2\text{ mm}$ pieces and sterilized using 70% (v/v) ethanol solution for 5 min, followed by UV irradiation for 1 h [27]. The sterilized nanofibers were placed in 96-well plates containing fibroblast cells pre-seeded on the well surface at a density of

1×10^4 cells well⁻¹. The nanofibers were incubated for 24, 48, 72, and 96 h. Following incubation, nanofibers were gently removed from wells before the addition of MTT reagent [2]. This procedure was carried out to prevent any potential material-related interference, including nonspecific adsorption of MTT/formazan products and background absorbance from the nanofiber during spectrophotometric measurement. Then, 10 μ l of MTT reagent was added to each well containing the adherent cells [31, 32]. After 2 h of incubation in the dark, the plates were centrifuged, the supernatant was discarded, and 100 μ l DMSO was added to each well. Absorbance was measured using a microplate reader (Varioscan, Thermo Fisher, USA) at 570 nm. The cell viability (%) was calculated using the following equation [33]:

$$\begin{aligned} \text{Cell Viability (\%)} \\ = [\text{Mean OD}_{\text{sample}} / \text{Mean OD}_{\text{control}}] \times 100. \end{aligned} \quad (8)$$

2.4.9. Cell attachment assay

The nanofibers (4×4 mm) were placed in 96-well plates, and 1×10^4 cells were seeded into each well. After incubation for 24 and 72 h, the culture media were removed, and the nanofibers were washed with PBS to eliminate non-adherent cells. The nanofibers were then fixed with 2.5% (v/v) glutaraldehyde overnight at 4 °C. To visualize cell nuclei, 20 μ l of DAPI staining solution was applied to each membrane, and the nanofibers were incubated in the dark for 5 min. The stained nuclei were examined using a fluorescence microscope (LEICA DM6 B, Germany) at 20 $\times$ magnification with the Leica Application Suite X (LAS X) software.

2.4.10. In vitro scratch assay

To assess the nanofiber's potential to support cellular activities relevant to wound healing, an *in vitro* scratch assay was performed to measure scratch area closure. Initially, fibroblast cells (1×10^5 cells well⁻¹) were seeded into 6-well plates and incubated at 37 °C for 24 h. The linear scratch was created using a sterile 200 μ l pipette tip, and the nanofibers were then placed in the wells. Six-well plates for incubation at 24, 48, 72, and 96 h were prepared separately. At the end of the 24 hour incubation period, the nanofibers were removed from the wells and imaged under a microscope. The same procedure was carried out for the six-well plates left for incubation at 48, 72, and 96 h. After incubation for 24, 48, 72, and 96 h, wound images were captured using a microscope-mounted camera (Dino-Lite Camera). The reduction in scratch area was quantified using ImageJ software based on the following equation [34]

$$\text{Relative Scratch Closure (\%)} = [(A_i - A_f) / A_i] \times 100 \quad (9)$$

where A_i denotes the initial scratch area, and A_f represents the final scratch area.

2.4.11. Mechanical characterization

Uniaxial tensile testing was performed on the nanofibers using a universal testing machine (AGS-X, 10 kN, Shimadzu, Japan) at a strain rate of 1×10^{-2} s⁻¹ [35]. The samples (10 mm wide, 40 mm long, and 0.47 mm thick) were subjected to mechanical testing. Force and displacement data were recorded from TRAPEZIUM-X software, and stress-strain curves were plotted. Ultimate tensile strength (UTS), elongation at break, and Young's modulus were calculated from the stress-strain curves using the following equation:

$$\text{UTS} = F_m / A_0 \quad (10)$$

where F_m is the maximum force, A_0 is the cross-sectional area of the nanofiber,

$$\text{Elongation (\%)} = (L_0 - L_x / L_0) \times 100 \quad (11)$$

where L_x is the length at break, and L_0 is the initial gauge length of the nanofiber [36].

2.5. Statistical analysis

The experiments were conducted in triplicate ($n = 3$), and the results were presented as mean $\pm$ standard deviation (SD). Graphs were plotted using OriginLab and Graphpad Prism software. Statistical analyses were conducted using GraphPad Prism 10. A one-way ANOVA test was used, and $p < 0.05$ was considered statistically significant.

3. Results and discussion

3.1. Extraction of *P. lanceolata*

In this study, the phytochemical profile of the *P. lanceolata* extract was analyzed by GC-MS. The results are represented in figure 1. GC-MS analysis revealed that the extract mainly contained fatty acids and esters (e.g. palmitic acid derivatives, linolenic acid), alcohols (1-dodecanol, phytol), hydrocarbons (heptadecane, hexadecane), ketone and diol derivatives, and terpenoid compounds (neophytadiene, phytol derivatives) (supplementary table 1).

Several of these compounds, including the n-hexadecanoic acid, octadecanoic acid, hexadecanoic acid, methyl ester, and 9,12,15-octadecatrienoic acid, have been previously reported as characteristic constituents of *P. lanceolata* [37]. Hexadecanoic acid, palmitic acid, and octadecatrienoic acid (commonly called linolenic acid) are fatty acids that have been reported to exhibit antibacterial and antifungal activity under certain conditions. Similar profiles of decanoic acid and its derivatives have also been reported in previous GC-MS analyses of *P. lanceolata*

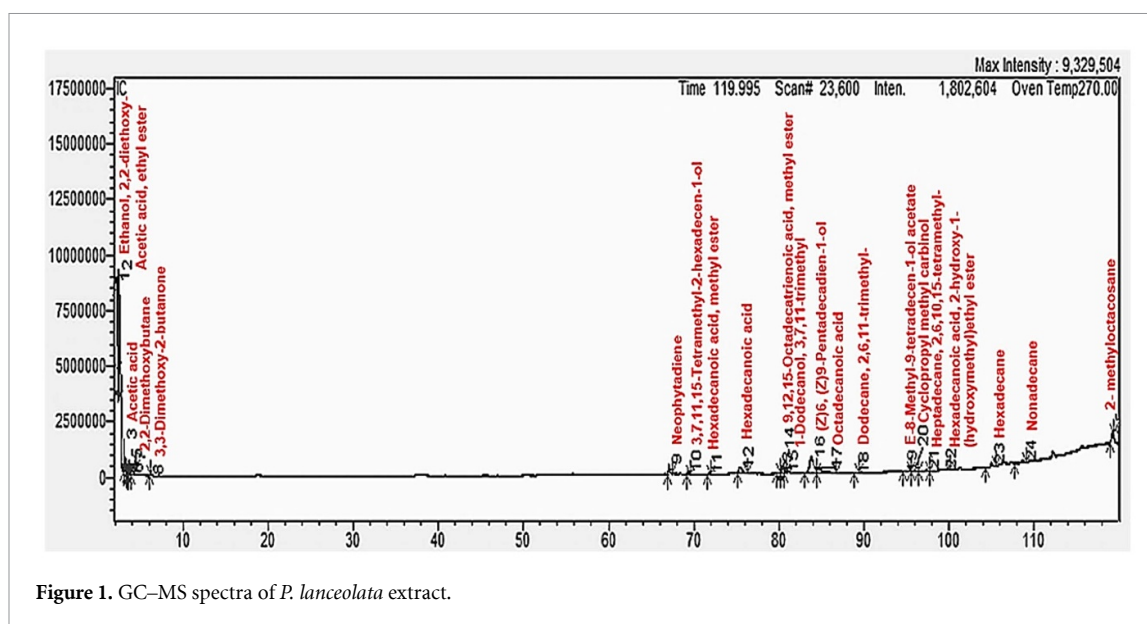


Figure 1. GC-MS spectra of *P. lanceolata* extract.

[12]. Our findings indicate that the chemical composition of the *P. lanceolata* extract is consistent with these earlier reports.

3.2. Characterization of electrospun nanofibers

3.2.1. Morphological characterization

The morphological characteristics of the nanofibers were examined using SEM, and the results are shown in figure 2. The extract- and oil-containing nanofibers were labeled ST2, ST3, and ST4, as shown in table 1.

SEM images revealed a homogeneous distribution of fibers across the nanofibers, and the incorporation of *P. lanceolata* extract and clove oil did not damage the fiber structure, resulting in a uniform, bead-free morphology. No visible signs of aggregation were observed, and both extract and oil appeared well integrated within the fibers.

The SEM images showed that increasing the concentration of *P. lanceolata* extract affected the morphology of the electrospun nanofibers. ST2 and ST3 exhibited relatively homogeneous fibers, whereas partial structural irregularities became more noticeable in ST4. This difference may be related to changes in solution properties after the addition of higher extract concentrations. Similar observations have been reported in electrospun systems containing plant-derived bioactive compounds, where variations in viscosity and intermolecular interactions influenced fiber formation and surface morphology. Despite these structural changes, the nanofibers maintained a continuous fibrous architecture without severe bead formation, indicating that the selected electrospinning parameters remained suitable for nanofiber production.

When the viscosity and polymer blend ratio are well balanced, chain entanglement increases, and fiber formation becomes more stable. In this study,

using 18% (w/v) total polymer concentration and a 6:4 (w/w) PCL/PEG ratio resulted in consistent, bead-free fibers [38].

The average fiber diameters and pore sizes of the nanofibers are presented in figure 3. The mean fiber diameters were 800.64 ± 161 nm, 768.21 ± 140 nm, 892 ± 206 nm, and 858 ± 213 nm for ST1, ST2, ST3, and ST4, respectively. The corresponding average pore sizes of the electrospun nanofibers were 6.20 ± 1.16 μ m, 4.58 ± 0.82 μ m, 4.19 ± 0.97 μ m, and 3.93 ± 0.97 μ m for ST1, ST2, ST3, and ST4, respectively.

Following the incorporation of the extract and oil, a thin coating layer was formed on the PCL/PEG nanofibers, resulting in a slight increase in fiber diameter and a reduction in pore size due to narrowing of the pore areas. Fiber diameters of ST1 and ST2 were comparable, whereas increasing extract concentration led to a noticeable increase in fiber diameter, particularly in ST3 and ST4. The observed increase in fiber diameter may be attributed to the elevated viscosity of the polymer solution, as the electrospinning process is sensitive to viscosity.

In a previous study, the average diameter of electrospun PCL/PEG fibers (3:1 ratio) containing 12.5% naringenin was reported as 666 ± 144 nm [39]. Similarly, 10% (w/v) PCL nanofibers demonstrated fiber diameters of 233.2 ± 84.2 nm, while the addition of 5.3% and 10.6% (w/v) *Plantago major* extract increased fiber diameters to 235 ± 72.2 nm and 378.5 ± 118.5 nm, respectively. These increases were attributed to solution instabilities caused by phase separation during electrospinning, likely due to differences in polarity between the polymer and the extract [14]. Moreover, increasing the clove oil concentration in PCL/gelatin nanofibers increased fiber diameters from 241 ± 96 nm to

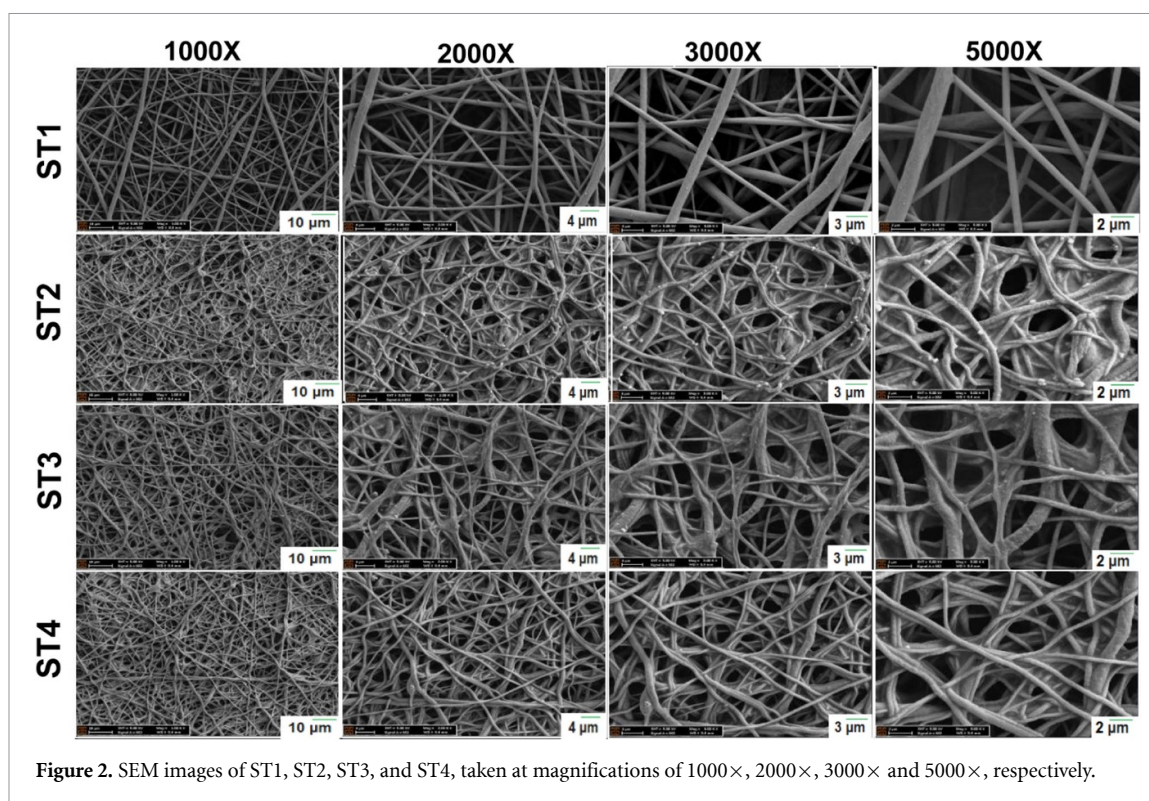


Figure 2. SEM images of ST1, ST2, ST3, and ST4, taken at magnifications of 1000 $\times$, 2000 $\times$, 3000 $\times$ and 5000 $\times$, respectively.

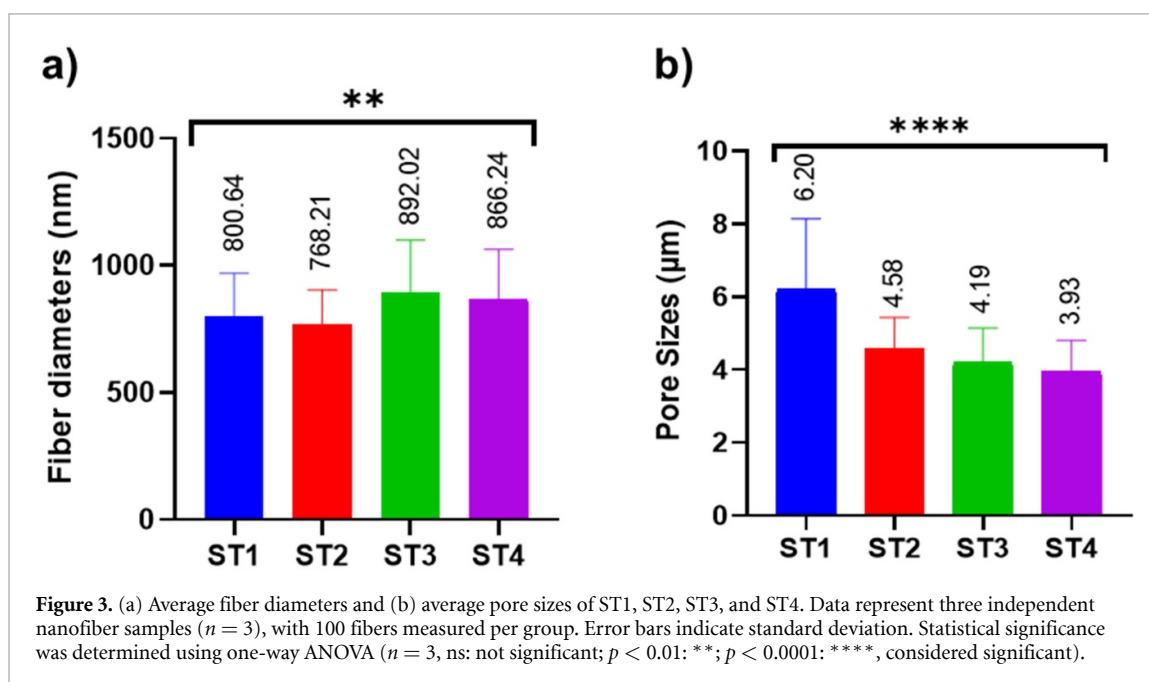


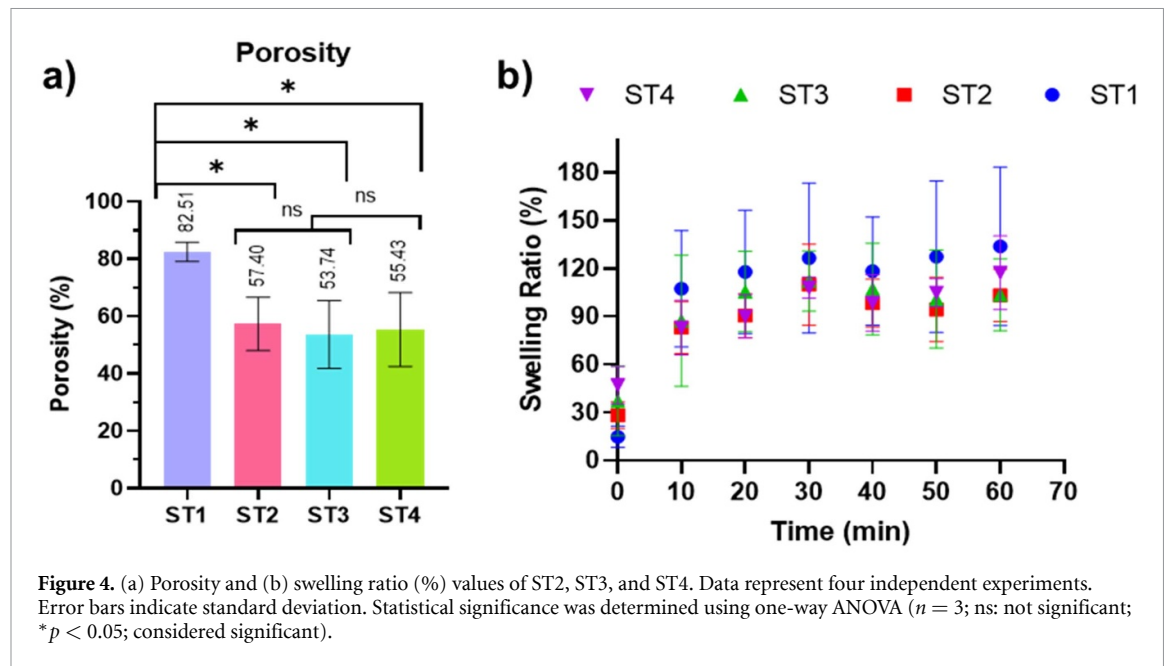
Figure 3. (a) Average fiber diameters and (b) average pore sizes of ST1, ST2, ST3, and ST4. Data represent three independent nanofiber samples ($n = 3$), with 100 fibers measured per group. Error bars indicate standard deviation. Statistical significance was determined using one-way ANOVA ($n = 3$, ns: not significant; $p < 0.01$: **; $p < 0.0001$: ****, considered significant).

305 ± 82 nm. This effect was attributed to interactions between the oil and polymer matrix, which reduced the solution's electric conductivity and increased its viscosity [24]. The addition of camptothecin to PCL fibers increased the fiber diameter from 300 ± 50 nm to 500 ± 20 nm, likely due to the compound's incorporation into the fibers [40]. For the wound dressing nanofibers, pore sizes ranging from 4 to $50 \mu\text{m}$ are considered suitable for gas exchange and molecular infiltration at the wound area [41].

3.2.2. Porosity and water absorption

Wound dressing nanofibers should efficiently absorb wound exudates to maintain a moist environment and possess sufficient porosity to allow oxygen permeability, both of which are essential for wound healing [19, 27, 42, 43]. As shown in figure 4(a), ST1 exhibited a porosity of $82.51 \pm 3.39\%$, while ST2, ST3, and ST4 demonstrated porosity of $57.4 \pm 9.32\%$, $53.73 \pm 11.84\%$, and $55.43 \pm 12.87\%$, respectively.

The water-absorption capacity of the electrospun nanofibers was assessed using a swelling test, and



the results are shown in figure 4(b). The swelling ratios were $133.93 \pm 40.45\%$, $103.23 \pm 16.42\%$, $103.63 \pm 22.61\%$ and $117.47 \pm 18.81\%$ for ST1, ST2, ST3, and ST4, respectively. Notably, the incorporation of extract and oil led to a coating over the nanofibers, increasing fiber diameter and resulting in a slight reduction in both porosity and swelling ratio for ST2, ST3, and ST4 compared to ST1.

Although PCL is hydrophobic, the nanofibers showed notable water uptake due to the hydrophilic nature of PEG [14]. In contrast, clove oil's hydrophobic nature reduces polymer–water interactions, limiting water absorption in the nanofibers. As a result, the swelling capacity decreased in ST2, ST3, and ST4 compared to ST1, which lacked clove oil [19].

In the literature, a 14% w/v PCL nanofibrous scaffold produced by electrospinning exhibited a porosity of $85 \pm 2.5\%$, which is very close to that of ST1 ($82.51 \pm 3.39\%$), containing only PCL and PEG [43]. In another study, increasing the casein content led to larger fiber diameters and increased solution viscosity, which, in turn, decreased the nanofibers' porosity. For example, polycaprolactone/casein nanofibers showed a porosity of 82% at a 95:5 weight ratio, whereas it dropped to 63% at 80:20 [44]. Similarly, the addition of *Hypericum perforatum* oil reduced the porosity of PCL/PEG nanofibers from 73% to 56% [45].

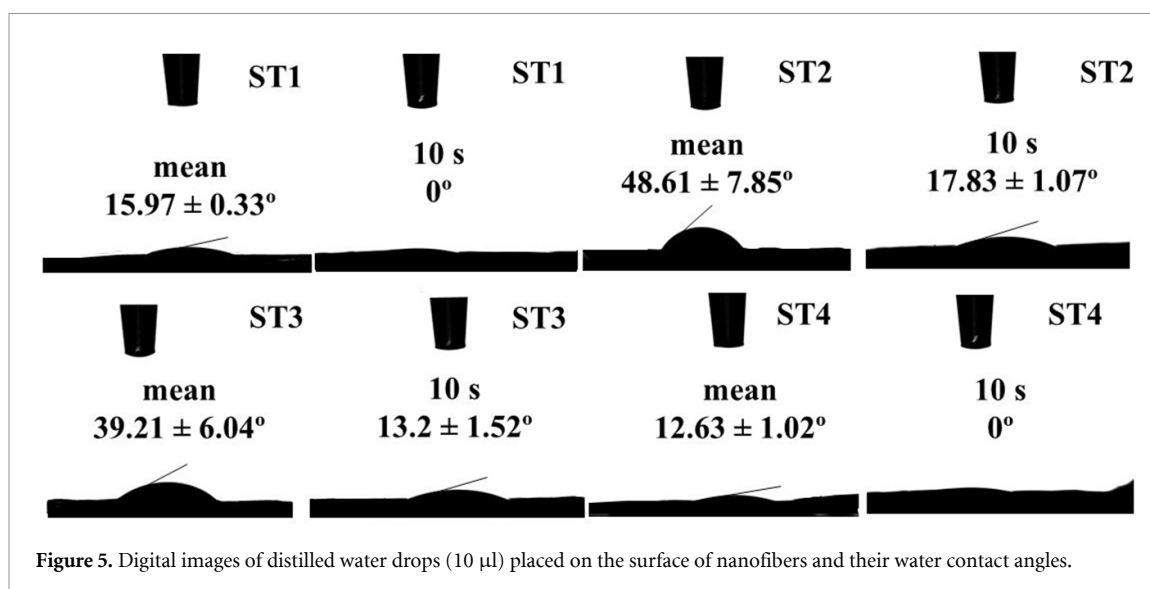
A wound dressing nanofiber should effectively absorb wound exudate to prevent tissue infection and should possess a porosity ratio between 60% and 90% to allow for adequate gas-liquid exchange [19, 46]. Maintaining a moist environment promotes tissue regeneration and accelerates epithelialization, thus requiring sufficient water absorption [14]. In this study, the nanofibers' porosity and swelling capacities meet key physicochemical requirements commonly

reported for wound-dressing applications, including exudate absorption and oxygen permeability.

3.2.3. Contact angle measurement

The wettability of the surface of electrospun nanofibers, one of the most desired material characteristics for wound dressing applications, may affect the initial adhesion and migration of cells, as well as their proliferation in the wound area [47, 48]. To assess the effects of *P. lanceolata* and clove oil on the wettability and hydrophilicity of PCL/PEG, contact angle measurements were performed. As shown in figure 5, the PCL/PEG scaffold (ST1) showed highly hydrophilic behavior. It was observed that the water droplet completely soaked the ST1 and, due to rapid absorption, made it difficult to determine the contact angle accurately. In our study, clove oil reduced the nanofiber's hydrophilicity due to its hydrophobic nature, but this effect was not significant. According to contact angle measurements taken in the 0–10 s range, the average contact angle for ST2 was $48.61 \pm 7.85^\circ$, and the contact angle at 10 s was $17.83 \pm 1.07^\circ$, demonstrating rapid absorption capacity. Compared to ST2, the contact angle decreased with increasing *P. lanceolata* concentration in ST3 and ST4, reaching 0° at 10 s in ST4, demonstrating superhydrophilic properties. The results of contact angle measurements showed remarkable wettability across all groups ($\theta < 90^\circ$).

The hydrophilic nature of PEG, when added to the naturally hydrophobic PCL, improves the wettability of PCL/PEG scaffold structures. The low contact angle observed with the addition of PEG and the resulting increase in hydrophilicity are attributed to the oxygen atoms in the PEG molecule, which are hydrogen-bond acceptors, thereby conferring PEG with an appropriate affinity for water molecules



[49, 50]. In the literature, pure PCL has a contact angle of 121.9°. However, when *Plantago major* extract is added, the contact angle of the fiber mats decreases from 39.4° to 0° as the extract concentration increases. *P. lanceolata* and *P. major* extracts have halogenated and OH-containing components, resulting in a high potential for hydrogen bonding and a strong affinity for water [14]. In a similar study, PCL-GEL nanofiber mats had a contact angle of 37 ± 8°, which decreased to 18 ± 3° with the addition of 1.5% (v/v) clove oil [20]. According to another study, chitosan nanoparticles encapsulating cinnamon essential oil were incorporated into poly(lactic acid) (PLA) composite fibers, thereby improving the fibers' hydrophilic properties [51]. Despite its hydrophobic nature, adding an appropriate amount of clove oil to the PCL/PEG nanofiber and loading it with the hydrophilic *P. lanceolata* has resulted in the nanofiber exhibiting enhanced surface wettability.

3.2.4. Chemical characterization

Figure 6 presents the FTIR spectra of the *P. lanceolata* extract and electrospun PCL/PEG nanofibers, both with and without including the extract and clove oil. The neat PCL/PEG nanofiber (ST1) exhibits characteristic peaks at 2877 cm⁻¹ (C–H aliphatic stretching) and 1095 cm⁻¹ (C–O stretching). A specific peak at 1719 cm⁻¹ is attributed to C=O stretching, indicating the ester carbonyl group of PCL. Additionally, the peak at 1467 cm⁻¹ is associated with the C–H bending of methylene (CH₂) groups in both PCL and PEG [45].

P. lanceolata extract showed a peak at 3275 cm⁻¹, corresponding to the O–H stretching vibrations of flavonoids, polyphenols, and phenolic compounds. As the extract concentration increased, the absorption in this region increased, indicating greater incorporation into the nanofiber. In addition, the peak at 1558 cm⁻¹, which is characteristic of *P. major*,

confirms the presence of the extract in the nanofiber structure [14].

In addition, the peak at 1514 cm⁻¹, which is associated with C=C aromatic bond vibrations, is attributed to eugenol, the main component of clove oil, and appears in the ST2, ST3, and ST4 nanofibers [24]. The peaks observed in the 1467–1341 cm⁻¹ are also related to the C–H bending of the PCL-PEG nanofiber [45]. These results confirm the incorporation of the extract-oil mixture into the electrospun PCL/PEG nanofibers.

3.2.5. Weight loss study

Figure 7 illustrates the *in vitro* weight loss profiles of the electrospun nanofibers over a 21 day period. The nanofibers showed weight losses of 25.92 ± 2.84%, 40.21 ± 4.00%, 54.32 ± 1.36% and 57.76 ± 0.92% for ST1, ST2, ST3, and ST4, respectively. Nanofibers containing *P. lanceolata* extract and clove oil showed higher degradation rates than the neat PCL/PEG nanofiber. This increase is likely due to the release of hydrophilic compounds, particularly the hydroxyl-rich constituents of the extract, into the aqueous environment [52, 53].

This result is further supported by the higher weight loss observed during the first week in extract-containing nanofibers, followed by a more stable degradation profile in the second and third weeks [54]. Similar findings have been reported for nanofibers incorporating HCC extract and henna rose, which also showed increased weight loss over time [5, 55].

The obtained results showed a significant difference between groups, especially between ST1 and the extract-loaded nanofibers (ST2, ST3, ST4). This suggests that incorporating bioactives affected nanofiber degradation. Overall, although the nanofibers exhibited more than 50% weight loss, they retained their physical integrity and morphology throughout the

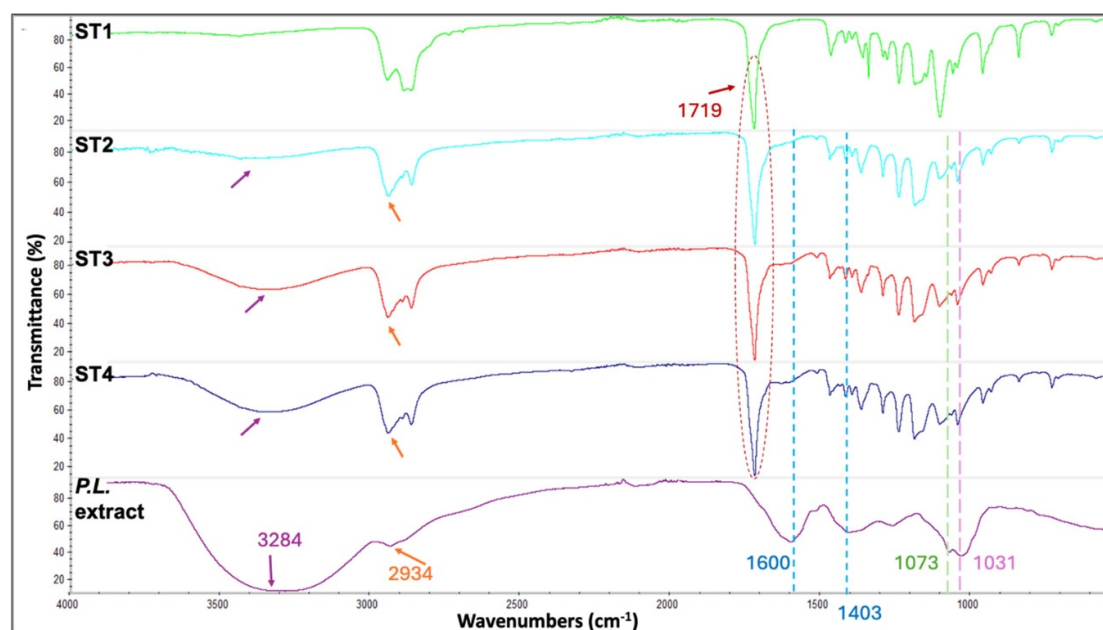


Figure 6. FTIR spectra of the *P. lanceolata* extract and electrospun nanofibers (ST1–ST4) showing characteristic peaks corresponding to the polymer matrix and incorporated bioactive components.

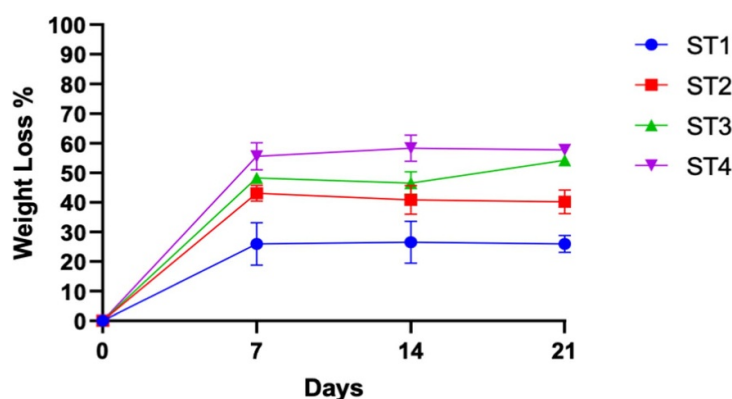


Figure 7. Weight-loss percentages for ST1, ST2, ST3, and ST4 nanofibers over 21 d. Error bars indicate standard deviation.

21 d, without signs of collapse or fragmentation. They remained structurally stable throughout the 21 d, supporting their suitability for short-term wound care [25, 30].

3.2.6. Cumulative release

The extract/oil loading capacity of PCL/PEG electrospun nanofibers was determined by the percentage of the amount of drug loaded per unit weight of each nanofiber, as represented in figure 8(b). Herein, ST2, ST3, and ST4 nanofibers demonstrated extract/oil loading capacities of $24.31 \pm 2.23\%$, $40.54 \pm 2.63\%$, and $48.22 \pm 8.10\%$, respectively. Similarly, in a study, *P. major* extract-containing PCL nanofibers with 5.3% and 10.6% *P. major* extract demonstrated drug loading capacities of 13.02% and 31.01%, respectively [14]. The drug content loaded

into electrospun nanofibers depends on several factors, including the compatibility between the polymer and the loaded drug (plant extract, essential oil), the hydrophilic/hydrophobic nature of the drug and the polymer, and the method used to load the drug [56]. The obtained loading capacities were consistent with previous reports on extract-loaded wound-dressing.

The *in vitro* release profiles of nanofibers are presented in figure 8(a). An initial burst release was observed during the first hour, with release percentages of $17.62 \pm 4.97\%$, $12.70 \pm 1.49\%$, and $11.30 \pm 0.48\%$ in PBS for ST2, ST3, and ST4, respectively. This rapid release is likely attributed to the diffusion of extract-related components physically adsorbed on or near the nanofiber surface [34]. Although clove oil is poorly water-soluble, it may still partially diffuse into the aqueous medium due

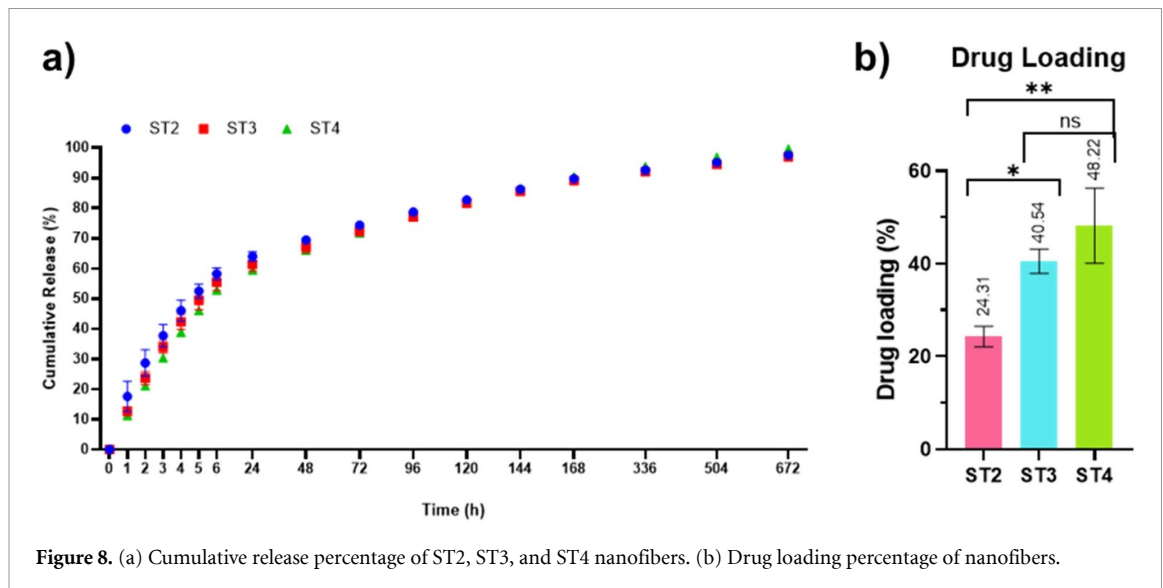
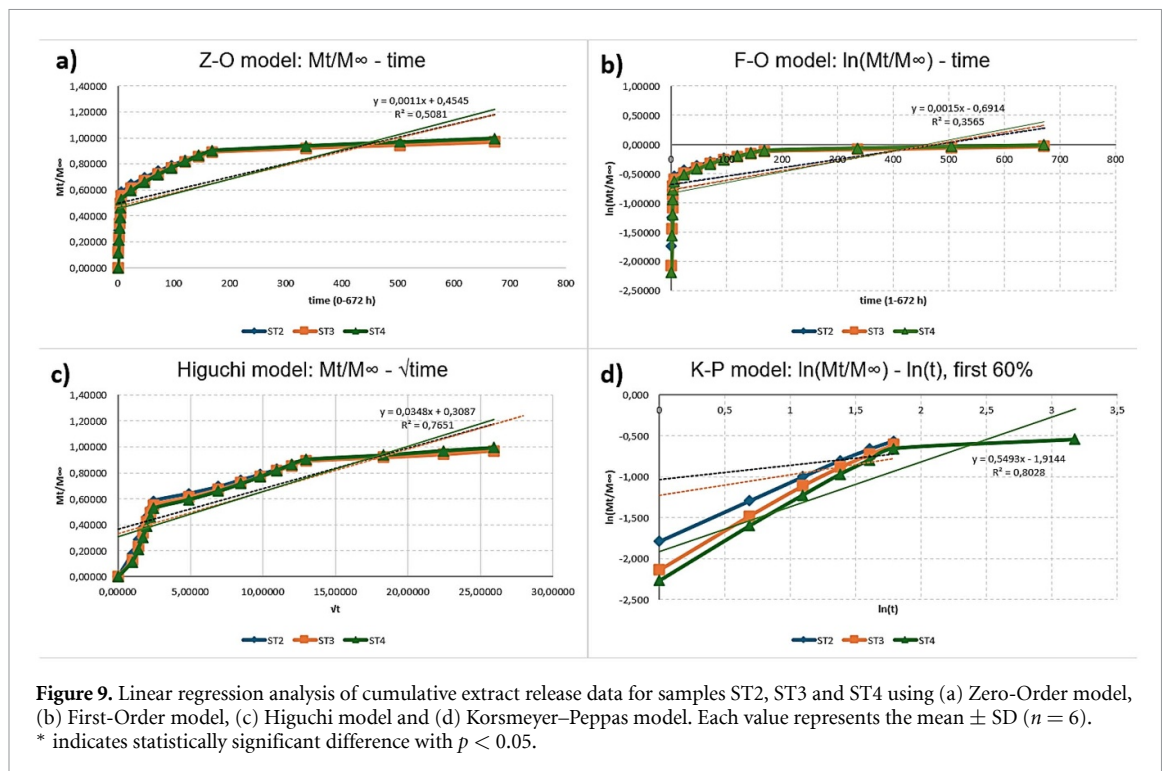


Figure 8. (a) Cumulative release percentage of ST2, ST3, and ST4 nanofibers. (b) Drug loading percentage of nanofibers.



to the presence of PEG and the nanofiber's porous structure. The release analysis in this study specifically focused on *P. lanceolata* extract using UV–Vis spectrophotometry.

The extended release after the initial burst may be due to the extract entering the porous fiber structure during immersion. Molecules on the surface are released quickly, while those deeper in the nanofiber take more time to diffuse. A similar two-phase release has been reported in extract-loaded nanofibers prepared by immersion [57–59].

Following the initial burst phase, the nanofibers exhibited a sustained release, with cumulative release values ranging from $52.83 \pm 0.92\%$ to $58.26 \pm 2.02\%$ within the first 6 h. By the end of 28 d (672 h),

cumulative release values of $97.62 \pm 0.90\%$ (ST2), $96.94 \pm 1.30\%$ (ST3), and $99.61 \pm 0.28\%$ (ST4) were obtained, indicating that the release profile approached a plateau under the experimental conditions.

The data align with a two-phase release: a fast initial release followed by a slower one as the extract diffuses from deeper parts of the fibers [27, 57]. Such a release profile can support early antibacterial protection, primarily attributed to clove oil, while maintaining bioactive availability over time.

Additionally, the degradation of the nanofibers in the aqueous medium over time contributes to the sustained release of the encapsulated bioactive components. The initial burst release is considered

advantageous for wound dressing applications, as it may support antimicrobial protection and promote healing during the initial stage of wound repair [57, 58]. A related study reported a 65% release from silk fibroin/polyethylene oxide nanofibers containing grape seed extract, which displayed burst, continuous, and quiescent release phases over 350 h [59]. Similarly, PCL/PEG nanofibers were shown to rapidly release naringenin over the first 2 h [39]. Another study demonstrated that PCL/PVP nanofibers loaded with *Tecomella Undulata* extract released 40% of the extract after 24 h [60].

The importance of burst release in delivering an initial antimicrobial effect has been widely noted, while the subsequent sustained release phase plays a critical role in inhibiting long-term microbial growth and proliferation [61].

The results indicate that the release profile approached a plateau under the applied *in vitro* conditions; however, this does not demonstrate complete release of all extract components. The drug release kinetics from *P. lanceolata* extract- and clove oil-loaded electrospun nanofibers can be described by the zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The results of the analysis were evaluated using the coefficients of determination (R^2 values), which indicate the quality of the fit. While the Z-O model indicates that release does not proceed at a constant rate due to the low R^2 value, the Higuchi model shows a higher R^2 value than the Z-O model, suggesting that matrix-mediated diffusion processes may also play a role in the release of extract and oil. The Korsmeyer–Peppas model provided a better fit for the early-stage release behavior of plant extracts and essential oils. The n values calculated from this model indicate that release can be influenced by the structural properties of the polymer matrix and potential relaxation/swelling behavior, in addition to diffusion. Although the cumulative release profile plateaued at 672 h, this was not interpreted as evidence of complete release. The Korsmeyer–Peppas model demonstrated a very high degree of fit for the ST2 and ST3 samples in the early release phase. For these samples, the R^2 values were 0.9987 and 0.9956, respectively. In the ST4 sample, however, the K–P model showed a lower fit, with an R^2 of 0.8028. The lower R^2 value for ST4 indicates that the early-stage release behavior of this nanofiber did not show the same linear fit observed for ST2 and ST3 (figure 9). This may be related to a more heterogeneous release progression in ST4, differences in scaffold density, or the inclusion of 24-hour data in the model under the condition $M_t/M_\infty \leq 0.60$, calculated with $N = 7$. Thus, ST4 exhibited a slower, more prolonged release [62, 63].

3.2.7. Antibacterial activity

The antibacterial activity of electrospun nanofibers was evaluated against *E. coli* (ATCC BAA-1025) and *S.*

aureus (ATCC 6538) using the Kirby-Bauer disc diffusion and LB-incubation methods. *S. aureus* is found in early wound infections, while *E. coli* is more common in chronic cases [64].

Table 2 and figure 10 show the inhibition zones. Ampicillin was the positive control, and the PCL/PEG nanofiber without additives (ST1) was used as the negative control. ST1 showed no inhibition zone against either *E. coli* or *S. aureus*. In contrast, nanofibers containing extract and oil showed clear zones of inhibition. Against *E. coli*, the inhibition zones were 10.25 ± 0.96 mm (ST2), 12.88 ± 0.63 mm (ST3), 14.00 ± 0.82 mm (ST4), and 21.38 ± 0.48 mm (ampicillin). Against *S. aureus*, the values were measured as 7.75 ± 0.96 mm (ST2), 9.00 ± 0.41 mm (ST3), 10.25 ± 0.87 mm (ST4), and 32.75 ± 0.50 mm (ampicillin).

Figures 11(a) and (b) further illustrate the bactericidal ratios in LB broth. Against *E. coli*, bactericidal activity was recorded as $5.88 \pm 2.23\%$ (ST1), $53.13 \pm 5.74\%$ (ST2), $79.80 \pm 2.84\%$ (ST3), and $84.35 \pm 1.03\%$ (ST4). Against *S. aureus*, corresponding values were $11.88 \pm 1.80\%$ (ST1), $60.12 \pm 7.79\%$ (ST2), $66.38 \pm 7.11\%$ (ST3), and $79.52 \pm 0.77\%$ (ST4). The low bactericidal ratios observed for ST1 are considered minimal baseline reductions inherent to the liquid assay and do not indicate a meaningful antibacterial effect. According to these results, the antibacterial activity of the nanofibers is primarily governed by clove oil, while increasing the extract concentration further enhances antibacterial performance within the composite system, consistent with previous reports on the antibacterial potential of *P. lanceolata* [65].

In the literature, ethanol, water, and acetone extracts of *P. lanceolata* leaves have demonstrated antibacterial activity against *S. aureus*, *E. coli*, *S. pneumoniae*, and *K. pneumoniae* [66]. The largest inhibition zones (23–24 mm) against *S. aureus* and *E. coli* were observed with *P. lanceolata* extracts prepared using chloroform/methanol and petroleum ether [11].

Although *P. lanceolata* has been reported to contain phytochemicals with antibacterial potential, the present results indicate that these components play a secondary role in the nanofibers' antibacterial performance. *P. lanceolata* contains several phytochemicals with known antibacterial effects, including hexadecanoic acid methyl ester and (Z)6,(Z)9-pentadecadien-1-ol [67, 68]. Fatty acids such as linoleic, linolenic, and palmitic acid can weaken bacterial nanofibers and cause cell damage, especially in *S. aureus*, *E. coli*, and *B. subtilis* [12]. Other identified compounds include nonadecane, heptadecane, and hexadecanoic acid ethyl ester [18]. Polyphenols in the extract may also interact with bacterial proteins via their phenolic hydroxyl groups, thereby contributing to both antibacterial and antioxidant activities [69].

Table 2. Kirby–Bauer disc diffusion inhibition zones of nanofibers.

Bacteria	Antibiotic	ST1	ST2	ST3	ST4
<i>E. coli</i>	21.38 ± 0.48 mm	0	10.25 ± 0.96 mm	12.88 ± 0.63 mm	14.00 ± 0.82 mm
<i>S. aureus</i>	32.75 ± 0.50 mm	0	7.75 ± 0.96 mm	9.00 ± 0.41 mm	10.25 ± 0.87 mm

**Figure 10.** Kirby–Bauer inhibition zone images of the nanofibers.

Flavonoids in *P. lanceolata* may influence membrane integrity, rigidity, and permeability, potentially contributing to antibacterial activity [69]. Clove oil contains eugenol, eugenol acetate, β -caryophyllene, and phenylpropanoids, which act through the disruption of nanofiber phospholipids and protein denaturation [21, 70]. In a study, clove oil produced inhibition zones of 9.17 ± 0.45 mm against *E. coli* and 15.24 ± 0.47 mm against *S. aureus* [71]. Similarly, clove oil-loaded PCL/GEL nanofibers exhibited activity against *S. aureus* within 6 h and *E. coli* after 24 h [24]. In the context of this study, such effects are considered supportive rather than primary, given the limited antibacterial activity observed for the extract alone.

In this study, adding *P. lanceolata* extract and clove oil to PCL/PEG nanofibers resulted in measurable antibacterial activity. A low amount of clove oil (1%) was used to avoid possible toxicity to healthy cells, and the extract concentration was adjusted to support both healing and antibacterial effects.

The antibacterial results for ST2, ST3, and ST4 support their potential use in wound dressing. An apparent dose-dependent enhancement was observed with increasing *P. lanceolata* content within clove oil-containing nanofibers, as assessed by both disc diffusion and bactericidal ratio assays in LB medium.

In the liquid assay, bacterial survival was evaluated by measuring OD after direct contact with the nanofibers. These findings indicated that higher extract levels further enhance the bactericidal performance of clove oil-loaded nanofibers within the composite formulation (supplementary figure 1). Besides, to separately evaluate the antibacterial effects of clove

oil and *P. lanceolata*, the antibacterial activity test was repeated on nanofibers (figure 11). According to the bactericidal ratio test, nanofibers containing 1% (v/v) clove oil (ST6) showed potent antibacterial activity against *E. coli* ($84.54 \pm 0.88\%$) and *S. aureus* ($74.03 \pm 1.29\%$). However, very similar results were obtained for ST4. ST4 showed antibacterial effects of $84.35 \pm 1.00\%$ against *E. coli* and $79.52 \pm 0.86\%$ against *S. aureus*. By contrast, 15% (w/w) *P. lanceolata* exhibited insufficient antibacterial activity with a bactericidal percentage of $31.81 \pm 1.44\%$ against *E. coli* and $34.54 \pm 1.46\%$ against *S. aureus*. These comparative results confirm that clove oil is the primary antibacterial agent in the system. At the same time, the presence of *P. lanceolata* provides a modest but consistent enhancement within the composite formulation rather than acting as an independent antibacterial component.

3.2.8. In vitro cell viability

Figure 12 shows the viability of human dermal fibroblasts (ATCC PCS201-010) on electrospun nanofibers over 24–96 h, based on MTT results. All nanofibers maintained cell viability above 95% throughout the test period. The presence of extract and oil supported cell growth, particularly in groups with higher extract content. This effect may be linked to the extract's antioxidant activity. Earlier studies have shown that it can scavenge hydroxyl, superoxide, and nitric oxide radicals [72], with flavonoids and verbascoside believed to play a role in this process [73]. Previous research has demonstrated that *Plantago* species possess a range of biological activities, including antimicrobial, antioxidant, analgesic, wound healing,

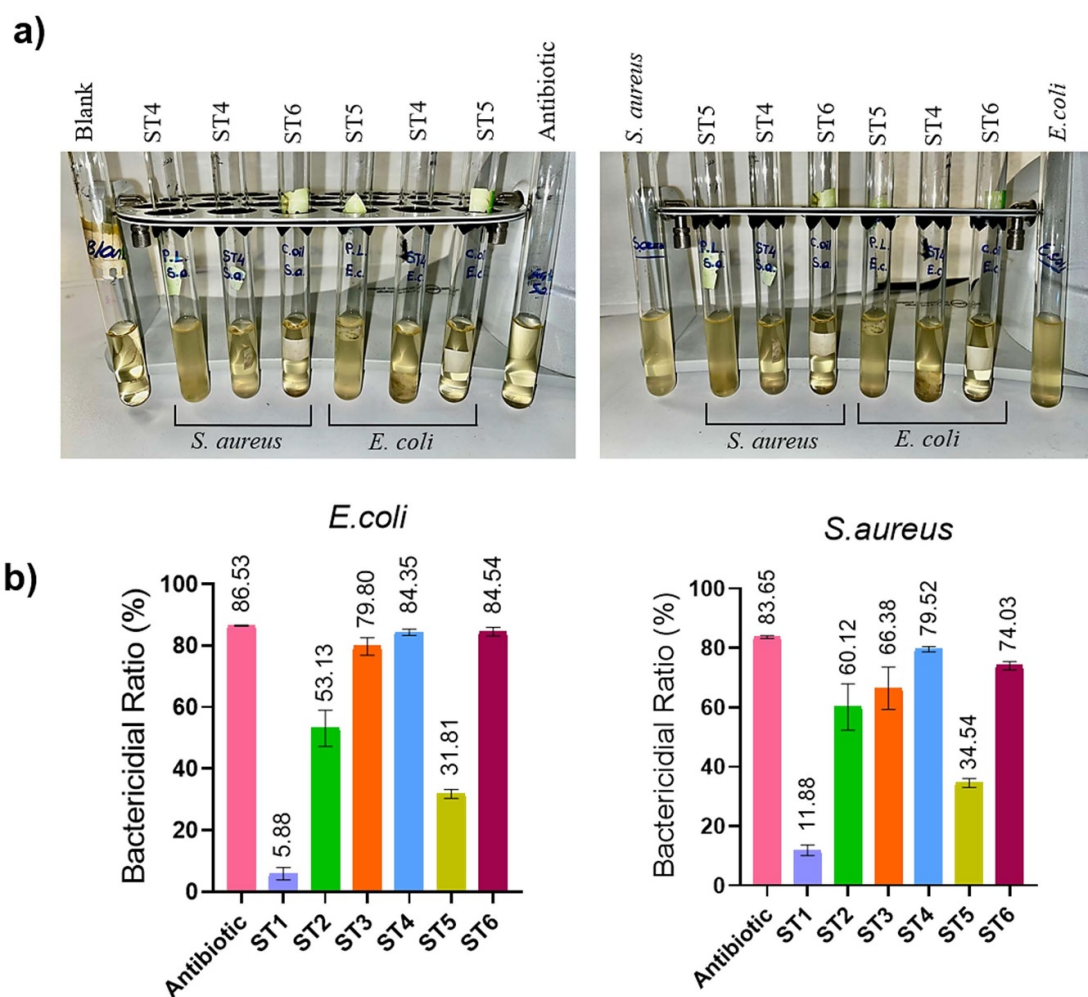


Figure 11. (a) Experimental setup for comparative evaluation of bactericidal ratio assay with ST5 (contains only 15% (w/w) *P. lanceolata*) and ST6 (contains only 1% (v/v) clove oil). (b) Bactericidal ratio percentage of nanofibers against *E. coli* and *S. aureus*. Error bars indicate standard deviation. Statistical significance was determined using one-way ANOVA ($n = 3$; *** $p < 0.0001$; considered significant).

anti-inflammatory, antispasmodic, and hepatoprotective effects, as well as cytotoxicity against cancer cells [72–75].

Clove oil has also been reported to improve cell viability through its antioxidant properties [24, 67]. These effects are mainly due to its phenolic constituents, especially eugenol and eugenol acetate, which help reduce oxidative stress in cells [76]. In one study, M5S cells treated with 15% clove oil showed around 85% viability, with the highest cell density (10^4 cells/ml) observed at this concentration [77].

However, excessive concentrations of essential oils or plant extracts can cause cytotoxicity [78]. Therefore, in this study, the concentrations of *P. lanceolata* extract and clove oil were optimized for the biocompatibility of the nanofibers. The results confirmed that PCL/PEG nanofibers containing *P. lanceolata* extract and clove oil exhibit high cellular compatibility, with no cytotoxicity. Based on these findings, the nanofibers demonstrate suitable biocompatibility for wound-dressing applications.

3.2.9. Cell adhesion

Fibroblast cells were cultured on the nanofibers, and their adhesion behavior was monitored for 24–72 h. Fluorescence microscopy images of DAPI-stained cells are shown in figure 13. DAPI is a membrane-permeable fluorescent dye that binds specifically to A-T-rich regions of DNA through electrostatic interactions, enabling the visualization of cell nuclei [2].

Cell adhesion improved with the addition of *P. lanceolata* extract and clove oil, especially in ST3. This improvement may be associated with the presence of polar functional groups from the extract and the resulting changes in surface characteristics, which can influence cell–material interactions.

Previous studies have shown that flavonoids support fibroblast growth, including in nanofibers containing henna extract [55]. In this study, stronger cell adhesion observed with higher extract concentrations may be related to bioactive functional groups present in *P. lanceolata*. A similar trend was noted in hydrophilic PCL/GO-g-PEG scaffolds, which showed

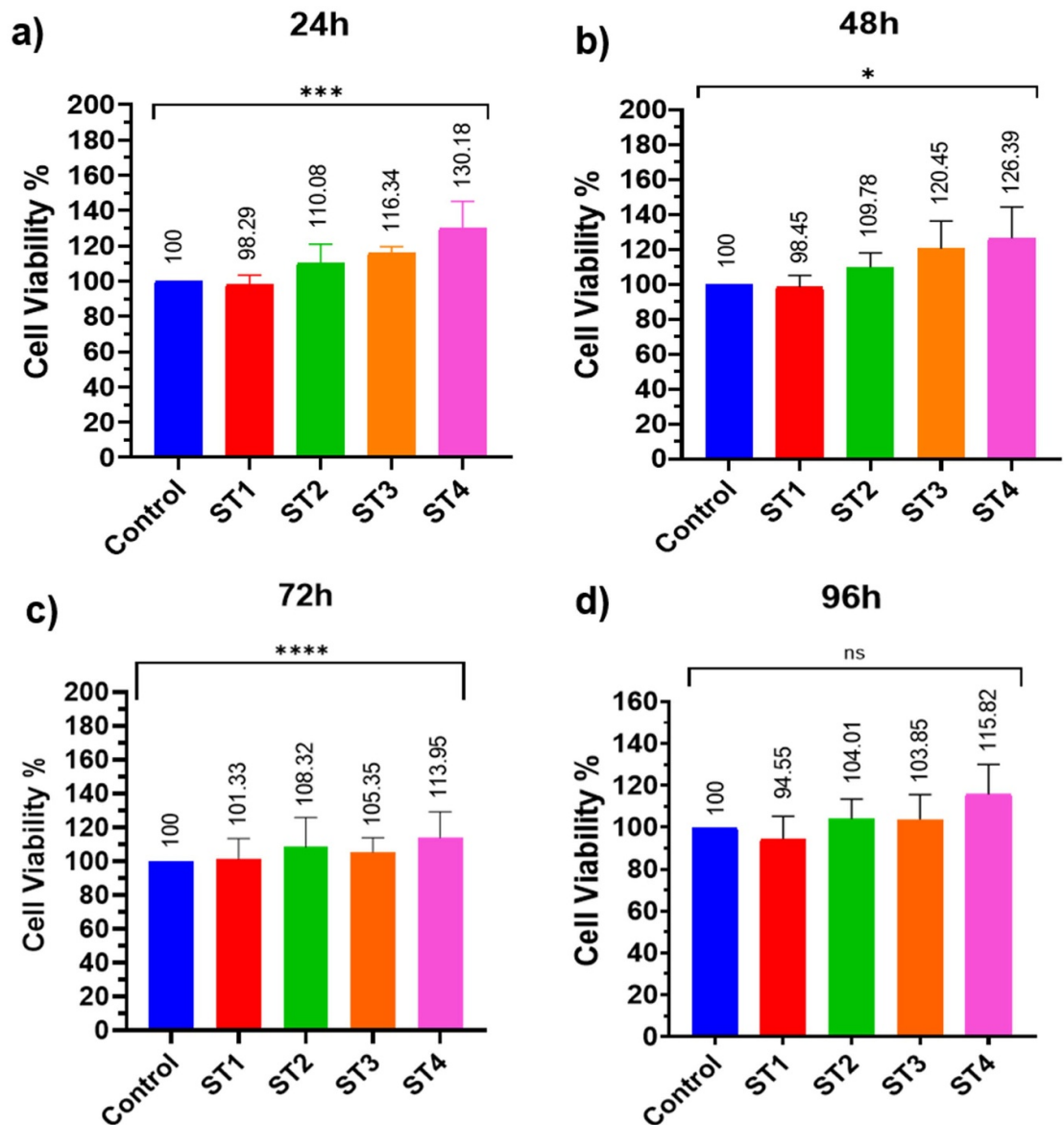


Figure 12. Cell viability of nanofibers at (a) 24 h, (b) 48 h, (c) 72 h, and (d) 96 h. Error bars represent standard deviation. Statistical significance was determined using one-way ANOVA ($n = 3$; ns: not significant; $*p < 0.05$, $***p < 0.001$, $****p < 0.0001$; considered significant).

better adhesion than neat PCL, suggesting that surface hydrophilicity plays a role in cell attachment [79].

Hydrophilicity helps cell attachment by supporting interactions between the material surface and membrane proteins [80]. However, in a previous study using PCL-GEL nanofibers with clove oil, NHDF cell adhesion was similar to that of the control group, indicating that clove oil alone may not significantly improve adhesion [24].

Based on these findings, the improved adhesion observed in this study is likely associated primarily with the presence of *P. lanceolata* extract and the resulting surface properties, rather than with clove oil alone. Furthermore, adding the extract/oil mixture to PCL/PEG nanofibers did not compromise the nanofibers' cell-adhesion capacity.

3.2.10. In vitro scratch assay

A scratch test was performed to evaluate the *in vitro* scratch area closure performance of the nanofibers, as shown in figures 14(a) and (b), with corresponding closure percentages shown in figure 15. The neat PCL/PEG nanofiber showed scratch area closure behavior comparable to that of the blank control. However, the incorporation of *P. lanceolata* extract significantly enhanced the reduction in scratch area, particularly in ST2, ST3, and ST4, whereas clove oil did not impair cellular migration.

Scratch area closure improved as the extract concentration increased, rising from $41.67 \pm 7.90\%$ (ST2) and $41.54 \pm 8.82\%$ (ST3) to $48.14 \pm 18.76\%$ (ST4) within 24 h. By 96 h, ST3 and ST4 showed near-complete scratch area closure, whereas ST1 (the control) and ST2 showed partial wound repair-related

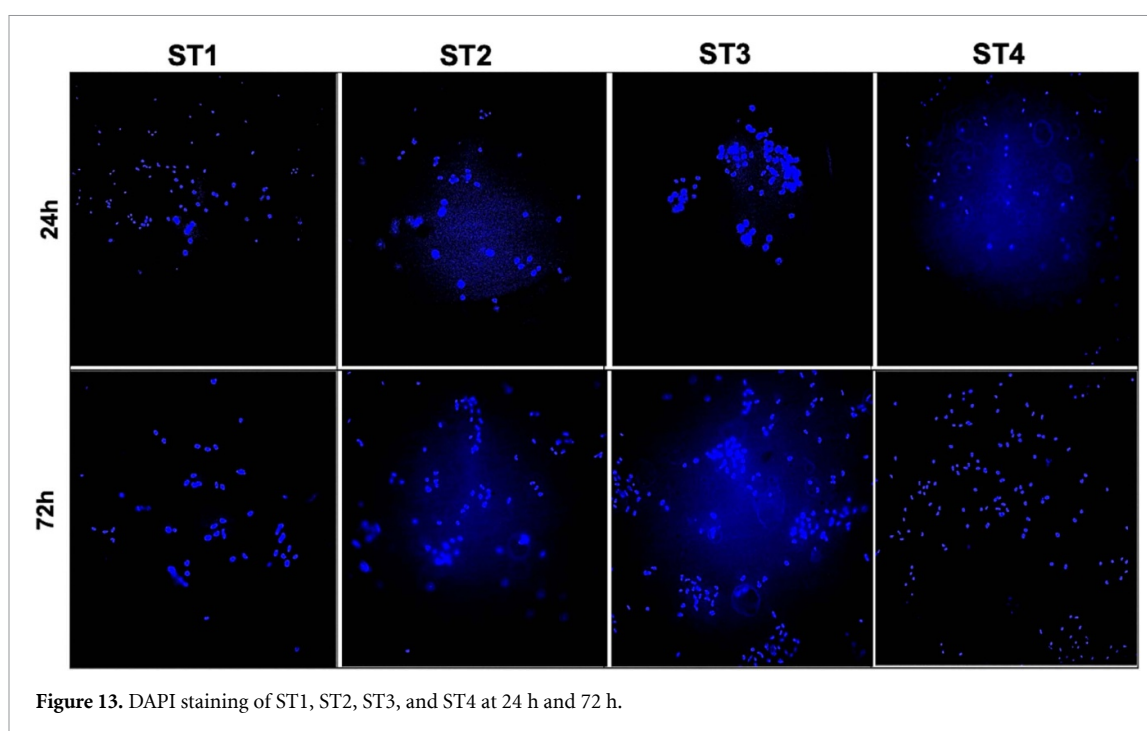


Figure 13. DAPI staining of ST1, ST2, ST3, and ST4 at 24 h and 72 h.

potential. These results indicate that ST3 and ST4 support effective *in vitro* responses associated with cell migration and proliferation, suggesting their potential for use in wound dressings. In our study, during the scratch test for ST1, ST2, ST3, and ST4 nanofibers, we also performed a separate test on a nanofiber loaded with *P. lanceolata* extract alone at 15% (w/w) to observe its potential to support cell migration. This nanofiber (referred to as ST5) showed $87.11 \pm 2.63\%$ closure at 72 h (figures 14 and 15). Thus, these findings suggest that the cell migration-supporting effect is mainly associated with *P. lanceolata* and that 1% (v/v) clove oil did not cause any toxic effects.

Cell migration increased in each sample from 0 to 96 h, indicating the supportive role of *P. lanceolata* extract in promoting cell proliferation and motility. At the same time, clove oil did not negatively affect these processes at the applied concentration. In the ST6 experimental group, 1 μ l of a mixture containing approximately 0.004 μ l of clove oil, within the safe range according to the literature, was loaded onto the nanofibers [19, 81]. When cell migration was examined with ST6 (1% (v/v)), the scratch closure rate was $62.75 \pm 8.84\%$ at 72 h, which was lower than the $72.97 \pm 6.02\%$ observed with ST1 and the $70.98 \pm 5.86\%$ observed with the control group. It cannot be concluded that clove oil is generally toxic at all time points measured for wound closure rates in the scratch assay [82]. However, when clove oil was applied alone to nanofibers in the ST6 experimental group, it did not promote cell migration; rather, it may slightly inhibit it over time due to increased release into the medium [24]. The

literature reports that clove oil and its main component, eugenol, can exhibit cytotoxic effects on fibroblasts and endothelial cells at concentrations above a threshold [83]. However, in our study, clove oil added to the nanofibers at 1% (v/v) did not cause any toxic effects in the *in vitro* scratch assay, as observed in the cell viability and proliferation experiments. This result indicates that although clove oil may have a mild inhibitory effect on cell migration when used alone, the biological response may be more balanced when combined with the plant extract, supporting the rationale for combining clove oil with *P. lanceolata* extract in the formulation (supplementary figure 2). Therefore, the limited reduction in the ST6 group suggests that the pro-migratory effect of clove oil alone may be weaker than that of the other control and test groups.

A study on *Calophyllum inophyllum* oil at varying concentrations (0.01%, 0.1%, and 1%) demonstrated enhanced cell migration with increasing oil content [84]. In another *in vivo* study, the ethanolic extract of *Plantago major* improved wound healing in a pig model, which can be related to its high polyphenol content [85]. In one study, a 10% (w/w) concentration of *P. lanceolata* extract showed particularly high efficacy and lower side effects than a 20% (w/w) concentration [13]. In the literature, LC-MS/MS analysis revealed that *P. lanceolata* contains substantial levels of verbascoside, a bioactive phenethyl alcohol glycoside known for its numerous healing-promoting activities [53]. The high antioxidant activity of the extract facilitated wound healing by neutralizing excess proteases and reactive oxygen species, thereby reducing inflammation in the

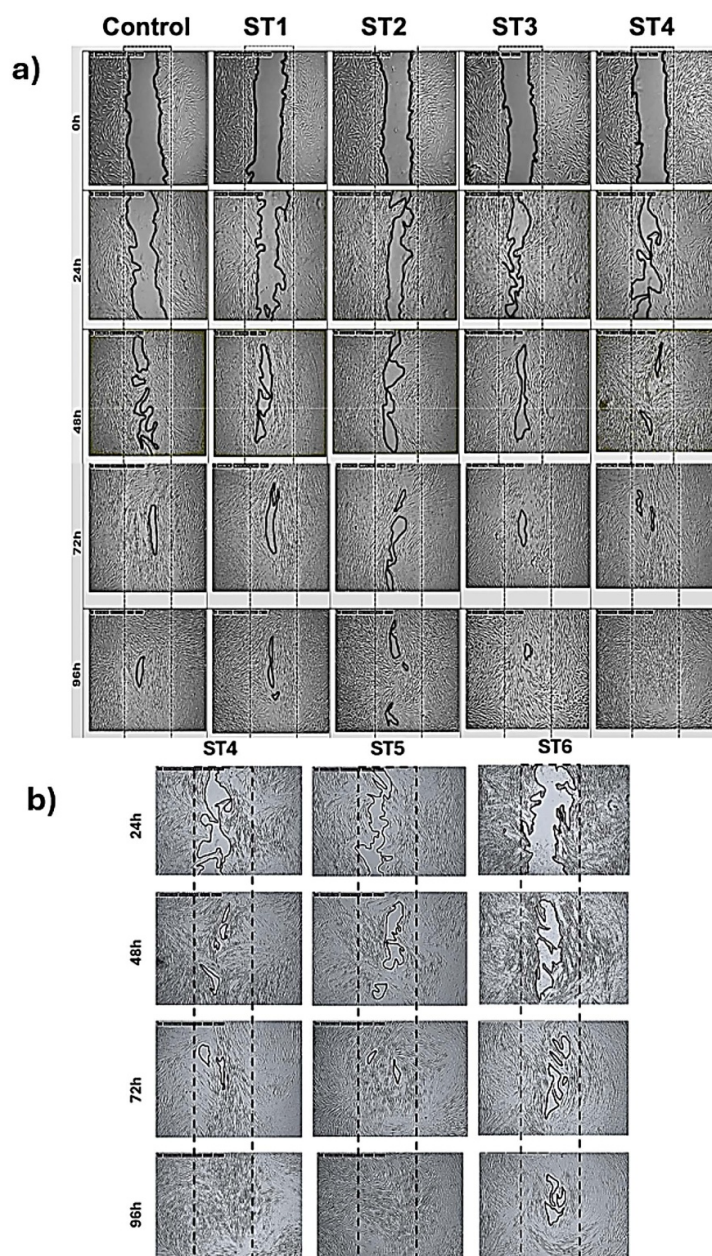


Figure 14. Microscopic images of nanofibers from the *in vitro* scratch test at 0 h, 24 h, 48 h, 72 h, and 96 h, (a) observation of cell migration activities of control, ST1, ST2, ST3 and ST4, and (b) cell migration activities in a repeated experiment comparing ST4, ST5 and ST6.

wound area [14]. Among these polyphenols, plantamajoside, a significant component in *P. lanceolata*, has been shown to promote fibroblast proliferation and accelerate wound repair. Additionally, flavonoids such as hispidulin and baicalein reduce histamine and prostaglandin release, thereby protecting tissue during early wound healing. The extract's triterpenoids may also inhibit cyclooxygenase (COX-1 and COX-2) activity, reducing prostaglandin synthesis and supporting tissue regeneration [86].

Other bioactive groups, such as coumarins, modulate immune responses at the wound site, and alkaloids improve tensile strength, epithelialization, and overall wound closure [85]. Furthermore, clove oil has been reported to enhance fibroblast migration

[87], and eugenol application has been shown to promote re-epithelialization in skin wounds within 20 d [77]. A study demonstrated that higher concentrations of clove oil inhibited both migration and proliferation of NHDF cells in a dose-dependent manner. In their research, there was no significant ($p < 0.05$) difference in percentage of scratch area closure between no clove oil and 1.5% clove oil added to nanofibers during 24 h [24].

Taken together, the results from the scratch test, MTT, and cell adhesion studies indicate that the electrospun nanofibers developed in this study are non-cytotoxic to fibroblast cells and actively promote cellular migration, proliferation, and *in vitro* wound repair-related potential.

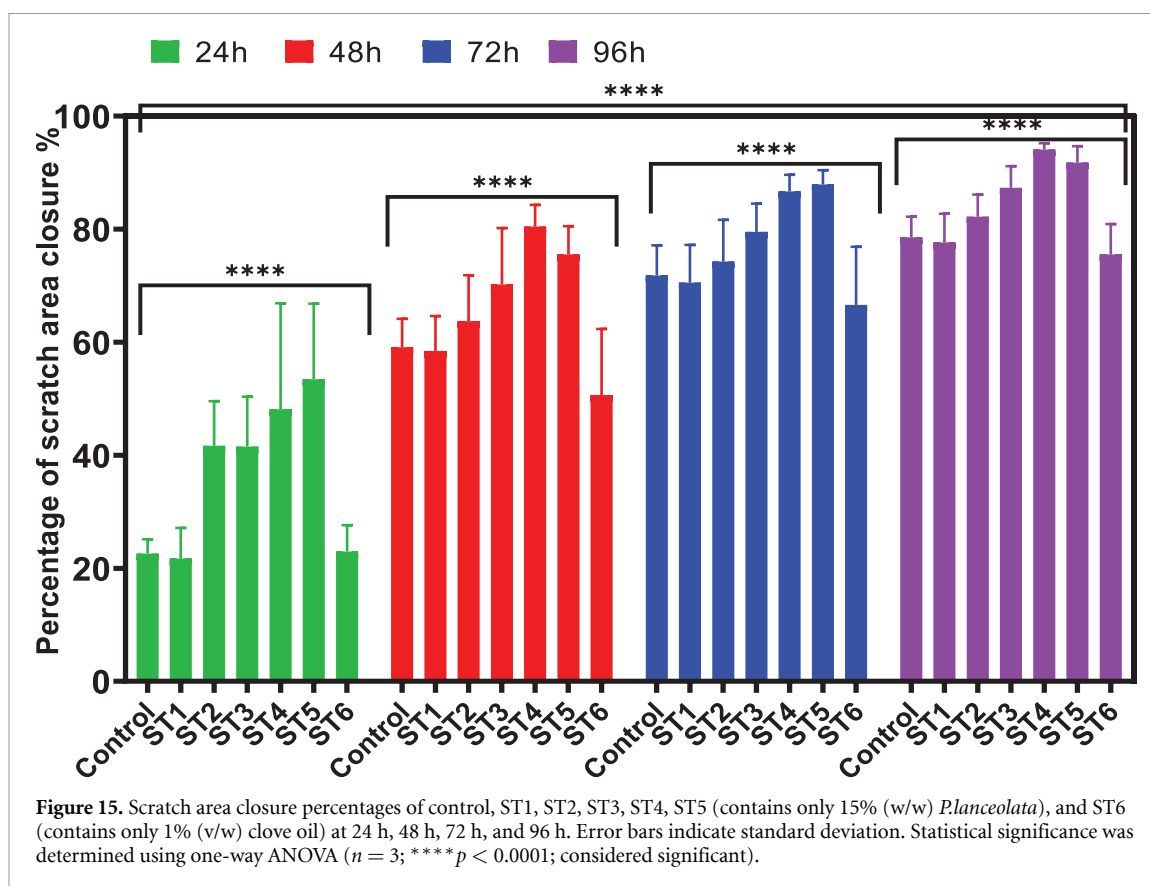


Figure 15. Scratch area closure percentages of control, ST1, ST2, ST3, ST4, ST5 (contains only 15% (w/w) *P.lanceolata*), and ST6 (contains only 1% (v/w) clove oil) at 24 h, 48 h, 72 h, and 96 h. Error bars indicate standard deviation. Statistical significance was determined using one-way ANOVA ($n = 3$; **** $p < 0.0001$; considered significant).

Table 3. Mechanical properties of nanofibers.

Nanofiber	Young's modulus (MPa)	Ultimate tensile strength (MPa)	Strain/ elongation at break (%)
ST1	1.65	1.24	276.83
ST4	3.92	3.55	375.88

3.2.11. Mechanical characterization

Figure 16 shows the stress-strain curves of the PCL/PEG electrospun nanofiber with and without *P. lanceolata* and clove oil. According to results, the immersion of the extract-oil mixture improved the UTS from 1.25 MPa (ST1) to 3.55 MPa (ST4), elongation from 276.8% (ST1) to 375.8% (ST4), and Young's modulus (table 3). It might be due to the immersion of *P. lanceolata* extract and clove oil in the PCL/PEG nanofibers. As indicated by SEM results, the extract-oil mixture surrounded the nanofibers, increasing the average fiber diameter and contributing to the observed improvement in mechanical properties [88]. Similar studies have reported that incorporating small molecules or nanoparticles can enhance tensile properties. In some cases, this may lead to reduced elongation due to reduced ductility.

For instance, a PCL/GO-g-PEG (1%) nanofiber scaffold exhibited nearly twice the elongation compared to a PCL/GO (1%) scaffold despite identical

GO content [79]. Pure PCL nanofibers have been reported to show an elongation of 115% and a tensile strength of 2.5 MPa. In comparison, curcumin-loaded PCL/PEG fibers demonstrated improved values of 167% elongation and 3.7 MPa tensile strength [9].

Our results demonstrate that an elongation at break of approximately 375.8% indicates high ductility and flexibility, which are advantageous for conformability and mechanical adaptability in wound-dressing contexts. Also, extract-oil-coated nanofibers may have promoted tighter fiber packing, increased interfacial adhesion, and greater nanofiber stiffness [89]. From a functional perspective, an enhanced modulus may benefit wound dressings intended for moderate to high mechanical stress areas (e.g. joints or mobile surfaces) by improving durability and stability. However, excessive stiffness should be avoided in fragile or superficial wounds; thus, the extract concentration can be tailored to the intended wound site [90].

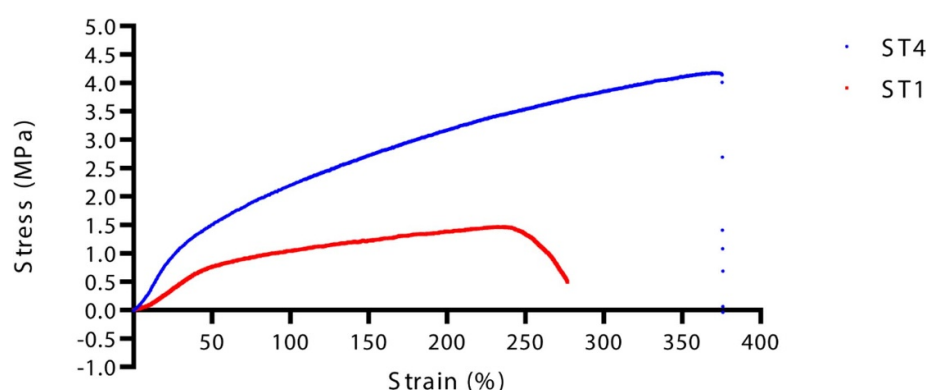


Figure 16. Stress-strain curves of ST1 and ST4.

4. Conclusion

In this study, electrospun PCL/PEG nanofibers incorporating *P. lanceolata* extract and clove oil were evaluated as dual-function wound dressings designed to provide antibacterial protection and support wound healing. Various extract concentrations were used to balance biological performance while maintaining non-cytotoxicity.

The nanofibers formed uniform, bead-free nanofibrous structures with suitable morphology and physicochemical properties for wound-dressing use. The addition of bioactive components increased surface wettability over time, and at higher extract concentrations, the nanofibers exhibited superhydrophilic behavior. FTIR analysis confirmed the presence of *P. lanceolata* extract and clove oil within the nanofiber structure. All nanofibers showed high water uptake during swelling tests.

Antibacterial performance was mainly determined by clove oil, as evidenced by the strong activity observed in the clove oil-only group, which was comparable to that of the highest-performing composite nanofiber. Within the clove oil-based system, increasing the *P. lanceolata* extract content modestly and consistently enhanced antibacterial performance at the composite level, rather than acting as an independent antibacterial component.

The nanofibers showed excellent cytocompatibility, and cell viability remained high across the tested time points. The wound-healing contribution of *P. lanceolata* was supported by the extract-only group (ST5), which showed strong scratch closure at later time points, consistent with its role in supporting healing. The developed nanofibers supported fibroblast responses and promoted wound closure, without cytotoxic effects from clove oil at the applied concentration.

Overall, electrospun PCL/PEG nanofibers incorporating *P. lanceolata* extract and clove oil provide a dual-function platform in which clove oil primarily contributes antibacterial protection, while *P. lanceolata* extract mainly supports wound healing and further enhances antibacterial performance within the composite formulation.

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Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

Supplementary figure 1 available at <https://doi.org/10.1088/1748-605X/ac7ebd/data1>.

Supplementary figure 2 available at <https://doi.org/10.1088/1748-605X/ac7ebd/data2>.

Supplementary table 1 available at <https://doi.org/10.1088/1748-605X/ac7ebd/data3>.

Conflict of interest

The authors hereby declare that they possess no known financial interests or personal relationships that could potentially influence the work presented in this paper.

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