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Review

Recent Developments in Electrospun Nanofibers as Delivery of Phytoconstituents for Wound Healing

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Abstract: Wound healing is an unresolved therapeutic challenge for the medical community, as wound assessment and management is a complex procedure involving numerous factors that play a significant role in the healing process. Several factors, including bacterial infections, underlying conditions, malnutrition, obesity, aging, and smoking are the most frequent causes of a delayed wound-healing process. The shortcomings related to the currently used wound dressings include poor antimicrobial properties, weak mechanical features, poor biodegradability, biocompatibility, etc. Modern medicine has expanded the use of phytoconstituents based on nanotechnology to regenerate and repair soft and hard tissues. Electrospun nanofiber platforms are the most recent and promising among many types of conventional wound dressings due to their distinct characteristics. Many plant extracts and their phytoconstituents are well-known as adequate substitutes for wound healing agents because of their wide range of active ingredients, accessibility, and limited side effects. Incorporating these phytoconstituents into electrospun nanofibers combines the structural properties of the nanofibers with the antibacterial and therapeutic properties of the plants, making the nanofibers ideal for use as wound dressings. This review focuses on the antibacterial and therapeutic applications of nanofiber wound dressings containing phytoconstituents and their potential to revolutionize wound healing.

Keywords: electrospinning; nanofibers; phytoconstituents; drug delivery; wound dressing; wound healing

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1. Introduction

The effective design of a skin wound therapeutic process, including dressing systems, is inextricably linked to an extensive understanding of the wound healing process and the included variables and local circumstances impacting the wound. As soon as a superficial wound occurs, many systems begin to clean up the wound milieu and restore the skin's main structure. This intricate healing process involves a wide range of inflammatory cells, cytokines, chemokines, nutrients, and matrix components discharged into the wound bed. Wound healing consists of three major steps: inflammation, proliferation, and remodeling (Figure 1) [1]. The inflammatory phase begins after hemostasis is complete and the pathogens and foreign materials are eliminated from the wound environment [2]. Vasodilation causes vascular permeability, allowing neutrophils and monocytes to concentrate inside the wound bed. This process is also influenced by a complex interaction of cytokines, transforming monocytes into macrophages. The differentiated macrophages perform two

critical functions: (1) phagocytosis and the digestion of tissue debris and neutrophils, and (2) the release of cytokines and growth factors that stimulate cellular proliferation and migration [3,4].

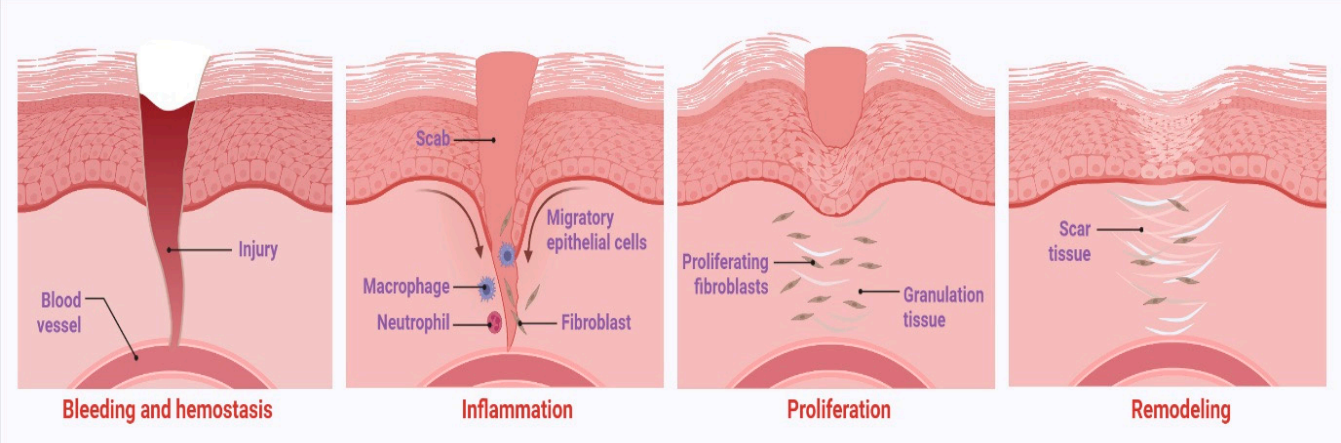

Figure 1. The basic mechanism of wound healing. Created with https://www.BioRender.com (accessed on 30 December 2022).

The proliferation stage begins after roughly 3 days and depends on fibroblast activity and the production of ground material and collagen. The fibroblasts in the region and those from the blood multiply and migrate, resulting in wound granulation tissue and a new ECM. Several fibroblasts are also transformed (differentiated) into myofibroblasts to aid in wound healing. Through molecular signaling, the as-formed ECM has a critical influence on the regulation of cell function throughout the wound-healing process. (Mainly by integrins). Later, similar signals activate cellular functions such as proliferation, differentiation, and even apoptosis. Keratinocytes and fibroblasts are the primary skin cells that produce integrins in response to ECM modification. ECM proteins also influence the behavior of cytokines and growth factors, such as TGF- and platelet-derived growth factor (PDGF), produced by macrophages and activated platelets, respectively [5,6]. ECM's indicated regulatory function in cellular activities augmented by its fibrous protein (collagens, elastin, and fibronectin) supporting structure. Cells anchor on a fibrous architecture, forming a vascular network and protecting growth factors from degradation. Endothelial cells rapidly proliferate and promote angiogenesis inside the granulation tissue during the proliferation phase [7]. After around 2–3 weeks, the wound state transitions to a remodeling (maturation) stage; the maturation of wound tissue results in further crosslinking and the creation of normal tissue. When maturation is complete, the vascular network rapidly returns to its less developed condition [8,9].

For many years, clinical practitioners have employed plant-based extracts to treat various conditions, such as burns, wounds, and infections. Herbs may hasten the healing of wounds and lessen the need for synthetic medications such as antibiotics, avoiding their adverse effects. Treating illnesses resistant to antibiotics is possible using various plants [10]. Since ancient times, natural plant products have been widely used to cure various ailments. Herbal remedies are well-known in modern medicine to have a favorable effect on fibroplasia, epithelization, collagenation, and wound contraction. The results from medicinally essential plants have created several pharmaceutical formulations for various diseases. The results of medicinally important plants have developed several pharmaceutical formulations for various diseases [11,12]. Phytochemicals have great potential for preventing and treating microbial infections and wounds. Antimicrobial, antioxidant, and wound-healing phytochemicals promote blood coagulation, combat infection, and fast wound healing. Many phytochemicals found in medicinal plants, such as triterpenoids and curcumin, have been proven to be important factors in homeostasis, re-epithelialization,

and regeneration by increasing fibroblast proliferation and collagen formation. Because of their astringent, antibacterial, and free radical scavenging capabilities, phenolic compounds aid wound healing. Polyphenolic components such as flavonoids may enhance good wound healing, most likely via antibacterial and anti-oxidative activities, by preventing lipid peroxidation, which leads to cell damage prevention and increased vitality of collagen fibrils. In wound dressings, carotenoids and triterpenoids decrease oxidative stress and enhance antioxidant activity. ROS are engaged in the healing process, recruitment of lymphoid cells, angiogenesis, and killing pathogens at the wound site by functioning as secondary messengers to immunocytes and non-lymphoid cells. Elevated ROS levels are associated with inadequate wound healing. Excessive ROS may change and destroy extracellular matrix proteins, negatively affecting dermal fibroblasts and keratinocytes and boosting pro-inflammatory cytokine release and the stimulation of matrix metalloproteases.

A wound infection slows the healing process, deforms the injured tissue, and may even be fatal to the patient. Antibiotic therapy is used to treat infections, and the development of infections resistant to antibiotics also places a heavy financial burden on the patient [13]. Therefore, a tool that efficiently stops microbial growth lowers the risk of rising antibiotic resistance, and is safe for human use is needed [14]. Commercially available topical antibiotic products for treating chronic wounds such as bacitracin-C, fusidic acid, gentamicin, mafenide acetate, metronidazole, mupirocin, and mupirocin calcium, neomycin sulfate, nitrofurazone, polymixin-B, retapamulin, silver sulfadiazine, and sulfacetamide sodium.

Resistance has led current synthetic antibacterial medications to become less effective or ineffective. Synthetic antibiotics commonly cause the following side effects: diarrhea, nausea, allergic reactions, contact dermatitis, vomiting, rash, and upset stomach, potentially causing metabolic acidosis, potential cross-reaction with other compounds, may cause local irritation, and neurological or renal adverse reactions. To address these difficulties, plant-derived compounds have shown promising benefits in preventing the evolution of antibiotic resistance in bacterial pathogens. The widespread presence of these compounds has shown therapeutic benefits in terms of antioxidant, antibacterial, and wound-healing properties. They may restore the therapeutic use of earlier antibiotics by improving their efficacy and, as a result, preventing the development of resistance. A rising number of research publications have recently focused on using natural herbal items as possible helpful agents in wound healing. Indeed, the primary benefits of these botanical treatments are their inexpensive cost, widespread availability, and lack of adverse effects. Plants include various bioactive phytochemicals, including alkaloids, carotenoids, flavonoids, tannins, terpenoids, saponins, and phenolic compounds.

Modern medicine has advanced phytoconstituents based on nanotechnology to repair and regenerate soft and hard tissues [15]. Electrospun nanofiber platforms are the most current and promising among the many wound dressings because of their distinctive properties [16]. The shape of these dressings is similar to that of the extracellular matrix. They have a high porosity level, which opens a large surface area to nutrient mobilization, gaseous or waste exchange, cell adhesion, and infiltration. These scaffolds are matting to properly apply damaged regions at burn sites instead of employing skin transplants. These scaffolds are used in novel methods to encapsulate phytoconstituents, administer drugs, and treat wounds. The effects of phytoconstituents-based nanofibers on wound healing include a variety of pharmacological targets, such as reducing oxidative factors and enhancing antioxidative enzymes, inhibiting the production of inflammatory cytokines and inflammatory transduction cascades, and encouraging neovascularization and angiogenic pathways by upregulating the expression of vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor [17–19].

Additionally, the electrospun nanofibers of plant extracts and their phytochemicals can improve their bioavailability, control their release as sustained delivery systems to the wound site, and enhance the permeability of these therapeutics to the underlying skin layers, all of which are essential for the healing process. The physical properties of the nanofibers' structure are combined with the antibacterial and medicinal properties of

the plants to create nanofibers that are perfect for wound dressing. Overall, several plant extracts and their natural constituents have shown excellent activity in treating wounds and may thus be anticipated to be future pharmaceutical medications. This review focuses on potential applications of electrospun nanofiber-based phytoconstituent delivery methods for wound healing.

2. Electrospinning Technique

A high-power source, a syringe pump, a syringe needle containing solutions, and a fiber deposition collector are the four major components of an electrospinning apparatus—the applied electric field between the needle and the collector. The positive electrode is attached to the needle, and the negative electrode is linked to the collector (Figure 2) [20,21]. Consequently, when a voltage is supplied, the repulsive charge builds up close to the needle's tip, which has a hemispherical shape. A Taylor cone is created when the repulsive charge exceeds the surface tension. The process produces fibers by directing the polymer solution to the negative electrode, which functions as the collector. The solvent from the polymer solution is vaporized, and the polymer solution is deposited as dry nanometer-to-micrometer-sized fibers on the collector [22,23]. Due to their distinct characteristics, electrospinning nanofibers may be used in several fields, including absorbent membranes, biosensors, tissue engineering, the packaging sector, filters, wound dressing, drug delivery, and cosmetics [24]. In the electrospinning procedure, a polymer solution flows through a capillary tip and toward a metallic collector while exposed to a substantial potential difference [25]. A syringe, a flat-tip needle, and a conducting collector are the only components needed for a conventional electrospinning setup [26]. Researchers may use used electrospinning process to collect oriented fibers [27]. Electrostatic forces overcome the surface tension of the polymer solution due to the potential voltage difference between the polymer solution and the collection plate, causing a jet of charged fluid to be pulled toward the collection plate and solidified [28]. The polymer jet divides, resulting in many nanofibers deposited at the collector. Electrospinning the jet causes the solvent to evaporate, leaving the collector with dry nanofibers. Electrospinning can produce continuous nanofibers from a variety of materials. Processional, physical, systemic, and solution parameters, among others, impact electrospun fibers' fiber form and properties.

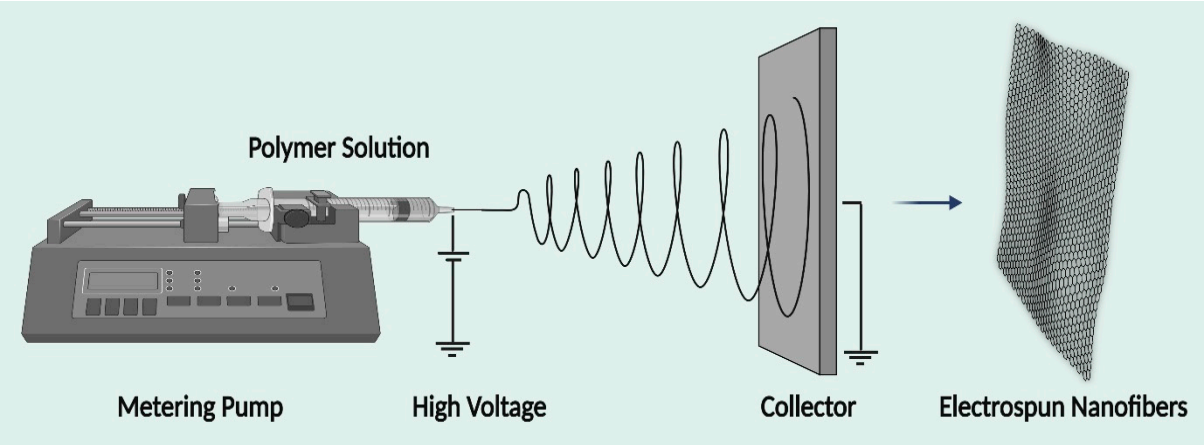

Figure 2. A schematic diagram of the electrospinning apparatus. Created with https://www.BioRender.com (accessed on 30 December 2022).

3. Factors Affecting Electrospinning

Electrospinning can produce continuous nanofibers from a variety of materials. Processional, physical, systemic, and solution parameters, among others, impact the fiber morphology and properties of electrospun fibers [29].

3.1. Solution-Related Parameters

The solution's parameters are crucial; it should have an ideal low surface tension and a sufficient charge density and viscosity to avoid the collapse of the jet into droplets before the solvent evaporates [30]. Polymer characteristics, including molecular weight, concentration, solution viscosity, surface tension, and solution conductivity, impact the shape and characteristics of nanofibers. Higher molecular weight produces viscous solutions compared to lower molecular weight because it indicates the length of the polymer chain, which determines the entanglements. During the process, these entanglements stop the jet from prematurely separating. A jet of a low-viscosity polymer solution fragments into tiny droplets or forms beaded threads. Viscous solutions promote chain entanglements and produce uniform fibers devoid of beads.

On the other hand, if the viscosity is too high, it will be challenging to pump the solution through the capillary, and it may dry up or drop at the tip. Surface tension reduces the solution's surface area and drives it to condense into spherical droplets. When the concentration is low, solvent molecules with a high ratio have a stronger propensity to join and take the form of beads or spheres. Solvents with a low surface tension are needed to create bead-free, homogenous fibers. The jet's electrostatic charge significantly increases when ions are present in the solution. For instance, increasing the jet stretching by a small amount of salt or polyelectrolyte in the electrospinning fluid might help generate smooth rather than beaded fibers [31].

3.2. Polymer Concentration

Droplets will form when the solution concentration is below the threshold value instead of fiber formation. High concentrations of a solution yield viscose solutions, which may pose processing problems. For instance, increased viscosity prevents the elongation and thinning of the jet and produces fibers with bigger diameters [25].

3.3. Processing Conditions

Electrospinning processing parameters include voltage, collector distance, flow rate, needle gauge, and collector type. High voltage provides the appropriate charges to the solution, which causes the jet to come out of the needle. With a relatively smaller Taylor cone, higher voltage accelerates a larger volume of electrospinning fluid [32]. The feed rate controls how much solution is present between the needle and the electrospinning target. Due to an increase in feed rate brought on by a voltage rise, the solution is stretched more and grows in diameter. Increased feed rate may also result in fiber fusing due to insufficient solvent evaporation before fiber collection. The reduction in distance causes a shorter flight time for the jet. So, the jet may not have enough time to solidify, resulting in the fusion of fibers. The diameter of the orifice also has an effect. Due to the jet's shorter exposure to the environment, a smaller interior diameter lowers clogging. Reduced needle internal diameter causes a rise in the solution's surface tension, which results in smaller droplets. The outcome was a decrease in the jet's acceleration. As a result, before deposition, the jet is further stretched and elongated, resulting in fibers with a reduced diameter. The parameters above significantly impact the web characteristics and fiber shape in electrospinning. The collector's design is another aspect. Regular electrospinning produces nanofibers that are randomly oriented. With a modification in collector design, it is possible to control the geometry of fiber deposition or get other desirable fiber patterns. One involves parallel bars with a space in the middle, resulting in aligned nanofibers.

3.4. Effect of Voltage

Raising the applied voltage would cause the polymer jet to discharge more forcefully, resulting in a rise in drawing tension [32]. The outcome is a reduction in fiber diameter, and as a result, the fiber diameter dispersion would rise, making process control more challenging. The ideal voltage is needed to start the polymer jet from the Taylor cone apex [33]. Before

jet formation, the applied voltage had a major impact on the morphology of the droplets: faster electrospinning and enhanced solution flow rate produced by higher voltage [24].

3.5. Volumetric Flow Rate

The flow rate needs to be adjusted within the right range to stabilize the Taylor cone. Due to the slow flow rate in the needle, the Taylor cone frequently vanishes, and the electrospinning process momentarily stops. The vacuum created a faster flow which may cause the solution to accumulate at the tip of the needle. The rate of charge withdrawal into the solution depends on how long the ions are in contact with the needle because the surface charge density falls as the flow rate rises. The diameter, porosity, and shape of nanofibers are the characteristics influenced by the solution flow rate [24]. A constant and steady flow rate is required in electrospun materials to decrease bead formation. The diameter of electrospun nanofibers decreased by a slow flow rate. Additionally, compared to a quicker flow rate, a slow flow rate produced fewer beads and a smaller diameter [34–36].

3.6. Distance of Collector

It exhibits a negative power relationship as increasing the distance causes the polymer jet's diameter to drop and the bending instabilities and whip action to lengthen. Surface charge density has a negative exponential connection. The surface charge density decreases as the gap distance increases. Fewer charged ions form as the distance between the charged solution and the collector grows [37]. Due to a reduction in the strength of the electric field between the two. The needle tip's diameter, which has risen with increasing needle tip diameter, is another process parameter [33]. However, there is no correlation between needle diameter and subsequent fiber [32].

3.7. Effect of Conductivity

Compared to poor conductivity, high conductivity allows polymer solutions to transport more charge. As a result, increased conductivity produces stronger tensile pressures following the applied voltage and a decrease in nanofiber diameter [34–36].

3.8. Effect of Solvent

Before electrospinning, a solvent's solubility and boiling point are crucial considerations. Due to the nanofibers' quick evaporation and dehydration, volatile solvents are the best choice [38]. Substances having very low boiling temperatures that promote rapid evaporation should be avoided to prevent obstructing or restricting the needle orifice before electrospinning. On the other hand, high boiling point solvents may not fully dehydrate before striking the target, resulting in flat ribbon-shaped fibers rather than circular ones [39]. Researchers must give particular attention to assessing and selecting electrospinning solvents since the solvent's volatility may alter the microscopic characteristics of electrospun fibers, such as porosity, shape, and size [40].

4. Advantages of Electrospun Nanofibers

The electrospinning process produces nanofibers with outstanding wound-healing capabilities (Figure 3). Their nanostructure is well adapted to the ECM structure of the human body, which encourages cell growth, proliferation, and adhesion. In addition, the high permeability and absorption rate may take in the exudate that forms on the wound surface and keep the healing environment moist [41]. The vast surface area is also advantageous for loading and distributing bioactive components such as medicines and growth hormones. Electrospun nanofiber materials are, thus, regarded as the best option for wound treatments [42]. A summary of available phytoconstituent-based nanofibers is shown in (Table 1).

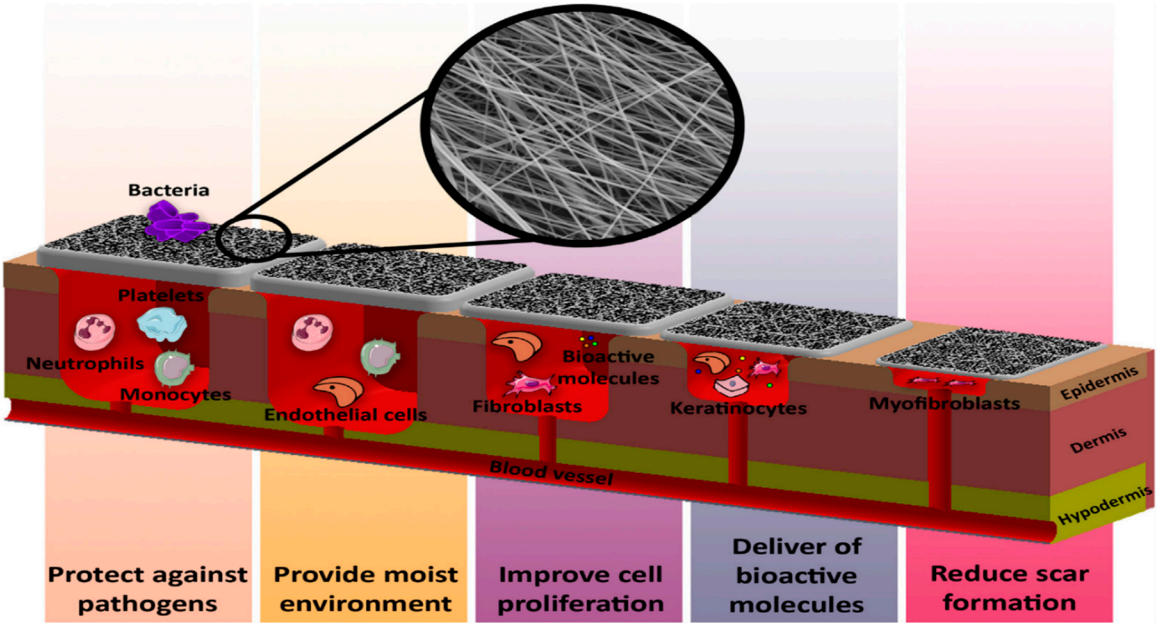

Figure 3. Advantages of electrospun nanofibers on wound healing (reproduced with permission from [20]. ©2018 Colloids and Surfaces B: Biointerfaces. Published by Elsevier Ltd.).

Table 1. A summary of available phytoconstituent-based nanofiber wound dressings and their biological properties.

Herbal Product Extract	Polymers for Electrospinning	Type of Study	Biological Properties	Ref.
Centella asiatica	Gelatin, CA, PCL	In vitro	Wound healing, Burns, Skin lesions, Antibacterial	[43]
Sorghum bicolor	Zein	In vitro	Antioxidant, Antibacterial	[44]
Spirulina agilis	PCL, Alginate	In vitro, in vivo	Anti-inflammatory, Antibacterial, Wound healing	[45]
Camellia sinensis	CS, PEO	In vitro, in vivo	Anti-inflammatory, Antibacterial, Antioxidant	[46]
Coptis chinensis	PVA	In vitro	Antifungal, Anti-inflammatory, Antioxidant	[47]
Hypericum perforatum	PCL	In vitro	Wound healing burns, Antibacterial, Antioxidant	[48]
Sorghum bicolor	PVA	In vitro	Treatment of skin infection, Antibacterial	[49]
Melilotus officinalis	CS, PEO	In vitro	Antibacterial, Treatment of chronic wounds	[50]
Gymnema sylvestre	PCL	In vitro	Antibacterial, Anti-inflammatory, Wound healing	[51]
Senegalia senegal	PCL	In vitro	Antibacterial, Wound healing	[52]
Lawsonia inermis	CS, PEO, PVA, PEO	In vitro, in vivo	Antioxidant, Analgesic, Anti-inflammatory, Antibacterial	[53]
Tridax procumbens	PVA	In vitro	Antibacterial, Wound healing	[54]
Vitis vinifera	SF, PEO	In vitro, in vivo	Wound healing, Antioxidant	[55]
Aloe barbadensis miller	PLGA, CS, PVA	In vitro, in vivo	Antifungal, Anti-inflammatory, Antibacterial	[56]
Moringa oleifera	PAN	In vitro, in vivo	Antibacterial, Wound healing	[57]
Garcinia mangostana	PLA, CS, PVA, PVP	In vitro, in vivo	Antibacterial, Anti-inflammatory, Antioxidant	[58]
Zataria multiflora	CS, PVA, PCL, PVA	In vitro, in vitro	Antibacterial, Antifungal, Anti-inflammatory, Anticoagulant	[59]
Quercus infectoria	PVA	In vitro	Antioxidant, Antiseptic, Anti-diabetic, Antibacterial, Antifungal	[60]
Matricaria chamomilla	PCL, PS	In vitro, in vivo	Antibacterial, Wound healing	[61]
Juniperus chinensis	PVA	In vitro	Antibacterial, Wound healing	[62]
Calendula officinalis	PG, PCL	In vitro, in vivo	Anti-inflammatory, Wound healing, Antibacterial	[63]
Beta vulgaris	Nylon 66	In vitro	Antimicrobial, Wound healing	[64]
Biophytum sensitivum	PCL	In vitro	Anti-inflammatory, Anti-diabetic, Antiseptic	[65]
Azadirachta indica	PCL	In vitro	Antimicrobial, Wound healing	[66]
Lavandula angustifolia	NaAlg, PAN, PVA	In vitro, in vivo	Antimicrobial, Anti-inflammatory, Pain relieving	[67]
Cinnamomum verum	PVA, NaAlg, CA	In vitro, In vitro	Antimicrobial, Wound healing	[68]
Syzygium aromaticum	PVA, NaAlg	In vitro	Antimicrobial, Antimicrobial	[69]
Zataria multiflora	Gelatin, PVP, CS	In vitro	Antibacterial, Antifungal, Anti-inflammatory, Anticoagulant	[70]
Curcuma longa	PLA, PCL, PEG, PU	In vitro, in vivo	Anticoagulant, Antioxidant, Antibacterial, Antifungal	[71]
Alkannin/shikonin	CA, PLA, PGA	In vitro	Antioxidant, Anti-inflammatory, Antibacterial, Wound healing	[72]
Astragaluspropinquus	SF, gelatin	In vitro	Antimicrobial, Wound healing	[73]
Zataria multiflora	PCL, PLA	In vitro, in vivo	Wound healing, Antibacterial	[74]

5. Polymers

Ideal wound dressings have focused on protecting the wound from dehydration and infection, requiring higher porosity, and providing a suitable barrier, higher gas permeability, better covering of the injury, inhibiting external microorganisms, and improving appearance after healing. Proteins, polysaccharides, and synthetic polymers are among the most frequently employed materials in producing nanofibers of all kinds. Specific protein polymers include soy, zein, keratin, collagen, gelatin, silk fibroin (SF), lysozyme, fibrin, eggshell membrane, and elastin [75,76]. Based on this sector's ever-growing research, nanofiber scaffolds are based on polysaccharides such as cellulose acetate (CA), starch, chitosan (CS), chitin, alginates, gums, pectins, heparin, hyaluronic acid (HA), chondroitin sulfate, and pullulan dressings are effective in wound healing management (Table 2) [77–79]. Specific synthetic polymers include polyethylene glycol (PEG), polylactic acid (PLA), polyvinyl alcohol (PVA), polyacrylic acid (PAA), polyethylene oxide (PEO), polycaprolactone (PCL), polyglycolide (PGA), polyvinylpyrrolidone (PVP), poly-lactic glycolic acid (PLGA), polystyrene (PS), and polyurethane (PU) display wound healing capabilities in vivo and in vitro. Because of its cell permeability, high surface-to-volume ratio, low antigenicity, non-toxicity, oxygen permeability, unique hemostatic, and mechanical properties, excellent biocompatibility, and sustained biodegradability. Ideally, it should stimulate the proliferation of human keratinocytes, re-epithelialization, and fibroblasts of endothelial cells, favoring tissue regeneration [80–82]. Some pure polymers, block copolymers, and blends have been reported as having been used successfully for wound healing therapy. Natural/synthetic hybrid polymers: Combining natural and synthetic polymers has been suggested as a potential remedy to solve the drawbacks of synthetic and natural polymers. This method combines the biocompatibility and bioactivity of natural polymers with the strength and resilience of synthetic polymers [83].

Table 2. Advantages of biopolymers and synthetic polymers in wound healing.

Biopolymers	Advantages	Ref.	Synthetic Polymers	Advantages	Ref.
Collagen	• Natural protein • Biocompatible • Biodegradable • Low antigenicity • Cheaper • Antithrombogenic • Mimics native ECM	[84]	PCL	• Good electrospinning properties • Soluble in most the organic solvents • Biocompatible • Biodegradable • FDA approved • Good mechanical property	[81]
Gelatin	• Biocompatible • Biodegradable • Low antigenicity • Cheaper • Antithrombogenic	[85]	PLGA	• Cytocompatible • FDA approved • Soluble in most the organic solvents • Excellent antiadhesive property	[82]
Chitosan	• Biocompatible • Bioactive • Biodegradable • Bactericidal material • Hydrophilic material • Nontoxic • Degradable by enzymes (chitosanase and lysozyme)	[86]	PU	• Creates a moist environment • Suitable coverage for burns • Good mechanical strength	[87]
Fibronectin/fibrin	• Adjustable mechanical properties • Hemostatic properties	[88]	PLLA	• FDA approved • Excellent cellular compatibility • Soluble in most the organic solvents • Suitable for drug delivery	[89]

Table 2. *Cont.*

Biopolymers	Advantages	Ref.	Synthetic Polymers	Advantages	Ref.
Alginate	• Biocompatible • Biodegradable • Nontoxicity • Water soluble • Nonimmunogenic • Inexpensive • Simply cross-linked • High stability • Zero shear viscosity	[90]	PLCL	• FDA approved • Suitable for drug delivery • Good mechanical strength	[91]
Cellulose	• Biocompatible • Biodegradable • Mechanical stability • Cost-effectiveness • Hydrophilic nature • Purity	[92]	PLA	• Good ductility • Good biocompatibility • Good processability • Biodegradability • Bioresorbability	[93]
Hyaluronic acid	• Biodegradable • Biocompatibility • Biopolymers are present in the majority of living organisms	[94]	PGA	• Supports various cell types • Good ductility • Good processability • Bioresorbability • Biodegradability • Good biocompatibility	[95]
Silk fibroin	• Biocompatibility • Water vapor transmission rate • Water retention capacity • Elasticity	[96]	PEO	• Easy modified • Biocompatible • Hydrophilic	[97]
Myoglobin/Hemoglobin	• Biocompatible • Excellent oxygen permeation • Alleviate wound hypoxia	[98]	PVA	• High-temperature stability • Long-lasting durability • Relatively low-cost • Biodegradability • High solubility	[99]
Starch	• Biodegradability • Low cost • Renewability • Hydrophilic	[100]	PEG	• Reasonable control over structural and compositional properties	[101]
Elastin	• High elasticity • Half-life > 70 years, and the monomer can reversibly stretch up to eight times its resting length	[102]	PVP	• Low toxicity • Excellent biocompatibility • Hydrophilic nature • Soluble in water/most organic solvents	[103]

6. Antibacterial Mechanism of Phytoconstituents

Phytoconstituents have shown significant promise in fighting bacterial illnesses. A diverse category of chemical substances is found naturally in plants. These chemicals' widespread presence has shown favorable benefits in terms of antioxidant, antibacterial, and antifungal activity. They may restore the therapeutic use of earlier antibiotics by improving their efficacy and, as a result, preventing the development of resistance [104–106]. Some phytoconstituents have antibacterial properties and are commercially accessible to consumers. Their chemical structures are divided into many key groups: alkaloids, sulfur-containing chemicals, terpenoids, coumarins, and polyphenols [107,108]. Phenolic compounds attack the phospholipids found in bacterial cell membranes, and the lipids on their cell walls result in increased permeability and, ultimately, cell lysis; such circumstances lead to cytoplasm leakage, a drop in pH, and the cessation of cellular functions, including protein synthesis, DNA transcription, and ATP generation. Additionally, it interferes with the active transport of nutrients across the cell membrane. It results in the coagulation of the contents of the bacteria's cells, both of which impair the cytoplasmic membrane's functionality (Figure 4) [107,108]. Antimicrobial agents' best-known and most-studied mechanisms of action are currently related to a wide range of bacterial targets and processes, including the inhibition of protein synthesis, inhibition of metabolic pathways,

interference with cell-wall synthesis, inhibition of DNA and RNA synthesis, and bacterial membrane lysis, among others (Figure 4).

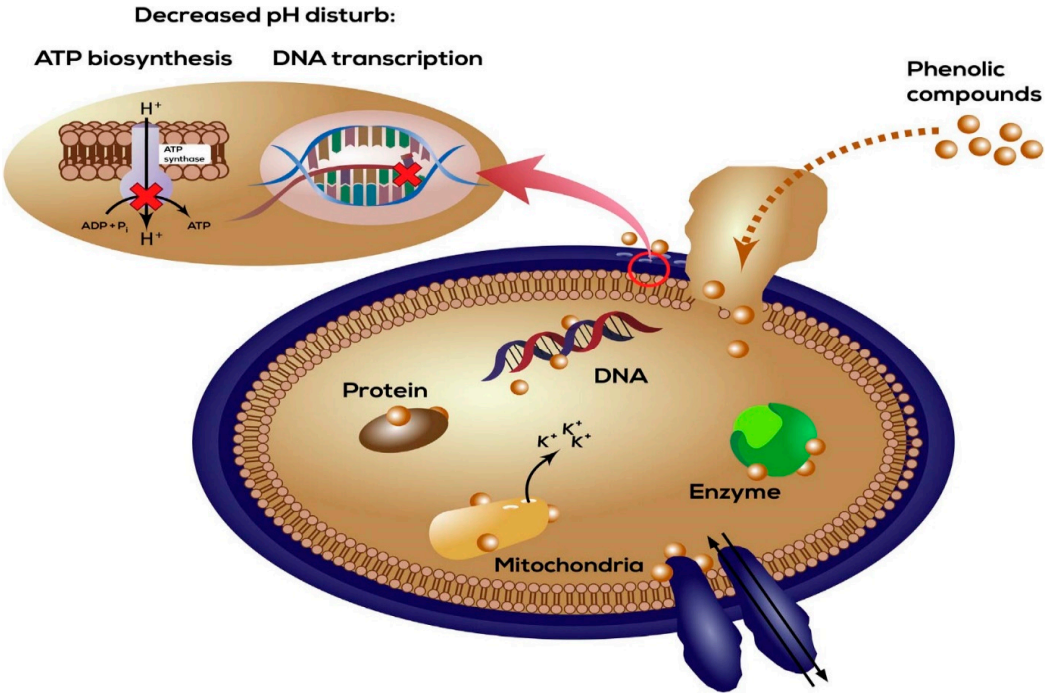

Figure 4. Representation of phenol component targets in bacteria. Reproduced with permission from Ref. [109], ©2018 European Journal of Pharmaceutics and Biopharmaceutics, published by Elsevier Ltd.

On the other hand, antibiotic modification by enzymes, antibiotic inactivation, and the development of efflux pumps are the most prevalent and well-researched mechanisms of bacterial resistance to antibacterial drugs. Phytochemicals have a wider range of target locations and action mechanisms than conventional antibiotics. Research into antimicrobial phytochemicals, their modes of action, and their potential use in therapies and treatments are moving forward quickly.

7. Phytoextract-Based Electrospun Nanofiber Wound Dressings

7.1. Curcuma longa

Curcuma longa, a member of the Zingiberaceae family, contains 3–4% curcumin (diferuloylmethane), its primary bioactive constituent. Curcumin is a polyphenolic molecule having qualities such as anti-inflammatory antioxidant, anticancer, angiogenic, inherent antibacterial properties, high biocompatibility, and biodegradability [110,111]. Curcumin's limited bioavailability, low solubility in water, instability to pH, heat treatment, and light restrict its medicinal uses and need alternative carriers, such as cyclodextrins [112]. Curcumin was described in the mat as an amorphous nano-solid dispersion. The outcome showed that a more significant crosslinking % is associated with a higher degree of hydrophobicity in the fiber mat and a lower release rate (Figure 5). Nguyen et al. formulated *C. longa*-loaded PLA nanofibers for wound healing. The in vivo results demonstrated that the PLA/*C. longa* nanofibers had a significantly higher wound closure rate than the control group [113]. Shahid, M.A. et al. formulated curcumin-infused PVA and polyethylene three-layer nanofibers [114]. The results of antibacterial testing revealed that 16% of curcumin fibers displayed antibacterial action without lowering the required percentage of cell viability. The exudates are absorbed using PVA, while polyethylene-polycaprolactone ensures favorable mechanical qualities and a non-adherence property to the wound [115]. Bui et al. created *C. longa* (0.5 wt%) and loaded The PCL and PCL/PEG nanofibers. The nanofibers had a reduced diameter due to the presence of *C. longa*, which also improved

their antibacterial activity against *S. aureus*. In animal testing, the PCL/PEG nanofibers with the most significant degree of wound closure (99%). Adding PEG to PCL led to the surface of the nanofibers becoming porous [116]. Shababdoust et al. created a *C. longa*-loaded PU electrospun nanofiber platform. Researchers utilized PCL and PEG-based polyurethane (PU) materials in their experiment. The results demonstrate that the presence of *C. longa* increases the diameter of nanofibers.

Additionally, the hydrophilicity of the PU structure is increased when PEG is added relative to PCL, PU, and *C. longa* is released from the scaffolds more rapidly [117]. Mutlua et al. formulated *C. longa* (0.1, 0.3, and 0.5 wt%) loaded PHBV nanofibers for wound treatment. According to studies, PHBV nanofibers have a beneficial impact on skin regeneration and wound healing. The findings demonstrated that adding more *C. longa* lowers the nanofiber diameter, raises swelling characteristics, and decreases mechanical qualities [118].

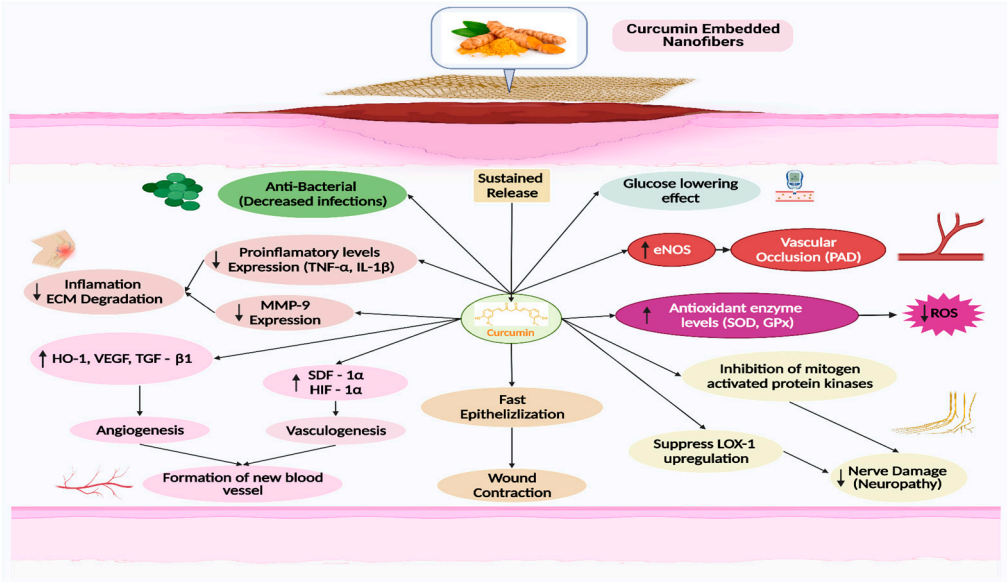

Figure 5. Curcumin mechanism of action in treating diabetic wounds. Reproduced from [119], Applied Nano (MDPI).

7.2. Aloe barbadensis Miller

Aloe vera may be used in nanofibrous mats even if it does not have suitable mechanical properties or electro-spinnability [120,121]. Researchers formulated aloe vera-loaded gelatin and PCL nanofibrous scaffold by two distinct syringes and double-nozzle co-electrospinning. The nanofibrous platform displayed an optimal uniform size distribution, low diameter, excellent biological qualities, and suitable mechanical features. Comparing Aloe vera-PCL and Gelatin-PCL scaffolds were shown that Aloe vera increased fibroblast proliferation [122].

7.3. Lawsonia inermis

Lawsonia inermis, often known as henna, henna leaf extract contains antibacterial, anthelmintic, immunostimulatory, anticancer, antioxidant, UV protecting, antimicrobial characteristics and wound healing; nevertheless, lawsone has limited solubility in water, preventing it from reaching its full medicinal potential [123]. One way to improve lawsone's solubility, stability, prolonged release, and bioavailability is by encapsulation [124–126]. M. Adeli-Sardou et al. formulated lawsone encapsulated gelatin and PCL nanofibrous mats by coaxial electrospinning. PCL is the outer shell polymer, while a gelatin-lawsone mix is an inner core. The scaffolds released lawsone for 20 days, and a 1% lawsone loaded mat increased re-epithelialization of the wound after 14 days to ensure the most remarkable healing. This mat also has outstanding properties that make it suitable for medication

and wound dressing. Gelatin and PLLA were combined with *L. inermis* solution to create hybrid nanofibrous scaffolds. The nanofibrous platforms show antibacterial capabilities against *E. coli* and *S. aureus*, which might help to prevent wound infection and hasten wound healing [127]. Mirei et al. created *L. inermis* leaf extract (1 wt%) loaded CS-PEO nanofibers for mice with second-degree burn wounds. They produced homogenous fibers without beads with an average diameter of 80 nm, which may have a more potent healing effect than traditional wound dressings and untreated nanofibers [128]. Avci et al. created *L. inermis* leaf extract (1.264 and 2.793 wt%) loaded PVA and PEO nanofibers. According to SEM, the average diameter increased when *L. inermis* leaf extract concentration rose. According to the antibacterial test findings, *L. inermis* leaf extract gives nanofibers their antibacterial capabilities. Nanofibers showed better antibacterial activity at a concentration of 2.793 wt% [53].

7.4. Zataria multiflora Boiss

Thymol is an essential oil and a significant component of *Z. multiflora*. Thymol is a naturally occurring antibacterial agent [129]. Due to its limited bioavailability, high volatility, and low water solubility, thymol is only permitted in some biological applications. Miguel, S.P. et al. created thymol loaded two layer nanofibrous scaffolds: a top layer made of PCL and SF to serve as a physical barrier at the wound site and a bottom layer made of HA, SF, and thymol to speed up the healing process and prevent infection. Ardekani et al. formulated *Z. multiflora* essential oil (10%) loaded CS, PVA, and gelatin electrospun nanofibers. It was nontoxic, had a high swelling capacity, biocompatible, and had antibacterial activity [70]. Pourhakak et al. formulated *Z. multiflora* extract-loaded CS and PVA electrospun nanofibers. The results demonstrated that decreasing the amount of CS in the mixture reduced the diameter. In addition, researchers produced nanofibers with a smaller diameter and more antibacterial qualities that may be used as a wound dressing.

7.5. Matricaria chamomilla L.

The *Asteraceae* family member and popular medicinal herb chamomile include a variety of potent compounds, including phenolics, flavonoids, patuletin, luteolin, quercetin, apigenin, and glucosides. The chamomile flower has the highest concentration of apigenin, which has a noticeable impact on wound healing. Motealleh et al. formulated chamomile extract (15%) loaded PCL/PS (35/65%) electrospun nanofibers. Researchers used the plant extract to reduce the nanofibers' diameter from 268 to 175 nm. ZOI for *S. aureus* was 7.6 mm. In drug release studies, almost 70% of the extract was released, which is advantageous for healing. A rat wound model study showed that a wound treated with an extract of nanofibers healed and closed in 14 days [61].

7.6. Isatis tinctoria

Isatis Root is used to treat infectious disorders, particularly skin conditions, due to its potent Antibacterial and anti-inflammatory properties to treat wounds, PVP and Isatis root fibers were electrospun by hand. The addition of 10 wt% Isatis to the nanofibers scaffolds improved surface wettability and air permeability, allowing for gaseous exchange, antibacterial activity, and faster wound healing [130].

7.7. Trigonella foenum-graecum

Fenugreek, which belongs to the *Leguminosae* family, has antioxidant characteristics that speed up the healing of wounds. Creating electrospun nanofibers from fenugreek and silk fibroin and treating it with ethanol vapor to bring structural changes in silk I (random coil) to silk II. antioxidant activity, high biocompatibility, wound healing, and collagen deposition were all shown by the fenugreek integration into silk nanofiber scaffold in the in vivo investigation. It also demonstrated excellent thermal, mechanical, and porosity properties [131].

7.8. Melilotus officinalis

Melilotus officinalis is the source of the herbal medication Semelil, which is used to treat diabetic foot ulcers. Researchers combined the Semelil extract from *M. officinalis* with CS and PEO to create nanofibers using electrospinning, according to Mirzaei, E. et al. The fibers can speed up wound healing and have the ability to release drugs [50].

7.9. Achillea lycaonica

Most of these *achillea* species are used in medicine and contain biological properties such as antioxidant, antibacterial, wound healing, and anti-inflammatory. The most excellent antioxidant properties were seen in a 1:1 ethanol-water extract. Pure PLA was combined with *A. lycaonica* plant extract to create nanofibrous mats. *A. lycaonica* may be released from the mat, which demonstrated excellent cell compatibility, enhanced cell viability, and was free of cytotoxic effects. The mat's adequate tensile strength also allows cell proliferation activity, leading to quicker and better wound healing. The scaffold's use of an Achillea lycaonica extract decreased the fiber's diameter [132].

7.10. Zea mays

Zein protein is a biologically active, nontoxic, biodegradable, flexible material with excellent temperature resistance that promotes cell adhesion, proliferation, and penetration in prospective medicinal applications. Zein PCL and gum arabic were combined to create new porous nanofibers. Zein and gum arabic may provide antibacterial properties, while PCL can give strength, elasticity, and degradability [133].

7.11. Lepidium sativum

A mucilage seed extract has historically been used as a therapy for skin conditions and other illnesses since it has biological qualities that include antibacterial, antioxidant, anti-inflammatory, and stimulator of cell development. PVA (10% *w/v*) was used to aid electro-spinnability and was added to aqueous mucilage extract before being electrospun into a nanofibrous mat. The biocompatibility, cell adhesion, and nanofibrous development are improved by adding mucilage [134].

7.12. Syzygium aromaticum

The blossom buds of the clove tree contain eugenol, an essential oil made from cloves and a naturally occurring phenolic substance. The antibacterial, analgesic, antioxidant, and anti-inflammatory therapeutic qualities of eugenol will speed up the healing of wounds. Eugenol, however, has the drawbacks of being poorly soluble in water, being unstable in the presence of enzymatic and chemical degradation, and losing its effectiveness via volatilization or heat breakdown [135]. Natural bioactive compounds' structural integrity and bioactivity are preserved when hydrophilic and hydrophobic bioactive molecules are included in emulsion electrospinning. Researchers employed chloroform and DMF solvent to dissolve PCL, water to dissolve PVA, and acetic acid to dissolve chitosan to generate the distinctive electrospun mats. The finished mat showed antibacterial activity against *P. aeruginosa* and *S. aureus*, biocompatibility, cytotoxic in vitro testing, and quick release, rising progressively up to 120 h, demonstrating the efficacy of Eugenol-loaded nanofiber as a possible wound healing mat.

7.13. Garcinia mangostana Linn

G. mangostana has been utilized in traditional medicine for treating ailments, including wound infections. Xanthone, gartanin, a, b, and c-mangostans, 8-deoxygartanin, and garcinone are all present in *G. mangostana. G. mangostana* extracts have anti-inflammatory, antioxidant, antibacterial, and antiproliferative properties. Thus, researchers may add *G. mangostana* extracts to the nanofibers platform to boost their antibacterial and antioxidant characteristics to promote wound healing [136]. Researchers created *G. mangostana*-loaded CS-EDTA/PVA nanofiber mats for wound healing in vivo. The outcome showed that the

mat has antibacterial, antioxidative, extract release, and stability properties. Additionally, the mats have the correct tensile strength, swelling qualities, and wound healing in vivo.

7.14. Gymnema sylvestre

G. sylvestre is used to treat wounds due to its antimicrobial, anti-inflammatory, and wound-healing characteristics. It contains gymnemic acids, anthraquinones, flavones, lupeol, gymnemasaponins, phytin, and stigmasterol as phytoconstituents. *G. sylvestre* leaf extract was used to create electrospun PCL nanofibrous mats, according to Ramalingam, R. et al. The outcome shows that the mat has excellent mechanical qualities, is wettable, is non-cytotoxic, and has good antibacterial efficacy [137].

7.15. Carica papaya

Carica papaya aqueous leaf extract has antibacterial, anti-inflammatory, anti-odor, and hydrophilic properties that help speed up wound healing. The vitamin C found in *carica papayas* is a co-factor for stabilizing the collagen's tertiary structure and promoting gene expression in collagen synthesis. The hydrophilic character of the papaya nanofibers, both on their own and when combined with specific polymers, promotes re-epithelialization and the healing of wounds. It has significant antibacterial activity against *E. coli* and *S. aureus*, is hemocompatible, and has no cytotoxicity against fibroblast cells [138].

7.16. Centella asiatica

The *C. asiatica* extract-containing electrospun PCL nanofibers were created by Manotham et al. They increased the ethanolic extract of *C. asiatica* by 0.5, 2.5, 5, and 10 wt% and obtained homogenous nanofibers free of beads. According to the study, adding the *C. asiatica* extract decreased the mean diameter of the fibers. For instance, the wavelength of pure PCL nanofibers reduced from 415 nm to 344 nm when researchers added *C. asiatica* extract (10 wt%). This reduction in wavelength may be the consequence of the *C. asiatica* extract's ability to reduce the viscosity of the polymer. From 3.36 MPa to 8.70 MPa for the nanofibers, the maximum tensile stress increased dramatically with the *C. asiatica* extract, which may be connected to a decrease in the diameter of the fibers. Additionally, the antibacterial activity of the nanofibers was brought about by adding *C. asiatica* extract to PCL. For *Micrococcus luteus* and *Bacillus cereus*, the inhibitory zone's mean diameter was 8 mm and 11 mm, respectively [139].

7.17. Sorghum bicolor

Yang et al. formulated *Sorghum* (*S. bicolor*) extract loaded zein electrospun nanofibers. Because of its tannin concentration, *S. bicolor* is a source of both antioxidants and antibacterials. Zein, a plant protein, is more readily available, degradable, and stable. Researchers used *K. pneumonia* and *S. aureus* to test the antibacterial effectiveness of nanofibers. According to the findings, increased *sorghum* extract concentration resulted in a significant reduction in the number of bacteria in nanofibers [44].

7.18. Camellia sinensis

Tea leaves contain phenolic chemicals called catechins, which are believed responsible for the plant's anti-inflammatory, antibacterial, and antioxidant activities. Researchers formulated *C. sinensis* extract-infused CS and PEO nanofibers in this work. When used as transporters of phytoconstituents, particularly for skin wound healing, the structure of CS nanofibers has shown some encouraging outcomes, such as exhibiting antibacterial characteristics, being biocompatible, and being biodegradable. The CS nanofibers are an excellent choice for wound dressings because of these qualities and their capacity to increase cell migration, adhesion, and proliferation. According to the findings, the plant extract-loaded nanofibers preserve the moisture on the wound site, lessen inflammation, and speed up wound healing [140].

7.19. Hypericum perforatum

Pourhojat et al. formulated *H. perforatum*-loaded PCL nanofiber as an efficient wound dressing. Due to its antibacterial characteristics, a medicinal plant has long been used in traditional medicine to heal burns and wounds. Electrospun nanofibers with 400–100 nm diameters and potent antioxidant activity were shown [48]. Karimi et al. created appropriate antibacterial thymol-loaded PCL/PLA nanofibers [48]. Antibacterial tests indicated that these thymol-loaded nanofibers had a better result against *S. aureus* than *E. coli*. Animal tests were conducted to compare the thymol-loaded nanofibers, demonstrating that they significantly impacted wound healing and closure [74].

7.20. Nepeta dschuparensis Bornm

N. dschuparensis contains flavonoids, essential oils, 1,8 cineole, β-Endemol, thujone, pinene, and β-caryophyllene; *Bornm* is widely used as an antibacterial, antioxidant, and anti-inflammatory traditional herbal medicine. Naeimi et al. created nectar from *N. dschuparensis* loaded PVA, CS, honey nanofibrous scaffold for burn therapy. Researchers also investigated the scaffold's capacity to promote wound healing [141].

7.21. Annona muricata

Aruan et al. formulated soursop leaves extract-infused PVA electrospun composite nanofibers. *Annona muricata L.*, sometimes known as soursop, is a plant with antibacterial qualities and the capacity to treat skin problems. The generated nanofiber mats had a mean diameter of 137–121 nm when 8–14% *A. muricata* leaf extract was used. It has significant antibacterial activity against *S. aureus*, and the inhibition zone measured 1, 2, and 4 mm for 8%, 12%, and 14% of the extract, respectively [49].

7.22. Tridax procumbens

A blooming plant endemic to the Americas is called *T. procumbens*, also known as *Tridax procumbens L.* Calcium, potassium, and sodium are all abundant in *T. procumbens* to treat wounds and promote healing. *T. procumbens* leaf extract is applied to the affected body area. The *T. procumbens* leaf extract-containing PVA nanofibers were created by Ganesan et al. When tested against *E. coli* and *S. aureus*, the nanofibers displayed a ZOI of up to 4.5 cm and 3.6 cm, respectively, demonstrating their antibacterial characteristics [54].

7.23. Vitis vinifera

Researchers have shown that the *V. vinifera* extract is around 20–50 times more effective than vitamin C or E and has a significant deal of potential to eliminate free radicals. Lin et al. formulated *V. vinifera* extract-loaded silk fibroin nanofibers. The *V. vinifera* extract has significantly more antioxidant activity. The biocompatibility and biodegradability of silk fibroin make it a safe and advantageous substance for human use. Silk fibroin increases collagen production and aids in wound healing, scar removal, and skin irritation reduction. To help fibroin's capacity to spin electrically and to enhance the nanofibers' mechanical qualities, PEO was added to the solution in this work. Data revealed that when PEO/fibroin nanofibers with 3 wt% *V. vinifera* extract were used instead of fibroin, they exhibited good biocompatibility and increased cell attachment. According to the results of this research, nanofiber mats containing *V. vinifera* have a bright future as treatments for wound healing, tissue regeneration, and skin protection [55].

7.24. Moringa oleifera

One of the native trees of India is the moringa, commonly known as *Moringa oleifera Lam. (M. oleifera)*, which may also be found in South America, Asia, and Africa. The *M. oleifera* extract's capacity to cure wounds has been established in the trials. Electrospun polyacrylonitrile (PAN)/*M. oleifera* extract nanofibers were used to create a wound dressing, which Fayemi et al. then tested for its ability to kill microbes and promote wound healing. Researchers found the most fantastic antibacterial activity in the PAN nanofiber scaffolds

loaded with *M. oleifera* extract. ZOI of 15 mm for *E. coli* and 12 mm for *S. aureus*. Various doses of *M. oleifera* extract were used in this investigation, ranging from 0.1 to 0.15 to 0.25 and 0.5. The outcomes of the experiments on animals also showed that the *M. oleifera* extract-infused nanofibers had superior healing abilities. Thus, the therapeutic benefits also increased with an increase in *M. oleifera* leaf extract concentration. Consequently, the nanofiber scaffold loaded with 0.5 g of *M. oleifera* extract showed excellent antibacterial activities [57].

7.25. Querqus infectoria

Q. infectoria has a high concentration of hydroxyl groups, tannins, which make up 50–70% of *Q. infectoria*, are antimicrobial. Yeganeh et al. formulated PVA nanofibers infused with *Q. infectoria* methanol extract. In this work, they contrasted *Q. infectoria*-containing PVA nanofibers with *Q. infectoria*—containing PVA films. The average diameter of their nanofibers was 500 nm. Researchers enhanced the *Q. infectoria* extract's antimicrobial effect by converting it to electrospun nanofibers. ZOI for the nanofibers against P. aeruginosa and *S. aureus* was 20 mm and 18 mm, respectively. Nanofibers generally showed improved moisture absorption rates, superior antibacterial properties, and controlled release, making them practical for wound healing [60].

7.26. Juniperus chinensis

East Asian nations are home to *J. chinensis*, also known as *Juniperus chinensis* L. which is often grown as an attractive plant. Three primary classes of *J. chinensis*' chemical constituents include flavones, lignans, and terpenes. It has been discovered to have potent antibacterial, antifungal, and anticancer properties. For electrospinning, Kim et al. employed PVA and a *J. chinensis* extract. The nanofibers have shown good antibacterial activity against *K. pneumonia* and *S. aureus* [62].

7.27. Beta vulgaris

Hosseinzadeh et al. formulated *B. vulgaris* extract-loaded nylon 66 skin scaffolds. Compounds found in *B. vulgaris* are mostly polysaccharides, particularly pectin, and pectin has been used extensively to heal skin wounds in traditional Iranian medical texts. The nanofiber scaffold produced has a tiny pore size and high porosity. The cell proliferation test findings and the investigation of this scaffold established its superiority in skin tissue engineering [64].

7.28. Biophytum sensitivum

The plant, *B. sensitivum*, possesses anti-inflammatory, antiseptic, and anti-diabetic effects. Namboodiri et al. developed antimicrobial *B. sensitivum* extract (10 wt%) loaded PCL nanofiber wound dressings. Fibers exhibited reasonable water absorption rates, were cellularly adaptable, and could transport water vapor. *S. aureus* and *E. coli* could not grow on the hybrid membrane, and their respective ZOI were 47 and 27 mm [65].

7.29. Lavandula

The essential oil from *L. angustifolia* possesses antibacterial and analgesic anti-inflammatory qualities and is beneficial in treating burns and wounds. Balasubramanian et al. formulated lavender essential oil-embedded sodium alginate nanofibers dressings for UV-induced skin burns. Animal experiments revealed that the animals recovered quickly without experiencing skin inflammation. Anti-inflammatory cytotoxin levels were up to 10 times lower in treated animals after 24 h than in untreated animals [67].

7.30. Boraginaceae

Shikonin is a naturally occurring compound in the roots of many *Boraginaceae* plants. Shikonin has demonstrated that it possesses antibacterial, anti-inflammatory, and wound-healing qualities. Han et al. created PTMC and PCL nanofiber scaffold with 1–5 percent

shikonin. The morphology of the nanofibers was unaffected, and the resulting nanofibers were homogeneous and bead-free. The findings demonstrated that the ratio of PTMC and PCL significantly influenced the diameter of the fibers. Due to their antibacterial activity and wound-healing qualities, nanofibers containing 5 wt% of shikonin may be used as a wound dressing [142].

7.31. Astragalus membranaceus

Shan et al. formulated *A. propinquus* incorporated gelatin and SF electrospun nanofiber mats for scar eradication and burned wound healing. Researchers added gelatin to fibroin to boost cell adhesion, and these nanofibers enhanced the healing of burn wounds [73]. The outcomes of a few representative research projects that used electrospinning to create phytoconstituent-loaded nanofibers are shown in (Table 3).

Table 3. Phytoconstituent-based nanofibers and their benefits.

Electrospun Nanofibrous Wound Dressings	Properties Investigated	Ref.
Chitosan/PEO/semelil (herbal extract drug)	release of semelil, high swelling	[138]
Chitosan/PVA/gelatin/*Zataria multiflora*	antibacterial properties, nontoxic and biocompatible	[70]
Cellulose acetate/gelatin/*Zataria multiflora*	antibacterial properties, wound healing, wound re-epithelialization, biocompatible	[143]
Vitamin E/starch nanoparticle/silk fibroin/PVA aloe Vera	nontoxic, biocompatible, release vitamin E, protect cells from toxic oxidation products	[144]
PVA/curcumin	nontoxic, biocompatible, antibacterial, release of curcumin	[145]
PVA/honey/curcumin	antibacterial activity, good moisture properties	[146]
PCL/gum tragacanth/curcumin	collagen deposition, regenerate epithelial layer, healing, fast wound closure	[147]
PCL/PVA/curcumin	antibacterial property, absorbable, biocompatible	[148]
Thiocarbohydrazide-modified gelatin/curcumin	nontoxic, antibacterial, release curcumin	[121]
PVA/gelatin/*Carica papaya*	hemocompatible, antibacterial, nontoxic, wound healing	[149]
PVA/mucilage	anti-inflammatory, promote cell growth and fibroblasts cells attachment, biocompatible	[134]
PLA/*achillea lycaonica*	compatible, nontoxic, release of achillea	[132]
PCL/gum arabic/Corn protein	antibacterial, biodegradable, porosity, good mechanical properties	[126]
Silk fibroin/Fenugreek (natural antioxidant)	antioxidant property, biocompatible, wound healing	[131]
Silk fibroin/soy protein isolate	nontoxic, biocompatible, biodegradable, wound healing activity	[133]
PCL/*Gymnema sylvestre* leave extract	antibacterial, biocompatible, mechanical properties, wettability	[137]
Polyvinyl pyrrolidone containing isatis root	Antibacterial, excellent wetting, permeable, active, wound closure	[130]
PCL/PVA/Chitosan/Eugenol	antibacterial action, biocompatible, nontoxic, release Eugenol	[135]
Silk fibroin-PCL/silk fibroin-hyaluronic acid, thymol	antioxidant and antibacterial properties, biocompatible, wound healing	[129]
Chitosan/PVA/honey/*Nepeta dschuparensis*	biodegradable, biocompatible, faster wound healing, tissue regeneration	[141]

8. Conclusions

Novel functional electrospun nanofiber wound dressings exhibit unique morphologies, a porous structure, a high surface area to volume ratio, hemostasis, the capacity to absorb exudates, the ability to be utilized as drug carriers, and the potential to speed up the healing of wounds. The production of electrospun nanofibrous materials may employ both natural and synthetic polymers. However, combining various synthetic and natural polymers will result in unique features for wound healing. Medicinal plants are readily available and easy to extract, and plant extracts have limited adverse side effects; we believe that electrospun wound dressings based on medicinal plants will increasingly replace synthetic antibiotics to impart antibacterial or other desirable properties. Adding herbal substances to these nanofibers may also enhance their characteristics.

Conversely, the rise in antibiotic resistance among pathogens and worries about the harmful effects of additives have prompted customers to prefer natural substitutes such as plants. Despite the notable characteristics of plant components, using plants in electrospinning has certain restrictions, such as including some of these compounds at a deficient level in the electrospinning solution. Additionally, several of these herbal components sometimes have various elements, which may make it challenging to locate a typical solvent for electrospinning. Further research is required on these plant resources' shelf life, usable life, and ideal storage conditions. Plants may also be employed for tissue engineering, bandages, bleeding fabrics, antimicrobial clothes, therapeutic pads, and the diversification of plant-based medicinal products in addition to dressing.

9. Future Perspective

In this paper, we have provided a thorough explanation of how herbal extracts may be used to design soft or hard tissues, influence the healing of wounds, or function as drug-eluting systems. These herbal extracts can be supplied using electrospun nanofibers, and in-depth descriptions of the electrospinning process for making scaffolds have been provided. The study focuses on novel approaches to replace conventional dressings with phytoconstituents in polymeric scaffolds. The review aims to provide cutting-edge ways to use herbal items in their raw or pure forms. Here, the use of nanofibers as a delivery mechanism for herbal medicines and crude extracts for diverse purposes has been thoroughly documented and tabulated for simple evaluation by researchers of the developments in this area. To better understand various consequences, examining the uses of electrospinning and other nanofiber creation processes is necessary. Herbal goods need to be investigated for any potential that researchers may show via a nanofiber composition. It is essential to develop new methods for obtaining clinically recommended, known-potency active components from medicinal plants that would increase the planned product's accessibility to various regulatory authorities. The best scaffolds must be identified to be conveniently used in clinical settings and design a specific application. It is necessary to comprehend the fundamentals of the nanofiber synthesis process. Researchers must first develop high-efficiency processes such as rotary jet spinning at the lab scale before being scaled up to big production units at the industrial setup in scaffold manufacturing. When it comes to releasing active ingredients in various release patterns defined by a particular application, the matrix system of these items must be prudently selected to guarantee the intended herbal product's specified release kind, immediate or sustained. For straightforward, practical translation in tissue engineering, researchers must create scaffolds with improved cellular biocompatibility and necessary mechanical robustness. The surface of the nanofibers may be modified, or researchers can use a combination of natural and synthetic polymers to accomplish this.

Additionally, researchers must investigate the potential use of plant-based extracts in tissue engineering to improve the lengthy shelf-life. In addition, examining the activity of purely natural ingredients rather than crude extracts would be more advantageous and valuable. Furthermore, there are still numerous barriers to overcome before researchers can use these items in clinical settings.

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