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Review

Nonwoven Electrospun Membranes as Tissue Scaffolds: Practices, Problems, and Future Directions

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Abstract: A flexible and dependable method that has been extensively employed to construct nanofibrous scaffolds that resemble the extracellular matrix made from polymeric materials is electrospinning (ES). ES is superior to other techniques because of its unique capacity to create nanofibers with a high surface-to-volume ratio, low cost, simplicity of setup, freedom in material choice, and ability to alter the surface attributes and usefulness of the nanofibers. However, the low productivity of nanofibrous membrane from conventional ES with the generation of tightly packed nanofibrous sheet-like two-dimensional membranes impedes cellular infiltration into scaffolds during tissue regeneration. Moreover, toxic organic solvents are desired for polymer dissolution for ES. Such solvents produce volatile organic compounds (VOCs) during electrospinning, which can degrade the indoor air quality of working place. Furthermore, when electrospun membranes containing traces of such VOCs are employed as tissue scaffolds, it may cause serious effect to cells and tissue. This justifies the need for alternative green solvents which are not only environmentally friendly, non-toxic, and low-cost but also biocompatible with medicinal values. Therefore, this review mainly focuses on summarizing the recent advances in ES machines, fabrication of three-dimensional (3D) spongy nanofibrous membrane, and introducing green solvent for polymer processing. Finally, based on the findings of the existing literature and our experience, this review mainly focuses on essential oils as future "greener" alternatives to current toxic solvents used in ES process.

Keywords: electrospinning; green solvents; tissue engineering; essential oils; volatile organic compounds

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1. Introduction

Over the last few decades, extensive strides have been taken in uncovering efficacious approaches to address damaged tissues arising from a multitude of causes. One promising approach proposed by nanoscientists is tissue engineering. In tissue engineering, scaffolds play a crucial role as they provide a supportive structure for cell growth, proliferation, and differentiation [1]. These scaffolds are required to possess specific characteristics such as high porosity, biodegradability, and non-toxicity to promote tissue regeneration. Several methods, including electrospinning (ES), solvent casting, freeze-drying, and gas foaming, can be employed to fabricate suitable tissue scaffolds. ES is considered one of the most promising processes for creating nonwoven membranes used in tissue scaffolds. It is highly recognized for its high output, ease of use, capacity to create fibres at the micro- and nanoscale that are different in size and shape, cost-effectiveness, reproducibility, and potential for industrial-scale application. Electrospinning, a flexible and straightforward process, has garnered significant interest over the past couple of decades. It makes it easier to produce nonwoven ultrafine fibres from a variety of substances, including organic and inorganic polymers, composites, and ceramics [2–4]. The technology has become a diverse area of research in materials science and engineering, showing significant potential for spinning materials at the micro- and nanoscale in both laboratory and commercial scale. Depending on the desired application, different polymers, ceramics, metals, and their composites can be effectively spun using different approaches [5–7]. The choice of technique provides distinct advantages. Melt electrospinning, for instance, offers enhanced safety and high production throughput. On the other hand, solution electrospinning is more multipurpose in terms of the range of electrospun materials and is more energy-efficient.

In addition, compared to melt electrospinning, solution electrospinning produces fibres with better electrical and mechanical characteristics. With the ability to customize the procedure to meet their unique material needs and application requirements, these various electrospinning techniques are available to researchers and industry practitioners [8,9]. Within the field of electrospinning, solution electrospinning has evolved into a diverse realm of biomaterials research within materials science. These biomaterials serve as synthetic frameworks, often referred to as scaffolds, matrices, or constructs, and they play a leading role in numerous biomedical applications. The objective of biomaterials in biomedical contexts is to develop synthetic materials that can repair or improve the function of damaged or injured body tissues, which enhances the overall quality of life.

Polymers have become popular biomaterials that are utilized to make scaffolds for tissue engineering and medical devices [10–12]. Polymeric scaffolds have captured substantial interest owing to their distinctive characteristics, which encompass a notable surface-to-volume ratio, significant porosity featuring small pore sizes, biodegradability, high mechanical properties, and favourable interactions with a variety of cell types present in the human body [13,14]. For a wide range of biomedical applications, synthetic polymers such as polyglycolide (PGA), polylactic acid (PLA), polyamide-6 (PA-6), poly(lactic-co-glycolic acid) (PLGA), poly(vinyl alcohol) (PVA), poly(vinyl pyrrolidone) (PVP), polycaprolactone (PCL), polyurethane (PU), poly(3-hydroxybutyrate), etc., are frequently electrospun into scaffolds due to their multifarious characteristics and capabilities [15,16]. Due to developments in the area of tissue engineering, it is now possible to combine cells, growth factors, or medications with polymers and electrospun nanofiber membranes into nano-scale scaffolds. Electrospun scaffolds are consummate for a wide range of tissue engineering applications, owing to their advantage of material flexibility and the ability to adjust scaffold parameters [17,18]. These applications encompass a variety of tissues, vessels, ligaments, bones, and skin. However, it is intriguing that most study in this area has focused on two-dimensional nanofibrous scaffolds rather than using three-dimensional scaffolds [19,20]. Traditionally, cells have been cultured primarily on the surface of electrospun materials rather than within the bulk material. Two-dimensional (2D) monolayer culture models are usually utilized due to their effortlessness and convenience, along with the ability to maintain good cell viability [21]. Nonetheless, the loose and highly porous three-dimensional (3D) structure of nanofibers holds great potential as a supportive substitute that can mimic the extracellular matrix, providing an environment for cells to grow [18,22]. Most research reports in the literature have focused on successful in vitro studies, demonstrating the suitability of electrospun materials for cell culture. Some studies have also delved into in vivo investigations, further emphasizing the potential applicability of electrospun scaffolds in tissue engineering applications [23].

Composite nanofiber scaffolds that are functionalized with osteogenic agents and nanostructured materials mimic natural bone properties. Inorganic particles like hydroxyapatite or ß-tricalcium phosphate enhance scaffold functionalities. Electrospun PLGA/collagen composite mat promotes cell attachment, proliferation, and ECM secretion for skin trauma treatment [24]. A composite 3D nanofibrous membrane is an advanced material that combines the properties of nanofibers with the benefits of a composite structure. These membranes are typically created through electrospinning, a technique that produces ultrafine fibres at the nanoscale. By incorporating various materials or nanoparticles into the nanofibers, composite 3D nanofibrous membranes can be engineered to possess a wide range of functionalities, such as enhanced mechanical strength, improved filtration efficiency, controlled release of drugs, or tailored surface properties. These membranes find applications in diverse fields, including filtration, tissue engineering, drug delivery, and sensors, where their high surface area, porosity, and customizability make them valuable for addressing complex challenges and creating innovative solutions. Overall, nanofiber scaffolds along with composite nanofiber scaffolds, present a promising avenue for tissue engineering and drug delivery, with their unique properties and functionalities enabling the development of advanced therapeutic strategies. While cells on electrospun surfaces have demonstrated adhesion within a 3D matrix, it is crucial to evaluate the use of electrospun nanofibers for tissue engineering at a 3D level, providing cells with an environment resembling natural tissues [25]. The evaluation of a 3D cellulose sponge for biomimetic mineralization and cell proliferation has shown promising results [26]. The as-fabricated cellulose sponge exhibited an excellent capacity to initiate hydroxyapatite formation from a simulated body fluid (SBF) solution. The mineralized 3D sponge displayed enhanced cell infiltration, growth, and proliferation compared to the cellulose mat. This highlights the significant potential of the 3D cellulose sponge, which was prepared through electrospinning and consequent post-treatment with sodium borohydride, for tissue engineering applications [27,28].

Various parameters play a vital role in shaping the morphology and characteristics of electrospun nanofibers, wherein the solvent assumes a crucial position. However, many conventional organic solvents used in electrospinning processes are toxic, flammable, and volatile. The presence of residual toxic solvents within the scaffold limits their applications in the biomedical field and can lead to adverse health effects [29]. For instance, Toluene is suspected to cause organ damage through prolonged exposure; Chloroform and DCM are considered carcinogenic by the WHO; and other solvents like dioxane, acetonitrile, acids, formaldehyde, tetrahydrofuran, dimethylformamide, tetrafluoroethylene, methylene chloride, dichloroethane, and pyridine have been connected with unfavourable human-health properties.

Therefore, the selection of environmentally friendly, biocompatible, and non-toxic solvents is crucial to ensure the safety and suitability of electrospun materials for various applications [30–32]. The use of essential oils from medicinal and aromatic plants as green solvents can effectively address these concerns. Essential oils, such as eucalyptus, cinnamon, lemongrass, peppermint, tea tree, thyme, mentha, and lavender oils, offer environmental friendliness, bio-activity, non-toxicity, and cost-effectiveness. They also aim to minimize or eliminate the use of hazardous organic solvents [33–35]. Employing benign solvents not only reduces toxicity but also enhances the enzymes, cell vitality, and bioactivity of genes, providing an opportunity to directly encapsulate cells within scaffolds.

This review emphasizes the ongoing efforts in exploring greener alternatives, specifically essential oils, as a substitute for volatile organic solvents in fabricating nonwoven electrospun fibres. The application of these fibres extends to biomedical tissue scaffolds, highlighting the potential for eco-friendly and biocompatible solutions.

2. Types of Tissue

Tissues are collections of cells that share a common structure and work collaboratively to carry out specific functions. The term "tissue" originates from an ancient French verb meaning "to weave" [36]. The body comprises four primary tissue types:

1. Connective;
2. Muscle;
3. Nervous;
4. Epithelial.

2.1. Connective Tissue

Connective tissue is a fibrous tissue that provides support, strength, cushioning, and elasticity to organs and tissues in the body. Specialized connective tissues like blood facilitate nutrient transport, waste removal, and gas exchange. Connective tissues consist of cells separated by an extracellular matrix (ECM), which includes ground substance and fibres [37]. The ECM's composition determines the specific structure and function of a tissue. Collagenous, elastic, and reticular fibres contribute to different aspects of connective tissue function. Connective tissue disorders, such as sarcomas, Marfan syndrome, and lupus, affect about 1 in 10 people and can cause various health issues [38]. There are three main types of connective tissues: fluid connective tissue, skeletal connective tissue, and fibrous connective tissue. This classification method categorizes connective tissues based on their distinct characteristics and functions [39].

2.2. Muscle Tissue

Muscle tissue consists of cells with the unique ability to contract, allowing for movement of the body parts. This highly cellular tissue is richly supplied with blood vessels. The cells, often referred to as muscle fibres, are elongated and slender, arranged in bundles or layers surrounded by connective tissue. The contractile proteins actin and myosin play a crucial role in muscle tissue [40].

Three varieties of muscle tissue exist in the body: cardiac muscle tissue, smooth muscle tissue, and cardiac skeletal muscle tissue. Skeletal muscle is voluntary and allows for movement, while smooth muscle is involuntary and found in organs like the intestines, blood vessels, uterus, and bladder. The heart contains cardiac muscle tissue, which is responsible for the pumping action that propels blood throughout the body. Cardiac muscle, situated in the heart, takes on the responsibility of pumping blood throughout the circulatory system. Skeletal and cardiac muscles are striated, while smooth muscle is not [41]. Duchenne muscular dystrophy is an example of a muscle tissue disorder that is distinguished muscle atrophy. It is hereditary, being inherited through genetic inheritance. It primarily affects males due to its association with the X chromosome [42,43].

2.3. Nervous Tissue

Nervous tissue is situated in the spinal cord, peripheral nerves, and the brain, forming the fundamental constituent of the nervous system. It has the ability to coordinate and control various body activities, including muscle contraction, environmental awareness, and functions related to emotions, memory, and reasoning. The key cells in nervous tissue are neurons, which generate and transmit impulses. Neurons consist of dendrites, the cell body, and an axon, with the cell body being the central functional component. Dendrites carry impulses toward the cell body, while the axon transmits impulses away from it [44,45].

Certain disorders affect nervous tissue, leading to symptoms like memory loss, mood swings, and confusion, as seen in Alzheimer's disease. Amyotrophic lateral sclerosis (ALS) causes a degeneration of nervous tissue, resulting in a gradual loss of higher brain functions. Multiple sclerosis is also among the nervous tissue disorders, wherein the immune system targets and harms the nervous tissue, leading to adverse effects. Huntington's disease is characterized by abnormal protein-induced neuron death, and Parkinson's disease impairs movement control due to insufficient dopamine production [46].

2.4. Epithelial Tissue

Epithelial tissue, known as epithelium, covers the surfaces of organs all over the body, including the skin, trachea, reproductive tract, and digestive tract lining. It serves a multitude of functions, encompassing fortification, absorption, discharging, sensory reception, excretion, filtration, and distribution. Epithelium acts as a protective barrier for organs, aids in the absorption of water and nutrients, eliminates waste, and produces enzymes and hormones [47,48].

All glands in the body originate from epithelial tissue. Epithelial cells possess varying shapes, such as cubical, squamous, or columnar, and can arrange themselves into single or multiple layers. Epithelial tissue diseases include skin conditions like eczema and psoriasis, which manifest as rashes. Carcinoma refers to cancer that originates from epithelial tissue. In the airways, inflammation of epithelial cells can lead to asthma, a condition characterized by breathlessness and airway inflammation [49,50].

3. Biomimetic from ECM and Polymeric Nanofibers

Biomimetics or biomimicry is the practice of imitating models, systems, and elements from nature to solve complex human problems. It involves drawing inspiration from natural selection solutions found in nature and applying those principles to human engineering [51]. Living organisms have developed specialized structures and materials through natural selection over millions of years. Biomimetics has facilitated the creation of innovative technologies that draw inspiration from biological solutions found at both macro and nanoscales. Nature has found solutions to engineering challenges such as self-healing, tolerance to environmental exposure, resistance, hydrophobicity, and self-assembly [52,53]. Designs inspired by biomimicry will ultimately enable human productions to be more efficient, resilient, and sustainable. Biomimicry has applications in various sectors of human activity, including medicine, research, industry, economy, architecture, urban planning, agriculture, and management. It can be directly or indirectly applied to all sectors. Some biomimetic processes have been in use for years, such as the artificial synthesis of certain vitamins and antibiotics. More recently, biomimetics have been proposed for use in electrospun nanofibrous scaffolds that mimic important characteristics of the native extracellular matrix (ECM). This provides a promising strategy for restoring functions and achieving positive outcomes in tissue regeneration [54,55].

Nanofibers in cellular scaffolds imitate the structure of native extracellular matrix (ECM) elements found in diverse tissues and organs such as bone, cartilage, tendon, and skin. This biomimetic approach is based on the principle of mimicking the natural fibrous organization of tissues at the nanoscale level [56]. The nanofibrous scaffold can provide cues to cells, promoting their growth and facilitating the synthesis of authentic extracellular matrices. The electrospun nanofibrous scaffold plays a pivotal role in determining the mechanical properties of tissue scaffold. The nanoscale structures of the scaffold enable interactions with cells, allowing for them to actively engage with the matrix, leading to functionalization, remodelling, and resembling the natural cellular remodelling process within the ECM [57,58]. Continuous efforts are being made to develop biomimetic scaffolds that provide structural support for cell growth, proliferation, and differentiation. These scaffolds are also employed for bringing bioactive molecules, such as growth factors and signalling cues, to support tissue regeneration and enhance cellular responses.

The objective of tissue engineering is to replicate the ECM, which is composed of a variety of proteins like collagen, laminin, and fibronectin that act as cell-binding ligands. In order to encourage cell adhesion between cellular frameworks and the surrounding environment of the ECM, integrin-recognizing peptide sequences are essential [59,60]. Traditional synthetic biodegradable aliphatic polyesters like PLA, PLGA, and PCL continue to be the ideal materials to produce biomimicking nanofibrous scaffolds owing to their exceptional processability, biocompatibility, and mechanical performance. These synthetic polymeric nanofibers have effectively replicated the physical dimensions and morphology of collagen, which serves as a key constituent of the native extracellular matrix (ECM) and the primary structural protein in the human body. Consequently, significant efforts have been made to create collagen-based scaffolds that can closely mimic the natural environment [61].

Various scaffolds have been developed successfully to imitate the three-dimensional (3D) structure of the interstitial ECM. However, limited progress has been made in reproducing the two-dimensional (2D) basement membrane (BM) of the ECM. These membranes play a crucial role in establishing the functional polarization of epithelial and endothelial cell layers throughout the body and are essential for artificial organ technologies [62,63]. Synthetic polymeric nanofibrous scaffolds hold the potential to act as an outstanding biomimetic platform for systematically studying cell–matrix interactions. Biomimetic nanofibrous scaffolds provide a platform for studying cell–matrix interactions and contribute to the design and fabrication of future biomimetic scaffolds in a precise and rational manner.

4. Background of Electrospinning

Since the emergence of nanotechnology, researchers have been interested in examining the distinctive properties and potential uses of nanomaterials [9,64,65]. Electrospun nanofibers are a distinct kind of nanomaterials, owing to their alluring properties in the form of membranes. The best and easiest method for creating nanofibers is electrospinning, which offers versatility, adaptability, and an enormous potential range of applications [10]. Strong electric fields are applied to a polymer blend solution or melt during ES, producing nanofibers that deposit on a grounded collector. ES is an alternative of electrostatic spraying, which has a very long history of 270 years for producing aerosols from fluid drops [11]. From 1934 to 1944, Formhals published a number of US patents outlining the electrospinning setup. Despite early discoveries, ES did not gain much recognition till the early 1990s, when interest in it was revived. The concept of electrospinning dates back to the early 17th century when William Gilbert, an English scientist, first described the phenomenon of electrically induced fibre formation. However, it was not until the 20th century that the modern electrospinning process was developed and refined. The growing popularity of electrospinning was attributed to the increased interest for nanotechnology and the availability of new devices and materials. Since that time, there has been a significant uptick in research concerning electrospinning, as seen by the tremendous increase in publications on the topic and the ongoing involvement of more than 200 research institutions and universities in the study of electrospinning for membrane fabrication. Electrospun nanofibers have found applications in various fields. In healthcare and biotechnology, they are used for drug delivery systems, tissue engineering scaffolds, wound dressings, and filtration media. In materials science, they are utilized for creating composite materials with enhanced properties. Electrospinning offers several advantages, including the ability to produce nanofibers with high surface area-to-volume ratios, tuneable properties, and controlled fibre diameters. The process is relatively simple and can be adapted for various materials [64]. Despite its many advantages, electrospinning has some challenges. The optimization of parameters for specific materials can be complex, and controlling the distribution of nanofibers can be challenging. Additionally, scaling up the process for industrial production can be difficult. Overall, electrospinning has revolutionized the field of nanomaterials and is continually evolving as researchers develop new techniques and applications. It has the potential to impact various industries by enabling the production of materials with unique properties and tailored characteristics [65].

5. Electrospinning Process and Membrane Morphology

Electrospinning has gained recognition for its ability to create scaffolds that mimic the extracellular matrix (ECM), making it a valuable addition to conventional scaffold-production techniques such as gas foaming, solvent-casting, fibre bonding, freeze-drying, particulate leaching, etc., [66,67]. Electrospinning is a highly versatile and cost-effective process that produces long, continuous fibres with diameters ranging from 10 nanometres to some micrometres, achieved by applying high electrical voltage [68–70]. A typical electrospinning setup as depicted in Figure 1 comprises four main components: a high voltage source, a spinneret (typically a hollow metal needle), a collector (grounded or negatively biased), and a syringe pump [71–73]. The syringe pump is employed to propel a polymer solution or melt through the spinneret. As the polymer liquid (solution or melt) is subjected to a high electrical potential, electric charges build up on the face of the liquid drop at the tip of the needle [71,74,75].

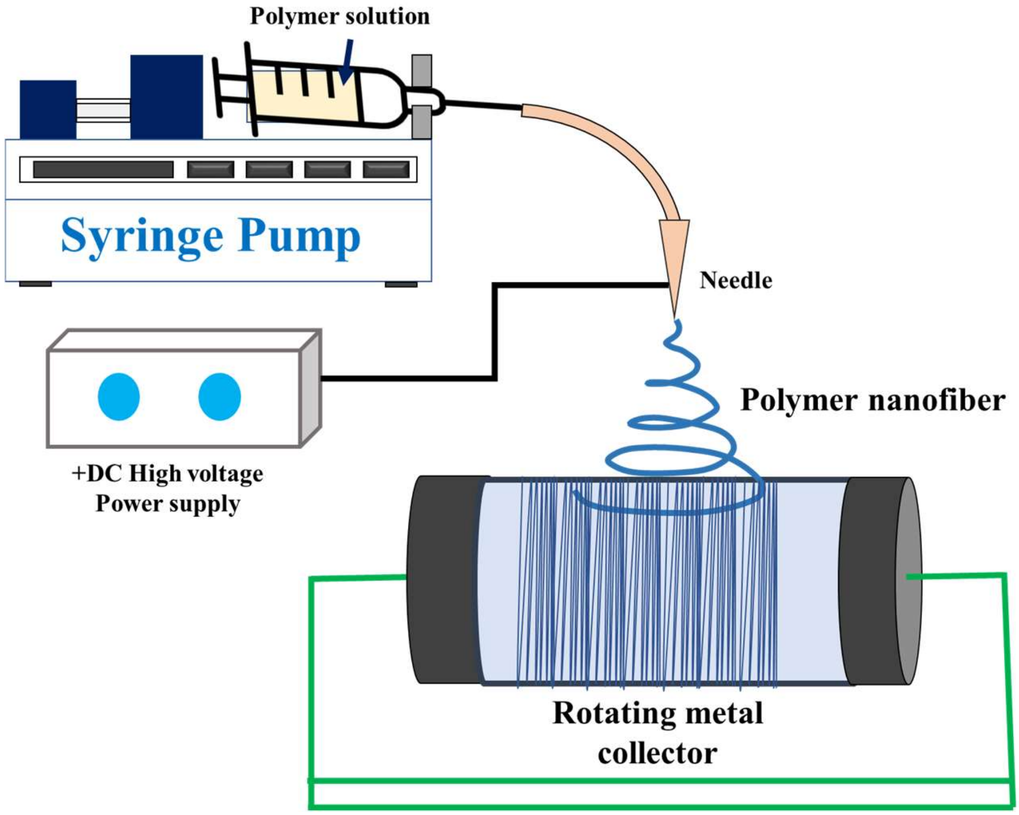


Figure 1. Schematic setup of simple electrospinning machine.

Once the electric field strength surpasses the surface tension of the droplet at a critical voltage, a charged jet is expelled from the tip of the droplet. The jet is continuously elongated and whipped by electrostatic repulsion until it reaches the grounded collector. Throughout this process, the solvent evaporates, and the jet solidifies, resulting in the formation of fibres. Ultimately, the collected fibres come together to form a nonwoven fibrous membrane [76,77].

Although the setup for electrospinning may seem simple, the actual production of fibres is a complicated process that demands cautious concern of various parameters for effective optimization. Nanofiber membranes produced through electrospinning can be tailored to achieve the desired morphology, structure, and functionalities by adjusting several operational, material, environmental, and post-processing parameters [78]. Operational parameters in electrospinning include the applied voltage, feed rate of the solution or melt, distance between tip and collector, collector, and speed.

Material parameters encompass the type and concentration of the polymer, molecular weight, viscosity, conductivity of the solution, surface tension, and the influence of additives. Environmental parameters refer to the ambient conditions within the chamber, such as humidity and temperature [79,80]. Post-processing strategies play a major role in determining the features of nanofibers. Factors such as drying conditions, heat treatment, and hot-pressing techniques greatly influence the final characteristics of the nanofiber membrane. It is crucial to consider all these parameters adequately in order to achieve optimized conditions for the formation of nanofiber membranes [81,82]. By controlling various parameter conditions, it is possible to produce different structures, morphologies, sizes, and functionalities of membrane fibres, as described in Table 1.

Table 1. Effect of parameters on morphology of nanofibrous membranes.

Parameters	Effect on Fiber Morphology
Solution (material) parameters	
Solvent vapor pressure	Increased porosity is associated with greater volatility [83].
Polymeric concentration	Higher concentrations (within the optimal range) lead to an increase in fiber diameter [84].
Solvent choice	The choice of solvent is crucial, as it can significantly affect the solubility and rheological properties of the spinning solution. Different solvents can lead to variations in fiber diameter and morphology [85].
Solution viscosity	Higher viscosity (within the optimal range) results in an increase in fiber diameter. However, exceeding the critical viscosity value can lead to the formation of beaded or deformed nanofibers, and may even cause clogging of the spinneret [86].
Solution surface tension	The surface tension of the spinning solution affects the ability of the solution to form a stable jet. A lower surface tension promotes the formation of thinner fibers, while a higher surface tension results in thicker fibers. Surfactants are sometimes added to adjust the surface tension and improve fiber formation [87].
Solution conductivity	Increasing the conductivity leads to a decrease in fiber diameter, and higher conductivity can result in more pronounced bending instabilities, leading to the formation of non-uniform or beaded fibers [88].
Processing (Operational) parameters	
Voltage	There is no definitive correlation between fiber diameter and voltage; however, it is commonly observed that increases in applied voltage cause a reduction in fiber diameter. Additionally, higher voltages may result in a higher probability of bead formation [89].
Flow rate	Enhancement of the fiber diameter and the occurrence of bead formation are commonly observed at higher feed rates (above the minimum rate) [90].
Needle-collector distance	Within the optimal range, the fiber diameter tends to decrease as the spinneret to the collector distances increases [91].
Ambient (Environmental) parameters	
Temperature	Increasing the temperature generally leads to a decrease in fiber diameter [92].
Humidity	Higher humidity levels tend to induce the formation of circular pores in the fibers [93].

6. Problem in the Electrospinning Process

6.1. Low Productivity

Electrospinning is a highly efficient and commonly used method for manufacturing nanofibers. Withal, conventional single-needle electrospinning systems are not very productive, often producing less than 0.3 g of fibre per hour. Although productivity can be improved by using multi-needle electrospinning systems, these systems have their weakness, such as taking up a large space and experiencing frequent blockages at the needle tip during the spinning process [94–96]. As a result, an alternative method called needleless electrospinning has been developed to eliminate the use of needles. In recent years, various types of spinnerets, such as disk, drum, spherical, spiral coil, or wire spinnerets (Figure 2), connected to a high-voltage source, have been employed by many researchers in needleless electrospinning systems.

In order to increase nanofiber production during the electrospinning process, a needleless electrospinning device using a toothed wheel as the spinneret was recently designed. Additionally, a bullet spinneret was utilized to address the issue of low fibre productivity during fibre production and enable the production of nanofibers at lower applied voltages [98,99]. Hence, the needleless electrospinning system has demonstrated its effectiveness in enhancing productivity. However, for industrial applications, it is crucial to thoroughly comprehend the parameters that influence the electrospinning process in order to accurately predict the quantity and quality of the produced fibres [100].

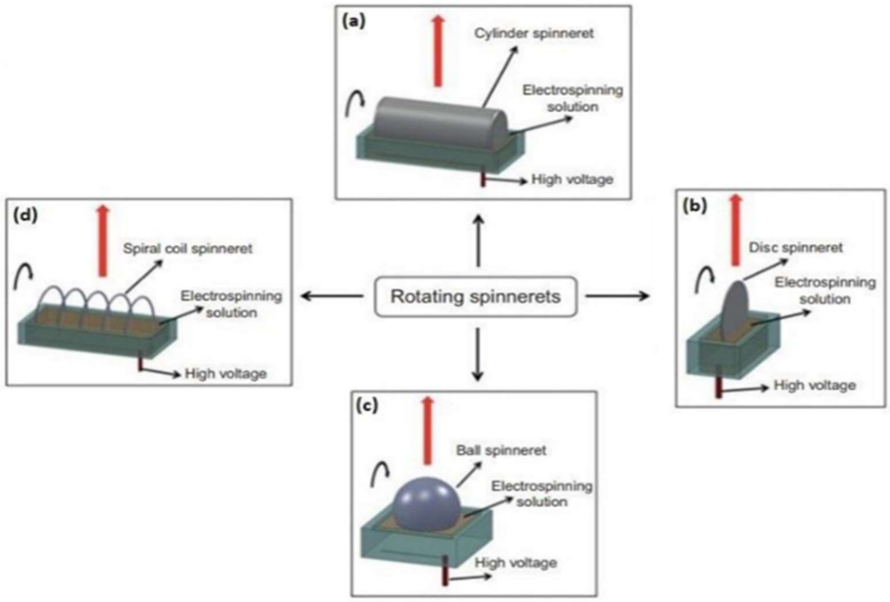


Figure 2. Schematic diagram depicting the (**a**) cylinder spinneret, (**b**) disc spinneret, (**c**) ball spinneret, and (**d**) wire/coil spinneret in needleless electrospinning [97].

6.2. Solvent Toxicity

The morphology of electrospun nanofibers is significantly influenced by numerous factors, such as the concentration of polymeric solution, the viscosity, nature of the solution, molecular weight of the polymer, the solvent, the applied voltage, and the distance between the tip and collector. These factors can be precisely controlled to produce electrospun nanofiber scaffolds with specific functionality. The choice of solvent is one of the factors that is crucial for producing smooth, well-formed nanofibers. Unfortunately, many conventional methods involve the use of harmful and toxic volatile organic solvents (VOCs) due to their high solubility and quick evaporation properties [101–103]. The use of such electrospun fibrous scaffolds is limited in in vitro applications due to the presence f residual solvents, which can be toxic and need to be removed completely before use. These residual solvents not only restrict their biomedical applications but also pose various health risks. For instance, solvents like formaldehyde, phthalates, toluene, chloroform, dimethylformamide, and p-dichlorobenzene can lead to serious health hazards such as nausea, infertility, neurological disorders, leukaemia, and cancer. The use of toxic, flammable, or environmentally harmful solvents appears unnecessary as these characteristics do not affect the function or progress of the electrospun fibres in biomedical applications [104–106].

6.3. Dense Compact Fibers

Electrospun nanofibers find a wide range of applications across various fields due to their unique properties and versatility. These nanofibers mimic the structure of native tissues and provide important cues for cell differentiation and migration. They are used in tissue scaffolds, drug release, biosensors, and the development of artificial implants such as bone, skin, or cartilage. However, a major challenge lies in achieving scalable and controllable assembly of nanofibrous structures. Most electrospun nanofibers are confined to two-dimensional (2D) membranes, which consist of densely packed layers of nanofibers. When cells are cultured on these membranes, they only form a layer on the surface, limiting their infiltration and growth throughout the fibre matrix [107]. The porous and three-dimensional (3D) structure of nanofibers offers great potential as a biomimetic support system that can replicate the extracellular matrix for cell growth.

Many studies have demonstrated successful in vitro experiments, and some have also investigated in vivo applications. Additionally, 3D electrospun fibres create interrelated porous networks with high surface-to-volume ratios and substantial empty spaces.

This unique structure facilitates nutrient supply and transport while also offering ample space for cell migration and attachment within the scaffold. Cell linkage, differentiation, movement, and propagation are influenced by the specific interactions between cells and the extracellular matrix (ECM). Therefore, it is sensible to anticipate that the 3D fibres, especially when surface-modified, would promote favourable cellular responses and have promising applications in tissue engineering [108]. Hence, various approaches have been explored to revise the conventional electrospinning system or the electrospun nanofibrous membranes in order to achieve a 3D architecture. It has been observed that a 3D multilayered nanofibrous structure outperforms conventional 2D electrospun nanofibers in terms of cellular infiltration and growth.

Numerous strategies were employed for fabricating 3D electrospun fibrous macrostructures, including post-modification of 2D electrospun fibres (such as folding, layer-by-layer stacking, electrospinning,) and through assembly using assisting elements (such as 3D templates and liquid collectors) [109]. The electrospun cellulose mat was subjected to treatment with sodium borohydride solution to create a 3D cellulose sponge suitable for tissue engineering purposes (Figure 3a–d). The morphology of the synthesized materials was investigated using an FE-SEM technique, as indicated in Figure 3e–j. The biomimetic mineralization and cell proliferation of the 3D cellulose sponge were assessed. The freshly prepared cellulose sponge demonstrated an excellent ability to initiate hydroxyapatite formation from simulated body-fluid solution. The mineralized 3D sponge exhibited enhanced cell infiltration, growth, and proliferation compared to the cellulose mat [110,111]. Consequently, the electrospun and post-treated cellulose sponge with sodium borohydride holds great promise for tissue engineering applications.

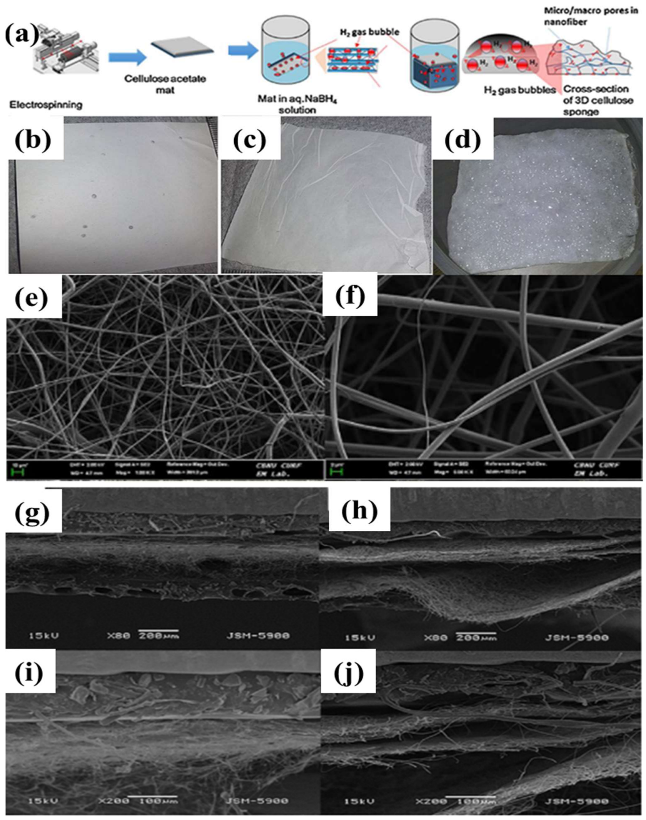


Figure 3. (**a**) Overall synthesis process of 3D cellulose sponge, (**b**) 2D cellulose mat, (**c**) regenerated cellulose mat, (**d**) 3D cellulose, (**c**,**d**). Digital images of showing images of (**a**) CA mat, (**b**–**d**) showing the conversion of 2D cellulose mat into 3D cellulose sponge, (**e**,**f**) FE-SEM images of 3D cellulose sponge at different magnifications, (**g**,**h**) cross-section images of 2D, and (**i**,**j**) cross-section images of 3D cellulose sponge [3]. Reprinted with permission from Carbohydrate Polymers. Copyright © 2015 Elsevier Ltd.

7. Recent Advancement of Electrospinning

7.1. Advancement in Electrospinning Machine

In addition to the traditional electrospinning technique, various modifications of this method have been recently developed. These include co-electrospinning or co-axial electrospinning, multi-needle, and needleless electrospinning. The multi-needle and needleless electrospinning techniques are employed to improve the productivity of the conventional electrospinning process [112]. On the other hand, co-axial electrospinning has been developed to produce core–shell and multilayer composite nanofibrous structures, offering improved functionalities and superior quality compared to conventional electrospinning methods. In co-axial electrospinning, two separate nanofiber components are fed through different coaxial capillary channels and combined to form core–shell composite nanofibers [113].

The introduction of co-axial electrospinning has played an important role in the comprehensive production of various functional nanomaterials. For instance, co-axial electrospinning has enabled the efficient production of two-layer core–shell polymer nanofibers. Co-electrospinning, on the other hand, is commonly employed to fabricate single-layer and bilayer nanofibers. However, these nanofiber structures have limitations in terms of assembly configurations and functionalities [114,115]. By increasing the number of nanofiber layers, the connectivity and functionalities of composite materials can be improved. Recent research has demonstrated the fabrication of multifunctional nanofibers with more than two layers using co-electrospinning. Additionally, the needleless electrospinning system has been widely adopted by researchers to increase fibre productivity [116]. This system utilizes two high voltage sources, one connected to the rotary drum collector and the other to the conductive wire, as illustrated in Figure 4.

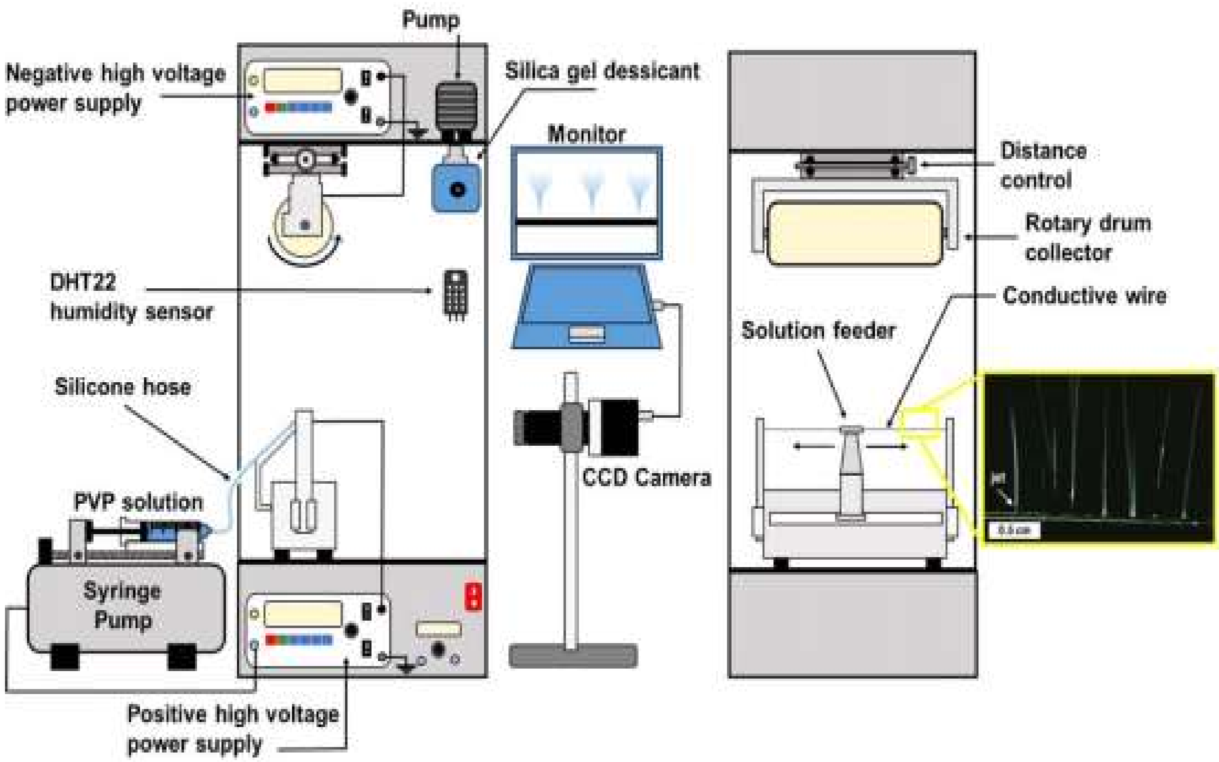


Figure 4. Schematic representation of needleless electrospinning setup [99].

7.2. Post-Electrospinning Process for Membrane Modification

Although the electrospinning setup is simple, the production of fibres is complex and requires careful consideration of multiple parameters for optimization. Electrospun nanofiber membranes can be tailored to achieve the desired morphology, structure, and functionalities by controlling various operational, material, environmental, and post-processing parameters, such as drying temperature and humidity [117,118]. After the formation of nanofibers on the collector, residual solvents may still be present in the mat.

Therefore, additional post-treatment methods are typically employed to ensure complete drying. The drying process is typically carried out in a dry or vacuum oven at a temperature slightly below the boiling point of the solvent employed [119]. This controlled temperature allows for the residual solvent to evaporate slowly without forming pores, which could occur if a higher temperature were used for drying. Maintaining low humidity during the drying process is crucial to prevent moisture from permeating the nanofiber membrane. High humidity could potentially cause phase separation or pore formation within the nanofibers, which should be avoided to preserve their integrity and desired properties [120,121].

7.3. Replacement of Toxic Organic Solvent by Green Solvent

Electrospinning has traditionally relied on the use of VOCs as solvent to dissolute polymeric materials. The selection of solvents is based on their capacity to dissolve the polymer chains effectively and evaporate rapidly over the short distance between the nozzle and the collector during the electrospinning process. During this process, large amounts of such toxic vapor may degrade the indoor air quality and cause serious health problems for humans. Moreover, in various applications such as tissue engineering, biomedical, and agriculture, the toxicity of these organic solvents is a critical concern [122,123]. Residual traces of these chemicals can have negative long-term environmental impacts and pose health hazards. For instance, prolonged exposure to toluene is suspected to cause organ damage, while chloroform and DCM are classified as likely carcinogens to humans according to the World Health Organization [124].

Similarly, acetonitrile, acids, formaldehyde, tetrahydrofuran, dimethylformamide, tetrafluoroethylene, methylene chloride, dichloroethane, and pyridine have also been connected to bad effects on human health. Additionally, many air fresheners contain five main ingredients: formaldehyde, phthalates, parabens, petroleum distillates, and p-dichlorobenzene, which can pose serious health hazards such as nausea, infertility, neurological dysfunction, leukaemia, and cancer [125]. This highlights the necessity for alternative, non-toxic, and environmentally friendly solvents [126].

8. Essential Oils as Green Solvent

Essential oils are organic, volatile, concentrated liquids that are secreted by tiny structures in a plant's various parts. They are also referred to as volatile oils, ethereal oils, or aetherolea. Each essential oil takes its name from the specific plant it is derived from. For example, the oil extracted from lavender flowers is known as lavender oil. These oils are a blend of natural compounds, including volatile organic compounds (VOCs) like terpenes, phenols, alcohols, and esters. Various methods such as steam distillation, cold pressing, solvent extraction, or effleurage are utilized to extract essential oils, depending on the plant and the desired outcome [127]. Different plant parts, such as flowers, leaves, stems, bark, roots, or seeds, can be used in the production process. The name "essential" was given to these oils because it was once believed that they captured the true essence of a plant, encompassing its distinctive odour, flavour, and applications due to the variety of constituents present in it. Figure 5 shows some major constituents of essential oils and their chemical structures.

Throughout history, essential oils have been used worldwide in the cosmetics, food industry, biomedical, and aromatherapy industries, as well as various household applications [129]. Figure 6 indicates the potential applicability of essential oils infused electrospun nanofibers.

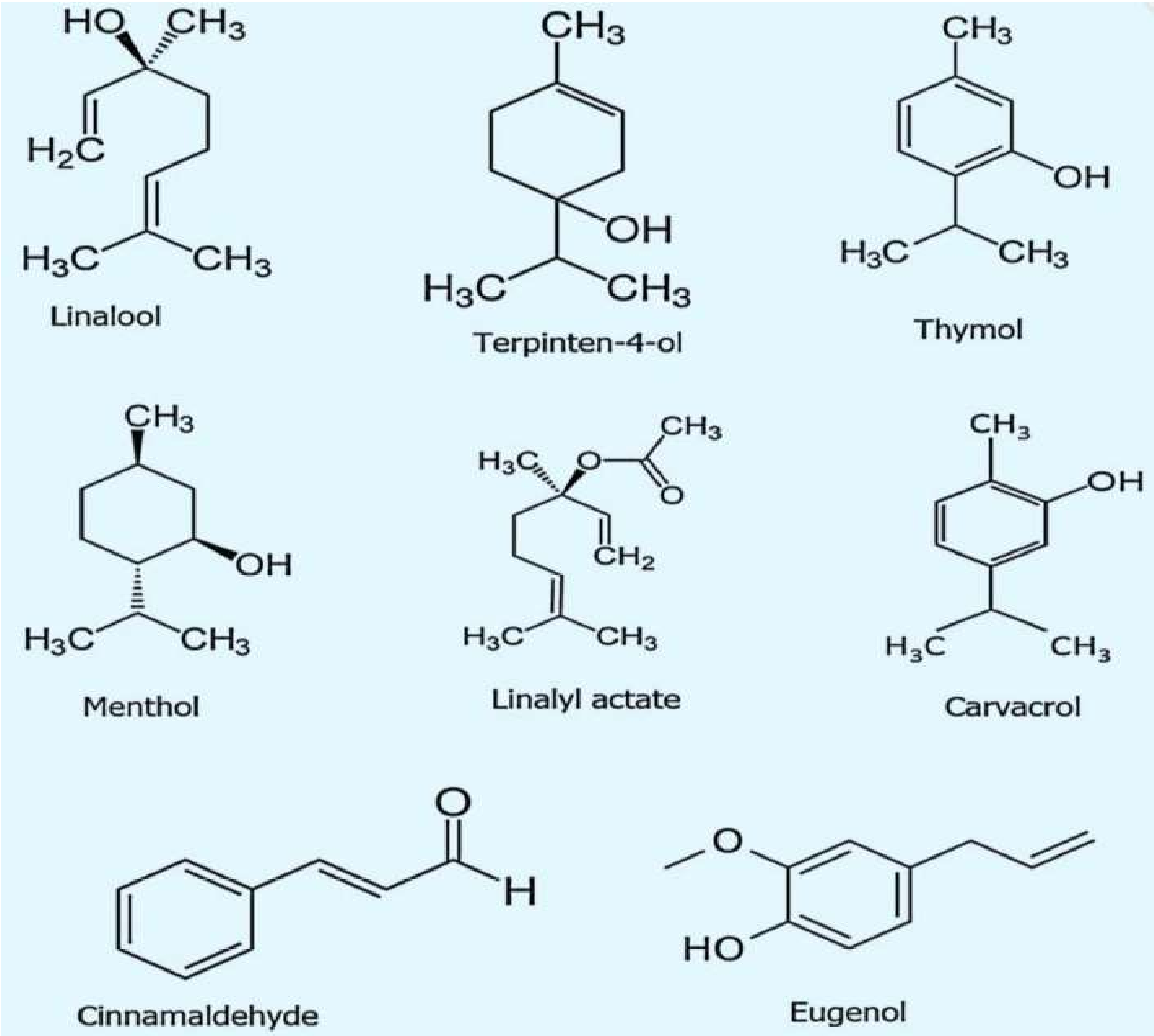


Figure 5. Chemical structures of some of the major constituents found in essential oils [128].

While it is challenging to pinpoint the exact origin of their usage, the first recorded instances of essential oils are believed to come from ancient civilizations in India, Persia, and Egypt. The trading of aromatic oils and ointments was prevalent among Greece, Rome, and Eastern countries, further spreading the use of essential oils across different cultures [127,130]. Essential oils are renowned for their therapeutic properties, which encompass calming, energizing, uplifting, and soothing effects. They have found applications in fabric fresheners, and medicines such as pills, powders, suppositories, ointments, scented baths, and more. Beyond their pleasing fragrances, some essential oils exhibit valuable antimicrobial, anti-inflammatory, and antioxidant properties, making them beneficial for natural health and wellness practices [131,132]. The quality of EOs depends upon the plant species along with geography and altitude in where they are grown. Their antibacterial, antifungal, antioxidant, anticancer and biocompatibility can vary with changing altitude, edaphic factors, and climatic conditions. This is due to the variation in types and concentration of secondary metabolic substances present in plant species.

Conversely, incorporating Essential Oils (EOs) into electrospun nanofibers can enhance their characteristics. Due to heightened pathogen antibiotic resistance and worries about additive-related side effects, consumers are seeking natural alternatives like herbal essential oils. Consequently, there has been a growing utilization of plant extracts, essential oils, and pure active components in electrospinning. This technique effectively merges nanofiber attributes with plant compounds as Eos [133,134]. Three methods have been developed for loading essential oils (EOs) into electrospun nanofibers (NFs). The simplest way involves directly electrospinning a mixture of EOs and polymer solution to create EO-blended NFs. Another approach involves loading EOs into a carrier before electrospinning to create NFs with EO-filled carriers. The latest method involves creating core–shell structured NFs by injecting core and shell substrates through separate syringes connected to a blunted loaded NF, so that products will emerge shortly [135,136]. In this context, different works have been performed to infuse essential oils into natural and synthetic polymers to enhance their broad application especially in biomedical field.

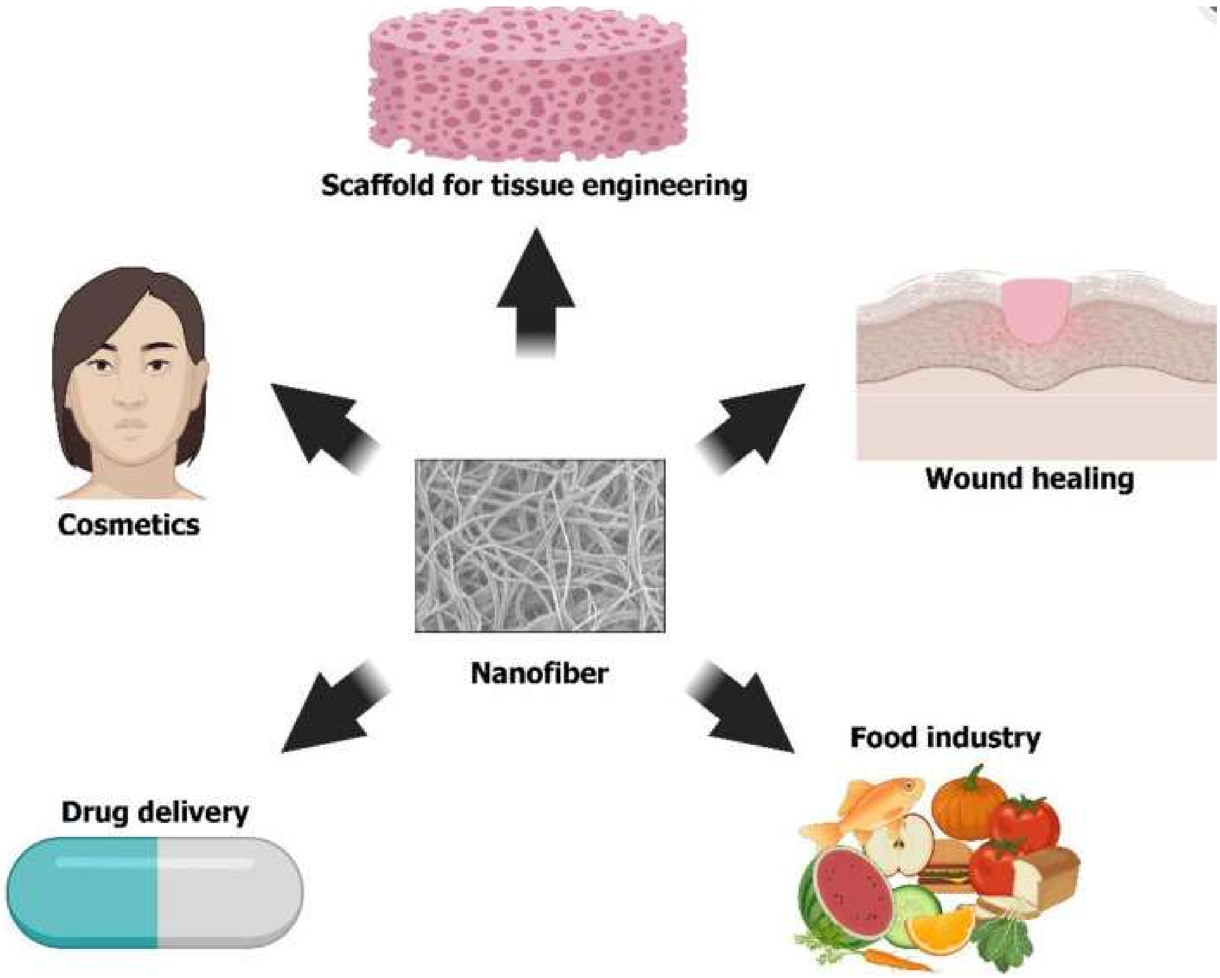
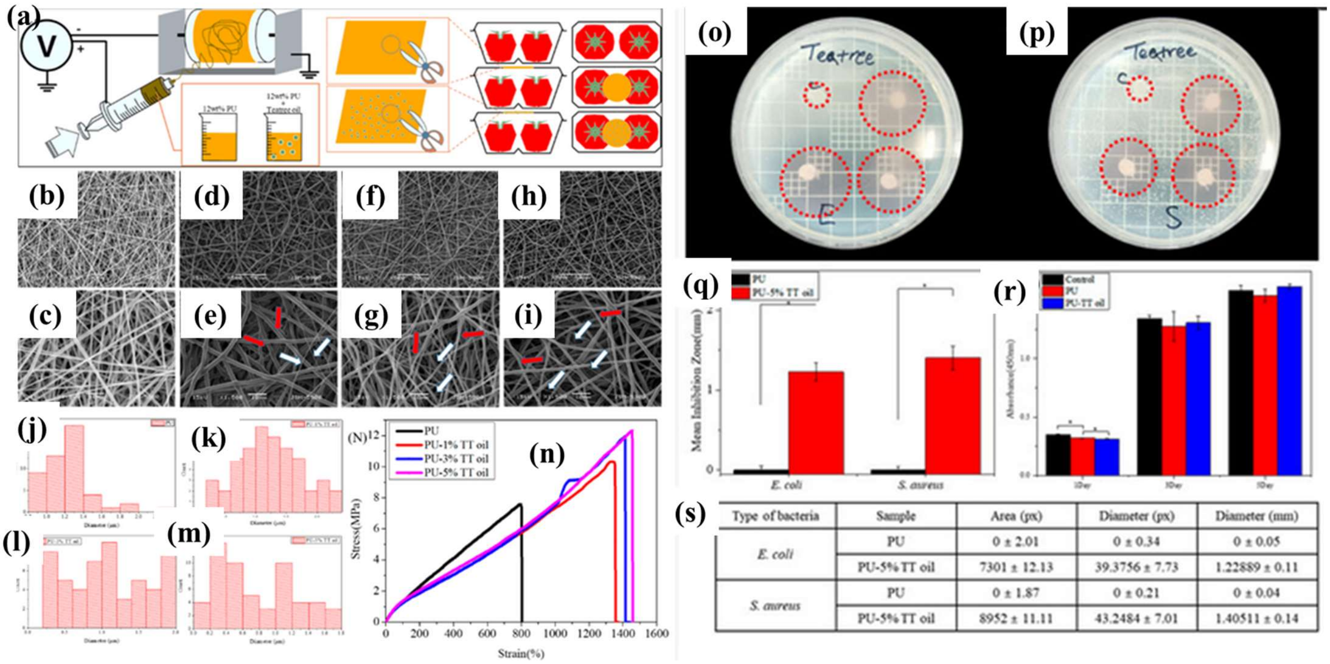


Figure 6. Potential applications of essential oils infused electrospun nanofibers [128].

There has been growing interest in essential oil (EO)-loaded electrospun dressings for wound healing. These dressings offer better wettability, biocompatibility, faster wound healing, and stronger antimicrobial effects. EOs likely stimulate fibroblast migration to wounds and have potential antimicrobial properties. This boosts collagen production and wound remodelling, while some EOs prevent infections. Diluted EOs are loaded into polymer solutions, stirred for dispersion, and then electrospun into fibres [137]. For example, chitosan/poly(ethylene oxide) (PEO) scaffolds blended with cinnamon EO treat *Escherichia coli* and *Pseudomonas aeruginosa* infections. Cinnamon EO's effectiveness against *E. coli* extends to cellulose acetate nanofibrous dressings. In food packaging, cinnamon EO combats microbial contamination and spoilage. Cinnamon EO and β-cyclodextrin in polylactic acid (PLA) fibres inhibit *E. coli* and *Staphylococcus aureus* growth. Lavender EO was electrospun with polyacrylonitrile (PAN) and sodium alginate to prevent skin wound colonization (*S. aureus, Klebsiella pneumonia*), exhibiting anti-inflammatory properties. Sodium alginate and lavender oil also demonstrated anti-inflammatory effects [135,136]. Gutarowska et al. [138] used herbal-infused *Hypericum perforatum* oil with polylactic acid for wound dressings, showing high antibacterial properties. Manikandan et al. [139] created a polyurethane scaffold with murivennai oil, enhancing hydrophilicity and blood compatibility. Mani et al. [140] combined neem essential oil and magnesium oxide in an electrospun polyurethane scaffold, yielding improved properties for wound healing applications. Park et al. [141] synthesized PU nanofibers infused tea tree essential oils (TTEO) of various concentrations (1, 3, and 5%) via the electrospinning technique, as indicated in Figure 7a. They investigated the effect of TTEOs concentration in the nanofiber diameter, mechanical strength, and antimicrobial properties. As the concentration of TTEO increased (Figure 7b–m), the diameter of nanofibers and mechanical strength increased simultaneously (Figure 7n). Moreover, 5 wt.% TTEO-infused PU nanofibers showed better antibacterial activity against Gram-negative/positive bacteria (Figure 7o–s).



Type of bacteria	Sample	Area (px)	Diameter (px)	Diameter (mm)
E. coli	PU	0 ± 2.01	0 ± 0.34	0 ± 0.05
	PU-5% TT oil	7301 ± 12.13	39.3756 ± 7.73	1.22889 ± 0.11
S. aureus	PU	0 ± 1.87	0 ± 0.21	0 ± 0.04
	PU-5% TT oil	8952 ± 11.11	43.2484 ± 7.01	1.40511 ± 0.14

Figure 7. (**a**) Schematic representation showing the overall synthesis process of PU/TTEO nanofibers, (**b**–**i**) FE-SEM images of PU/TTEO nanofibers with 1, 3, and 5% of TTEO, (**j**–**m**) histogram showing diameter of PU/TTEO nanofibers with 1, 3, and 5% of TTEO, (**n**) stress–strain curve, and (**o**–**s**) antibacterial test of PU/TTEO-5% nanofibers [141].

Furthermore, Milanesi et al. [142] created nano-textured fibres using PLA solutions with black pepper essential oil (BP-EO) or limonene. These porous nanofibers were then coated with chitosan, boosting antibacterial properties, biocompatibility, and support for cell adhesion and growth. Antibacterial tests on *S. aureus*, *S. epidermidis*, *E. coli*, and *P. aeruginosa* demonstrated chitosan and EOs working together synergistically. Fibers with BP-EO and limonene exhibited stronger antibacterial activity compared to pure PLA. Coated fibres outperformed uncoated ones in microbial activity, indicating chitosan's positive impact on stopping bacterial growth in PLA-EOs fibres.

In a separate study, lemon balm and dill essential oils were enclosed within collagen hydrolysates taken from bovine tendons and rabbit skins. These were combined with chitosan using coaxial electrospinning, with a focus on their potential use in wound dressings. In vivo tests indicated strong biocompatibility of the resulting electrospun samples, indicating that they have potential as wound dressings [143,144]. Phan et al. [145] successfully synthesized AgNPs and coated orange essential oil (OEO) onto cellulose (CL) nanofibers. The combined AgNPs and orange EO showed strong antibacterial properties against *E. coli* and *B. subtilis*. Orange EO coating allowed for sustainable silver release over 48 h. *E. coli* exhibited notable antibacterial synergy, while orange EO content did not impact effectiveness against *B. subtilis*. OEO and AgNPs in cellulose nanofibers could serve as biomaterial to prevent bacterial infections in masks, clothing, and packaging though further research needed for commercial applications [146].

In other study, Berechet et al. [147] created biocompatible, antimicrobial nanofibers using collagen hydrolysate and thyme/oregano essential oils (EOs). They used electrospinning to incorporate the essential oils, resulting in nanofibers with diameters of 471–580 nm and a porous structure. The composite showed no cytotoxicity up to 1000 $\mu g \cdot mL^{-1}$ for collagen and 500 $\mu g \cdot mL^{-1}$ for the oils. Optimized electrospinning led to collagen nanofiber mats with thyme/oregano essential oils for potential use in wound dressings, tissue engineering, or protective clothing.

In recent times, essential oils have been integrated into electrospun fibres, serving not only to impart bioactivity but also to manipulate the thermal characteristics of the resulting mats [148]. In one study by Souza et al. [149], the use of 20% Linalool led to an 18% decrease in the glass-transition temperature (Tg) of PLA fibres. In a separate investigation, incorporating 15% candeia EO into PLA fibres resulted in a Tg reduction of 30%. In both instances, the natural extracts functioned as plasticizers for PLA, influencing polymer chain mobility and decreasing interactions between chains. All the aforementioned research revealed that essential oils continue to be cherished and utilized as a green solvent in a diverse range of applications across the globe. Common essential oils are schematically represented in Figure 8a–e; their fundamental characteristics and potential medical uses are detailed below.

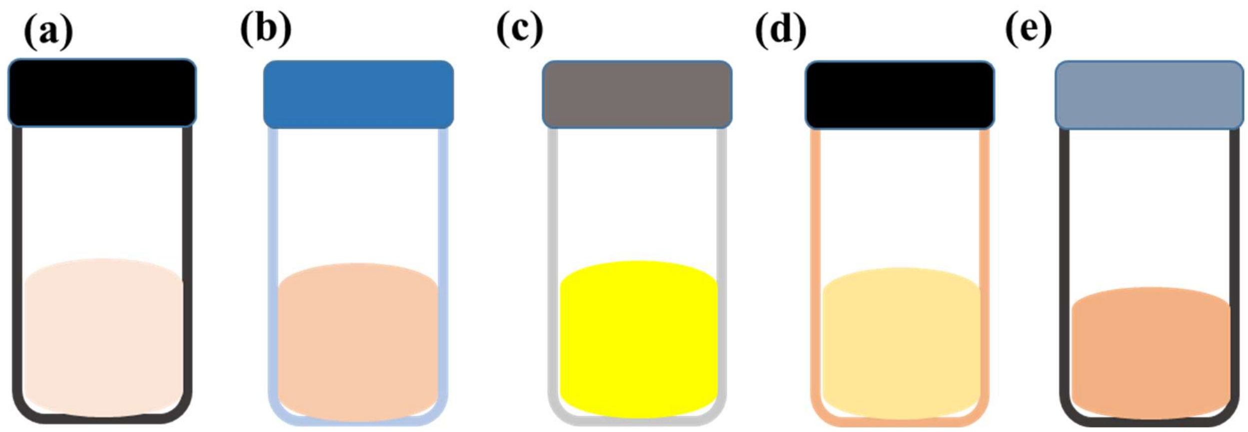


Figure 8. Schematic representation of different types of essential oils; (**a**) lavender oil, (**b**) eucalyptus oil, (**c**) lemon oil, (**d**) tea tree oil, and (**e**) clove oil.

8.1. Lavender EO

Lavender oil, extracted from *Lavandula angustifolia* flowers through steam distillation, is primarily composed of linalyl acetate, linalool, lavandulol, 1,8-cineole, lavandulyl acetate, and camphor [150,151]. Lavender essential oils (LEOs) exhibit effective antimicrobial properties against various bacteria, filamentous fungi, and yeasts. Additionally, lavender oil has shown antipseudomonal activity, making it potentially beneficial in combating *Pseudomonas* infections [35,152,153].

8.2. Eucalyptus EO

Eucalyptus oil is extracted from eucalyptus leaves and contains 1,8-cineole, α-pinene, limonene, and other compounds [154]. It has antimicrobial properties against both Gram-negative and Gram-positive bacteria. Research suggests it may enhance the immune response and could be used in immune suppression, infectious diseases, and tumour chemotherapy [155].

8.3. Lemon EO

Lemon essential oil is extracted from fresh lemon peels through steam extraction or cold-pressing [22,156]. It can be applied topically when diluted or diffused for inhalation. The oil mainly comprises terpenes and oxygenated terpenes. It demonstrates antifungal properties against the *Candida species*, making it a potential remedy for candidiasis caused by *C. albicans* [157,158].

8.4. Tea Tree EO

Tea tree oil is obtained through steam distillation of *Melaleuca alternifolia* leaves. It effectively treats fungal infections and boosts immunity [34]. It is a potent remedy for acne, reducing acne-causing bacteria, and drying out active acne. It is ideal for oily skin [159].

8.5. Clove Oil

Clove oil is extracted from the leaves, stem, and buds of Syzygium aromaticum through water distillation and contains eugenol, eugenyl acetate, carvacrol, thymol, cinnamaldehyde, β-caryophyllene, and 2-heptanone [160,161]. It is renowned for therapeutic properties and is commonly used in dentistry. Additionally, it exhibits antibacterial and antifungal activities [162,163].

8.6. Cinnamon Oil

Cinnamon oil is extracted from the leaves and barks of *Cinnamomum verum*. The major components of the oil include (E)-cinnamaldehyde, linalool, -caryophyllene, eucalyptol, and eugenol and it shows antioxidant, antiproliferative antimutagenic, and antimicrobial properties [164]. The chief chemical component of cinnamon oil is cinnamaldehyde which is also known as cinnamic aldehyde, which comprises between 60–90% of cinnamon oil. Other constituents include cinnamyl acetate, cinnamyl alcohol, cuminaldehyde, eugenol, linalool, and pinene. It has antimicrobial activity against Gram-negative bacteria (*E. coli*) as well as Gram-positive bacteria (*S. aureus*) and also exhibits cell proliferation properties [165].

8.7. Wintergreen Oil

Wintergreen essential oil is obtained from the steam or hydrodistillation of the leaves of the *Gaultheria species.* The major component of the oil is methyl salicylate [166]. The essential oil shows antioxidant and antimicrobial activities**.** It reduces pain and swelling in the underlying tissue and is also used to kill germs on the skin [167].

9. Significance of Essential Oils in Nanofiber Formation

Essential oils have gained significant attention in various fields, including nanofiber formation, due to their unique properties and potential benefits. Essential oils are recognized as natural, environmentally friendly, biocompatible, non-toxic, and cost-effective solvents [168]. When incorporated into nanofiber materials, essential oils can enhance the performance and functionality of the resulting products and also help to minimize or eliminate the need for hazardous organic solvents in various applications [169]. The combination of essential oils with nanofibers has shown potential advantages and unique properties, leading to their impact and significance in several areas.

9.1. Enhanced Antimicrobial Properties

Many essential oils possess natural antibacterial and antimicrobial properties. By incorporating these oils into nanofibers, the resulting materials can effectively inhibit the growth of bacteria and microorganisms. These essential oil-infused nanofibers could find applications in wound dressings, air filtration systems, and other medical or hygienic products, contributing to better infection control and prevention. For example, orange essential oil has been successfully used as a green solvent replacement for toluene in the production of polystyrene nanofibers [170]. These eco-friendly nanofibers can find application in areas like wound healing and active food packaging. Using orange essential oil as an alternative solvent instead of toxic volatile organic compounds (VOCs) helps to reduce the toxicity of electrospun fibres [171,172]. Motealleh et al. [173] prepared PCL/PS nanofibers containing 15% of the chamomile extract by electrospinning technique and used them for wound dressing applicaitons. The photographs in Figure 9a,b showed the change in colour of nanofibrous mat with the addition of chamomilla extract. The diameter of the nanofibers was decreased from 268 to 175 nm by adding the M. chamomilla extract, as indicated by FE-SEM images in Figure 9c,d. The created inhibition zone was 7.6 mm for both *S. aureus* and *C. albicans*. In the release study, about 70% of the M. chamomilla was released at the wound site, which is a positive feature for wound healing. The examination of the rat wound model also showed that within 14 days, the wound treated with the extract containing nanofibers was completely closed and healed as indicated in Figure 9e,f.

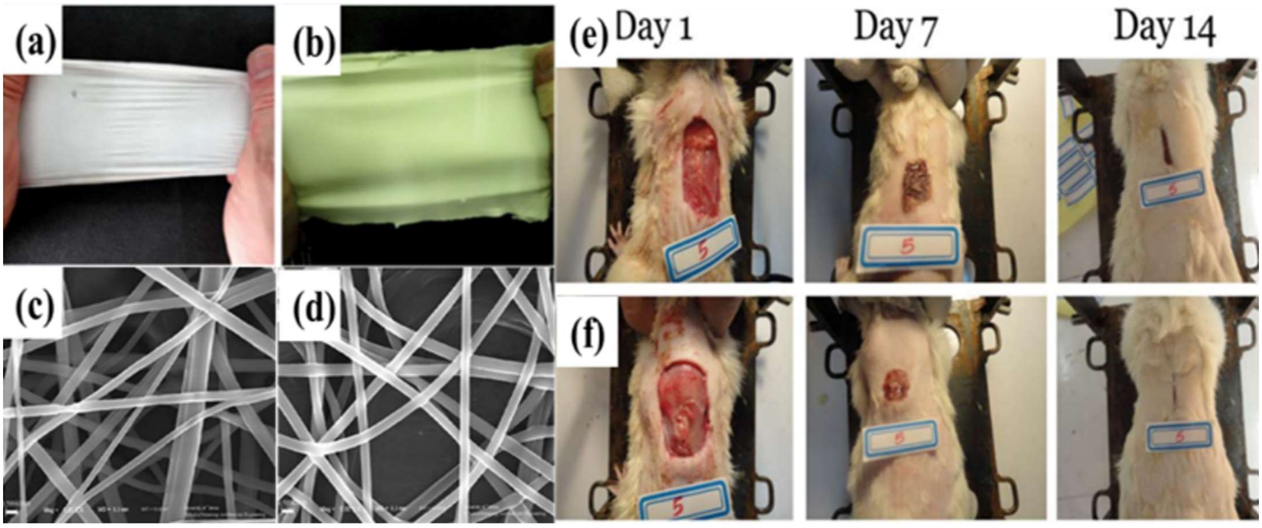


Figure 9. Digital photographs: (**a**) PCL/PS nanofibers, (**b**) the PCL/PS nanofibers with chamomile extract. FE-SEM images: (**c**) PCL/PS nanofibers, (**d**) the PCL/PS nanofibers with chamomile extract, and in vivo wound healing investigation: (**e**) skin wound treated with pure PCL/PS nanofibers and (**f**) skin wound treated with pure PCL/PS nanofibers containing chamomile [173]. Adopted with the permission from Journal of Biomedical Materials Research part A, John Wiley and Sons, © 2013 Wiley Periodicals, Inc.

The study conducted by Khataei et al. [174] focused on the production of electrospun fibres composed of PA-6 (polyamide-6), PVP (polyvinylpyrrolidone), and TTO (tea tree oil). The research aimed to investigate the potential applications of these fibres, particularly in wound healing. The findings of the study showed several positive attributes of the produced electrospun fibres: (a) inhibition of free radicals and pathogenic bacteria, and the presence of TTO in the fibres imparted them with antioxidant and antibacterial properties. This means that the fibres have the ability to neutralize harmful free radicals, which can cause cellular damage, and also possess the capacity to combat pathogenic bacteria, reducing the risk of infections in wound healing. (b) Cell adhesion support: The study revealed that as the content of TTO increased in the electrospun fibres, they exhibited enhanced support for cell adhesion. This suggests that the fibres promote the attachment and growth of cells, which is crucial for tissue regeneration and wound healing.

Based on these findings, they concluded that the PA-6/PVP/TTO electrospun fibres have great potential as a suitable scaffold for wound healing applications. The combination of PA-6 and PVP with the added benefits of TTO makes these fibres promising materials for use in wound dressings or tissue engineering scaffolds. Their antioxidant and antibacterial properties can aid in the healing process by protecting the wound from oxidative stress and preventing infections. Additionally, their ability to support cell adhesion encourages tissue growth and repair.

9.2. Bioactive and Biocompatible

Essential oils derived from natural sources are generally considered bioactive and biocompatible [175]. When integrated into nanofiber materials, they are less likely to cause adverse reactions or toxicity, making them suitable for biomedical applications like tissue engineering, drug delivery, and wound healing [176–178]. Wang et al. [179] selected clary sage and black pepper essential oils to prepare PLA nanofiber, and studies have shown that these essential oils impart antibacterial, anti-inflammatory, or anti-oxidant properties on electrospun fibres. The inclusion of essential oils resulted in changes in the chemical, thermal and surface properties of the electrospun fibres, as demonstrated by SEM investigations (Figure 10a–d). The resulting composite fibres, which also exhibited antibacterial properties, have potential biomedical applications as dressings that are able to prevent bacteria colonisation in wounds and promote skin regeneration (Figure 10e–j). Particularly, the nano-topography created on the surface of the PLA/EO fibres is attractive to the development of scaffolds that provide both physical and chemical cues for skin repair.

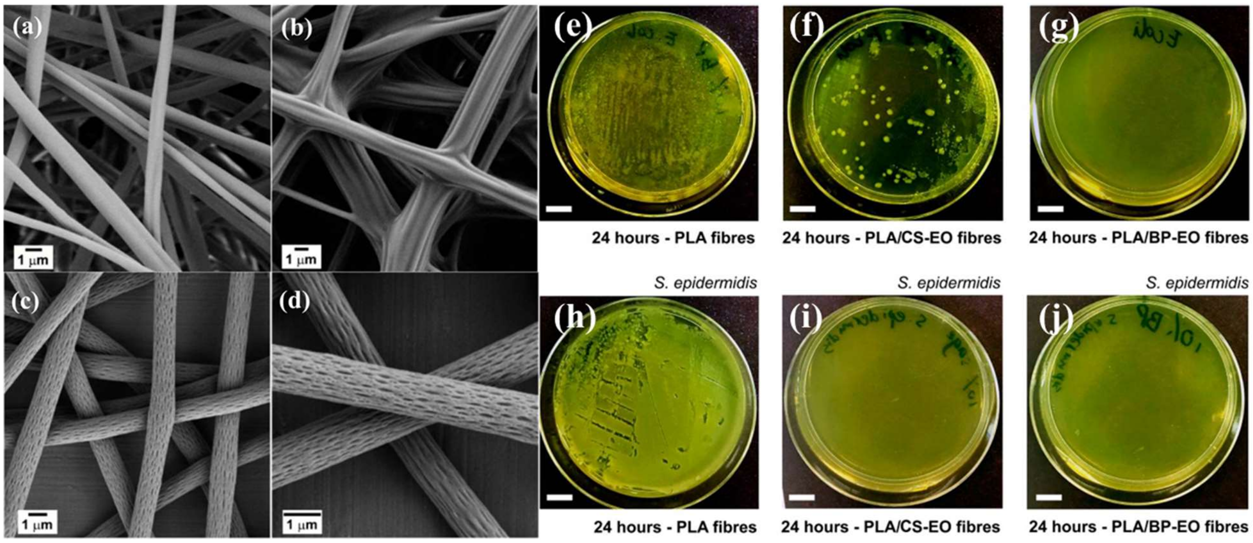


Figure 10. FE-SEM images; (**a**) PLA nanofibers, (**b**) PLA/Cs-EO (10% *v*/*v* CS-EO) nanofibers, and (**c**,**d**) PLA/BP-EO ((10% *v*/*v* BP-EO) nanofibers at different magnifications. Photographs of growth of *E. coli* (**e**–**g**) and *S. epidermidis* (**h**–**j**) after incubation with PLA, PLA/Cs-EO (10% *v*/*v* CS-EO), and PLA/BP-EO ((10% *v*/*v* BP-EO) nanofibers, respectively [179].

9.3. Improved Mechanical Properties

The integration of essential oils into nanofibers can indeed have a significant impact on the mechanical properties of the resulting materials [180]. When essential oils are incorporated into nanofibers they can interact with the polymer matrix and alter its properties in several ways, leading to improved mechanical characteristics. The mechanical properties of nanofibers play a crucial role in determining their potential applications in various fields. Depending on the type of essential oil and its concentration, the following improvements in mechanical properties can be observed.

Enhanced tensile strength: Certain essential oils, when integrated into nanofibers, can reinforce the polymer matrix and enhance the overall tensile strength of the material. This means that the resulting nanofibers can withstand higher levels of mechanical stress and stretching without breaking or deforming. Improved tensile strength is especially desirable in applications where strength and durability are critical, such as in protective clothing or filters [181].

Increased flexibility: Essential oils can enhance the flexibility and elasticity of nanofibers, making them more pliable and adaptable to different shapes and surfaces. This property is valuable in applications where the material needs to conform to complex geometries, such as tissue engineering scaffolds or wound dressings [182].

Impact on toughness: Essential oils may improve the toughness of nanofiber materials, making them more resistant to cracking or fracturing under stress. This can be beneficial in applications where the material will experience repeated mechanical forces [183].

On the whole, the improved mechanical properties of nanofibers due to the incorporation of essential oils open up new possibilities for their use in various fields [184]. The enhanced tensile strength and flexibility make them attractive candidates for applications such as protective clothing in harsh environments, advanced filters for air and water purification, and tissue engineering scaffolds for regenerative medicine [185].

9.4. Controlled Release of Active Compounds

Nanofibers have a high surface area to volume ratio, which allows for the efficient encapsulation and controlled release of active compounds like essential oils. By modifying the nanofiber structure or using different carrier materials, it is possible to control the release rate of the essential oils, making them suitable for sustained drug delivery or long-lasting fragrance applications [186,187].

9.5. Aromatherapy and Wellness

Essential oils are well-known for their aromatherapy benefits. When integrated into nanofibers, they can release their pleasant and therapeutic scents gradually, promoting relaxation (sleep masks), stress-relieving factors, and overall well-being. Such nanofiber-based products can be used in air fresheners, personal care items, and even in healthcare settings to create a soothing atmosphere [188].

9.6. Natural and Sustainable Materials

Essential oils are derived from plant sources and are generally considered natural products. When used in nanofiber formation, they can help create sustainable materials that are biodegradable and eco-friendly. This aspect is particularly relevant in the context of reducing environmental impact and developing green technologies [189]. Marina Stramarkou et al. [184] successfully incorporated rosemary essential oils into bio-polymeric matrices (PLA and zein) using the innovative method of electrospinning and the conventional method of extrusion. The superior encapsulation efficiency of electrospun fibres was 91.3%. In conclusion, the produced structures have the potential to be integrated in greenhouse and low-tunnel films with the aim of providing pesticide activity and replacing agrochemicals.

9.7. Food Packaging and Preservation

Some essential oils such as clove oil, peppermint oil, citronella oil, etc., possess natural antioxidant and antimicrobial properties that can help extend the shelf life of food products and prevent spoilage. By incorporating essential oils into nanofibers, it becomes possible to create food packaging materials with improved preservation capabilities [190].

Incorporating essential oils into nanofiber formation offers multifarious advantages, including antimicrobial properties, aromatherapy benefits, controlled release of active compounds, enhanced mechanical properties, eco-friendliness, biocompatibility, and flavour/fragrance applications [191,192]. As research in nanotechnology and essential oils advances, we can expect to see even more innovative applications and uses for these unique essential oil-infused nanofibrous materials. Various essential oils have been used in electrospun fibres for different applications, as listed in Table 2.

Table 2. EOs-blended electrospun nanofibers membranes and their applications.

Essential Oils	BP (°C)	Main Component	Polymeric Solution	Application Areas
Green tea oil	165	Terpinene	Chitosan-PEO	Wound healing [193]
Chamomile oil	161	Terpenoids organic acids	PCL-PS	Wound healing [173]
Tea tree oil liposomes	165	Terpinene	Chitosan-PEO	Antimicrobial properties [194]
Cinnamon oil	194–234	Cinnamadehyde	PVA	Food packaging [195]
Clove oil	251	eugenol	PLA	Antimicrobial activity [196]
Cinnamon oil	194–234	Cinnamadehyde	Chitosan-Gelatin	Antibacterial activity [197]
Oregano oil	239	Thymol	Cellulose Acetate	Antimicrobial properties [198]
Cinnamon oil	194–234	Cinnamadehyde	Xanthan-chitosan	Antimicrobial properties [199]
Lavender oil	204	Linalool	Polyacrylonitrile	Antimicrobial properties [200]
Mustard oil	170	Erucic acid	Polyurethane	Blood compatibility test [201]
Black pepper oil	166	Trans-aryophyllene	Polylactic acid	Wound healing [142]
Palmarosa	100	Geraniol	Polyvinyl Alcohol	Wound healing [202]
Lemongrass oil	228	Citral	Nylon-6,6	Air freshener [203]

9.8. EOs as Next Generation Green Solvent

From the reported works discussed in above sections, we found that a sufficient amount of EOs are miscible with polymer solutions and easily able to produce EO-infused polymer electrospun nanofibers. These results clearly show that polymers should be dissolved in some EOs and can produce electrospun nanomembranes without using traditional toxic organic solvents. Recently, our research team achieved a significant breakthrough in the field of polymer processing by identifying locally available Himalayan essential oils, namely cinnamon, wintergreen, and lemongrass, as green solvents for FDA-approved polycaprolactone (PCL) polymer (unpublished work). This innovative research has led to the successful fabrication of electrospun membranes of PCL-EOs using the electrospinning method, employing these essential oils as solvents. The outcomes of this research have far-reaching implications as the electrospun membranes exhibited remarkable properties, including antimicrobial activity and the ability to promote cell proliferation. The use of essential oils as green solvents is a groundbreaking development in the realm of polymer processing. Traditional solvents often pose environmental and health hazards due to their toxicity and adverse effects. In contrast, essential oils are known for their non-toxic, biocompatible, and eco-friendly characteristics. This pioneering research opens doors to a more sustainable and environmentally responsible approach to polymer fabrication and processing.

10. Conclusions and Future Remark

Electrospun nanofiber scaffolds/membranes produced through the electrospinning method have shown great potential in various fields. These include filtrating, enzyme confinement, sensors, cosmetics, shielding clothing, affinity membranes, tissue scaffolds, drug delivery, and wound dressing applications. Due to the unique features of electrospun nanofibrous membrane, the electrospinning method plays a crucial role in biomedical fields, particularly in tissue engineering. Progress is being made to develop electrospun nanofiber scaffolds with improved cell infiltration capabilities, enabling them to function as 3D scaffolds.

Despite their unique properties, electrospun nanofibers have limitations. One challenge is the proper handling and disposal of nanofiber-based products, as many of them contain harmful and toxic organic solvents. It is crucial to explore and select environmentally friendly and non-toxic alternatives, such as essential oils, for electrospun fibrous membranes. In the future, the replacement of toxic solvents with safer options like essential oils, along with the use of synthetic biocompatible and biodegradable polymers, will be thoroughly investigated to promote the production of environmentally friendly membranes. There is no doubt that electrospun fibres prepared by using essential oils will play significant role in future biomedical applications.

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