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REVIEW

Electrospun Nanofibers from Plant Natural Products: A New Approach Toward Efficient Wound Healing

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Abstract: Globally, wound care has become a significant burden on public health, with annual medical costs reaching billions of dollars, particularly for the long-term treatment of chronic wounds. Traditional treatments, such as gauze and bandages, often fail to provide an ideal healing environment due to their lack of effective biological activity. Consequently, researchers have increasingly focused on developing new dressings. Among these, electrospinning technology has garnered considerable attention for its ability to produce nano-scale fine fibers. This new type of dressing, with its unique physical and chemical properties—especially in enhancing breathability, increasing specific surface area, optimising porosity, and improving flexibility—demonstrates significant advantages in promoting wound healing, reducing the risk of infection, and improving overall healing outcomes. Additionally, the application of natural products from plants in electrospinning technology further enhances the effectiveness of dressings. These natural products not only exhibit good biocompatibility but are also rich in pharmacologically active ingredients, such as antibacterial, anti-inflammatory, and antioxidant compounds. They can serve as both the substrate for nanofibers and as bioactive components, effectively promoting cell proliferation and tissue regeneration, thereby accelerating wound healing and reducing the risk of complications. This article reviews the application of plant natural product nanofibers prepared by electrospinning technology in wound healing, focussing on the development and optimisation of these nanofibers, discussing the advantages and challenges of using plant natural products in this technology, and outlining future research directions and application prospects in this field.

Keywords: plant-derived natural products, electrospinning, nanofibers, wound healing

Introduction

Wound care is a significant global public health issue, imposing a substantial burden on individuals and the economy.¹ Treating chronic wounds such as diabetic foot ulcers, pressure ulcers, and venous ulcers often necessitates long-term care and high medical costs.² Statistics indicate that the annual cost of wound care in the United States exceeds 25 billion US dollars, and the wound care market in Europe is also rapidly expanding.³ These chronic wounds severely impact patients' quality of life and increase the strain on the medical system.⁴ Additionally, treating infectious wounds is more complex, further exacerbating the economic burden. And because the wound healing process includes four stages: hemostasis, inflammation, proliferation and reconstruction. Its complexity and multi-stage nature make it an important topic in current medical research to effectively promote wound healing and reduce infection.⁵ Wound dressings are crucial in promoting wound healing by protecting the wound from external risks and accelerating the healing process.⁶ However, most dressings used in wound healing are still primarily composed of traditional gauze, cotton wool, and bandages.⁷ This often results in the gauze adhering to the wound skin during dressing changes, causing the wound to tear and increasing patient suffering.⁸ Additionally, these dressings primarily provide physical protection and absorption, with limited

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efficacy in promoting the wound healing process itself. Therefore, developing efficient, cost-effective, and rapid-healing wound care materials is an urgent priority. In response to the needs of wound treatment, an increasing number of researchers are focussing on new types of medical dressings. Among these, nanofiber dressings prepared through electrospinning technology are gaining attention due to their unique advantages.⁹

Electrospinning technology is an advanced method for preparing nanofibers, offering significant advantages over traditional wound dressings. By applying a high voltage, electrospinning technology can stretch polymer solutions or melts into continuous nanofibers, forming a fibrous network structure. The core principle lies in the electric field force acting on the polymer solution or melt. The polymer solution is injected at a constant rate through an injection system, and a high voltage is applied between the needle and a grounded collector. The electric field force acts on the droplet at the tip of the needle, forming nanometer-scale fibers that accumulate on the collector, resulting in a non-woven fibrous network. The nanofiber membranes produced by electrospinning exhibit excellent breathability, high specific surface area, and high porosity.¹⁰ These characteristics make them superior in promoting wound healing, reducing infection risk, and enhancing healing quality. More importantly, by adjusting the composition, diameter, and arrangement of the fibers, the physical and chemical properties of electrospun nanofibers can be customised to meet the needs of different wounds, optimising their functional performance.¹¹ Studies have shown that embedding bioactive molecules such as antibacterial drugs, anti-inflammatory drugs, or growth factors into the fibers can achieve controlled drug release, inhibit infection, and accelerate cell proliferation and tissue regeneration.¹² Such nanofiber dressings not only accelerate the wound healing process but also reduce scar formation, showing significant advantages in treating chronic and infectious wounds. Moreover, the three-dimensional structure of electrospun nanofibers mimics the natural cell growth environment, forming a highly porous and large surface area scaffold that effectively supports cell adhesion, migration, and proliferation.¹³ By precisely controlling the morphology and composition of the fibers, these dressings provide ideal support for new tissue formation in the wound bed.¹⁴ In summary, electrospun nanofiber dressings not only provide physical protection for wounds but also promote wound healing through customised design and drug loading. Their tremendous potential in modern wound care is driving treatment towards more efficient and personalised directions.

However, most electrospun dressings currently rely on synthetic polymers, lacking the biocompatibility and sustainability of natural materials. In recent years, plant-based materials have become an important research direction in electrospinning technology due to their natural biodegradability, antibacterial properties, and anti-inflammatory effects. Materials like cellulose, plant proteins, and alginates are extensively studied for wound dressing due to their biocompatibility and inherent antimicrobial and anti-inflammatory properties.¹⁵ These plant-derived fibers can closely interact with wounds without causing irritation, supporting healing processes and reducing environmental impact through natural degradation. Moreover, electrospinning allows for the functionalisation of these dressings by incorporating natural antioxidants, vitamins, or bioactive compounds, which can directly enhance cell proliferation and tissue regeneration, thus speeding up wound healing.¹⁶ Cellulose-based nanofibers, for instance, can be infused with natural healing agents like curcumin or witch hazel extract, enhancing the therapeutic efficacy of the dressings. Overall, plant-based electrospun nanofiber dressings offer an efficient and sustainable solution for wound care, while actively support the biological processes of healing through their natural components, showing significant promise in modern wound management.

In the current research on electrospun nanofibers and their application in wound healing, there are many important papers discussing the progress in this field. For example, Guo et al¹⁷ and de Almeida Bertassoni et al¹⁸ introduced the application of plant-based nanofibers and discussed their mechanism of action in wound healing. Although these studies provide important theoretical support, they mainly focus on the preparation techniques, mechanisms, or applications of specific plant components. They have not yet fully covered the diversity of different plant sources and the broader applications of plant components in nanofibrous structures. Based on this, this review aims to systematically explore the application of electrospun nanofibers derived from plant natural products in wound treatment. It focuses on their specific roles as electrospun nanofiber matrix materials and bioactive components. According to the plant-derived natural products commonly used as electrospinning nanofiber-based materials, they are divided into plant cellulose, alginate, and plant protein. The emphasis is on their use of plant natural products as nanofiber bases in wound healing treatment under the action of electrospinning significant advantages. Next, the review summarises the application of major plant-derived active components, such as flavonoids, polyphenols, and plant extracts, in wound treatment. It highlights the role

of electrospinning technology in improving plant-based natural products, emphasising the advantages of nanofibers prepared by different electrospinning techniques in wound healing. Finally, we summarise the use of vegetable oils as both a nanofiber base and a bioactive ingredient for wound treatment. Our review presents significant innovation and uniqueness compared to existing literature. We not only cover the latest results of in vitro and in vivo experiments, but also expand the literature coverage to include a wider range of plant ingredients, especially the diversity in plant source selection. Compared with the existing literature, our review systematically classifies and analyses the potential and specific applications of more diverse plant ingredient nanofibers, striving to provide a more comprehensive perspective for further research in this field.

Selection of Natural Products

When preparing plant-based nanofiber dressings, selecting suitable natural products is crucial. The selection of plantbased natural products for nanofiber substrates must meet several key criteria. Firstly, these materials must exhibit excellent biocompatibility and low immunogenicity to avoid adverse reactions during application.¹⁹ Secondly, they should possess good mechanical properties and processability, enabling the formation of stable nanofiber structures during electrospinning.²⁰ Additionally, an appropriate degradation rate is crucial, allowing the materials to be gradually absorbed by the body during wound healing.²¹ For instance, plant-derived natural products like alginate, cellulose, and plant proteins perform well in electrospun nanofiber preparation. Alginate is ideal for wound dressings due to its biocompatibility and antimicrobial properties; cellulose is valued for its mechanical strength and biodegradability;²² plant proteins offer adhesiveness and stability, making them promising candidates for wound care materials.²³

As active ingredients in nanofibers, plant-derived natural products must meet specific criteria. They should exhibit significant biological activity, such as antimicrobial and anti-inflammatory properties, and promote cell proliferation. For instance, tea tree oil, rich in terpenes, has strong antimicrobial effects that effectively inhibit various pathogens;²⁴ linalyl acetate and linalool in lavender oil reduce inflammation and promote wound healing;²⁵ asiaticoside from *Centella asiatica* extract accelerates tissue regeneration by promoting skin fibroblast proliferation.²⁶ These plant-derived active components, with their potent biological activities, enhance the therapeutic effects of nanofiber dressings and provide a natural and effective solution for wound management.

Chemical stability is another crucial factor when selecting natural products. The chemical components must remain stable during electrospinning and storage to ensure their biological activity is preserved. For example, thermal stability is essential, as some plant extracts may decompose under the high temperatures involved in electrospinning, making it necessary to choose extracts with good thermal stability.²⁷ Additionally, pH stability is important, as some components may lose activity with changes in pH.²⁸

Finally, the availability, cost-effectiveness, and cost effectiveness of natural products are important factors that determine their practical application. For example, materials like aloe²⁹ and *Centella asiatica*,³⁰ which are widely available and sustainably sourced, are ideal choices for large-scale procurement. By considering these criteria comprehensively, it can be ensured that the selected materials not only possess good therapeutic effects but also meet economic feasibility and market competitiveness.

Application of Electrospun Nanofibers from Plant Natural Products in Wound Healing

In the previous section, we studied the selection of natural products. Next, we would like to mention specific roles of plant-derived natural products in wound healing. This section will be classified into two parts. One part will focus on the role of plant-derived natural products in the form of a nanofiber-based material in wound healing. The other part will discuss the role of plant-derived natural products as an active substance in wound healing. The purpose of this study is to discover how electrospinning technology improves the properties of plant-derived natural products. It also aims to explore how these improved plant-based nanofibers facilitate wound healing. We shall strive to explore the potential of this technology for an increase in medical applications of plant natural products, especially in the field of wound treatment.

The Role of Plant-Derived Natural Products as Nanofiber Bases in Wound Healing

When preparing nanofibers for wound healing, selecting the appropriate fiber base material is crucial. Compared to synthetic materials or animal sources, plant-derived natural products offer unique advantages as nanofiber bases. Materials like cellulose, alginate, and plant proteins are sustainably sourced and generally exhibit higher biocompatibility and biodegradability.³¹ These characteristics enable better integration with human tissues without causing allergic reactions, thus promoting natural wound healing. It is worth noting that the unique chemical and physical structures of plant-derived fibers provide an excellent support environment for cell attachment and proliferation, which is essential for wound healing.³² This section will detail the specific applications and benefits of three main plant-derived natural products commonly used in electrospinning technology for wound healing: cellulose, alginate, and plant proteins, in the preparation of nanofiber-based dressings.

Cellulose

Cellulose, as a nanofiber base, boasts remarkable mechanical properties and biocompatibility.³³ In a study conducted by Adhikari et al,³⁴ they crafted a dual-layer nanofiber scaffold comprising regenerated cellulose and quaternized CS-hyaluronic acid/collagen. This scaffold not only showcased the synergistic effects of these materials but also underscored cellulose's pivotal role. The cellulose layer plays a crucial role in providing mechanical support for structural stability. Additionally, it acts as a foundational substrate, facilitating cell adhesion and migration on the more bioactive hyaluronic acid/collagen layer. By harnessing the advantages of cellulose nanofibers, this structural design significantly improves the scaffold's biocompatibility and therapeutic efficacy. In addition, other research has explored combining cellulose-based nanofibers with natural products. For instance, electrospun nanofibers created by combining cellulose with acacia extract and CS exhibited excellent mechanical properties and biocompatibility.³⁵ Notably, these nanofibers demonstrated potent antifungal activity in vitro and promoted wound healing in animal models, suggesting exciting clinical applications.

Cellulose-based nanofibers exhibit remarkable antibacterial and anti-inflammatory properties, critical for preventing wound infections.³⁶ In research conducted by Ullah et al,³⁷ cellulose acetate (CA) nanofiber mats infused with Manuka honey (MH) showed remarkable antibacterial and antioxidant effects. In vitro experiments confirmed significant inhibition of *Escherichia coli* and *Staphylococcus aureus* growth, alongside high cell compatibility when co-cultured with NIH 3T3 cell lines.

Moreover, cellulose-based electrospun nanofibers can be functionalised for controlled drug release, further promoting wound healing. Khalek's study³⁸ incorporated the antibiotic ciprofloxacin (CIP) into hydrophobic ethyl cellulose (EC) and hydrophilic polyvinylpyrrolidone (PVP) nanofibers. This enhanced the material's antibacterial properties and enabled sustained drug release, ensuring prolonged antibacterial protection. The in vitro drug release test showed that hydrophilic fibers released drugs significantly faster than hydrophobic fibers, with EC nanofibers exhibiting near zero-order release characteristics over three days. This functional modification controlled the drug release rate through the polymers' physicochemical properties. It significantly improved the antibacterial efficacy of cellulose nanofibers and effectively inhibited the growth of both gram-positive and gram-negative bacteria. This sustained and effective treatment notably accelerated the wound healing process.

Alginate

Alginate is a natural polysaccharide extracted from brown algae. It is widely used in electrospun nanofiber bases due to its excellent biocompatibility, low cost, renewability, and biodegradability.³⁹ Alginate-based nanofibers offer significant advantages in wound healing, particularly in promoting cell proliferation, antibacterial activity, and controlled drug release.⁴⁰ Alginate's biocompatibility and biodegradability ensure compatibility with human tissues and natural degradation without harmful metabolites.⁴¹ Alginate's production process is simpler and safer than animal-derived collagen systems. This reduces the risk of complications during prolonged use and ensures no adverse effects on the wound or surrounding tissues.⁴²

Secondly, alginate-based nanofibers excel in moisture absorption and breathability, maintaining a moist environment around the wound.⁴³ This environment promotes cell migration and proliferation, accelerating new tissue formation and

speeding up wound healing. Dodero et al⁴⁴ found that alginate nanofiber ENMs exhibit exceptional water absorption capacity and biocompatibility in both in vitro and in vivo tests, creating an ideal microenvironment for wound healing.

In addition, alginate-based nanofibers demonstrate excellent antibacterial activity. Their porous structure and chemical properties effectively inhibit the growth of various pathogenic microorganisms, including both gram-positive and gram-negative bacteria. This antibacterial activity reduces the risk of wound infection and facilitates smooth healing. A study by Smith et al⁴⁵ demonstrated that alginate nanofiber dressings form an antibacterial barrier on the wound surface, preventing bacterial invasion. This barrier also promotes biofilm formation at the wound base, significantly improving treatment outcomes and patient recovery rates.

As a carrier for drug delivery systems, alginate-based nanofibers exhibit remarkable drug loading capacity and precise controlled release characteristics. These nanofibers can encapsulate various drugs, such as antibiotics, growth factors, and anti-inflammatory agents. They release the drugs directly at the wound site, achieving high local concentrations and ensuring sustained release. This maximises therapeutic efficacy while minimising side effects. In a recent study,⁴⁶ alginate/polyvinyl alcohol(PVA) composite fibers prepared by electrospinning were used to load paclitaxel, an anticancer drug. The nanofibers achieved slow and sustained release, significantly enhancing the therapeutic effect on chronic diabetic wounds.

Alginate-based nanofibers also serve as excellent carriers of bioactive substances, effectively binding and releasing compounds like growth factors and antioxidants to enhance therapeutic effects. For example, Hu's⁴⁷ team developed a composite wound dressing that combines alginate and PCL fibers. The highly absorbent alginate maintains a moist environment, while PCL promotes cell adhesion. Additionally, plasmid DNA encoding platelet-derived growth factor-B (PDGF-B), complexed with polyethyleneimine (PEI), forms cationic nanoparticles that are adsorbed onto alginate fibers. Wound healing experiments showed that PDGF-B-loaded fibers accelerate wound closure and promote collagen formation, offering a promising multifunctional solution for wound care.

Based on the above, alginate-based nanofibers have great potential as carriers for bioactive substances. In the future, researchers can further optimise the fabrication process of alginate nanofibers and explore their functional modifications or synergistic effects with other bioactive substances, enhancing their role in wound care.

Plant Protein

Plant proteins, such as soy protein isolate (SPI) and zein, are preferred for electrospun nanofibers due to their high biocompatibility, environmental friendliness, and cost-effectiveness. These proteins are less likely to cause immune reactions and carry a lower risk of disease transmission than animal-based proteins.⁴⁸ Their natural hydrophilicity and optimised cell adhesion properties make them ideal for wound healing applications. Furthermore, the presence of the abundant disulphide bonds in their molecular structure provide water stability, maintaining structural integrity and functionality in practical applications, ensuring long-term safety and environmental sustainability.⁴⁹

SPI stands out in wound healing because of its remarkable biological properties. Rich in amino acids, SPI offers favourable biocompatibility and stability. Its structure closely resembles the extracellular matrix (ECM), which makes it well-suited for electrospinning.⁵⁰ In addition to serving as an effective matrix, SPI also possesses antioxidant and antiinflammatory properties. These characteristics help reduce oxidative stress and inflammation at the wound site, facilitating faster healing.⁵¹ Khabbaz et al prepared electrospun nanofiber mats (ENMs) and cast films (CFs) made from PVA and SPI that exhibit favourable physical, chemical, mechanical, and biological properties for wound healing. These materials can effectively absorb wound exudates, maintain a moist environment, promote cell migration and proliferation, and stimulate new tissue formation and healing.⁵² Furthermore, SPI/cellulose nanofiber scaffolds successfully mimic the physicochemical properties of natural skin by simulating the ECM and exhibiting high water retention capacity. In vitro, CA/SPH nanofibers promote fibroblast proliferation, migration, infiltration, and integrin β 1 expression. In vivo, CA/SPH scaffolds accelerate re-epithelialisation and epidermal thinning, while reducing scar formation and collagen anisotropy, confirming their potential as novel wound dressings.¹⁵ Furthermore, multifunctional electrospun nanofibers were made from Eudragit[®]/soy protein isolate, with ZnO-loaded halloysite nanotubes and allantoin. These nanofibers possess excellent antibacterial, anti-inflammatory, and antioxidant properties. They exhibit good biodegradability and strong mechanical properties. They also support significant cell proliferation. In addition, they demonstrate antimicrobial activity, especially against S. aureus. These characteristics highlight their potential for wound healing applications.⁵³

Zein, a hydrophobic plant protein extracted from corn, has good biocompatibility and film-forming properties, making it ideal for electrospun nanofibers.⁵⁴ In wound healing, zein-based nanofibers perform exceptionally well. For example, aloe-loaded nanofiber scaffolds (NFs/ZnO/Alv) were prepared by combining zein with polycaprolactone (PCL) and collagen. These scaffolds exhibited favourable morphology, mechanics, thermal stability, and hydrophilicity.⁵⁵ Studies indicate these scaffolds have good cell compatibility, promoting fibroblast proliferation and adhesion, and exhibit significant antibacterial activity against *S. aureus* and *E. coli*, making NFs/ZnO/Alv samples effective for wound healing.

Other plant proteins, such as pea protein and soy protein isolate, have also been used to prepare electrospun nanofibers. These materials show similar biological activity and have broad potential for biomedical applications. Nanofibers based on plant proteins (like potato, pea, and soy protein isolate) produced by Kalouta⁵⁶ using an eco-friendly water-based electrospinning method demonstrated high protein content and excellent biological properties. Pea and soy protein isolate, with their rich β -sheet content, form strong, dense nanofibers that decompose slowly in water, showing broad potential for biomedical applications. However, pea protein's application in wound healing is less explored. While it is cost-effective and nutritionally beneficial, it lacks bioactivities that promote cell growth and migration, essential for wound repair. Additionally, pea protein fibers may not meet the mechanical strength and durability required for clinical use, especially in moist environments, and may degrade too quickly, reducing their effectiveness in wound care.

Based on the above summary, which includes examples from <u>Table S1</u> highlighting the role of plant-derived natural products as nanofiber bases in wound healing, plant-based electrospun nanofiber materials show great potential for wound healing. Several factors, however, may limit their standalone use. First, some plant-derived fibers may lack sufficient structural stability and mechanical strength, making them unsuitable for some applications on their own. Second, while some plant-based materials offer good biocompatibility, they may not provide enough biological activity on their own, such as promoting cell adhesion and tissue regeneration. Additionally, the production cost and supply fluctuations of plant-derived fibers may restrict their large-scale production and use. Therefore, while plant-based materials have advantages in biocompatibility and environmental friendliness, overcoming technical and production challenges is key to their wider application. To meet the multifunctional requirements of wound healing dressings, plant-based materials are often combined with other functional materials. These composite materials are better suited to clinical needs and enhance the overall performance of the dressings.

Plant-Derived Natural Products as Active Ingredients

Plant-derived natural products possess unique bioactive properties that make them highly advantageous for wound healing.⁵⁷ These substances, derived from sustainable sources, offer a wide range of chemical diversity, allowing for targeted therapeutic interventions at various stages of the healing process. In contrast to synthetic compounds, the active ingredients from plants generally have lower toxicity and enhanced biocompatibility, supporting cell regeneration and exhibiting anti-inflammatory and antibacterial effects.⁵⁸ In electrospinning technology, these plant-based active substances are categorised into several classes: flavonoids, polyphenols, and plant extracts. Each type exhibits unique chemical and biological properties and plays a key role in various wound healing aspects. Next, we will explore the applications and benefits of these specific plant-derived active components in wound healing, highlighting how they optimise the therapeutic performance of nanofiber dressings through their unique mechanisms.

Application of Flavonoid Electrospun Nanofibers in Wound Healing

Flavonoids, prevalent secondary metabolites in the plant kingdom, possess unique chemical structures that exhibit significant pharmacological activity, particularly antioxidant and anti-inflammatory effects during wound healing.⁵⁹ These compounds consist of two aromatic rings (A and B) connected by a three-carbon unit (C ring).⁶⁰ This structural diversity endows flavonoids with potent bioactivity, effectively alleviating inflammation, promoting angiogenesis and cell migration, and accelerating wound healing. Electrospinning technology overcomes the poor water solubility and low bioavailability of flavonoids by encapsulating them within nanofibers, enhancing their direct application.

Quercetin

Quercetin (QE), a bioactive flavonoid obtained by hydrolysis of rutin (Ru), is widely found in fruits and vegetables.⁶¹ Its pharmacological activities include antioxidant, anti-inflammatory, and antimicrobial effects, as well as vascular nerve protection and pain relief.⁶² Despite its benefits in wound healing, the effectiveness of quercetin and its plant-derived derivatives is limited by poor water solubility and low bioavailability.⁶³

To address this, Zhou⁶⁴ developed a novel electrospun nanofiber membrane composed of PCL, chitosan oligosaccharides (COS), and a combination of QE/Ru for use as a bioactive dressing for wound healing. By incorporating COSs into the PCL scaffold at an optimised molar ratio, the hydrophilicity and water absorption properties of the membrane were improved. The antioxidant and antimicrobial activities of the QE/Ru-loaded nanofiber ENMs were tested. Among all the membranes, the PCL-COS-QE film outperformed the others. In another study, Zhang⁶⁵ and colleagues used electrospinning to load quercetin into a composite nanofiber dressing made of CS, PVP, and dihydroquercetin (DHQ). The results revealed that this membrane had good morphology, thermal stability, and hydrophilicity. It also displayed antimicrobial and antioxidant activities while being non-toxic to Hacat cells. Most importantly, animal experiments demonstrated that the CS-PVP-DHQ nanofiber membrane could accelerate wound healing. It achieved this by inducing autophagy pathways, increasing the expression of pan-cytokeratin, vascular endothelial growth factor (VEGF), and CD31.

The Croitoru research team⁶⁶ created a novel microscale matrix using PLA and graphene oxide (GO) as base materials through electrospinning. They loaded quercetin onto the fiber matrix to explore its potential as a model drug for wound dressing applications. The study aimed to establish an electro-responsive drug delivery system, utilising external electrical stimuli to control and locally deliver drug molecules to target tissues. This significantly accelerates the drug release rate. With the application of appropriate electric fields, the release rate of QE increased by up to 8640 times. Antimicrobial tests confirmed that these scaffolds could prevent bacterial biofilm growth. Moreover, these scaffolds could be loaded with more effective drugs for cancer, infection, and osteoporosis treatments. When cultured on these scaffolds, L929 fibroblast cells were evenly distributed, with the highest cell survival rate of 82.3% observed on the 10% PLA/0.5% GO/Q scaffold. This further validates the potential of electrospinning technology in overcoming quercetin's limitations and highlights its significant promise for wound healing and electro-responsive drug delivery systems. Overall, the electrospinning technique has significantly improved quercetin's shortcomings, and the prepared scaffolds have shown good effects in wound repair, further proving their potential for application.

Naringenin

Naringin (NR), a bioactive flavonoid from grapefruit peel, features a sugar group linked to a flavonoid skeleton. Its pharmacological activities include antioxidant, anti-inflammatory, lipid-lowering, anti-cancer, and cardiovascular protective effects, making it a promising candidate for wound healing.⁶⁷ Unfortunately, NR is easily metabolised in the intestines and liver, leading to low bioavailability in the body and limiting its applications.⁶⁸

To address this, Farzaei and colleagues⁶⁹ used electrospinning technology to incorporate water-insoluble NR into PCL/polyethylene glycol (PEG) nanofibers, creating a wound dressing with notable antibacterial properties. These nanofibers exhibit a linear morphology with a uniform, smooth surface, as confirmed by SEM images. The dressing ensures sustained release of NR under high-concentration conditions. FT-IR analysis reveals cross-linking between the OH groups of NR and the C=O groups of PCL, enhancing its antibacterial effects. In vitro MTT assays and in vivo rat wound model experiments demonstrate that the dressing is non-toxic to human fibroblasts and significantly improves cell viability. It shows re-epithelialisation and wound closure effects comparable to commercially available phenytoin ointment. This highlighting its potential as a biodegradable antibacterial wound dressing.

Tottoli et al⁷⁰ developed an advanced biopolymer dressing to prevent hypertrophic scars (HTS) in complex wounds. This dressing, composed of poly-L-lactide-co- ε -caprolactone (PLA-PCL) fibers loaded with 2.0% w/w NR, exhibits moderate hydrophobicity, good absorbency, and moisture permeability, providing an ideal healing environment. The fibers demonstrated excellent toughness and elongation in simulated wound fluid, ensuring flexibility and adaptability to the body surface. What's more, the slow release of NR exerted a sustained anti-fibrotic effect on human dermal

fibroblasts over three days. By downregulating major fibrotic factors (TGF- β 1, COL1A1, and α -SMA), it significantly prevented HTS formation, demonstrating potential to minimise hypertrophic scarring during early wound healing.

Lastly, the Arezomand team's research⁷¹ combined copolymerisation and electrospinning technologies from nanomedicine to create new biomimetic nanofiber composites, highlighting NR's multifunctionality. This technique involves melt polymerisation of proline (Pr) and hydroxyproline (Hyp), followed by graft copolymerisation with CS, producing PHPC with amino acid grafting, drug-loaded, and porous nanofiber structures. Scaffolds based on PHPC are more effective in absorbing wound exudate and releasing drugs faster, with better compatibility with MDF cells and antibacterial activity against multidrug-resistant Staphylococcus aureus. In vivo studies further showed that PHPCbased scaffolds accelerate wound healing during cell migration, proliferation, and remodelling phases compared to CSbased scaffolds, promoting better collagen content, wound contraction, epithelialisation, and neovascularisation.

These studies demonstrate the immense potential of electrospinning technology in enhancing NR's functionality, as well as highlight the effectiveness of optimising wound healing dressings through nanotechnology. These advancements drive technological innovation in wound treatment and lay a solid scientific foundation for future clinical applications, showcasing the broad application prospects of natural medicines in modern healthcare.

Astragaloside

Astragaloside IV (AS) possesses pharmacological properties such as immune modulation, anti-inflammatory, antiviral, anti-apoptotic, and blood sugar reduction.⁷² Despite its benefits in wound healing, AS and its derivatives suffer from low bioavailability and stability in the human body, leading to poor drug absorption. To address these issues, Liu and colleagues⁷³ developed a novel AS/CS/PLA nanofiber dressing using electrospinning technology to enhance diabetic wound healing. Experiments showed that the dressing significantly promoted cell proliferation, adhesion, and migration in vitro and increased collagen deposition and granulation tissue formation in vivo, aiding wound healing in diabetic rats. Early on, the AS/CS/PLA nanofiber dressing also enhanced the expression of CD31 and TGF- β factors, accelerating the healing process.

Further validating the efficacy of electrospun dressings, Zhang's research⁷⁴ demonstrated that AS-loaded nanofiber dressings significantly promoted wound healing in rat models, especially in the early stages. These dressings enhanced angiogenesis, improved immune function at the wound site, and regulated collagen alignment to inhibit scar formation. Preliminary mechanistic studies suggested that SF/GT nanofiber dressings loaded with AS increased macrophage numbers at the wound site. This promoted VEGF secretion and improving local immune function, thereby facilitating wound healing. Additionally, these dressings suppressed α -SMA expression, preventing myofibroblast formation and inhibiting scar formation.

Wang's research⁷⁵ utilised coaxial electrospinning technology to create a novel nanofiber dressing for chronic diabetic wounds. Coaxial electrospinning offers greater surface area and porosity and allows for adjustable drug release, enhancing therapeutic efficacy. This dressing, composed of AS, PVP, and PLA, featured nanofibers with a fast-first-then-slow release characteristic. Antioxidant tests showed a free radical scavenging rate of 61%. In vitro cell tests showed the dressing promoted L929 fibroblast proliferation, adhesion, and migration, with good biocompatibility. In a diabetic rat model, the dressing group achieved a wound healing rate of 96.54 \pm 0.29% by day 14. Overall, the coaxial AS/PVP/PLA nanofiber dressing shows significant advantages in improving drug release efficiency, promoting wound healing, and antimicrobial properties, holding broad prospects for application.

Others

In addition to the aforementioned common flavonoids, other flavonoids derived from natural sources have also shown unique advantages in the application of electrospun nanofibers. Firstly, chrysin (Chr) is a naturally occurring flavonoid with significant bioactivity, known for its anticancer, anti-inflammatory, and antioxidant properties.⁷⁶ Unfortunately, its application in wound healing is limited due to low water solubility and rapid metabolism. Researchers have addressed these issues by integrating Chr into PCL and PEG nanofibers through electrospinning technology. These nanofibers release Chr slowly, increasing the drug's concentration and duration at the target site, enhancing its bioactivity. Experimental results show that Chr nanofibers significantly improve cell viability and inhibit oxidative stress and

inflammation in models, indicating that electrospinning technology effectively enhances Chr's application in wound treatment.⁷⁷

Puerarin (PUE), a flavonoid extracted from kudzu root, is known for its strong antioxidant and anti-inflammatory activities.⁷⁸ Nevertheless, like other flavonoid drugs, it faces the same limitations. Sun's research⁷⁹ utilized electrospinning technology to prepare a composite nanofiber membrane of SF/PVP/PUE, incorporating PUE, natural silk fibroin (SF), and synthetic PVP. This fibrous membrane, with increased fiber diameter and porosity, significantly enhanced cell adhesion and proliferation. Moreover, the nanofiber membrane exhibits excellent antioxidant properties and effectively reduces cellular inflammatory responses induced by lipopolysaccharide (LPS). Mechanistic studies reveal that the nanofibers suppress the activation of the Toll-like receptor 4/myeloid differentiation factor 88/nuclear factor kappa B (TLR4/MyD88/NF-κB) and phosphoinositide 3-kinase/protein kinase B (PI3K/AKT) signalling pathways. This significantly reduces inflammation and promoting rapid wound repair. These findings provide theoretical support for the design of innovative wound dressings and demonstrate their potential for clinical application.

In summary, these nanofibers offer a high surface area and excellent biocompatibility, allowing localized and sustained release of flavonoid compounds while maintaining their bioactivity and minimising systemic side effects. By adjusting the fiber composition and structure, precise control of drug release can be achieved, enhancing therapeutic outcomes. In addition, these nanofiber dressings can be combined with antimicrobials and other functional materials to create a multifunctional therapeutic system, significantly improving wound healing efficiency.

Application of Electrospun Nanofibers of Polyphenols in Wound Healing

Polyphenolic compounds are widely distributed in nature and typically contain multiple phenolic structures. These structures form complex multi-ring configurations, endowing polyphenols with excellent antioxidant and anti-inflammatory properties.⁸⁰ The immense potential of these substances is evident; yet, their limited water solubility and bioavailability remain significant challenges.⁸¹ Encapsulating polyphenolic compounds in nanofibers through electrospinning technology addresses these challenges and takes advantage of the high surface area and excellent biocompatibility of nanofibers. This approach allows for controlled release of active ingredients, maintains the stability of active components, and reduces systemic side effects.

Curcumin

Curcumin (CU), a bioactive polyphenolic compound extracted from turmeric rhizomes, possesses antioxidant, antiinflammatory, anti-tumour properties, and offers cardiovascular, nervous system protection, and digestive improvement.⁸² However, its clinical application is limited by poor water solubility and low bioavailability.⁸³

In the study by Moradkhannejhad et al⁸⁴ electrospinning technology effectively encapsulated curcumin in PLA nanofibers, enhancing wound dressings by adjusting the fibers' physical and chemical properties. The study optimised fiber hydrophilicity by varying the molecular weight and proportion of PEG, improving curcumin's bioavailability and accelerating wound healing by controlling the drug release rate. In another study, the Chagas team⁸⁵ used electrospinning to create a top layer of PLA nanofibers and a bottom layer of PLA/CU ultrafine fiber blend. This combined curcumin's protective and antimicrobial properties, providing an effective solution for wound protection, infection prevention, and healing. The dual-layer asymmetric nanofiber membrane design prevented curcumin's photodegradation and enhanced its stability under sun exposure, crucial for externally used wound dressings.

Finally, the study expanded the application of electrospinning technology in wound treatment by integrating multiple bioactive functions such as antioxidant, anti-inflammatory, and angiogenesis. Xi⁸⁶ designed a multifunctional elastomeric PLA-poly(citrate-siloxane)-CU@polydopamine hybrid nanofiber scaffold (PPCP matrix). The PPCP nanofiber matrix significantly promoted the adhesion and proliferation of normal skin cells by enhancing early angiogenesis and accelerating skin wound healing in both normal and bacteria-infected mice. This scaffold's development demonstrated the potential of nanofibers in treating skin injuries and infections. It also highlighted the key role of electrospinning technology in preparing advanced dressings with high biocompatibility and therapeutic functionality.

Resveratrol

Resveratrol (RS) is a natural polyphenolic compound known for its antioxidant, anti-inflammatory, anti-cancer, and cardiovascular protective effects.⁸⁷ Electrospinning, an advanced method for producing nanofiber materials, significantly improves the stability and bioavailability of resveratrol by mixing it with polymers and subjecting it to the electrospinning process.⁸⁸ For instance, Karakucuk et al⁸⁹ demonstrated that resveratrol nanocrystals physically adsorbed onto PCL nanofibers significantly enhanced resveratrol's solubility and bioactivity. This modification not only improved fiber-skin contact quality but also increased the antibacterial effect against Propionibacterium acnes, suggesting potential advantages in treating acne and other skin conditions.

Electrospinning technology enables the uniform dispersion of resveratrol within nanofibers, creating a drug delivery system with well-controlled release properties, thereby enhancing its pharmacological activity and efficacy. Kanaujiya⁹⁰ successfully incorporated resveratrol into PVP and PVA nanofibers using electrospinning for burn wound treatment. This novel nanofiber mat not only provided sustained and controlled release of resveratrol but also significantly enhanced antimicrobial activity against, highlighting the broader application potential of resveratrol in drug development and functional foods.

In ischaemic wound treatment, Lakshmanan⁹¹ developed a resveratrol-loaded nanofiber scaffold using electrospinning, significantly improving wound healing efficiency. The sustained release of resveratrol directly activates VEGF expression, driving new blood vessel formation, crucial for enhancing oxygenation and nutrient supply to wounds. By reducing local oxidative stress and inflammation through its antioxidant and anti-inflammatory effects, resveratrol alleviated conditions that typically inhibit VEGF function. Furthermore, resveratrol enhanced cell proliferation and migration by activating the PI3K/Akt and ERK/MAPK signalling pathways, essential for wound healing. This promoted angiogenesis and increased cell survival in the wound area by upregulating the anti-apoptotic effect of Bcl-2.

In summary, electrospinning technology effectively enhances resveratrol's bioavailability and demonstrates broad application potential in various therapeutic areas.

Catechins

Catechins, polyphenolic compounds found in plants like tea leaves and cocoa, possess various pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, antiviral, anticancer, and cardiovascular protective effects, making them highly valued in pharmaceutical development.⁹² Electrospinning, an advanced method for producing nanofiber materials, protects catechins from degradation caused by light, heat, and oxygen, and controls their release rate, thereby enhancing their absorption and efficacy. Studies have shown that catechin nanofibers prepared by electrospinning significantly extend antioxidant activity, enhance anti-inflammatory effects, and improve bioavailability.⁹³

Hu⁹⁴ utilised uniaxial electrospinning to load catechins onto PVA/CS nanofibers, optimising them for diabetic wound infections. These nanofibers exhibit excellent antibacterial and antioxidant properties, effectively controlling both grampositive and gram-negative bacteria. In addition, by dynamically releasing catechins, these nanofibers significantly promote cell migration and proliferation, offering a low-cost and efficient treatment option for diabetic wounds.

Dual-nozzle electrospinning, compared to uniaxial electrospinning, can simultaneously spin two different polymer solutions, achieving more uniform distribution and complex structural control in composite materials. Mohammadi⁹⁵ integrated catechins into gelatin/PLA fiber structures using dual-nozzle electrospinning, creating a hybrid composite fiber structure. This technique ensures even distribution of catechins within the fiber structure, enhancing the mechanical strength and bioactivity of the fibers. The improved fibers demonstrate increased antibacterial activity and enhance cell adhesion. They also increase fiber diameter, which improves cell viability and promotes cell migration, both crucial for rapid wound healing.

The primary advantage of coaxial electrospinning over dual-nozzle electrospinning is its ability to precisely generate nanofibers with a core-shell structure. This structure encapsulates active ingredients in the core layer, providing protection and controlled release. Coaxial electrospinning also enables the creation of complex composite functional materials, crucial for drug delivery systems requiring multifunctionality, delayed release, or environmental sensitivity. Li⁹³ used coaxial electrospinning to create a poly(L-lactide-co-caprolactone) (PLCL)/gelatin/epigallocatechin gallate (EGCG) nanofiber membrane with a core-shell structure. This advanced structure stabilises EGCG encapsulation in the

core layer, while the outer gelatin layer provides mechanical support and additional bioactivity. The nanofiber membrane demonstrated excellent biocompatibility, antibacterial, and antioxidant capabilities in both in vitro and in vivo experiments. It significantly promoted cell proliferation, inhibited inflammatory responses, and accelerating wound closure.

Progressing from basic to advanced technology, each application of electrospinning has markedly improved the therapeutic effects of catechins. This demonstrates broad potential in complex wound management, especially in promoting rapid healing and enhancing clinical outcomes.

Others

To further demonstrate the widespread application of plant-derived natural products in wound healing, let us discuss several other polyphenolic compounds and their applications in nanofiber technology, beyond the commonly used ones.

Anand⁹⁶ developed a silk-based ferulic acid (FA) carrier nanofiber mat for treating diabetic foot ulcers. Electrospinning technology allows precise control over the diameter (100–250 nm) and porosity of the fibers, optimising the loading and release of FA. Both in vitro and in vivo experiments have shown that this nanofiber mat can continuously release FA, demonstrating low cytotoxicity and significant wound healing effects, especially in restoring normal skin structure. Lan⁹⁷ developed a novel core-shell structured nanofiber membrane using coaxial electrospinning technology, containing antioxidant tea polyphenols (TP) in the core and antimicrobial ε -polylysine (ε -PL) in the shell. This design achieves rapid release of ε -PL and sustained release of TP, aiding in rapid antibacterial action and long-term antioxidant protection, effectively promoting wound healing. These nanofibers exhibit excellent antibacterial performance, particularly against Escherichia coli and Staphylococcus aureus, and good cellular compatibility, indicating their potential as ideal wound dressings.

In <u>Table S2</u>, I have summarized the application of plant-derived natural product monomers as active ingredients in nanofibers for wound healing over the past five years. These examples of polyphenolic compounds highlight the broad application and promising prospects of plant-derived natural product nanofibers in wound healing. Electrospinning technology offers innovative carrier designs for these natural products, enhancing their biological activity and clinical potential.

Application of Electrospun Nanofibers from Plant Extracts in Wound Healing

Compared to individual flavonoids and polyphenols, plant extracts contain a more complex and diverse array of bioactive components, including terpenes, alkaloids, glycosides, and polysaccharides.⁹⁸ This diversity enhances their therapeutic efficacy and offers a broader range of biocompatibility and mechanisms, from anti-inflammatory and antibacterial effects to promoting cell proliferation and repair. This gives them a significant advantage in wound treatment applications. Through electrospinning technology, these complex plant extracts can be effectively encapsulated into nanofibers, creating smart dressings that release multiple active components at specific treatment stages, providing multidirectional therapeutic support.

Firstly, Doostan et al⁹⁹ used electrospinning to create PVA/CS nanofiber scaffolds, meticulously controlling pore size and surface structure, greatly enhancing the antioxidant and anti-inflammatory properties of flaxseed extract. This technology ensured uniform distribution of active ingredients, accelerated wound healing, and reduced inflammation duration through controlled release dynamics. Similarly, Shahid¹⁰⁰ optimised the antibacterial and healing-promoting effects of licorice extract by integrating it into PVA nanofibers using electrospinning. Active components in licorice, such as glycyrrhizin and glycyrrhetinic acid, were stably encapsulated and slowly released, providing long-term antibacterial protection and promoting tissue regeneration. In another study, Fahimirad¹⁰¹ prepared PCL nanofibers as the first support layer using electrospinning. Subsequently, a mixed solution of PVA/Quercus infectoria galls (QLG)/biosynthesised CuNPs was electrospun as the second bioactive external layer. The combined use of Crepe Myrtle extract with copper nanoparticles demonstrated enhanced antibacterial properties, long-lasting antioxidant protection. It also promoted wound healing through the complex nanofiber structure, showcasing technological advancements in integrating multiple functions to combat complex wounds.

Ramalingam's team¹⁰² developed a poly-ε-caprolactone/gelatin composite pad containing *Gymnema sylvestre* extract to prevent bacterial colonisation. Electrospinning technology ensured the uniform distribution and effective release of the

extract, providing continuous protection against bacterial invasion. This composite fiber mat significantly enhanced the activity and proliferation of human primary dermal fibroblasts and keratinocytes. It accelerated wound closure and improved the formation and quality of new skin tissue. This sped up the healing process and improved the functionality and aesthetics of the skin post-treatment.

Almasian and colleagues¹⁰³ incorporated peppermint extract into polyurethane (PU) nanofibers for diabetic wound healing. The addition of F127 to the polymer matrix enhanced the absorption capacity of the wound dressing. They precisely controlled the fiber structure and encapsulation of the extract. This optimised the sustained release curve of peppermint extract, ensuring a stable effect over a long period. The system continuously inhibited bacterial growth and reduced inflammation.

Furthermore, this nanofibre controlled-release system was tailored for diabetic wounds, ensuring the active components provided assistance when most needed at the wound site. This targeted release technology enhanced local treatment effectiveness and reduced the possibility of systemic side effects, making these nanofibers an efficient solution for diabetic wounds.

In addition to single plant extracts, Zehra et al¹⁰⁴ developed a PLA-PHBV double-layer electrospun film incorporating extracts from both bearberry and licorice. During wound healing, arbutin reduces oxidative stress and inflammation, protecting tissues from free radical damage and minimising scar formation and pigmentation. The film's design includes one layer for the rapid release of glycyrrhetinic acid from licorice, providing early-stage antibacterial and antiinflammatory effects. Concurrently, a second layer ensures the gradual release of arbutin from bearberry, providing a continuous supply of antioxidants that promote cellular growth. Electrospinning technology precisely controls the loading and release rates of these extracts. The film support various stages of wound healing. It begins with the rapid action of licorice extract to reduce inflammation and prevent microbial infection. This is followed by the sustained release of bearberry extract, which promotes tissue growth and aids in wound closure. This innovative development demonstrates the potential of electrospun nanofiber dressings in modern wound management and highlights the enhanced therapeutic outcomes achievable through the synergistic use of multiple plant extracts.

In <u>Table S3</u>, we summarize the application of plant extracts as active ingredients in electrospun nanofibers for wound healing in recent years. In summary, the application of electrospun nanofibers combined with plant extracts in wound healing demonstrates a powerful combination of innovation and natural efficacy. Electrospinning technology can effectively encapsulate plant extracts, ensure their uniform distribution and control their release, by precisely regulating the load and release rate of the extracts. In addition, plant extracts contain a variety of active ingredients that can cope with different types of wounds, such as diabetic wounds or chronic wounds, providing more possibilities for personalized treatment. The development of this technology has opened up new prospects for wound management and demonstrated the therapeutic advantages brought by the fusion of plant extracts and advanced technologies.

Application of Electrospun Nanofibers from Vegetable Oil in Wound Healing

Essential oils are highly concentrated plant-derived liquids extracted from various parts of plants, such as flowers, leaves, bark, roots, seeds, or peels, through distillation or cold pressing.¹⁰⁵ Their complex chemical composition includes terpenes, alcohols, ketones, aldehydes, esters, and phenols, which provide a range of biological activities, including antibacterial, anti-inflammatory, antioxidant, analgesic, and antidepressant effects.¹⁰⁶ Unlike plant extracts, which typically serve a single function in electrospun nanofibers, essential oils can serve dual roles. They act as both the base material for nanofibers and as bioactive components due to their exceptional biocompatibility and pharmacological properties. This multifunctionality grants essential oils broader potential in design and application.

Fiaschini et al¹⁰⁷ created a three-layer core-shell membrane dressing using electrospinning technology, encapsulating neem oil and St. John's wort oil in the core layer. This design offers antibacterial, anti-inflammatory, and antioxidant benefits. Neem oil (Azadirachta indica) is known for its broad-spectrum antibacterial and anti-inflammatory properties, while Hypericum perforatum is rich in antioxidants that scavenge free radicals and protect cells from oxidative stress. The multilayer structure ensures sustained release of active ingredients and provides excellent protection and usability through the mechanical strength of the outer medical-grade PCL. This design showcases the application of electrospinning technology in controlled-release therapeutic systems, paving the way for more complex dressing designs.

Irem Unalan's¹⁰⁸ research advanced the use of electrospinning technology in wound dressings by incorporating peppermint essential oil (PMO) into PCL fiber mats, boosting the dressing's antibacterial and analgesic properties. Key components of PMO, like menthol and menthone, exhibit notable antibacterial, anti-inflammatory, and mild analgesic effects. By optimising spinning parameters, reducing fiber diameter, and enhancing the release efficiency of PMO, the dressing demonstrated excellent efficacy against pathogens such as *S. aureus* and *E. coli*.

Sofi et al's study¹⁰⁹ showcases the advanced technique of simultaneously incorporating lavender oil and silver nanoparticles into PU fibers. Lavender essential oil (LEO) is renowned in wound care for its anti-inflammatory and cell growth-promoting effects, while silver nanoparticles (AgNPs) are valued in medical materials for their strong antibacterial properties. The PU/lavender oil/silver nanoparticle composite fibers, created using electrospinning technology, not only demonstrated excellent antibacterial activity but also enhanced fibroblast proliferation and migration, significantly speeding up the wound healing process.

Hussein¹¹⁰ explored PU and PVA/Gel nanofiber scaffolds using dual-nozzle electrospinning, incorporating cinnamon essential oil (CEO) and nCeO2 to enhance performance. Analysis using STEM, DSC, and FTIR revealed that CEO and nCeO significantly improved the scaffolds' mechanical and thermal stability. Cytotoxicity tests showed that CEO and nCeO-enriched scaffolds enhanced cell viability and effectively inhibited Staphylococcus aureus, indicating their potential for diabetic wound management.

Rezk's research¹¹¹ developed nanofiber scaffolds loaded with pumpkin seed oil (PSO) using electrospinning technology. These scaffolds showed significant antibacterial activity and excellent wound healing effects in animal models. Rich in fatty acids and antioxidants, PSO reduces inflammation and promotes tissue regeneration. In experiments on skin and oral wounds, the PSO nanofiber scaffolds demonstrated high healing rates and good biocompatibility, particularly excelling in treating skin and oral wounds.

Liu et al¹¹² employed in situ electrospinning to directly deposit zein and thyme essential oil (TEO) membranes onto wounds. This method improved treatment convenience and precision, ensuring perfect dressing adherence and significantly enhancing therapeutic efficacy. Zein's excellent film-forming properties and biocompatibility, combined with TEO's potent antibacterial and antioxidant properties, further boosted the dressing's therapeutic effects.

In <u>Table S4</u>, we still summarize the application of plant essential oil nanofibers in wound healing. Based on the above studies, we can observe that essential oils, when applied through electrospinning technology, exhibit significant therapeutic potential in the field of wound healing. Electrospinning technology offers greater possibilities for the use of essential oils by combining them with nanomaterials, successfully enabling the controlled release of the oils' multiple bioactive properties. This enhances their antimicrobial, anti-inflammatory, and antioxidant effects, providing a more efficient and precise solution for wound treatment.

Summary and Perspective

Overall, we can clearly see the significant advantages of plant-derived electrospun nanofibers in wound healing. Plantderived materials have excellent biocompatibility, mechanical properties and degradability, and can provide good support for wound repair under the action of electrospinning technology. Secondly, the natural active ingredients in plant-derived materials have pharmacological activities that are beneficial to wound healing, helping to control infection, reduce inflammation and accelerate wound healing. In addition, electrospinning helps plant-derived natural products overcome challenges like poor water solubility, low bioavailability, and instability while preserving their pharmacological activity. This integration has allowed better development and utilisation of these natural products.

Although plant-derived electrospun nanofibers have so many advantages in wound healing, the diversity and selectivity of plant sources are not comprehensive. We look forward to seeing more plant-derived natural product nanofibers enter the field of wound treatment in the future. Similarly, we expect to further understand how plant active ingredients interact with human cells and biomolecules and their role in different stages of wound healing. In addition, there is still a lot of room for development in the wide application of plant-derived natural products and their multiple mechanisms of action in wound healing, which deserves further exploration.

Data Sharing Statement

The data in this study are derived from clinical studies and do not have ethical conflicts, so this does not apply.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

References

- 1. Balaha M, Cataldi A, Ammazzalorso A, et al. CAPE derivatives: multifaceted agents for chronic wound healing. Arch. Pharm. 2024;357(10): e2400165. doi:10.1002/ardp.202400165
- 2. Cui Y, Hong S, Jiang W, et al. Engineering mesoporous bioactive glasses for emerging stimuli-responsive drug delivery and theranostic applications. *Bioact. Mater.* 2024;34:436–462. doi:10.1016/j.bioactmat.2024.01.001
- 3. Parvin F, Vickery K, Deva AK, Hu H. Efficacy of surgical/wound washes against bacteria: effect of different in vitro models. *Materials*. 2022;15(10):3630. doi:10.3390/ma15103630
- 4. Marques R, de Lopes MVO, Neves-Amado JD, et al. Integrating factors associated with complex wound healing into a mobile application: findings from a cohort study. *Int Wound J.* 2024;21(1):e14339. doi:10.1111/iwj.14339
- 5. Han Y, Cao J, Li M, et al. Fabrication and characteristics of multifunctional hydrogel dressings using dopamine modified hyaluronic acid and phenylboronic acid modified chitosan. *Front Chem*. 2024;12:1402870. doi:10.3389/fchem.2024.1402870
- Lee H, Kim J, Myung S, et al. Extraction of γ-chitosan from insects and fabrication of PVA/γ-chitosan/kaolin nanofiber wound dressings with hemostatic properties. *Discover Nano*. 2024;19(1):1–14. doi:10.1186/s11671-024-04016-6
- Dehghani P, Akbari A, Saadatkish M, Varshosaz J, Kouhi M, Bodaghi M. Acceleration of wound healing in rats by modified lignocellulose based sponge containing pentoxifylline loaded lecithin/chitosan nanoparticles. *Gels.* 2022;8(10):658. doi:10.3390/gels8100658
- Singh V, Marimuthu T, Makatini MM, Choonara YE. Biopolymer-based wound dressings with biochemical cues for cell-instructive wound repair. *Polymers (Basel)*. 2022;14(24):5371. doi:10.3390/polym14245371
- 9. Xu S, Lu T, Yang L, Luo S, Wang Z, Ye C. In situ cell electrospun using a portable handheld electrospinning apparatus for the repair of wound healing in rats. *Int Wound J.* 2022;19(7):1693–1704. doi:10.1111/iwj.13769
- Du L, Li T, Wu S, Zhu HF, Zou FY. Electrospun composite nanofibre fabrics containing green reduced Ag nanoparticles as an innovative type of antimicrobial insole. RSC Adv. 2019;9(4):2244–2251. doi:10.1039/C8RA08363K
- Li J, Liu Y, Abdelhakim HE. Drug delivery applications of coaxial electrospun nanofibres in cancer therapy. *Molecules*. 2022;27(6):1803. doi:10.3390/molecules27061803
- 12. Jiang Z, Zheng Z, Yu S, et al. Nanofiber scaffolds as drug delivery systems promoting wound healing. *Pharmaceutics*. 2023;15(7):1829. doi:10.3390/pharmaceutics15071829
- Xu T, Yao Q, Miszuk JM, et al. Tailoring weight ratio of PCL/PLA in electrospun three-dimensional nanofibrous scaffolds and the effect on osteogenic differentiation of stem cells. *Colloids Surf. B.* 2018;171:31–39. doi:10.1016/j.colsurfb.2018.07.004
- Adeli H, Khorasani MT, Parvazinia M. Wound dressing based on electrospun PVA/chitosan/starch nanofibrous mats: fabrication, antibacterial and cytocompatibility evaluation and in vitro healing assay. Int J Biol Macromol. 2019;122:238–254. doi:10.1016/j.ijbiomac.2018.10.115
- Ahn S, Chantre CO, Gannon AR, et al. Soy protein/cellulose nanofiber scaffolds mimicking skin extracellular matrix for enhanced wound healing. Adv. Healthcare Mater. 2018;7(9):1701175. doi:10.1002/adhm.201701175
- 16. Azimi B, Maleki H, Zavagna L, et al. Bio-Based Electrospun Fibers for Wound Healing. J Funct Biomater. 2020;11(3):67. doi:10.3390/jfb11030067
- 17. Guo S, Wang P, Song P, Li N. Electrospinning of botanicals for skin wound healing. Front Bioeng Biotechnol. 2022;10:1006129. doi:10.3389/ fbioe.2022.1006129
- de Almeida Bertassoni B, de Abreu Garófalo D, Monteiro M, et al. In vivo wound healing activity of electrospun nanofibers embedding natural products. Arabian J. Chem. 2024;17(12):106019. doi:10.1016/j.arabjc.2024.106019
- 19. Li A, Jing Z, Liu Y, Wang Y. Nanofiber-based wound dressing in wound healing of elderly patients. *Postepy Dermatol Alergol.* 2024;41 (1):121–127. doi:10.5114/ada.2024.136034
- de Morais MG, Vaz Bda S, de Morais EG, Costa JA. Biological effects of Spirulina (Arthrospira) biopolymers and biomass in the development of nanostructured scaffolds. *Biomed Res Int*. 2014;2014:762705. doi:10.1155/2014/762705
- 21. Mao Z, Fan B, Wang X, et al. A systematic review of tissue engineering scaffold in tendon bone healing in vivo. *Front Bioeng Biotechnol*. 2021;9:621483. doi:10.3389/fbioe.2021.621483

- 22. Gheorghita Puscaselu R, Lobiuc A, Dimian M, Covasa M. Alginate: from food industry to biomedical applications and management of metabolic disorders. *Polymers*. 2020;12(10):2417. doi:10.3390/polym12102417
- 23. Cheng J, Liu J, Li M, et al. Hydrogel-based biomaterials engineered from natural-derived polysaccharides and proteins for hemostasis and wound healing. *Front Bioeng Biotechnol*. 2021;9:780187. doi:10.3389/fbioe.2021.780187
- Kaur K, Singh A, Monga A, Mohana P, Khosla N, Bedi N. Antimicrobial and antibiofilm effects of shikonin with tea tree oil nanoemulsion against Candida albicans and Staphylococcus aureus. *Biofouling*. 2023;39(9–10):962–979. doi:10.1080/08927014.2023.2281511
- de Melo Alves Silva LC, de Oliveira Mendes FC, de Castro Teixeira F, et al. Use of Lavandula angustifolia essential oil as a complementary therapy in adult health care: a scoping review. *Heliyon*. 2023;9(5):e15446. doi:10.1016/j.heliyon.2023.e15446
- 26. Liu YQ, Zhang D, Deng J, Liu Y, Li W, Nie X. Preparation and safety evaluation of centella asiatica total glycosides nitric oxide gel and its therapeutic effect on diabetic cutaneous ulcers. Evid Based Complement Alternat Med. 2022;2022:1419146. doi:10.1155/2022/1419146
- Jurić M, Donsi F, Bandić LM, Jurić S. Natural-based electrospun nanofibers: challenges and potential applications in agri-food sector. *Food Bioscience*. 2023;103372.
- Davidov-Pardo G, Gumus CE, McClements DJ. Lutein-enriched emulsion-based delivery systems: influence of pH and temperature on physical and chemical stability. *Food Chem.* 2016;196:821–827. doi:10.1016/j.foodchem.2015.10.018
- Garcia-Orue I, Gainza G, Gutierrez FB, et al. Novel nanofibrous dressings containing rhEGF and Aloe vera for wound healing applications. Int J Pharm. 2017;523(2):556–566. doi:10.1016/j.ijpharm.2016.11.006
- Bozkaya O, Arat E, Gün Gök Z, Yiğitoğlu M, Vargel İ. Production and characterization of hybrid nanofiber wound dressing containing Centella asiatica coated silver nanoparticles by mutual electrospinning method. Eur. Polym. J. 2022;166:111023. doi:10.1016/j.eurpolymj.2022.111023
- 31. Tian L, Chen C, Gong J, et al. The Convenience of Polydopamine in Designing SERS Biosensors with a Sustainable Prospect for Medical Application. *Sensors (Basel)*. 2023;23(10):4641.
- Hajialyani M, Tewari D, Sobarzo-Sánchez E, Nabavi SM, Farzaei MH, Abdollahi M. Natural product-based nanomedicines for wound healing purposes: therapeutic targets and drug delivery systems. *Int j Nanomed*. 2018;Volume 13:5023–5043. doi:10.2147/IJN.S174072
- Torabizadeh F, Fadaie M, Mirzaei E, Sadeghi S, Nejabat G-R. Tailoring structural properties, mechanical behavior and cellular performance of collagen hydrogel through incorporation of cellulose nanofibrils and cellulose nanocrystals: a comparative study. *Int J Biol Macromol.* 2022;219:438–451. doi:10.1016/j.ijbiomac.2022.08.006
- 34. Adhikari J, Dasgupta S, Das P, et al. Bilayer regenerated cellulose/quaternized chitosan-hyaluronic acid/collagen electrospun scaffold for potential wound healing applications. Int J Biol Macromol. 2024;261:129661. doi:10.1016/j.ijbiomac.2024.129661
- 35. Ribeiro AS, Costa SM, Ferreira DP, et al. Chitosan/nanocellulose electrospun fibers with enhanced antibacterial and antifungal activity for wound dressing applications. *React Funct Polym.* 2021;159:104808. doi:10.1016/j.reactfunctpolym.2020.104808
- 36. Kefayat A, Hamidi Farahani R, Rafienia M, Hazrati E, Hosseini Yekta N. Synthesis and characterization of cellulose nanofibers/chitosan/ cinnamon extract wound dressing with significant antibacterial and wound healing properties. J Iran Chem Soc. 2022;19(4):1191–1202. doi:10.1007/s13738-021-02374-x
- 37. Ullah A, Ullah S, Khan MQ, et al. Manuka honey incorporated cellulose acetate nanofibrous mats: fabrication and in vitro evaluation as a potential wound dressing. Int J Biol Macromol. 2020;155:479-489. doi:10.1016/j.ijbiomac.2020.03.237
- Khalek MAA, Gaber SAA, El-Domany RA, El-Kemary MA. Photoactive electrospun cellulose acetate/polyethylene oxide/methylene blue and trilayered cellulose acetate/polyethylene oxide/silk fibroin/ciprofloxacin nanofibers for chronic wound healing. Int J Biol Macromol. 2021;193:1752–1766. doi:10.1016/j.ijbiomac.2021.11.012
- Singha Deb AK, Mohan M, Govalkar S, Dasgupta K, Ali SM. Functionalized carbon nanotubes encapsulated alginate beads for the removal of mercury ions: design, synthesis, density functional theory calculation, and demonstration in a batch and fixed-bed process. ACS Omega. 2023;8 (35):32204–32220. doi:10.1021/acsomega.3c05116
- Abid S, Wang L, Haider MK, et al. Investigating alginate and chitosan electrospun nanofibers as a potential wound dressing: an in vitro study. Nanocomposites. 2024;10(1):254–267. doi:10.1080/20550324.2024.2362534
- Hasany M, Talebian S, Sadat S, et al. Synthesis, properties, and biomedical applications of alginate methacrylate (ALMA)-based hydrogels: current advances and challenges. *Appl. Mater. Today.* 2021;24:101150. doi:10.1016/j.apmt.2021.101150
- Dodero A, Scarfi S, Pozzolini M, Vicini S, Alloisio M, Castellano M. Alginate-based electrospun membranes containing ZnO nanoparticles as potential wound healing patches: biological, mechanical, and physicochemical characterization. ACS Appl. Mater. Interfaces. 2019;12 (3):3371–3381. doi:10.1021/acsami.9b17597
- Hajimohammadi K, Parizad N, Bagheri M, Faraji N, Goli R. Maggot therapy, alginate dressing, and surgical sharp debridement: unique path to save unresponsive diabetic foot ulcer. Int J Surg Case Rep. 2023;111:108907. doi:10.1016/j.ijscr.2023.108907
- Dodero A, Alloisio M, Castellano M, Vicini S. Multilayer alginate-polycaprolactone electrospun membranes as skin wound patches with drug delivery abilities. ACS Appl. Mater. Interfaces. 2020;12(28):31162–31171. doi:10.1021/acsami.0c07352
- Tang Y, Lan X, Liang C, et al. Honey loaded alginate/PVA nanofibrous membrane as potential bioactive wound dressing. Carbohydr. Polym. 2019;219:113–120. doi:10.1016/j.carbpol.2019.05.004
- 46. Wang Y, Ding C, Zhao Y, et al. Sodium alginate/poly (vinyl alcohol)/taxifolin nanofiber mat promoting diabetic wound healing by modulating the inflammatory response, angiogenesis, and skin flora. *Int J Biol Macromol.* 2023;252:126530. doi:10.1016/j.ijbiomac.2023.126530
- 47. Hu -W-W, Lin Y-T. Alginate/polycaprolactone composite fibers as multifunctional wound dressings. *Carbohydr. Polym.* 2022;289:119440. doi:10.1016/j.carbpol.2022.119440
- Qu R, Dai T, Wu J, et al. The characteristics of protein-glutaminase from an isolated Chryseobacterium cucumeris strain and its deamidation application. Front Microbiol. 2022;13:969445. doi:10.3389/fmicb.2022.969445
- Yan S, Wang Q, Yu J, Li Y, Qi B. Soy protein interactions with polyphenols: structural and functional changes in natural and cationized forms. Food Chemistry: X. 2023;19:100866. doi:10.1016/j.fochx.2023.100866
- Vogt L, Liverani L, Roether JA, Boccaccini AR. Electrospun zein fibers incorporating poly (glycerol sebacate) for soft tissue engineering. Nanomaterials. 2018;8(3):150. doi:10.3390/nano8030150
- Chang C-Y, Jin J-D, Chang H-L, et al. Antioxidative activity of soy, wheat and pea protein isolates characterized by multi-enzyme hydrolysis. Nanomaterials. 2021;11(6):1509. doi:10.3390/nano11061509

- Khabbaz B, Solouk A, Mirzadeh H. Polyvinyl alcohol/soy protein isolate nanofibrous patch for wound-healing applications. *Progress Biomater*. 2019;8(3):185–196. doi:10.1007/s40204-019-00120-4
- 53. Jaberifard F, Ramezani S, Ghorbani M, Arsalani N, Moghadam FM. Investigation of wound healing efficiency of multifunctional eudragit/soy protein isolate electrospun nanofiber incorporated with ZnO loaded halloysite nanotubes and allantoin. Int J Pharm. 2023;630:122434. doi:10.1016/j.ijpharm.2022.122434
- 54. Li T, Shen Y, Chen H, et al. Antibacterial properties of coaxial spinning membrane of methyl ferulate/zein and its preservation effect on sea bass. *Foods*. 2021;10(10):2385. doi:10.3390/foods10102385
- Ghorbani M, Nezhad-Mokhtari P, Ramazani S. Aloe vera-loaded nanofibrous scaffold based on Zein/Polycaprolactone/Collagen for wound healing. Int J Biol Macromol. 2020;153:921–930. doi:10.1016/j.ijbiomac.2020.03.036
- Kalouta K, Stie MB, Sun X, Foderà V, Vetri V. Eco-friendly electrospun nanofibers based on plant proteins as tunable and sustainable biomaterials. ACS Sustainable Chem. Eng. 2024;12(27):10118–10129. doi:10.1021/acssuschemeng.4c00895
- 57. Sarbadhikary P, George BP. A review on traditionally used African medicinal plant annickia chlorantha, its phytochemistry, and anticancer potential. *Plants (Basel)*. 2022;11(17). doi:10.3390/plants11172293
- 58. Feng X, Jia P, Zhang D. Nanocarrier drug delivery system: promising platform for targeted depression therapy. *Front Pharmacol.* 2024;15:1435133. doi:10.3389/fphar.2024.1435133
- 59. Gu M, Zheng AB, Jin J, et al. Cardioprotective effects of genistin in rat myocardial ischemia-reperfusion injury studies by regulation of P2X7/ NF- κ B Pathway. Evid Based Complement Alternat Med. 2016;1(1):5381290. doi:10.1155/2016/5381290
- Asati V, Srivastava A, Mukherjee S, Sharma PK. Comparative analysis of antioxidant and antiproliferative activities of crude and purified flavonoid enriched fractions of pods/seeds of two desert legumes Prosopis cineraria and Cyamopsis tetragonoloba. *Heliyon*. 2021;7(6):e07304. doi:10.1016/j.heliyon.2021.e07304
- 61. Wang J, Wang K, Ding L, et al. Alleviating effect of quercetin on cadmium-induced oxidative damage and apoptosis by activating the Nrf2-keap1 pathway in BRL-3A cells. *Front Pharmacol.* 2022;13:969892. doi:10.3389/fphar.2022.969892
- Song XY, Meng X, Xiao BL, et al. MWCNTs-CTAB and HFs-Lac nanocomposite-modified glassy carbon electrode for rutin determination. *Biosensors*. 2022;12(8). doi:10.3390/bios12080632.
- Orihuela-Campos RC, Tamaki N, Mukai R, et al. Biological impacts of resveratrol, quercetin, and N-acetylcysteine on oxidative stress in human gingival fibroblasts. J Clin Biochem Nutr. 2015;56(3):220–227. doi:10.3164/jcbn.14-129
- 64. Zhou L, Cai L, Ruan H, et al. Electrospun chitosan oligosaccharide/polycaprolactone nanofibers loaded with wound-healing compounds of Rutin and Quercetin as antibacterial dressings. Int J Biol Macromol. 2021;183:1145–1154. doi:10.1016/j.ijbiomac.2021.05.031
- Zhang J, Chen K, Ding C, et al. Fabrication of chitosan/PVP/dihydroquercetin nanocomposite film for in vitro and in vivo evaluation of wound healing. Int J Biol Macromol. 2022;206:591–604. doi:10.1016/j.ijbiomac.2022.02.110
- 66. Croitoru A-M, Karaçelebi Y, Saatcioglu E, et al. Electrically triggered drug delivery from novel electrospun poly(lactic acid)/graphene oxide/ quercetin fibrous scaffolds for wound dressing applications. *Pharmaceutics*. 2021;13(7):957. doi:10.3390/pharmaceutics13070957
- 67. Jin H, Zhao Y, Yao Y, et al. Intratracheal administration of stem cell membrane-cloaked naringin-loaded biomimetic nanoparticles promotes resolution of acute lung injury. *Antioxidants (Basel)*. 2024;13(3):282.
- 68. Yuan D, Guo Y, Pu F, et al. Opportunities and challenges in enhancing the bioavailability and bioactivity of dietary flavonoids: a novel delivery system perspective. *Food Chem.* 2024;430:137115. doi:10.1016/j.foodchem.2023.137115
- Farzaei MH, Derayat P, Pourmanouchehri Z, et al. Characterization and evaluation of antibacterial and wound healing activity of naringenin-loaded polyethylene glycol/polycaprolactone electrospun nanofibers. J Drug Delivery Sci Technol. 2023;81:104182. doi:10.1016/j.jddst.2023.104182
- Tottoli EM, Benedetti L, Chiesa E, et al. Electrospun naringin-loaded fibers for preventing scar formation during wound healing. *Pharmaceutics*. 2023;15(3):747. doi:10.3390/pharmaceutics15030747
- Arezomand Z, Mashjoor S, Makhmalzadeh BS, Shushizadeh MR, Khorsandi L. Citrus flavonoids-loaded chitosan derivatives-route nanofilm as drug delivery systems for cutaneous wound healing. *Int J Biol Macromol.* 2024;271:132670. doi:10.1016/j.ijbiomac.2024.132670
- 72. Jin H, Jiao Y, Guo L, et al. Astragaloside IV blocks monocrotaline-induced pulmonary arterial hypertension by improving inflammation and pulmonary artery remodeling. *IntJ Mol Med*. 2021;47(2):595–606. doi:10.3892/ijmm.2020.4813
- Liu Z, Zheng G, Wang L, Wang H, Che X. Pharmacodynamic study: astragaloside IV/chitosan/polylactic acid composite electrospinning scaffold for wound healing in diabetic rats. J Drug Delivery Sci Technol. 2024;96:105632. doi:10.1016/j.jddst.2024.105632
- 74. Zhang D, Li L, Shan Y, et al. In vivo study of silk fibroin/gelatin electrospun nanofiber dressing loaded with astragaloside IV on the effect of promoting wound healing and relieving scar. J Drug Delivery Sci Technol. 2019;52:272–281. doi:10.1016/j.jddst.2019.04.021
- Wang H, Wang L, Liu Z, Luo Y, Kang Z, Che X. Astragaloside/PVP/PLA nanofiber functional dressing prepared by coaxial electrostatic spinning technology for promoting diabetic wound healing. *Eur. Polym. J.* 2024;210:112950. doi:10.1016/j.eurpolymj.2024.112950
- Li Y, Yang R, Huang X, et al. Chrysin targets myeloid-derived suppressor cells and enhances tumour response to anti-PD-1 immunotherapy. *Clin Translational Med.* 2022;12(9). doi:10.1002/ctm2.1019.
- Deldar Y, Pilehvar-Soltanahmadi Y, Dadashpour M, Montazer Saheb S, Rahmati-Yamchi M, Zarghami N. An in vitro examination of the antioxidant, cytoprotective and anti-inflammatory properties of chrysin-loaded nanofibrous mats for potential wound healing applications. *Artif. Cells Nanomed. Biotechnol.* 2018;46(4):706–716. doi:10.1080/21691401.2017.1337022
- 78. Ye Z, Wu H, Chen X, et al. Puerarin inhibits inflammation and oxidative stress in female BALB/c mouse models of Graves' disease. *Translational Pediatr.* 2024;13(1):38. doi:10.21037/tp-23-370
- Sun S, Ding C, Liu X, et al. Silk protein/polyvinylpyrrolidone nanofiber membranes loaded with puerarin accelerate wound healing in mice by reducing the inflammatory response. *Biomaterials Adv.* 2022;135:212734. doi:10.1016/j.bioadv.2022.212734
- Oyedemi SO, Oyedemi BO, Arowosegbe S, Afolayan AJ. Phytochemicals analysis and medicinal potentials of hydroalcoholic extract from Curtisia dentata (Burm.f) C.A. Sm Stem Bark. Int J Mol Sci. 2012;13(5):6189–6203. doi:10.3390/ijms13056189
- Aatif M. Current understanding of polyphenols to enhance bioavailability for better therapies. *Biomedicines*. 2023;11(7):2078. doi:10.3390/ biomedicines11072078
- Carolina Alves R, Perosa Fernandes R, Fonseca-Santos B, Damiani Victorelli F, Chorilli M. A critical review of the properties and analytical methods for the determination of curcumin in biological and pharmaceutical matrices. *Crit. Rev. Anal. Chem.* 2019;49(2):138–149. doi:10.1080/ 10408347.2018.1489216

- Jamal Z, Das J, Gupta P, Dhar P, Chattopadhyay S, Chatterji U. Self Nano-Emulsifying Curcumin (SNEC30) attenuates arsenic-induced cell death in mice. *Toxicol Rep.* 2021;8:1428–1436. doi:10.1016/j.toxrep.2021.07.010
- Moradkhannejhad L, Abdouss M, Nikfarjam N, Shahriari MH, Heidary V. The effect of molecular weight and content of PEG on in vitro drug release of electrospun curcumin loaded PLA/PEG nanofibers. J Drug Delivery Sci Technol. 2020;56:101554. doi:10.1016/j.jddst.2020.101554
- Chagas PA, Schneider R, Dos Santos DM, Otuka AJ, Mendonça CR, Correa DS. Bilayered electrospun membranes composed of poly (lactic-acid)/natural rubber: a strategy against curcumin photodegradation for wound dressing application. *React Funct Polym.* 2021;163:104889. doi:10.1016/j.reactfunctpolym.2021.104889
- Xi Y, Ge J, Wang M, et al. Bioactive anti-inflammatory, antibacterial, antioxidative silicon-based nanofibrous dressing enables cutaneous tumor photothermo-chemo therapy and infection-induced wound healing. Acs Nano. 2020;14(3):2904–2916. doi:10.1021/acsnano.9b07173
- Guo D, Xie J, Zhao J, Huang T, Guo X, Song J. Resveratrol protects early brain injury after subarachnoid hemorrhage by activating autophagy and inhibiting apoptosis mediated by the Akt/mTOR pathway. *Neuroreport*. 2018;29(5):368–379. doi:10.1097/WNR.00000000000975
- Saleem Z, Rehman K, Hamid Akash MS. Role of Drug Delivery System in Improving the Bioavailability of Resveratrol. *Curr Pharm Des*. 2022;28(20):1632–1642. doi:10.2174/1381612828666220705113514
- Karakucuk A, Tort S. Preparation, characterization and antimicrobial activity evaluation of electrospun PCL nanofiber composites of resveratrol nanocrystals. *Pharmaceutical Development Technol.* 2020;25(10):1216–1225. doi:10.1080/10837450.2020.1805761
- Kanaujiya S, Arya DK, Pandey P, et al. Resveratrol-ampicillin dual-drug loaded polyvinylpyrrolidone/polyvinyl alcohol biomimic electrospun nanofiber enriched with collagen for efficient burn wound repair. *Int j Nanomed.* 2024;Volume 19:5397–5418. doi:10.2147/IJN.S464046
- Lakshmanan R, Campbell J, Ukani G, et al. Evaluation of dermal tissue regeneration using resveratrol loaded fibrous matrix in a preclinical mouse model of full-thickness ischemic wound. Int J Pharm. 2019;558:177–186. doi:10.1016/j.ijpharm.2019.01.001
- Montone CM, Aita SE, Arnoldi A, et al. Characterization of the trans-epithelial transport of green tea (C. sinensis) catechin extracts with in vitro inhibitory effect against the SARS-CoV-2 papain-like protease activity. *Molecules*. 2021;26(21):6744. doi:10.3390/molecules26216744
- Li A, Li L, Li X, et al. Antibacterial, antioxidant and anti-inflammatory PLCL/gelatin nanofiber membranes to promote wound healing. Int J Biol Macromol. 2022;194:914–923. doi:10.1016/j.ijbiomac.2021.11.146
- 94. Hu Y, Hu L, Zhang L, et al. Novel electro-spun fabrication of blended polymeric nanofibrous wound closure materials loaded with catechin to improve wound healing potential and microbial inhibition for the care of diabetic wound. *Heliyon*. 2024;10(6).
- Ranjbar-Mohammadi M, Nouri M. Production and in vitro analysis of catechin incorporated electrospun gelatin/poly (lactic acid) microfibers for wound dressing applications. *Journal of Industrial Textiles*. 2022;51(5_suppl):75298–7544S. doi:10.1177/15280837211060883
- 96. Anand S, Pandey P, Begum MY, et al. Electrospun biomimetic multifunctional nanofibers loaded with ferulic acid for enhanced antimicrobial and wound-healing activities in STZ-Induced diabetic rats. *Pharmaceuticals*. 2022;15(3):302. doi:10.3390/ph15030302
- 97. Lan X, Liu Y, Wang Y, et al. Coaxial electrospun PVA/PCL nanofibers with dual release of tea polyphenols and ε-poly (L-lysine) as antioxidant and antibacterial wound dressing materials. *Int J Pharm*. 2021;601:120525. doi:10.1016/j.ijpharm.2021.120525
- Khamis T, Diab -A-A-A, Zahra MH, et al. The antiproliferative activity of Adiantum pedatum extract and/or piceatannol in phenylhydrazine-induced colon cancer in male albino rats: the miR-145 Expression of the PI-3K/Akt/p53 and Oct4/Sox2/Nanog Pathways. *Molecules*. 2023;28(14):5543. doi:10.3390/molecules28145543
- Doostan M, Mohammadi P, Khoshnevisan K, Maleki H. Flaxseed extract-loaded polyvinyl alcohol/chitosan nanofibrous scaffolds: anti-oxidant, anti-bacterial activity, and acceleration of wound healing process. *Int J Biol Macromol.* 2022;S0141-8130(22):03139.
- Shahid MA, Khan MS, Hasan MM. Licorice extract-infused electrospun nanofiber scaffold for wound healing. OpenNano. 2022;8:100075. doi:10.1016/j.onano.2022.100075
- 101. Fahimirad S, Satei P, Ganji A, Abtahi H. Wound healing performance of PVA/PCL based electrospun nanofiber incorporated green synthetized CuNPs and Quercus infectoria extracts. J biomater sci Poly ed. 2023;34(3):277–301. doi:10.1080/09205063.2022.2116209
- 102. Ramalingam R, Dhand C, Leung CM, et al. Antimicrobial properties and biocompatibility of electrospun poly-ε-caprolactone fibrous mats containing Gymnema sylvestre leaf extract. *Mater Sci Eng C*. 2019;98:503–514. doi:10.1016/j.msec.2018.12.135
- 103. Almasian A, Najafi F, Eftekhari M, Shams Ardekani MR, Sharifzadeh M, Khanavi M. Preparation of polyurethane/pluronic F127 nanofibers containing peppermint extract loaded gelatin nanoparticles for diabetic wounds healing: characterization, in vitro, and in vivo studies. *Evidence-Based Complement Alternat Med.* 2021;2021(1):6646702. doi:10.1155/2021/6646702
- 104. Zehra A, Bokhari N, Nosheen S, et al. Electrospun bilayer membranes carrying bearberry/licorice extract to ameliorate wound healing. J Polym Environ. 2024;32(2):735–748. doi:10.1007/s10924-023-03007-5
- 105. Lu M. Is aromatic plants environmental health engineering (APEHE) a leverage point of the earth system? *Heliyon*. 2024;10(9):e30322. doi:10.1016/j.heliyon.2024.e30322
- Al-Khayri JM, Banadka A, Nandhini M, Nagella P, Al-Mssallem MQ, Alessa FM. Essential oil from Coriandrum sativum: a review on its phytochemistry and biological activity. *Molecules*. 2023;28(2):696. doi:10.3390/molecules28020696
- 107. Fiaschini N, Carnevali F, Van der Esch SA, et al. Innovative multilayer electrospun patches for the slow release of natural oily extracts as dressings to boost wound healing. *Pharmaceutics*. 2024;16(2):159. doi:10.3390/pharmaceutics16020159
- Unalan I, Slavik B, Buettner A, Goldmann WH, Frank G, Boccaccini AR. Physical and antibacterial properties of peppermint essential oil loaded poly (ε-caprolactone)(PCL) electrospun fiber mats for wound healing. *Front Bioeng Biotechnol*. 2019;7:346. doi:10.3389/fbioe.2019.00346
- 109. Sofi HS, Akram T, Tamboli AH, Majeed A, Shabir N, Sheikh FA. Novel lavender oil and silver nanoparticles simultaneously loaded onto polyurethane nanofibers for wound-healing applications. Int J Pharm. 2019;569:118590. doi:10.1016/j.ijpharm.2019.118590
- Hussein MAM, Gunduz O, Sahin A, Grinholc M, El-Sherbiny IM, Megahed M. Dual spinneret electrospun polyurethane/PVA-gelatin nanofibrous scaffolds containing cinnamon essential oil and nanoceria for chronic diabetic wound healing: preparation, physicochemical characterization and in-vitro evaluation. *Molecules*. 2022;27(7):2146. doi:10.3390/molecules27072146
- 111. Rezk MY, Ibrahim S, Khalil EA, et al. Pumpkin seed oil-loaded chitosan/polyvinyl alcohol electrospun nanofiber scaffold for dermal and oral wound dressing. *ChemistrySelect.* 2023;8(26):e202300722. doi:10.1002/slct.202300722
- 112. Liu J-X, Dong W-H, Mou X-J, et al. In situ electrospun zein/thyme essential oil-based membranes as an effective antibacterial wound dressing. ACS Appl. Bio Mater. 2019;3(1):302–307. doi:10.1021/acsabm.9b00823

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