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Electrospun nanofibers based on plant extract bioactive materials as functional additives: possible sources and prospective applications

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Electrospun nanofibers based on plant extracts have garnered increasing interest as valuable bioactive materials for medicinal and packaging applications. This concise review examines recent studies on functional plant extract nanofibers, emphasizing their fabrication techniques, antimicrobial characteristics, and potential applications. Plant extracts having bioactive compounds are generally obtained from diverse natural sources that can be incorporated into electrospinning solutions to develop functional nanofibers with enhanced germicidal activities. Key findings suggest that nanofibers integrated with natural bioactive materials possess adequate antibacterial, antioxidant, anti-inflammatory, and anticancer properties and are considered expedient biocompatible materials for use in biomedical and food packaging. The potential biomedical applications of these nanofibers include wound healing, drug delivery, and tissue engineering owing to their germicidal activity, biodegradability and biocompatibility, while packaging applications leverage antibacterial and food preservation capabilities. However, some constraints, including insolubility of some extracts, insufficient mechanical robustness for electrospinning, and lack of green solvents to mitigate bio-toxicity, have hindered their diversified applications. The current review, therefore, summarizes future research avenues concerning the scope of overcoming the limitations in this burgeoning field. Overall, plant extract functional nanofibers demonstrate their potential for utilization in biomedical and food packaging applications, but more research is needed to scale up production and make these eco-friendly biocomposite materials commercially available.

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Introduction

The emergence of electrospinning technology to produce fibrous structures with micro and nano dimensions has drawn significant attention in recent years due to its predominant advantages over other techniques.[1] This electrofluidodynamic technique involves the interaction of the polymer solution moving at a constant flow rate with a high-voltage electric field at the tip of the needle that is directly connected to a power supply.[2] A significant number of natural and synthetic polymeric materials, including polyamide, polyester, PCL, polyacrylonitrile, chitosan, collagen, starch, PVC, PEO, and PVA, have been used individually and collectively in electrospinning, maintaining the required processing parameters for particular application.[3,4]

The formation of nano-inscribed biomaterials utilizing this method is a contemporary issue because of their potential to provide professional protection in health care, military personnel, and other day-to-day emergency response applications.[5–13] Electrospun nanofibers can also act as effective barriers against microorganisms, particles, and liquids, as well as enhance the mechanical, thermal, and chemical properties of the protective products.[14,15] For example, electrospun nanofibers can be used to fabricate masks, respirators, and personal protective equipment (PPE) for medical and healthcare applications. Conventionally, the development of nano biomaterials with various functionalities, including germicidal activity, involves the usage of metal nanoparticles and synthetic antibiotics. However, their detrimental effects on the environment and human health, and/or bacterial resistance issues have triggered a surge in the use of natural antimicrobial compounds which are expected to be non-toxic, sustainable, and less prone to creating resistant bacteria.[16,17]

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Plant extracts, with the advantage of their inherent medicinal properties, have been used for numerous purposes, especially in treating various diseases from time immemorial, and are considered to be the most prominent sources of biomolecules, which can be screened from different parts of a plant, for example, seeds, leaves, stems, flowers, *etc.*[18] With the advent of various solvents and advanced extraction methods, the extraction of such biomolecules from medicinal plants has become more effective in terms of quantity and purity for their use in specific purposes. The commonly used techniques for plant extraction include maceration,[18] digestion,[19] decoction,[20] infusion,[21] percolation,[22] Soxhlet extraction,[23] superficial extraction,[24] ultrasound-assisted extraction,[25] and microwave-assisted extraction.[26] Successful extraction also involves employing various solvents of different polarity, including polar to nonpolar, with a reasonable quantity for appropriate and excellent yields of extracts and biomolecules.[27]

Several studies have proposed that solvents such as ethyl acetate,[28] hexane,[29] dichloromethane,[30] chloroform,[31] acetone,[32] ethanol,[33] methanol,[34] and butanol,[35] and/or a combination of solvents in suitable ratios are the best solvent systems for extracting plant extracts. Because of improved biocompatibility, biodegradability, low toxicity, and intrinsically large surface area, nanofibrous mats are currently fabricated by incorporating such medicinal extracts as functional additives for enhanced biological activities and have emerged as novel materials for various biomedical applications, such as wound dressing,[36] tissue engineering,[37] and drug delivery.[38–40] A significant number of research studies are therefore conducted on developing plant extract-based nanofibers to explore their formation, characterization, and potential applications in various fields. For instance, preparation of electrospun nanofibrous mats incorporating *Azadirachta indica*,[41] *Curcumin longa*,[42] chitosan,[43] henna,[44] *Aloe vera*,[45] moringa,[46] sericin,[47] lignin,[48] honey,[49] ginger,[50] keratin,[51] propolis,[52] *etc.* in combination with various carrier polymers for wound dressing and other biomedical purposes has been rigorously investigated in several contemporary research studies. Increasing efforts towards the process optimization and functionalization of the nanomats are also being made to

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diversify their use. To date, fewer than 200 experiments have focused on developing plant extract-based nanofibers, a small number compared to the extensive research on electrospinning post-commercialization (Fig. 1a). This figure is expected to grow as interest in sustainable and bioactive materials increases. Fig. 1b illustrates the diverse research interests in electrospinning technology, with a significant emphasis on polymer science (41%), highlighting its foundational role in nanofiber production. The substantial focus on agricultural and food chemistry (18%) and biomedical materials (16%) underscores the potential of electrospun nanofibers in biodegradable packaging and advanced medical applications, respectively. The notable portions dedicated to biochemistry and pharmaceutics (15%) and nanoscience (10%) indicate ongoing efforts to enhance pharmaceutical formulations and understand nanofiber properties at the nanoscale, demonstrating the technology's multidisciplinary impact. The novelty of this paper lies in its comprehensive examination of the integration of plant extracts into electrospinning solutions, highlighting the innovative techniques used for fabricating advanced functional nanofibers and their potential applications in biomedical and packaging fields. Additionally, it provides a detailed discussion of the benefits of green electrospinning as a sustainable alternative to metallic nanoparticles.

Considering the current research gap, the purpose of the present review is to compile the existing research on plant extract bioactive materials and their integration into electrospinning solutions for creating functional nanofibers. This review aims to highlight the fabrication techniques, potential applications, and challenges in developing plant extract-based nanofibers, offering insights into overcoming these limitations for future advancements. Besides, the adverse effects of metallic nanoparticles and the importance of green electrospinning, followed by the formation and characterization of functional nanofibers, have been explained meticulously. Various challenges in fabricating plant extract-based nanofibers and potential scopes to overcome the limitations have also been discussed in detail.

Electrospinning fundamentals

Electrospinning is defined as a process of fabricating ultrafine nanofibers (nanometer size) by ejecting a charged polymer solution or melting through a spinneret under a high-voltage electric field, followed by its solidification in the form of filament.[53,54] Key steps include preparing the polymer solution, loading it into a syringe, applying high voltage to create a Taylor cone, forming nanofibers as the solution is ejected towards a grounded collector, and collecting the fibers on a non-woven mat.[55] Challenges such as controlling fiber diameter and morphology, scalability, and ensuring uniform nanoparticle distribution are crucial considerations. The electrospinning technique was initially invented by J. F. Cooley in 1900, and W. J. Morton improved the design of the electrospinning setup immediately thereafter, in 1902.[56,57] Later on, J. Zeleny described the behavior of fluid droplets at the extremity of metal capillaries, and since then, the utilization of needle-equipped spinnerets has become a common practice.[58] The work of A. Formhals, who patented 22 improvements of the electrospinning technique between 1931 and 1944, significantly enhanced the field.[59–61] This work not only dealt with the process itself but also resulted in an improved apparatus for preparing nanothreads. In 1938, N. Alber, N. D. Rosenblum, and I. Kurchatov promoted the first commercial application of nanofibers.[62] They developed filter materials known as ''Petryanov filters'' from electrospun fibers and were awarded the Stalin Prize for their efforts.[58,60,63]

The theory behind electrospinning was developed by Sir G. I. Taylor in 1969 and was the first mathematical modeling of

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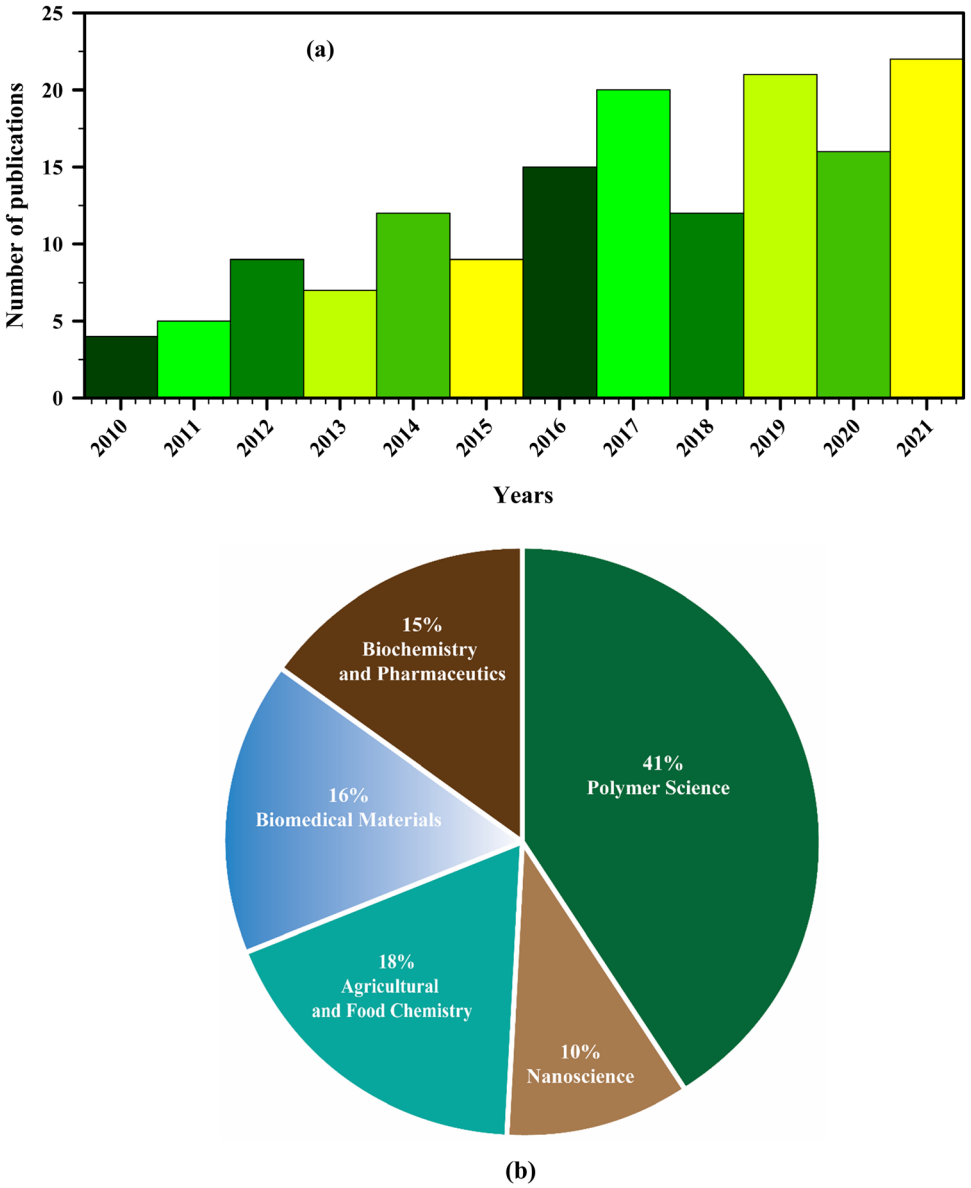

Fig. 1 Published research articles relevant to plant extract-based nanofibers: (a) quantity of papers published based on year and (b) data analyses according to subject area (data obtained from SciFinder, searching for "plant extract nanofibrous").

electrified fluids.[64] He modeled the behavior of fluid droplets under the effect of an electric field and mathematically explained the formation of the cone, later named the Taylor cone.[64] In the last 20 years, a number of patents and patent applications have been developed on the topic of electrospinning by large industry players such as Elmarco, Dienes, eSpin Technologies, Nano Technics, KATO, Donaldson Company, Freudenberg Tech, *etc.* As of now, around fifty thousand (50 000) articles, patents, and books have been published on electrospinning.[65]

The incorporation of plant extracts into nanofibers presents significant challenges and limitations, primarily due to the potential for variability in extract composition and concentration, which can affect the consistency and reproducibility of the nanofibers' properties. Additionally, the stability of plant extracts during the electrospinning process and their long-term stability within the nanofibers are critical issues. Various electrospinning techniques also pose challenges, including controlling fiber diameter and morphology, scalability for industrial production, and ensuring uniform distribution of nanoparticles within the fibers.[66] These limitations necessitate ongoing research and optimization to fully leverage the benefits of plant extract nanofibers.

Classification of electrospinning

The electrospinning process can be classified into four broad types: solvent-free electrospinning, electrospinning from solution, electrospinning from ionic liquids (ILs), and colloid electrospinning, also known as suspension electrospinning.

Several techniques of electrospinning are illustrated in Fig. 2 (with needle) and Fig. 3 (needleless). Solvent-free electrospinning is particularly well suited for tissue engineering and wound dressing materials since the produced fibrous materials are suitable for further treatment. However, only a few researchers have paid attention to this solvent-free electrospinning process.[67]

Melt electrospinning, supercritical CO_2-assisted electrospinning, anion-curing electrospinning, UV-curing electrospinning, and thermo-curing electrospinning are all examples of solvent-free electrospinning. The most significant benefits of these systems are efficient, controlled, and environmentally friendly processes that produce harmful residue-free ultrafine fiber. As a result, it is very engaged in biomedicine, tissue engineering, and textile engineering. However, because of the high setup requirements due to the precursor's comparatively greater viscosity, large diameter fibers due to no solvent evaporation, and electrical bending instability, this technique is not widely employed.[67]

Solution electrospinning, the most extensively used method, requires the use of suitable solvents to solubilize the polymers and form homogeneous polymer solutions. It has a number of distinct advantages, including the availability of solvents, an elevated level of interest in biomaterial manufacturing, and the ability to commercialize the technique for bulk nanofiber manufacture.[36,68] Because most biopolymers do not dissolve in water, this method of electrospinning requires the use of appropriate solvents. Even though some polymers are dissolvable in water, the surface tension of water might make it difficult to obtain smooth nanofibers. However, this method has notable drawbacks, including challenges related to the dielectric constant, conductivity, and volatility of the solvents used.[68]

Green solvents, such as ionic liquids (ILs), are an emerging research area in biopolymer dissolution. Environmentally friendly nature, effective dissolving of carbohydrate materials, good thermal stability, low vapor pressure, and variable viscosity are only a few of the benefits of ILs.[69–72] The different types of ionic liquids result from how various forces work together, such as coulombic, van der Waals, and hydrogen bonding forces. These bonds and forces allow properties including viscosity, density, solubility, melting temperature, and hydrophobicity to be tailored to fulfill a variety of processing needs.[73] These solvents also have the benefit of being able to be separated and recovered fast, unlike traditional solvents.

In addition to the abovementioned electrospinning methods, colloid or suspension electrospinning is a unique method of producing nanofibers. Like the solution electrospinning, this system requires three essential components: application of high voltage, needle, and collector. The fundamental benefit of this technique is that it keeps colloids in fibers immobilized. Colloids in the electrospinning feed, on the other hand, complicate the prediction of a system's theoretical features of physicochemical parameters.[74]

Physiological and ecological aspects of metal nanoparticles

In healthcare applications, such as cosmetics, pharmaceuticals, and food industries, synthetic antibiotics and metallic compounds utilized in biomedical nanofibers have been linked to elevated health and environmental risk.[17] To date, several investigations on

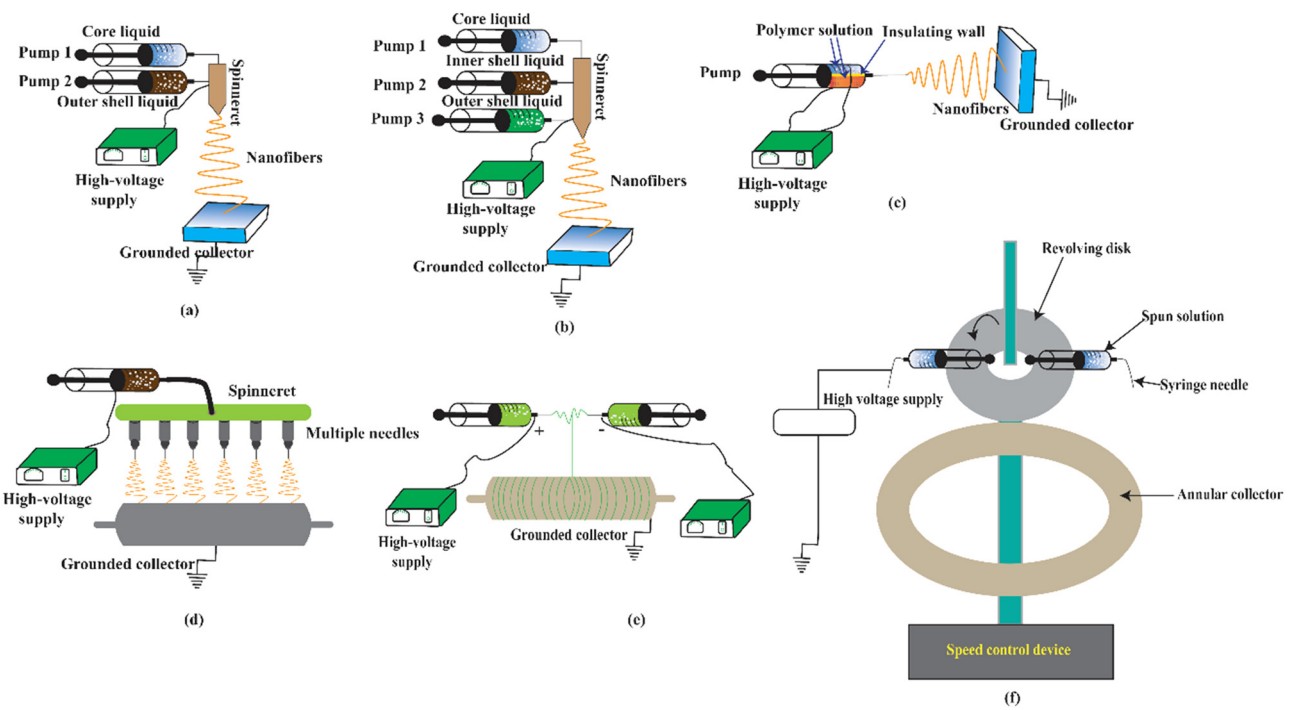

Fig. 2 Schematic diagram of forming nanofibers using different electrospinning techniques with needle: (a) co-axial, (b) tri-axial, (c) side-by-side bi-component, (d) multi-needle based, (e) conjugate, and (f) centrifugal electrospinning.

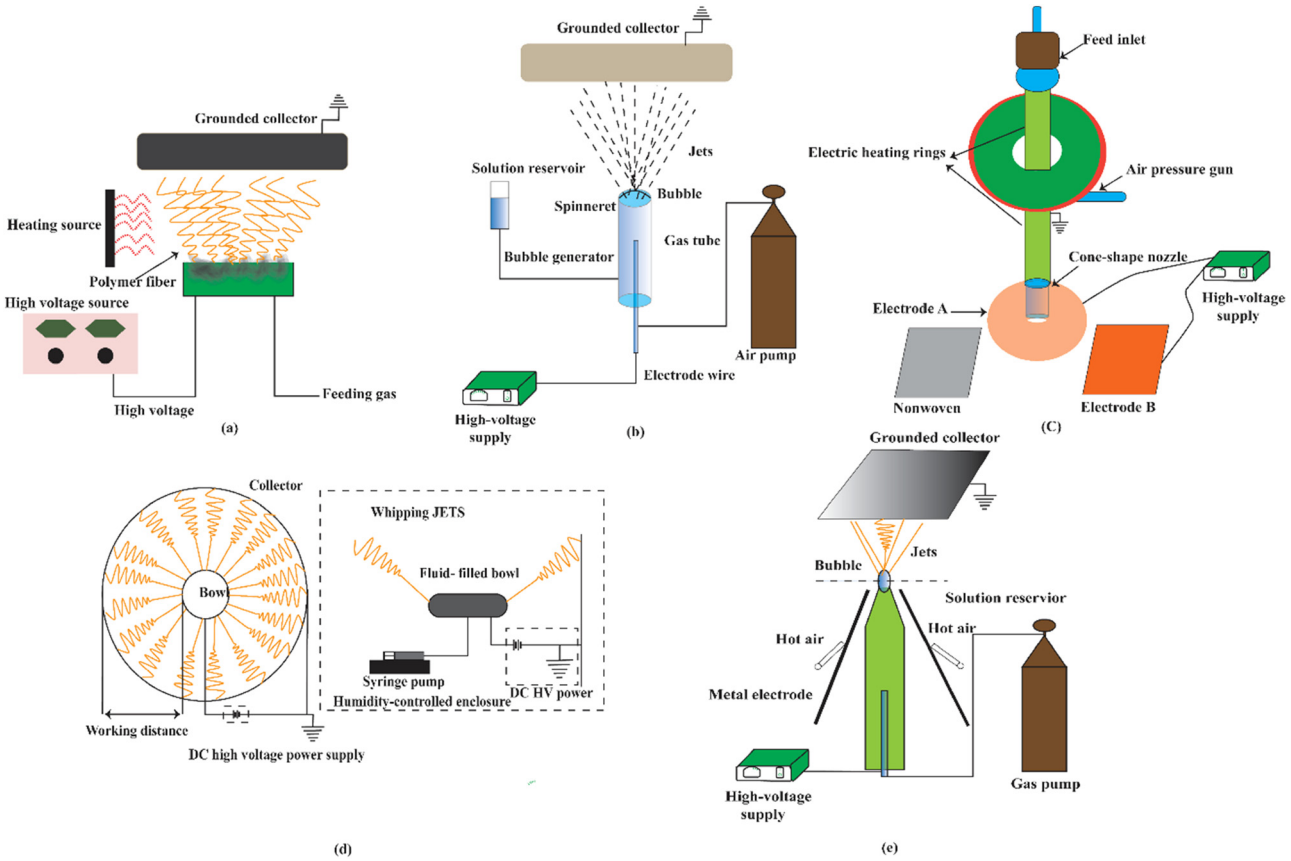

Fig. 3 Schematic diagram of forming nanofibers using different needleless electrospinning techniques: (a) multi-bubble, (b) single-bubble, (c) gas-assisted melt differential, (d) edge, and (e) blown bubble electrospinning.

metal particle-based nanofibers for biomedical applications have been conducted. Silver, gold, and zinc particles are the most used metal particles, as shown in Table 1. These particles have no negative impact on the human body when used in moderate amounts.[75,76] Nonetheless, these nanoparticles have a number of distinct advantages when used in biomedical electrospun nanomats. Silver nanoparticles (AgNPs) are the most extensively employed substance in nanomats. The efficacy and antibacterial and bactericidal effects of AgNPs have been studied in a number of investigations. The efficiency of these nanoparticles against multi-resistant and biofilm-forming bacteria was their main advantage.[77–79] Bergin and Adhaya *et al.* showed that AgNPs and silver sulfadiazine were beneficial in treating chronic wound and burn infections.[80,81]

However, despite these benefits, metallic compounds have several detrimental impacts on health and the environment. According to Adhaya *et al.*, these chemicals could cause tissue toxicity.[81] Furthermore, some researchers claim that silver-based biomedical nanomaterials cause blue-gray coloration on the skin after a prolonged time due to increased melanin production caused by silver, resulting in skin diseases such as argyria[100] and reoccurrence of silver-resistant bacteria.[101–103] Szmyd *et al.* reported that high AgNP concentrations impair keratinocyte viability, metabolism, and migration by activating

Table 1 Health hazards associated with metallic nanoparticles

Metallic particles	Potential adverse effects	Ref.
Silver nanoparticles and silver nitrate	Tissue toxicity, skin diseases such as argyria, cell death, and dose-dependent DNA damage, highly toxic to mammalian cells, sperm cell damage	81–89
Zinc oxide nanoparticles	Hazardous to mammalian cells	83, 84, 90 and 91
Gold nanoparticles	They can easily enter the cell membrane and assemble into vacuoles	84, 92 and 93
Iron oxide nanoparticles	DNA damage, oxidative stress, mitochondrial membrane dysfunction, and changes in gene expression	88 and 94
Piroxicam	Ulcers, bleeding, or holes in the stomach or intestine	95
Titanium dioxide nanoparticles	Vesicle formation after internalization, apoptosis, cytotoxic	96
Silicon dioxide nanoparticles	Reactive oxygen species (ROS) generation, lipid peroxidation – oxidative stress	97
Copper oxide nanoparticles	Dose-dependent oxidative stress, genotoxic effects, kidney, liver, and spleen are the target organs	98 and 99

caspase 3 and 7, which are implicated in cell death and dose-dependent DNA damage.[82]

A series of studies have demonstrated that AgNPs are highly toxic to mammalian cells[104–106] including brain cells,[107] liver cells,[107] and stem cells.[104] McAuliffe *et al.* revealed in another significant investigation that AgNPs harmed male reproduction due to their high toxicity. According to this study, AgNPs pass the blood–testes barrier and are deposited in the testes, causing sperm cell damage.[108] Takenaka *et al.* found in their studies that AgNPs can cause damage to the cardiovascular system. They looked at the pulmonary and systemic distribution of inhaled ultrafine elemental AgNPs in rats and discovered silver in the lungs after the exposure had finished. They also discovered that Ag was present in significant amounts in the blood, kidney, spleen, nose, brain, and heart.[109] Because of their large surface area and small particle size, AgNPs can interact with membrane surfaces and propagate throughout the human body. This contact with membranes may produce extremely reactive and harmful radicals, such as reactive oxygen species, which can induce inflammation and damage mitochondrial cells. It has also been connected to neurological issues, gastrointestinal distress, headache, and fatigue.[110]

Similarly, ZnONPs are widely used in various hydrogel-based wound dressing materials.[90,111] ZnONPs, on the other hand, have been reported to be less hazardous to mammalian cells than AgNPs.[112,113] Coatings, cosmetics, packaging, and medicinal applications are only a few of the applications of these nanoparticles.[114,115] Most investigations looked into the cytotoxicity of ZnONPs concerning their extracellular dissolution.[116] This occurs because of an increased level of $[Zn^{2+}]$. A study revealed that 300 mg kg^{-1} ZnONPs cause cellular damage in the liver of mice after 14 days of subacute oral therapy. In addition to high alanine aminotransferase and alkaline phosphatase levels, there were pathological lesions in the liver. ZnONPs increase lipid peroxidation to demonstrate oxidative stress. The liver was subjected to oxidative stress, which generated Fpg-specific DNA damage.[117]

AuNPs are also employed in nanofiber fabrication. These particles are used in wound therapy because of their chemical stability. They have antibacterial and healing properties both *in vitro* and *in vivo*, as investigated by Arafat *et al.*[118,119] AuNPs are usually considered to be bioinert, but questions have been raised regarding their safety. However, Lu *et al.* found that these particles' cytotoxicity is linked to their high concentration. AuNPs trapped in the liver can affect the function of this organ.[120] The deleterious consequences of AuNPs were investigated by Nadine *et al.*, who showed that particles as small as 14 nm could easily enter the cell membrane and assemble into vacuoles. In dermal fibroblasts, this penetration resulted in aberrant actin filaments and extracellular matrix constructs.[121] Research indicates that cells can endocytose nanoparticles of gold and form cytotoxic aggregates. HL7702 cells were used to study the interaction between gold nanoparticles and glutathione, and the impact of this interaction on apoptotic signaling (human liver cell line).[122]

Titanium dioxide nanoparticles (TiO_2NPs) exhibit unique physical and chemical properties in cosmetics and pharmaceuticals because of their high surface-to-mass ratio. However, researchers used TiO_2NPs on rat and human glial cells to study the activities of the nervous system (C6 and U373). They found that the immunolocalization of F-actin is inhibited by TiO_2NPs.[123] Long-term inhalation of TiO_2NPs may harm the brain.[96] Animals exposed to TiO_2NPs develop lung inflammation. The effects of intratracheal TiO_2NPs on chronic pulmonary injury were evaluated for ninety days. The results suggested that the usage of TiO_2NPs irritated the lungs and caused hemorrhage. TiO_2NPs increased lung antioxidant capacity and lipid peroxidation in rats.[124]

Copper oxide nanoparticles (CuONPs) are widely employed in material development, including nanofabrication. CuONPs are lethal to mammalian cells due to the induction of oxidative stress. It is still unknown whether CuONPs constitute a genotoxicity risk to people. There is a correlation between p53 and the lung epithelial cell toxicity of CuONPs (A549). CuONPs reduced, in a dose-dependent manner, the viability of cells exposed to them. CuONPs result in glutathione depletion, lipid oxidation, an increase in catalase activity, and the activation of superoxide dismutase. They promoted the activation of the inflammation detecting Hsp70 protein. CuONPs had a similar positive effect on Rad51 and MSH2 DNA repair proteins. CuONPs have been shown to induce A549 cells to perish as a result of oxidative stress.[98] The Hodge and Sterner scale classifies CuONPs as moderately hazardous. They target the kidneys, liver, and spleen, among other organs. These nanoparticles damaged the kidneys, liver, and spleen of mice; however, micro copper particles had no effect.[99]

Despite the health issues, these nanoparticles are linked to threats to the environment and biological organisms.[125] The utilization of nanoparticles has enhanced artificial synthesis. Increased exposure of modified nanoparticles to biotic and abiotic ecosystem components will result from their rapid production and utilization. While nanomaterials are widely used, their long-term presence and prolonged exposure can be harmful to the environment. To examine the environmental implications of nanoparticles, it is crucial to comprehend their negative effects, how their dissolution in water influences their toxicity, their propensity to aggregate or settle, and their fate during wastewater treatment and incineration. However, it is necessary to study the acute and long-term effects of customized nanoparticles on the skin, gastrointestinal tract, and respiratory system.[126] The use of metal nanoparticles in electrospun nanofibers for biomedical and food packaging applications poses significant risks, including oxidative stress, DNA damage, and ecological disruption.[127] Rigorous safety assessments are crucial, encompassing comprehensive evaluations of biodistribution, metabolism, long-term effects, and both acute and chronic toxicity. In pharmaceuticals and cosmetics, detailed characterization and toxicological evaluations are essential to ensure that the benefits outweigh the risks. Continuous research, strict regulatory adherence, and proactive risk management are vital for safely harnessing nanotechnology's advantages.

In essence, nanotechnology has been utilized in both commercial and medical applications. Following this technology, metallic nanoparticles are widely used in healthcare applications despite having an elevated risk to health and the environment.

The physicochemical features of nanoparticles facilitate medical and industrial applications. They are utilized by the electro/photocatalytic-environmental-space-cosmetic-medical-pharmaceutical industries.

Therefore, it is necessary to understand how the released nanoparticles interact with their surroundings, which requires a thorough understanding of the long-term effects of nanotechnology-designed particles on human health, as well as the detection and evaluation of nanotechnology's dangers and risks.[125] Alternative ways, such as incorporating green materials and processes, could be a viable means to address their health and environmental issues. The following section illustrates the green electrospinning technique to avoid the utilization of these metallic nanoparticles.

Green electrospinning is a novel technique for increasing the production of electrospun fibers with little or no toxicity, particularly for medical, filtration, tissue, and food engineering (Fig. 4). It is an environmentally friendly and safe method and is particularly useful in medical and food applications. According to a number of studies, natural and synthetic polymers used in green electrospinning include PVA,[128] PEO,[129] PVP,[128] collagen,[130] silk,[131] fibroin,[132] polyimide,[133] and PAA.[134]

Water or mild solvents such as acetic acid might be used to make a solution to avoid toxicity; only the Class 3 solvent tested was capable of sufficient polymer solubilization and subsequent fiber formation. However, many biopolymers, such as chitin, chitosan, and cellulose, are not dissolved in water. As we discussed previously, metallic compounds have tremendous detrimental effects on health and the environment, and organic solvents are also responsible for health and environmental issues.[136] Most often, electrospun biomaterial productions require toxic, hazardous fluorinated solvents, including HFIP (hexafluoro isopropanol), FA (ferulic acid), chloroform, and TFA (trifluoroacetic acid). DMF (*N*,*N*-dimethylformamide) and HFP (hexafluoropropylene) are very harmful to both humans and the environment. On the other hand, toxic or flammable organic solvents are still used in emulsion electrospinning, limiting its utility in *in vivo* medicinal and agricultural applications.[135] These volatile organic compounds may affect the product user and producer and evaporate into the air, affecting water, air, and soil quality.[137–139]

However, research conducted by Hsieh *et al.* demonstrated the water solubility of chitosan after carboxymethylation and subsequent electrospinning with water-soluble PVA.[140,141] Velankar *et al.* showed the use of oil–water emulsion electrospinning using polystyrene and PEO liquid phase. However, emulsion electrospinning still employs toxic or flammable organic solvents, limiting its utility in *in vivo* medicinal and agricultural applications.[142]

As a result, scholars are motivated to develop nanomats using harmless substances to reduce the aforementioned problems associated with health, safety, and the environment. Over the last decade, there have been significant advances in plant extract-based nanofibers. Due to the negative side effects of synthetic compounds reported by Srindhar *et al.*,[143] plant extract encapsulated nanofibers have been developed for cosmetics, medicine, and the food industry.

Plants, indeed, contain a wide variety of bioactive chemical compounds possessing antimicrobial properties[144,145] and with the potential to kill bacteria that cause infections. A range of phytochemicals are derived from plants and classified by Cowan *et al.* as phenolics, terpenoids, and alkaloids.[146–148] These compounds can target pathogens by disrupting cell membranes, binding to cellular components, depriving the cells of essential nutrients, and inhibiting enzyme activity.[131] The plant's crude extract can be derived from the plant's leaf, bark, stem, seeds, and flowers using a variety of organic solvents such as ethanol,[149] methanol,[150] and ethyl acetate.[151]

Because plant extracts are too brittle and have inadequate mechanical qualities to be electrospun alone, numerous biopolymers are utilized as carrier polymers to provide good mechanical properties, such as PVA,[128] PEO,[129] PVP,[128] collagen,[130] silk fibroin,[132] polyimide,[133] PAA,[134] alginate,[152] and gelatin.[153] Cellulose,[154] chitin,[155] and chitosan[156] are some of the natural and synthetic biopolymers. The fibrous structure, due to its nano- to micro-scale thickness, lacks the mechanical strength needed for use in clothing, so the fibrous web is usually laminated to enhance its durability and provide adequate reinforcement.[5] However, all synthetic biopolymers cannot be dissolved in non-toxic solvents, limiting their use in medical applications. Embedding nanofibers in traditional clothing greatly improves the functional properties of self-cleaning, water repellency, and flame retardancy.[157]

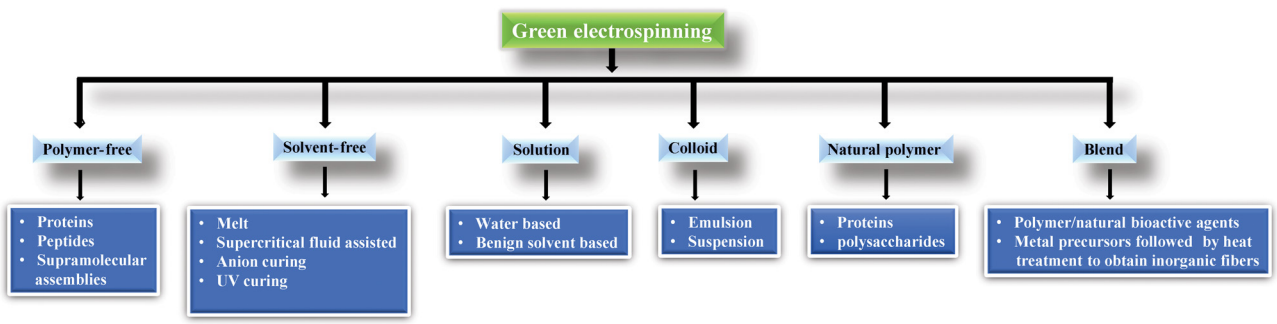

Fig. 4 Classification of green electrospinning.[135]

Sources of bio-based materials forming nanofibers

Plant sources

Exploring a wide range of plant sources for bioactive agent-infused nanofibers offers a highly promising opportunity to develop advanced materials.[158] The substances derived from different botanical sources such as leaves, seeds, stems, flowers, oils, and fruits have a crucial part in the complex creation of nanofibers, enhancing their capabilities. Several extracts found in the plant include those derived from *Azadirachta indica* (neem), which is well known for its strong antimicrobial properties; *Achillea lycaonica*, recognized for its noticeable anti-inflammatory effects; and *Lawsonia inermis* (henna), which possesses distinct medicinal qualities.[159] Seeds, such as *Trigonella foenum-graecum* (fenugreek) and *Allium sativum* (garlic), coupled with mucilage, are important sources of bioactive compounds. The stems of plants such as *Curcuma longa* (turmeric), *Zingiber officinale* (ginger), and *Glycyrrhiza glabra* (licorice) contain unique bioactive compounds that have potential applications.

The use of bioactive agents from flowers such as Matricaria recutita (chamomile), *Isatis tinctoria*, and *Helianthus annuus* (sunflower) broadens the spectrum of bioactive compounds that can be incorporated into nanofibers. The inclusion of *Eugenia caryophyllata* (clove) and *Olea europaea* (olive) oils in nanofibers can enhance their intrinsic capabilities due to the presence of unique bioactive components. Fruits such as *Garcinia mangostana*, *Citrus sinensis* (orange), *Ananas comosus* (pineapple), and *Momordica charantia* add to the variety of bioactive substances that can be used to create nanofibers.

Animal sources

The importance of animal sources in the production of bioactive nanofibers should not be underestimated, especially when combined with plant-derived materials. Proteins like silk fibroin, gelatin, and keratin possess exceptional characteristics that can be strategically utilized for specific purposes. Silk fibroin, obtained from silkworms, demonstrates exceptional tensile strength and compatibility with living organisms.[160] Gelatin, derived from collagen, offers flexibility and is known for its inherent biodegradability. Keratin, obtained from several animal sources, enhances the mechanical robustness and stability of nanofibers, hence broadening their range of functionalities.

Mineral sources

The use of mineral sources expands the range of materials accessible for the fabrication of bioactive nanofibers. Polysaccharides such as cellulose and chitin, obtained from plants and animals respectively, play a crucial role in enhancing the structural stability of nanofibers. Zein, a protein component, adds complexity to mineral sources for bio-based nanofibers.[161,162]

The incorporation of these many natural sources into electrospun nanofibers not only guarantees biocompatibility but also harmonizes effortlessly with environmentally sustainable methods. The resulting materials exhibit great potential for a wide range of applications in fields such as medicine, agriculture, and environmental remediation, highlighting the extensive possibilities and adaptability of nanofibers that contain bioactive agents.

Humans have used plant-based medications since prehistoric times. Since bioagents make it possible to cross-link scaffolds, the use of bioactive materials in tissue engineering has grown over the past few decades. Materials with bioactive compounds integrated offer special properties for tissue engineering matrices. Plants provide therapeutic substances and are the source of these compounds: leaves, stems, seeds, bark, flowers, and oils.[163]

The extraction process has employed biomaterials from these natural plant sources to prevent the development of acute or chronic toxicity associated with biocompatible and biodegradable materials derived from them. Natural polysaccharides, including alginate, cellulose, and starch, have been extensively used in tissue engineering. Protein extracts from plants and animals are also important sources of biomaterials.[164] Plant extract cannot be electrospun alone due to numerous challenges; consequently, a variety of synthetic and natural biopolymers are loaded to create nanofibrous fibers (Fig. 5).

The overview of plant-extract bioactive nanofibrous production conditions, opportunities, and difficulties of applying the nanomembrane for biomedical applications are the main points of the review. The development of the nanofibrous process, including its bioactive compounds and several plant-derived medicinal extracts from diverse plant parts, including leaves, stems, flowers, seeds, and oil, is discussed in the following section.

Bioactive agents or extract

Leaves

The *Aloe vera* plant belongs to the Liliaceae family, and it possesses several properties such as anti-inflammatory, antiarthritis, antibacterial, and antifungal properties. It contains several compounds such as amino acids, vitamins, sugars, minerals, and enzymes. In the Indian subcontinent, *Azadirachta indica*, often known as neem, contains more than 140 bioactive ingredients and has antimalarial, antiulcer, antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, and anticarcinogenic properties.[165–167] *Achillea lycaonica*, a common species found in Turkey and a member of the Asteraceae family, has been claimed to have antioxidant, wound healing, antibacterial, and cytotoxic characteristics by many researchers.[168,169] Reneta Gevrenova *et al.* used ethyl acetate, methanol, and water extracts of the aerial parts and roots of two *Achillea* species (*A. alecppica* and *A. santolinoides*) in another investigation. They discovered that hydroxybenzoic and hydroxycinnamic acids, phenolic acid glycosides and sugar esters, acylquinic acids, *O*-glycosyl flavones and flavonols, and flavonoid aglycons are present as bioactive constituents in these species. The extracts (Fig. 6) of these species may have the phytotherapeutic potential for Alzheimer's disease and industrial applications.[170]

Korean angelica is another name for these small plants, mostly used as a medicinal herb in Asia. The dried roots of this

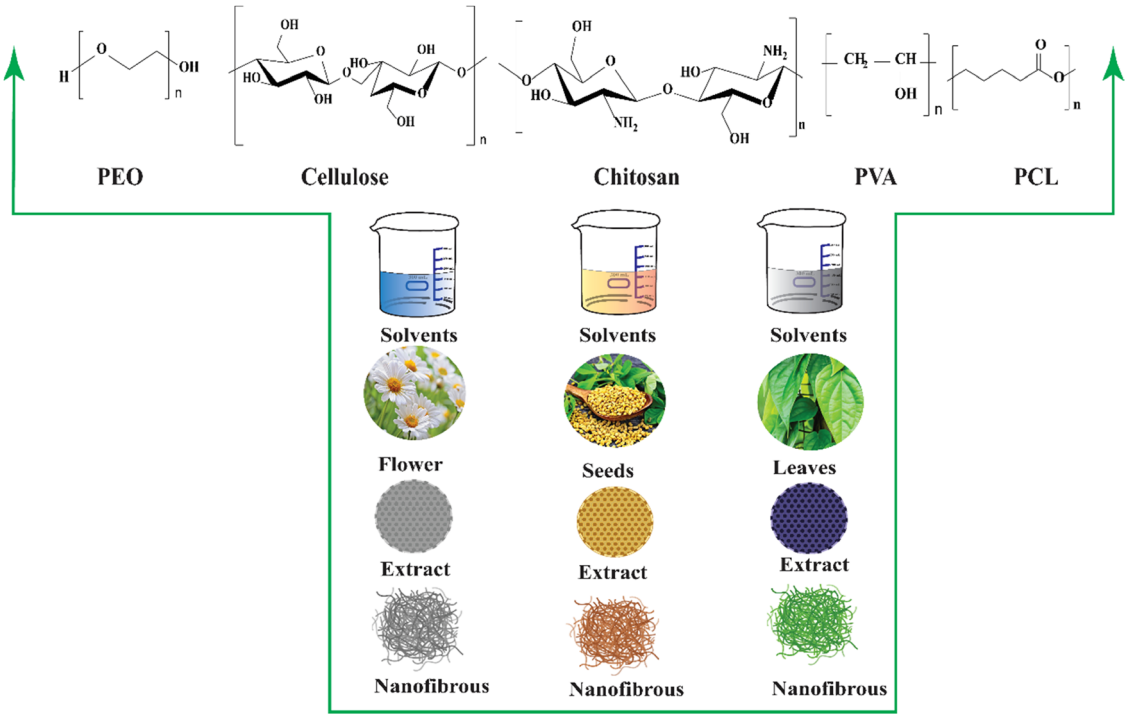

Fig. 5 Carrier biopolymers (PEO, cellulose, chitosan, PVA, PCL) and different bioactive compounds extracted from plant sources (flowers, seeds, leaves) using appropriate solvents for converting them into nanofibrous materials for various applications.

plant are commonly used to treat anemia, pain, infection, and articular rheumatism. The medicinal dose is prepared by boiling the dried roots in water. Decursinol angelate is the most common medicinal compound of this plant, and various studies have shown that it can treat cancers, such as bladder cancer, colon cancer, leukemia, lung cancer, melanoma, myeloma, prostate cancer, and sarcoma.[171–176] *Carica papaya* is a type of papaya fruit that belongs to the *Caricia* genus included in the Caricaceae family.[177] It contains phenolics, flavonoids, and alkaloids (tryptanthrin and isatin), among other phytochemical

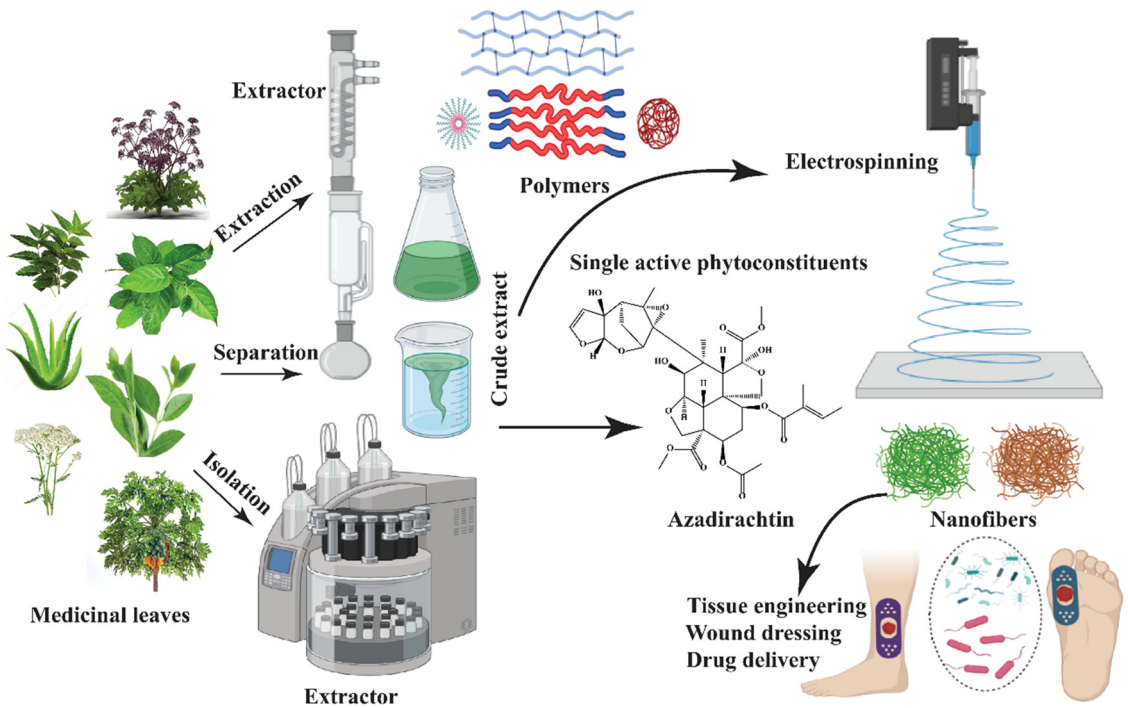

Fig. 6 Schematic diagram of producing bioactive nanofibers utilizing extracts from medicinal plant leaves.

substances (Fig. 7). It has antioxidant, antibacterial, anticancer, anti-inflammatory, antiulcer, antidiabetic, and many other properties due to these chemical substances.[178] The medicinal plant *Gymnema sylvestre* is a perennial woody vine native to Asia, Africa, and Australia. It contains phytochemical compounds such as gymnemasaponins, anthraquinones, flavones, phytin, lupeol, and stigmasterol. Therefore, this plant is utilized for many purposes like microbial infection, wound healing, inflammation, obesity, arthritis, constipation, and cancer.[179–182]

A natural red-orange dye, also known as hennotannic acid, is derived from the henna plant.[136] This plant has been used for natural hair and skin dyes for over 5000 years. It contains lawsone (2-hydroxy-1,4-naphthoquinone) and exhibits various biological activities such as antioxidant, analgesic, anti-inflammatory, antibacterial, antifungal, and anticancer.[183–185] *Nepeta dschuparensis* is a herbaceous aromatic plant that belongs to the Lamiaceae family. It is a flavonoid-rich plant that is used mostly in traditional herbal therapy. These plants contain flavonoids such as caryophyllene, 1,8-cineole, thujone, eudesmol, and pinene, which demonstrate antibacterial, antioxidant, and anti-inflammatory properties.[186–188]

Ginseng is found in Korea, China, and Siberia and it belongs to the *Panax* genus. Ginseng root contains polysaccharides, amino acids, polyacetylene alcohols and fatty acids that are all found in most ginseng species. Ginsenoside ingredients are the main active chemical compounds, and they have the structure of triterpenoid dammarane saponins. Approximately 30 ginsenosides have been obtained until now, although additional substances have also been found. In addition to its antioxidant properties, ginseng has been shown to have impacts on the cardiovascular system, immune system, and central nervous system, and it has anticancer properties.[189] It has been used in medical applications for a long time. Its pharmacological activity in the human body, including the skin, cardiovascular,

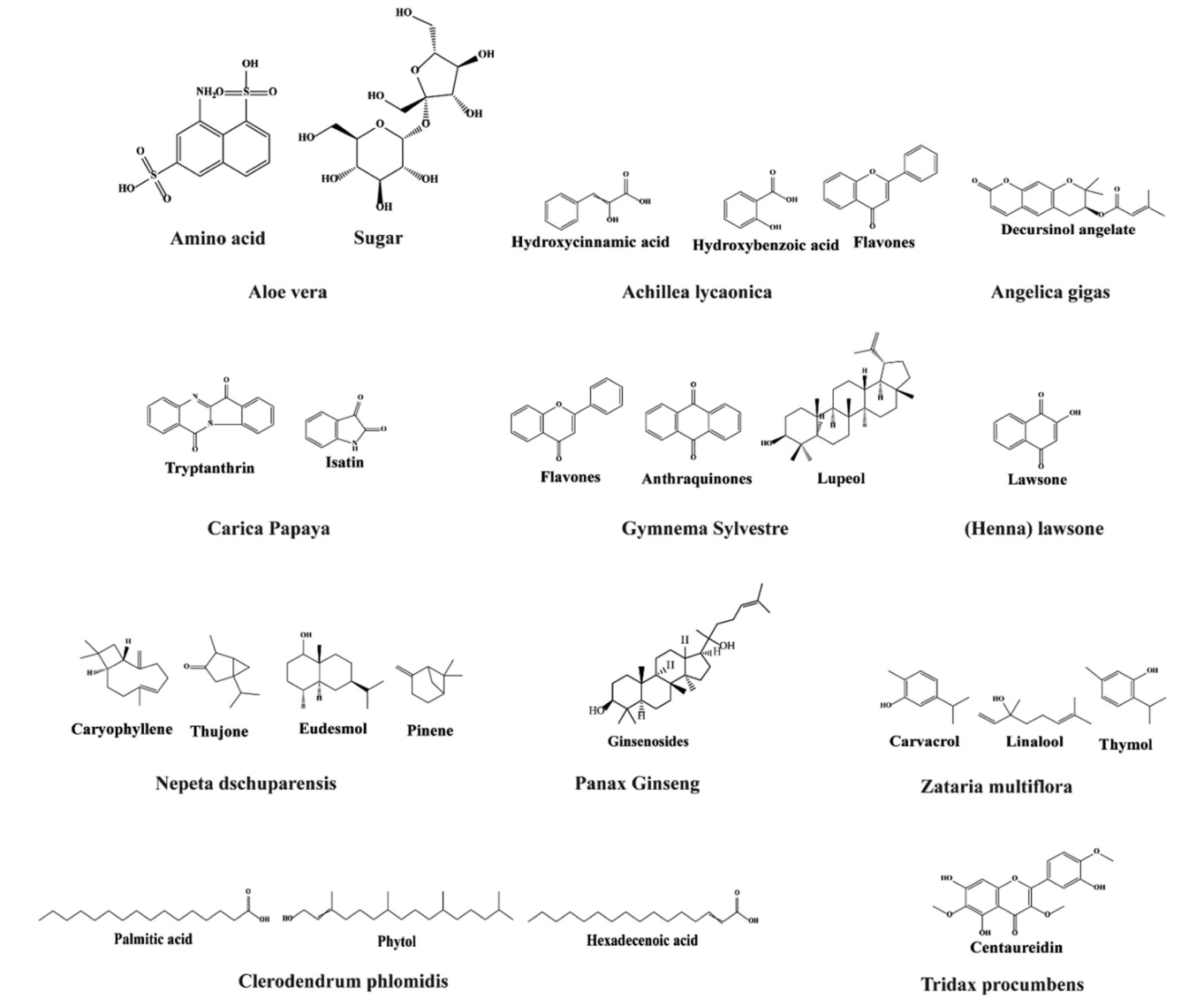

Fig. 7 Bioactive compounds extracted from various plant leaves for developing functional nanofibers.

immunological, endocrine, and neurological systems, has been described in a number of investigations. It also promotes collagen synthesis in dermal fibroblast cells.[190–193]

The Lamiaceae family includes *Zataria multiflora*, widely grown in Iran, Pakistan, and Afghanistan. Carvacrol, thymol-carvacrol, and linalool are found in the essential oil of *Zataria multiflora*. However, the earlier studies found only carvacrol and thymol.[194] These therapeutic constituents can help in the improvement of infectious wounded areas in the human body. They possess a wide range of biological activities, including spasmolytic, antinociceptive, antioxidant, anti-inflammatory, antifungal, and antibacterial effects.[194–196] Terpenoids, flavonoids, phytol, hexadecenoic acid, and palmitic acid are among the more than 40 phytochemical components found in the flowering plant *Clerodendrum phlomidis*, which belongs to the Lamiaceae family. The *Tridax procumbens* flowering plant, also referred to as coat-buttons or coat buttons, is a member of the Asteraceae family; it is a pest and widespread weed plant. Although it is native to the subtropical America, it has been found everywhere. The aerial part of *Tridax procumbens* contains procumbenetin. It also contains flavonoids (centaureidin and centaurein), alkyl esters, sterols, pentacyclic triterpenes, fatty acids, and polysaccharides.[197–200]

The leaves of *Tridax procumbens* are used to treat wound healing and blood clotting.[201–204] Its drink is effective against bronchitis, diarrhea, and dysentery. The active ingredients of this plant extract possess antihyperuricemia, antioxidant, antibacterial, antifungal, and antileishmanial activities.[197–200] Therefore, Sharbidre *et al.* utilized this against SARS-CoV-2 by implementing computational methodologies.[205] The Moringaceae family of flowering plants contains only one genus of *Moringa*, which has been used for generations to cure wounds and various ailments, such as diabetes and cold. A few phytoconstituents in *Moringa* species include alkaloids, saponins, tannins, steroids, phenolic acids, glucosinolates, flavonoids, and terpenes. The broad variety of phytochemicals in this species are useful in various medicinal applications.[206]

Seeds

Fenugreek, also known as methi, is a Leguminosae family member commonly used in cuisine preparations, especially in south Asian countries. The main constituents of fenugreek seeds include nonvolatile and volatile oil (in small amount) (Fig. 9). These seeds are rich in sugars, proteins, lipids, alkaloids, flavonoids, steroid saponins, sterols, vitamins, and minerals.[207] The major bioactive compounds present in fenugreek seeds are diosgenin, rhaponticin, and isovitexin, as shown in Fig. 8.[208] These seeds demonstrate hypoglycemic[209], hypocholesterolemic,[210] antioxidant, and anti-ulcerogenic effects.[211] Flavonoids and polyphenols are bioactive constituents in plant-derived *mucilage*, which is made up of various phenolic compounds (Fig. 8). These bioactive substances prevent diseases related to oxidative damage.[212,213] Moreover, a glue-type polysaccharide found in most plants exhibited several biological activities such as antibacterial, antioxidant, and anti-inflammatory. It is also found in *Trigonella foenum-graecum* and exhibits antioxidative, antimicrobial, and anti-inflammatory properties.[213–215] Mucilage from cress seeds possesses a high mannose and galactose ratio. However, due to the different chain conformations and repulsive forces among the poly anions in solution, its application in electrospinning is limited.[216] However, Bonino *et al.* reported that PVA and PEO were employed to minimize repulsive forces.[217]

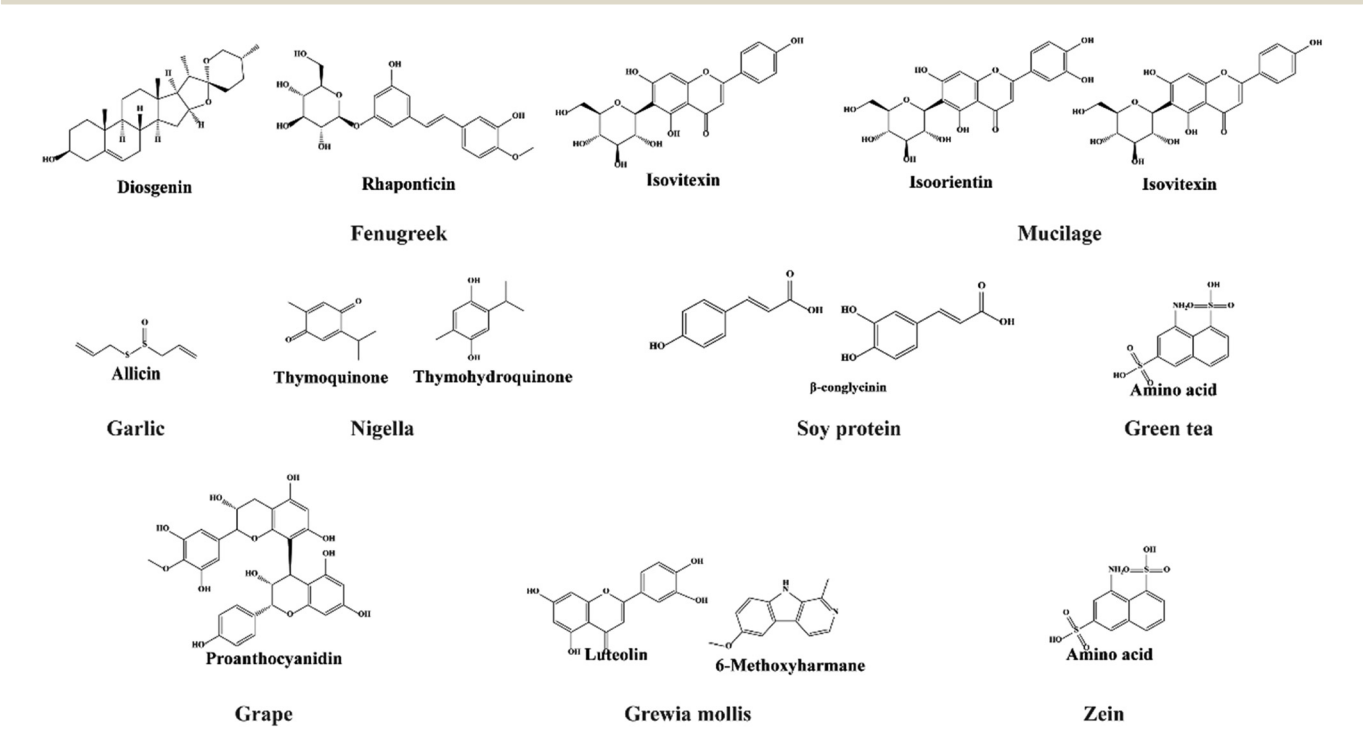

Fig. 8 Molecular structures of bioactive compounds extracted from various seeds and incorporated into electrospun nanofibers.

Garlic is a bulbous flowering plant that belongs to the genus *Allium*. Allicin, the main phytochemical component of garlic, has a variety of biological actions, including antibacterial, antioxidant, antibiotic, anticancer, and antiviral properties.[218–220] Garlic contains organosulfur compounds that are water- and oil-soluble.[221] The latest work conducted by Yongxu *et al.* using CS/PVA/GO with allicin showed its excellent long-lasting antibacterial property against *S. aureus* bacteria and was suggested as a potential wound dressing material. Furthermore, the nanofiber was found to be highly hydrophilic, with a high capacity for natural retention and pH-responsiveness.[222]

The ancient medicinal seed *Nigella sativa*, which belongs to the Ranunculaceae family, is widely available. Thymoquinone (TQ) and thymohydroquinone (THQ) are the major important therapeutic constituents in nigella. Due to the presence of these groups in *Nigella sativa*, it has anti-inflammatory, antioxidant, antibacterial, immunological, antidiabetic, hepatoprotective, anticestodal, and antiaflatoxin properties.[223–225] Soybean protein isolates are another name for soy protein containing β-conglycinin and glycinin as the major important chemical constituents. Usually, the glycinin peptide is superior to β-conglycinin in terms of antibacterial activity. The compound has the potential to be used in biomedical applications.[226,227] Antimicrobial peptides kill microbes by penetrating and damaging the cell membrane of microbes. Soy protein is an example of an antimicrobial peptide derived from soybeans, and it contains protein levels of 53%, 74%, and 93% in different forms.[228] It also contains significant reactive functional groups, such as NH_2, OH, and SH, and is applied extensively in biomedical applications.[229]

Green tea is made from *Camellia sinensis*, which originated in China and later spread out throughout East Asia. It contains flavanols, flavonoids, amino acids (theanine or 5-*N*-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, and lysine), and phenolic acids. Due to these functional groups in green tea, it provides a wide range of health benefits such as prevention of cancer and cardiovascular diseases and anti-inflammatory, antiarthritic, antibacterial, antiangiogenic, antioxidative, antiviral, neuroprotective, and cholesterol-lowering effects.[230]

A series of papers reported the fabrication of nanofibers from green tea extracts for healthcare applications. Sadri *et al.* developed three types of nanofiber composites using CS and PEO for wound healing applications that showed antibacterial activity against Gram-positive and Gram-negative bacteria with good moisture performance (Table 2).[231] PCL was also electrospun with green tea extract for cancer therapy, which showed an outstanding inhibition effect on tumor cells.[232] Pusporini *et al.* incorporated PVP to fabricate nanofibers for antioxidant activities a few years ago. All these studies showed the fine fiber production of green tea extract-loaded nanofibers. Grape seeds are utilized to create grape seed extract. Numerous health advantages are related to blueberries' antioxidants and oligomeric proanthocyanidin complexes, in addition to treating high cholesterol, atherosclerosis, macular degeneration, and nerve damage.

Grewia mollis, a floral species indigenous to Yemen and Oman, is widespread within the Malvaceae family and is indigenous to tropical Africa. It was shown that ethanol stem bark extracts, including tannic acid, phenolic components, and tannic acid and saponins, have antibacterial and anti-inflammatory

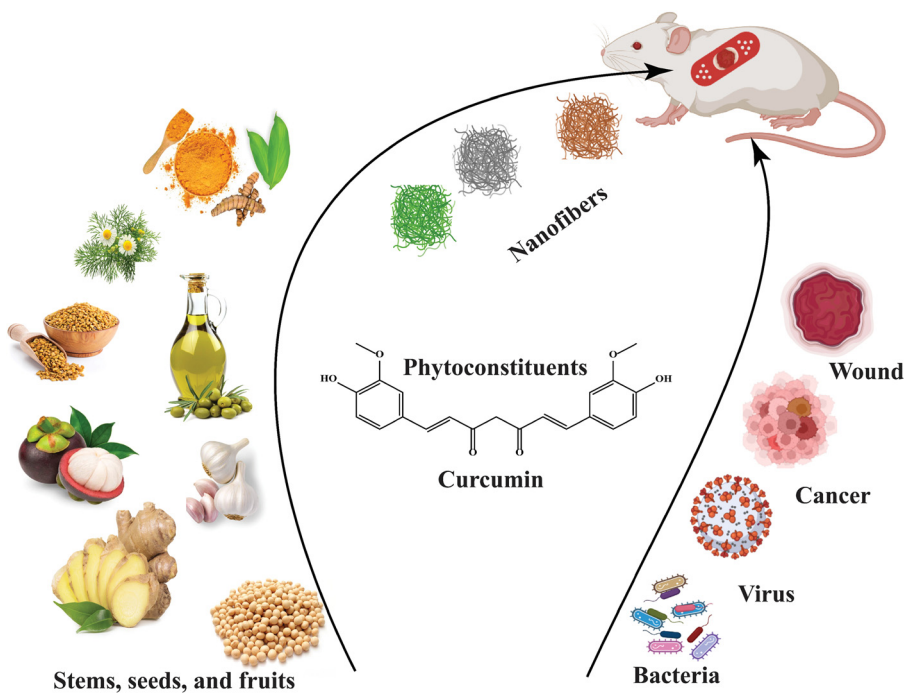

Fig. 9 Functional electrospun nanofibers incorporated with stems, seeds, and fruit extract and their biomedical applications. The functionality and performance of the nanofibrous mat increased considerably after adding bioactive compounds into nanofibers during the fabrication.

Table 2 Plant sources, extraction, fabrication, and findings of nanofibers

Plant name	Extractor	Carrier polymers	Solvents	Electrospinning condition: Voltage (kV)	(TCD) (cm)	Feed rate (mL h^{-1})	Fiber diameter (nm)	Antibacterial activity	Properties	Application	Ref.
Section 1: leaf extract nanofiber formation conditions, properties, and applications											
Aloe vera	—	Zein/collagen/PCL	Ethanol/chloroform	15	10	1.00	50–150	*S. aureus* and *E. coli*	Cytocompatibility/suitable thermal stability and mechanical properties	Wound healing	233
Aloe vera	—	PLGA/PVA	HFIP/DIW	12	12	1.00	112–562	*S. aureus* and *S. epidermidis*	Hydrophilic/antibacterial	Wound healing/wound dressing	234
Aloe vera	—	PLGA	HFIP	10	8	2.7	420–340	—	Good handling properties	Wound healing	235
Azadirachta indica (neem)	Methanol	PVA/CS	AA/DIW	20	16	3.00	152–298	*S. aureus*	Bi-layered/antibacterial/good tensile properties/good thermal and absorbance properties	Wound dressing	167
Azadirachta indica (neem)	Ethanol	PVA	DIW	20	15	3.50–4.00	185	*S. aureus*	Biocompatibility/antibacterial	Wound dressing	149
Achillea lycaonica	Ethanol/water	PLA	DMSO/chloroform	24–32	17	9–12	124–1094	—	Antibacterial/controlled drug release/good tensile strength/no risk of melting in the human body	Tissue engineering	150
Angelica gigas	Ethanol	PVA	DIW	25	15	1.00	75–170	—	Fast dissolving mat	Oral cancer	236
Cariica papaya	Ethanol/water	PVA/Gel	AA/chloroform	10–15	10–15	0.45–0.60	140–160	*S. aureus* and *E. coli*	Hydrophilic, antibacterial, and anti-inflammatory	Scaffold/wound healing	237
Carica papaya/honey	—	PU	DMF/chloroform	16	15	0.75	19–190	—	Hydrophilic/porous morphology	Burn injury	238
Clerodendrum phlomidis	*n*-hexane, ethyl acetate, ethanol, and methanol	PCL	Chloroform	12	12	1.00	300–400	*S. aureus*, *E. coli*, *P. aeruginosa*, and *S. typhi*	Antibacterial and antioxidant activity/superior mechanical, thermal and moisture properties	Wound dressing	239
Gymnema sylvestre	Ultrasonic extraction	PCL	TFE	12	12	1.00	79–377	*S. aureus*, *E. coli*, *P. aeruginosa*, and *S. typhi*	Biocompatibility/antibacterial	Wound dressing	41
Gymnema sylvestre	Methanol	PCL	Chloroform/methanol	13	12	1.00	50–206	*S. aureus* and *P. aeruginosa*	Antibacterial/infection control/superior mechanical properties and good wettability	Wound dressing	240
(Henna) lawsone	DMF	PCL/gel	TFE	10–22	12–18	0.30	10–297	*S. aureus* and *P. aeruginosa*	Antibacterial/cell proliferation	Wound healing, tissue engineering	241
(Henna) lawsone	—	PLLA/Gel	Chloroform/DMF/AA	16–18	15	0.40	196–520	*E. coli* and *S. aureus*	Biocompatibility/antibacterial	Wound dressing	242
(Henna) lawsone	Ethanol	CS/PEO	AA	25	10–20	0.10–1.50	64–87	*E. coli* and *S. aureus*	Antibacterial/cell viability	Tissue engineering	243
Nepeta dschuparensis/honey	Ethanol	PVA/CS	DIW/HCL	17	—	0.50	95–150	—	Antibacterial/antifungal/anti-inflammatory	Wound healing	244
Panax ginseng	Ethanol	PCL	DCM	16	12	1.50	250–660	—	Higher proliferation/hydrophilic	Bone tissue engineering	245
Zataria multiflora	Water	PVA/CS/Gel	DIW/AA/	21	—	0.20	58–218	*S. aureus*, *P. aeruginosa*, and *C. albicans*	Antibacterial/antifungal/anti-inflammatory	Wound healing	195
Tridax procumbens	DIW	PCL	DCM/DMF	—	—	—	100–124	*E. coli* and *S. aureus*	Antibacterial	Wound healing	202
Moringa	—	PAN	—	20	10	0.15		*E. coli* and *S. aureus*	Cost-effective and biodegradable nanofibers, antibacterial	Wound healing	246

Table 2 (*continued*)

Plant name	Extractor	Carrier polymers	Solvents	Electrospinning condition: Voltage (kV)	(TCD) (cm)	Feed rate (mL h^{-1})	Fiber diameter (nm)	Antibacterial activity	Properties	Application	Ref.
Section 2: seed extract nanofiber formation conditions, properties, and applications											
Fenugreek	HFIP	Fibroin	HFIP	25	10	0.50	38–339	—	Good mechanical and thermal properties/antibacterial/ biocompatibility	Wound dressing/scaffold	247
Garlic	Grinding	PU	DMF	10.5	15	0.20	150–578	—	Biocompatible	Wound dressing	248
Mucilage/ chan and linaza	DIW	PVA	Acetone	30	20	1.00	350	—	Antibacterial, antioxidant, anti-inflammatory and promoter of cell growth	Tissue engineering	249
Nigella	Methanol	PVA	AA	20	16	2.50	178–188	*S. aureus* and *E. coli*	Biocompatibility/hydrophilic/ antibacterial	Wound dressing	223
Nigella	—	PCL/PLA	DMF/DCM	10–20	15	0.80	638–707	*S. aureus* and *E. coli*	Good handling properties/ antibacterial	Wound dressing	250
Nigella	Methanol	PVA	AA	20	15	1.5	223	*S. aureus*	Antibacterial/good moisture management and thermal properties	Wound dressing	251
Soy protein	Ethanol	Fibroin	FA	—	—	—	71–160	—	Anticancerous/anti-inflammatory/ good moisture management	Tissue engineering	252
Green tea	—	CS/PEO	AA	17–20	10	0.3–0.5	100	*S. aureus* and *E. coli*	Keeps wound surface moist, reduces inflammation and increases the speed of recovery and healing	Wound dressing	231
Grape	—	Silk/PEO	*tert*-Butyl 29 hydroperoxide (*t*-BHP)	14	15	0.3	420		Grape extract can be released from the nanofibers in a sustained manner	Skin care, tissue regeneration and wound healing	253
Grewia mollis	Methanol	PLGA	DCM/DMF	15	10	—	—	*S. aureus* and *E. coli*	Potential effective antimicrobial membrane	Wound dressing	254
Zein	Citric acid	HA	—	17.5	15	1	100–300	—	Cell proliferation	Bone tissue engineering	255
Section 3: stem extract nanofiber formation conditions, properties, and applications											
Curcumin	—	PCL/GT	AA	15	15	1.00	23–288	*S. aureus*	Better healing performance/ antibacterial	Wound healing	256 and 257
Curcumin	—	CA	DMAc/acetone	17.5	15	1.00	314–340	*S. aureus* and *E. coli*	Anti-tumor/antioxidant/anti-inflammatory	Wound healing	258
Curcumin	Methanol/ethanol	PCL/PVA	DMF/DCM	12–24	16	1–3	—	*S. aureus* and *E. coli*	Water absorbability, antibacterial, and biocompatibility	Wound dressing	259
Curcumin	—	PVA	AA	15	10	1.00	47–138	*S. aureus* and *E. coli*	Good mechanical properties/ hydrophilic	Wound dressing	260
Curcumin	DIW	PVA	DIW	15	20	0.50	250–350	*S. aureus* and *E. coli*	More even fibers/drug release/ antioxidant/anti-inflammatory	Biomedical	261
Curcumin	AA	Gel	DIW/EDC	26	12	1.70	500	*E. coli*	Antibacterial and anti-inflammatory	Wound healing	262
Curcumin	—	CA/PU/GO	DMF/THF/ acetone	17	15	0.40	44–678	*S. aureus*	Antibacterial and anti-inflammatory	Wound healing	263
Curcumin/ honey	Ethyl acetate	PVA	DIW	20	15	—	340	*S. aureus*	Antibacterial, anti-inflammatory/ good moisture management	Wound healing	151
Ginger	NaOH	CS/PVA/ cellulose	AA	—	—	—	100–200		Antibacterial, high mechanical strength	Medical and packaging areas	264

Table 2 (*continued*)

Plant name	Extractor	Carrier polymers	Solvents	Electrospinning condition: Voltage (kV)	(TCD) (cm)	Feed rate (mL h^{-1})	Fiber diameter (nm)	Antibacterial activity	Properties	Application	Ref.
								B. cereus, *E. coli*, *S. aureus* and *S. typhimurium*			
Licorice		PVA		25	15		245	*S. aureus*	Better moisture absorbing material	Wound healing	265
Section 4: flower extract nanofiber formation conditions, properties, and applications											
Chamomile	—	CECS/PCL/PVA	AcA/DIW/AA	15–18	18	0.20	19–248	*S. aureus* and *C. albicans*	Superior mechanical properties and great phosphate buffer uptake/controllable release behavior/antibacterial and antioxidant	Wound dressing	266
Chamomile	—	PCL/PS	DMF/chloroform	18	15.50	0.46	175	*S. aureus* and *C. albicans*	Antibacterial and antifungal/drug release	Wound healing	267
Isatis tinctoria	Alcohol	PVP	—	10	5–8	—	—	*S. aureus* and *E. coli*	Antibacterial, excellent wetting surface	Wound healing	268
Sunflower	DIW	PVA	NaOH	20	15	0.5–0.75	304–400		Hydrophobic and hydrophilic nanofibers	Aqueous food systems	269
Section 5: oil-based nanofiber formation conditions, properties, and applications											
Eugenol (clove oil)	—	PCL/PVA/CS	DMF/AA/chloroform	75	13	—	162–387	*S. aureus* and *P. aeruginosa*	Biocompatibility/hydrophilic/antibacterial	Wound dressing	270
Olive oil	—	PEO/CS/PCL	AA/methanol/DCM	15–25	7–20	0.20–1.00	95–131	*S. aureus* and *E. coli*	Antibacterial/antifungal/anti-inflammatory	Wound dressing	271
Cinnamomum zeylanicum	DIW	PVA	—	17	15	0.5	80	—	—	Highly effective for use in stored product pest control	272
Lavender oil	—	PU	THF/DMF	15	15	0.5	371–979	*S. aureus* and *E. coli*	Excellent bactericidal properties, multifunctional wound dressings	Wound dressing, promoting the regeneration of new tissue	273
Cinnamon oil	—	PEO/cyclodextrin		25	12	0.6	350–450	*B. cereus*	Extends the shelf life of beef	Active food packaging	273

activities.[274] Typically, zein protein has been utilized as a film or nanofibrous scaffold for wound healing and tissue engineering purposes. Higher quantities of amino acids, including glutamic acid, proline, leucine, and alanine, and lower levels of basic and acidic amino acids can be found in zein proteins.

Stems

Curcumin is a yellow pigment found in turmeric, a flowering plant of the *ginger* family which is commonly used as a curry spice, especially in south Asian countries. There are three major types of curcuminoids found in turmeric: curcumin or diferuloylmethane (responsible for yellow color), demethoxycurcumin, and bisdemethoxycurcumin[275] (Fig. 10). Many investigations have been conducted to determine the phytochemical constituents of turmeric that result in antioxidant, anti-tumorigenic, anti-inflammatory, anticancer, and many other properties.[238] Due to these therapeutic properties turmeric has been used for a long time to heal many diseases like cough, rheumatism, diabetes, biliary disorders, anorexia, sinusitis, hepatic disorders, cancer, and alzheimers.[276,277] Traditional civilizations have used ginger for a range of purposes. Chemicals like phenolic (gingerols, shogaols, and paradols) and terpene (β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene) compounds are abundant in ginger. For thousands of years, ginger has been used in Chinese and Indian medicine to treat illnesses, including stomach pains and nausea. Ginger has antiviral, antibacterial, and anti-inflammatory properties. It is commonly known that ginger has medicinal qualities. Licorice is a flowering Fabaceae plant called *Glycyrrhiza glabra* and is well known for its fragrant, sweet root. Sugars, carbohydrates, bitters, resins, essential oils, tannins, inorganic salts, and tiny amounts of nitrogenous substances like proteins, amino acids, and nucleic acids can all be found in licorice extract.

Flower

Chamomile is a daisy-like plant that belongs to the Asteraceae family and is commonly used to make herbal infusions for beverages. Apigenin, quercetin, patuletin, luteolin, and glucosides are phenolic and flavonoid compounds found in this plant.[278] Its flower yields an essential oil that possesses antibacterial, anti-inflammatory, and antioxidant activities due to the presence of these functional compounds. A series of research studies have indicated that it could be used in cancer therapy,[279–281] diabetic wound healing,[282] and periodontal injury repair.[283] *Isatis tinctoria*, a flowering plant from the Brassicaceae family, has remarkable therapeutic properties due to the presence of a diverse spectrum of compounds and is primarily found in Asian countries. Among the bioactive substances are alkaloids (tryptanthrin and isatin), flavonoids (isoorientin and isovitexin), polysaccharides, glucosinolates, carotenoids, fatty acids, and volatile components. A great deal of investigation reported that it has good antibacterial and anti-inflammatory activities.[284–289]

Sunflower (*Helianthus annuus* L.) contains active ingredients. The roots, stems, leaves, and seeds of the sunflower plant, as well as the flower, contain flavonoids and phenols. These chemical constituents have antimicrobial and antioxidant activity, and hydrophobic and hydrophilic nanofibers were developed by Shaneazadeh *et al.* (Table 2).

Oil

Cloves are members of the Myrtaceae family and are mostly found in Indonesia. Clove oil, also known as eugenol, is a phenolic substance with antioxidant, antibacterial, antifungal, and anti-inflammatory properties[290] (Fig. 11). The predominant component, eugenol, has an inhibitory effect on oxidative stress due to radical scavenging property. The ancient olive fruits belong to the Oleaceae family and contain the major medicinal components, including phenolic and polyphenolic compounds such as oleuropein and hydroxytyrosol,[291] resulting in antioxidant, anti-inflammatory,[291] and antibacterial activity against *S. aureus* and *S. typhimurium* bacteria.[292]

Fruits

Garcinia mangostana is a member of the Guttiferae family and is known as the "Queen of Fruits" in Southeast Asia. Xanthone,

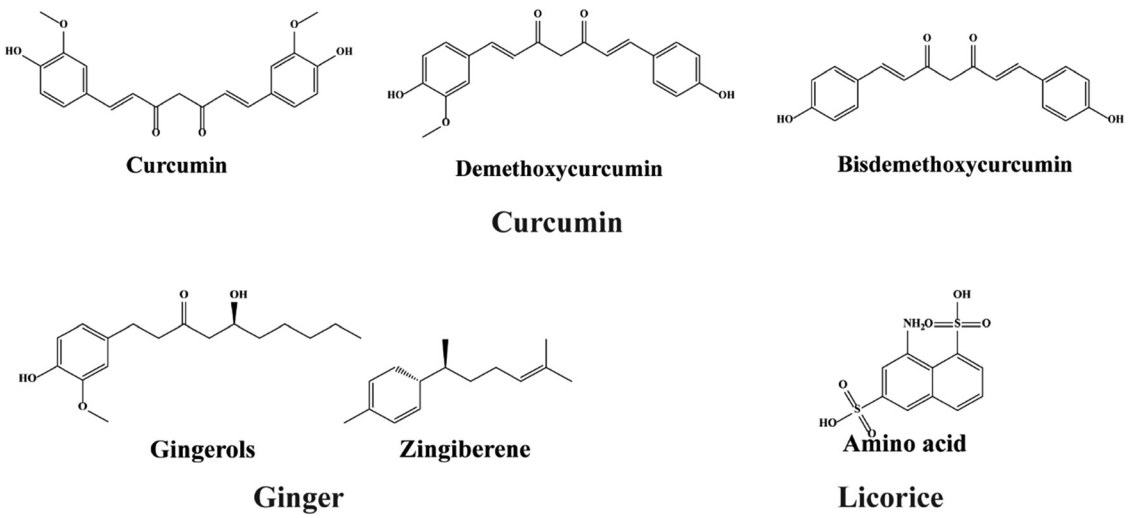

Fig. 10 Bioactive compounds isolated from various plant stems and incorporated into electrospun nanofibers.

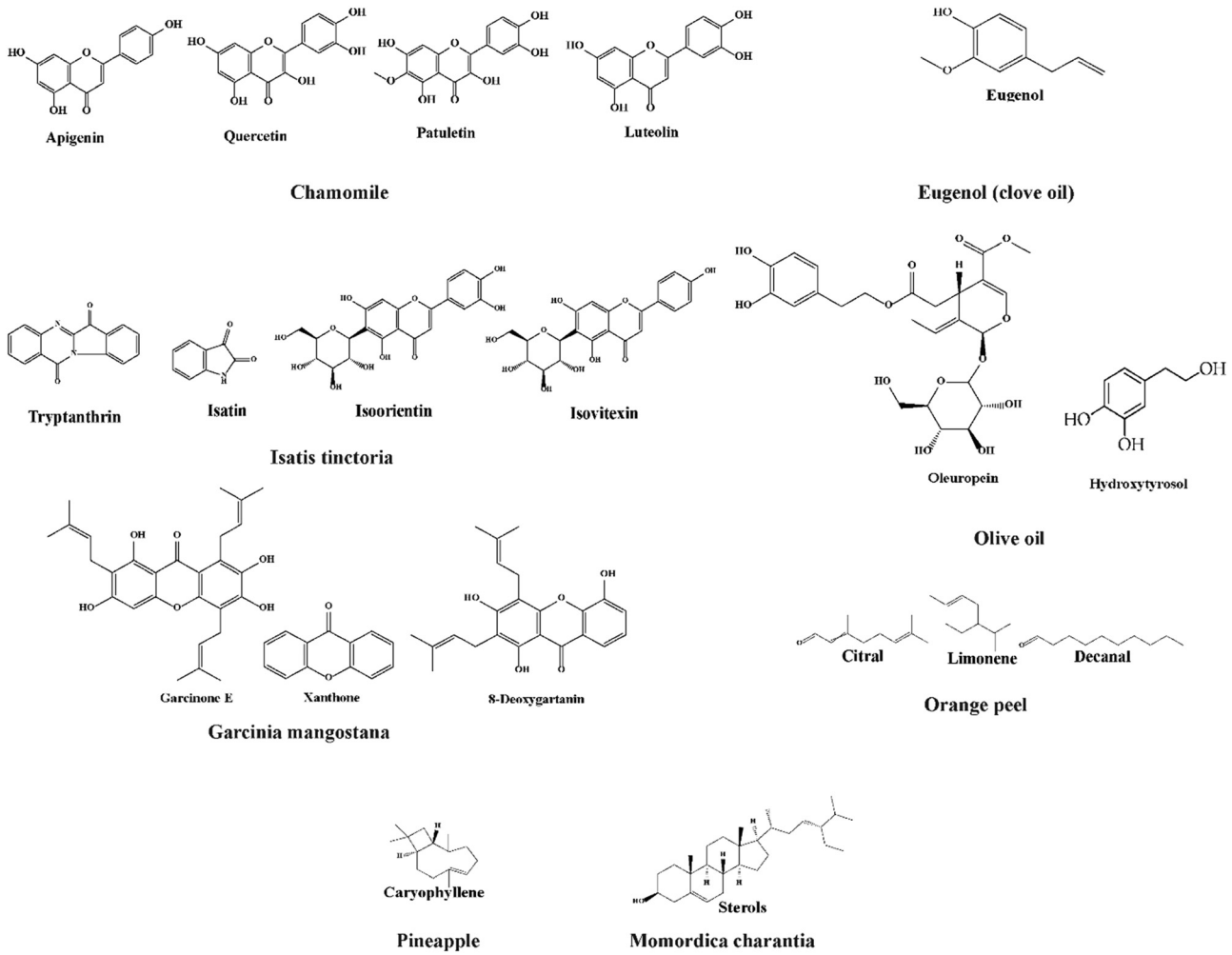

Fig. 11 Chemical structures of medicinal compounds derived from fruits, oils, and flowers for nanofiber production.

α, β, and γ-mangostins, garcinone E, 8-deoxygartanin, and gartanin are all found in *Garcinia mangostana*.[278] Much research reported its antioxidant, antitumoral, antiallergic, anti-inflammatory, antibacterial, and antiviral activities. Due to these properties, it has been used in a wide variety of illness treatments such as dysentery,[293] diarrhea,[294] hemorrhoids,[295] food allergies,[295] arthritis,[295] wounds,[296] tuberculosis,[297] inflammation,[298] ulcers,[299] micosis,[298] cholera,[300] leucorrhea,[301] fever,[302] and suppuration.[301] *Oranges* are the fruit of several citrus species in the Rutaceae family. Orange peels, the main byproduct of the citrus processing industry, are low in protein and high in pectin, cellulose, and hemicellulose. Additionally, the weight of fresh fruit is virtually entirely made up of orange peels. *Ananas comosus*, the pineapple, is economically the most significant Bromeliaceae plant. Pineapples have been cultivated for centuries and are native to South America. Flavonoids, phenolic acids, and other polyphenolic chemicals are present in pineapple which contribute to antioxidant activity. *Momordica charantia* from Cucurbitaceae is a tropical and subtropical vine used for its delicious fruit in Asia, Africa, and the Caribbean. This fruit has many bioactive substances categorized as carbs, proteins, fats, and more in the literature. Triterpenoids, saponins, polypeptides, flavonoids, alkaloids, and sterols are found in *Momordica charantia*.

Prospective applications of plant-based electrospun nanofibers

Biomedical applications

Recent interest has been drawn to quantitative research of electrospinning based on PLA, PCL, PEO, PVA, gelatin, chitosan, starch, *etc.*, which is not surprising given the significance of material development for biomedical applications.[303–305] The outcomes of this study will help improve the production of bio-based nanofibers. Polycaprolactone (PCL) fibers incorporated with *Inula graveolens* (L.) plant extract were fabricated by an electrospinning process.[306] The resultant nanofibers had a ribbon-like twisted form and showed no toxic effect on cell cultures (Fig. 12). After evaluating the tensile properties, hydrophilicity, cell toxicity, and biocompatibility, the authors claimed that the *Inula graveolens* (L.) plant extract/PCL scaffold

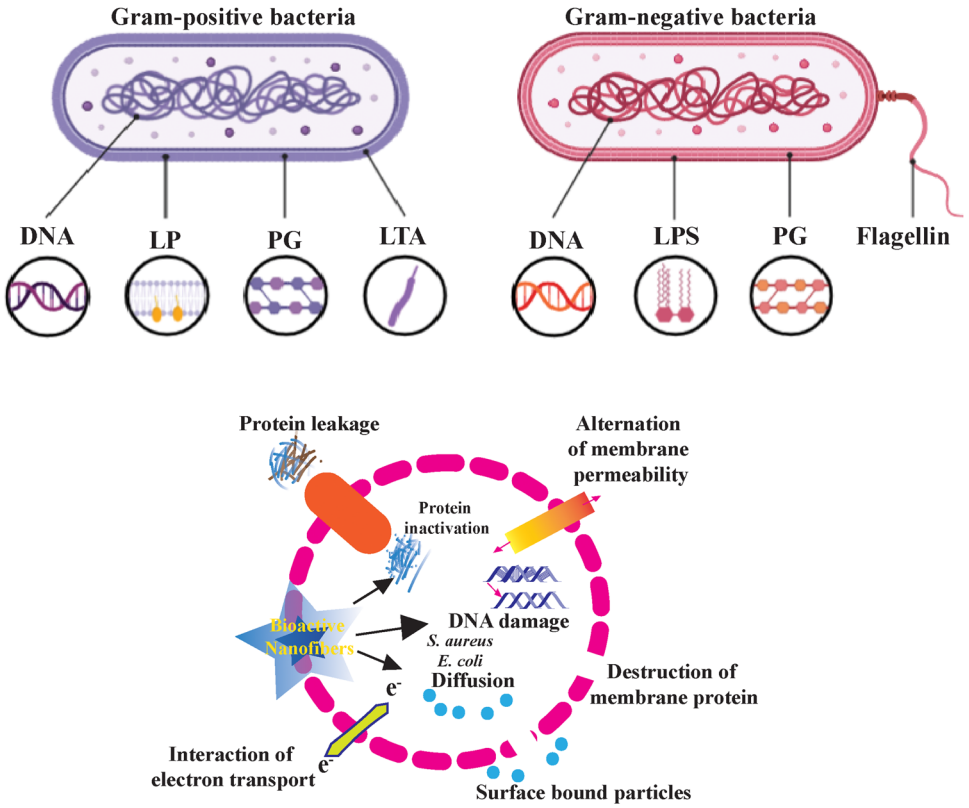

Fig. 12 Mode of the bacterial killing mechanism. This figure shows how nanoparticles inhibit the growth of Gram-positive and Gram-negative bacteria. The nanoparticle adheres to bacteria's surfaces, disrupting membrane structure and function. DNA damage and protein inactivation occur when nanoparticles enter bacterial cells. It illustrates how nanoparticles interact with lipoprotein, peptidoglycan, lipoteichoic acid, lipopolysaccharide, and flagellin in the bacterial cell wall and how nanoparticles damage bacteria's electron transport chains, reducing energy production.

could be used as a potential material for wound healing and tissue regeneration applications. Ferulic acid is a naturally occurring polyphenolic plant constituent. It was isolated from the *Parthenium hysterophorus* plant and encapsulated in the PLGA/PEO electrospun nanofibrous matrix.[307] Microscopic analysis showed that ferulic acid was found in the core of PLGA/PEO fibers.

The ferulic acid encapsulated PLGA/PEO nanofibers exhibited better cytotoxic potential against HepG2 cells. Seyed and co-workers studied the effect of electric potential on the morphology of polyvinyl alcohol (PVA)/sodium alginate (SAlg) electrospun nanofibers containing herbal extracts of *Calendula officinalis*.[308] The produced nanofiber mats have high porosity and a high surface-to-volume ratio. The diameters of Calendula-induced nanofibers were more compared to Calendula-free nanofibers for all applied potentials (5, 10, 15, and 20 kV).

Nanofibrous scaffolds of polylactic-*co*-glycolic acid (PLGA)/chitosan were synthesized through the emulsion electrospinning technique.[309] This technique doesn't require common solvents for either polymers or grafting. Furthermore, this allows the blending of polymers from natural and synthetic origins at different ratios. PLGA/chitosan scaffolds are hydrophilic due to the presence of chitosan and are mechanically strong because of having PLGA. Polyblends are highly useful in biomedical fields, like skin tissue engineering applications, as they have improved cell–scaffold interactions.

The development of nanofibrous hydrogel membranes by electrospinning has received tremendous attention in the research community in recent years. The hydrogel nanofibrous membranes are scaffolds that are extensively studied for their application in drug delivery systems, regenerative biomaterials for skin and tissue engineering, bone repair, *etc.*[310,311] The advances in the synthesis and development of PVA-polysaccharide-based electrospun membranes are extensively reviewed recently.[312]

The inclusion of bioactive additives, nanoparticle additives, medicaments, and medicinal plants in hydrogel nanofibrous membranes was also discussed. The advances in the usage of natural therapeutic compound loaded electrospun nanofiber membranes for wound dressing applications are highlighted in a mini-review by Younes *et al.*[313] Trends in tissue repair and regeneration using herbal scaffolds have been reviewed recently.[314] The fabrication techniques, such as electrospinning, solvent casting, freeze-drying, additive manufacturing, and hydrogel formation, are discussed.

Packaging applications

The potential usage of functional plant-based nanofibers for food packaging applications is getting wider acceptance among the research community in recent days. Electrospun nanofibers encapsulated with natural antioxidants/ingredients are considered as a prospective packaging material for preserving the food

materials and releasing nutrients to the food during preservation (Fig. 13).

Cinnamaldehyde (CNMA) is a bioactive chemical and packaging systems based on electrospun nanofibers with the inner area encapsulated with CNMA and the outer layer with compression-molded polyhydroxybutyrate (PHB) are reported.[316] The virucidal activity of CNMA was tested against norovirus surrogates, murine norovirus (MNV), feline calicivirus (FCV), and hepatitis A virus (HAV). The study reported that the CNMA-incorporated multilayer films inactivated FCV and offered better protection against MNV and HAV. An interesting study on strawberry preservation with conventional low-density polyethylene (LDPE) *vs.* electrospun PVA/cinnamon essential oil (CEO)/β-cyclodextrin (β-CD) was reported by Wen *et al.*[317] Unlike other essential oils such as clove and eucalyptus, CEO was chosen in their study as it was anticipated to give better food preservation and inhibit bacterial colony formation. The efficacy of fibrous PVA/CEO/β-CD mats against *E. coli* and *S. aureus* showed that the inhibition zones were 29 and 30 mm, respectively, and the fruits preserved with PVA/CEO/β-CD were stable without losing their flavor even after six days.

Cyclodextrin inclusion complexes (CD-ICs) are plant extracts used in the food industry. They are generally used as drug carriers and can form complexes with hydrophobic compounds. To improve the shelf-life and minimize the volatility of natural organic compounds, CD-ICs were used in nanofibers as carriers of plant extracts in food packaging applications.[17]

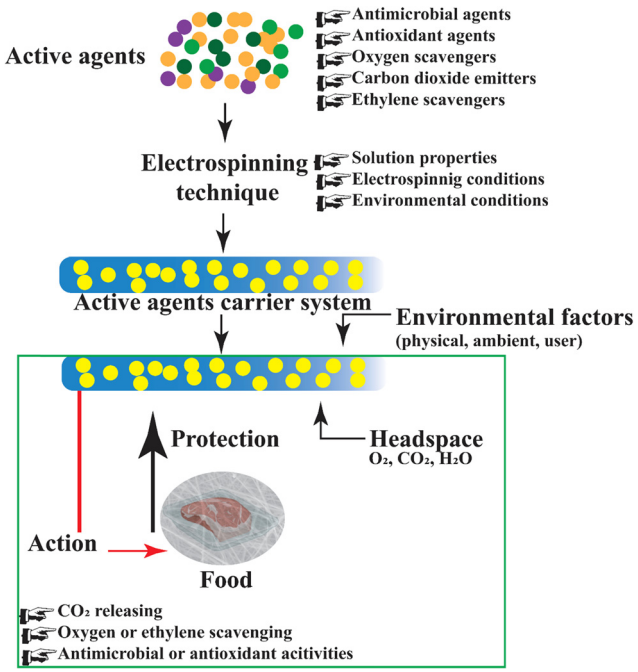

Fig. 13 Antibacterial activities of bioactive plant extract nanofibers in food packaging.[315] Bioactive nanofibers are used to fabricate smart food packaging that extends shelf life and improves food safety. Plant-based electrospun functional nanofibers, as packaging materials, regulate ambient gases (O_2, CO_2, H_2O), diminish oxygen or ethylene, release carbon dioxide, and protect food by utilizing their antibacterial or antioxidant properties. These mechanisms reduce spoilage germs, slow down lipid and vitamin oxidation, and preserve food color, flavor, and texture efficiently.

A detailed review of electrospun nanofibers having antioxidant, antibacterial, and antifungal properties for food packaging applications is available.[318]

Corn zein prolamine, in addition to chitosan ultrathin electrospun water resistant nanofibers, has intriguing utilization in food technology due to the bioactive and antimicrobial film-forming properties, such as a reinforcing fiber in plastic food packaging and as an edible carrier for encapsulating food additives or changing food qualities.[319] Neo *et al.* also incorporated zein prolamine co-loaded with garlic acid; the resulting nanofibers demonstrated potential applications for food packaging materials owing to their antibacterial and antioxidant properties.[320]

Red raspberry extract with bioactive anthocyanins loaded with soy protein isolate was studied by Wang *et al.* for nanofiber development.[321] The resultant fibers demonstrated excellent potential for active packaging due to their greater concentration of bioactive anthocyanins and improved antibacterial activity against *Staphylococcus epidermidis* in thermoplastic wheat gluten films electrospun from whey and soy protein isolate and zein loaded multilayer nanofibers developed by Farba *et al.*[322] Encapsulated alpha-tocopherol release was prolonged and the water vapor barrier performance of the wheat gluten film was improved, highlighting the potential of hybrid hydrocolloid structures with active chemicals in the creation of innovative multifunctional food packaging materials (Fig. 14). Ethyl cellulose and soy protein were loaded with orange peel extract to develop nanofibers for antimicrobial, antioxidant, and safe food packaging materials as reported by Rashidi *et al.*[323]

By combining glutenin and PVA to form composite nanofibers, Han *et al.* were able to increase the average diameter and homogeneity while lowering the diameter and quantity of beads and showed that PVA/glutenin nanofibers were more elongated and could absorb more water than pure PVA nanofibers.[324] Gelatin and

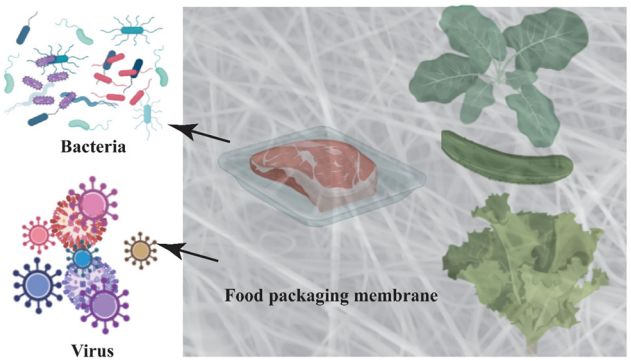

Fig. 14 Bioactive nanofibrous membrane creating barrier layers to prevent harmful microbes from getting into food packaging. The nanolayer, which is composed of microscopic structures with bactericidal characteristics, shields encapsulated food from harmful microorganisms by either blocking their entry or neutralizing them. The figure shows a piece of meat with fresh veggies inside the nanolayer barrier, illustrating how versatile this technology is. The nanolayer is ideal for a wide variety of food packaging applications due to its transparency and flexibility. This infographic highlights how nanotechnology has the ability to completely change the food industry and make food security much more reliable.

zein were encapsulated with curcumin extract with the addition of green tea extract for bioactive food packaging application as reported by Ali *et al.*[325] While the gelatin coatings demonstrated promising release behavior when exposed to fatty meal simulants, the results indicated that zein-based coatings would be better suited for packaging foods with high water content.

A recent study reported the fabrication of nanofibers employing lavender oil loaded with PVP for active food packaging applications.[326] Nanofiber mats infused with lavender have antioxidant properties *in vitro*. Testing on minced lamb *in situ* confirmed this influence. Meat's shelf life was extended by lavender oil-loaded PVP nanofibers, lowering yeast molds, psychotropic bacteria, and aerobic mesophilic bacteria that cause damage to meat.

Similarly, another study showed the development of nanofibers loaded with PLA/Ag for wound dressing applications that exhibited enhanced tensile strength, absorbency, and antibacterial properties with no cytotoxicity effects.[327] Mi Li *et al.* produced biodegradable active packaging materials that demonstrated a hydrophobic nature with a eugenol layer inside and exhibited remarkable antioxidant and antibacterial activity against Gram-positive and Gram-negative bacteria.[328]

Yadong *et al.* developed edible packaging materials in addition to gelatin with chamomile essential oil.[329] The results showed that increasing the oil concentration led to an increase in fiber diameter while still maintaining uniform fibers. The developed samples exhibited excellent antioxidant and antibacterial activities. The latest study by Ceylan *et al.* developed nanofibers loaded with grape oil to produce high-quality products in the food industry. Aslaner *et al.* used grape extract with PEO and flour for electrospinning. The fibers were suggested to be utilized in protective multilayer packaging.[330] The insights derived from recent research indicate a notable trend toward embracing nanofibers for advanced applications in food packaging. The encapsulation of natural antioxidants through electrospinning emerges as a favored strategy for preserving food materials and facilitating controlled nutrient release.

However, in biomedical contexts, the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require comprehensive preclinical and clinical evaluations for nanoparticles in medical devices and pharmaceuticals. This includes extensive toxicity testing, biodistribution studies, and detailed risk assessments to ensure that therapeutic benefits outweigh potential adverse effects.[331,332] For food packaging, agencies like the FDA and the European Food Safety Authority (EFSA) focus on migration testing, toxicological evaluations, and comprehensive safety assessments to ensure that nanoparticles do not pose health risks to consumers. These guidelines mandate thorough risk assessments, including data on the potential migration of nanoparticles into food, their toxicokinetic properties, and any health impacts. Comparing the toxic effects and biocompatibility of different types of nanoparticles, such as silver, zinc oxide, gold, and titanium dioxide, allows for selecting the safest materials for specific applications.[333] By adhering to these regulatory guidelines and safety standards, the risks associated with the use of metal nanoparticles in biomedical and food packaging applications can be effectively managed, ensuring that nanoparticles are thoroughly tested and evaluated for safety before reaching consumers. Continuous research and strict adherence to these guidelines are essential to harnessing the benefits of nanotechnology while safeguarding public health and the environment.

Challenges, prospects, and conclusions

While plant-based polymeric nanofibers offer a wide range of characteristics suitable for biomedical applications, they also present certain challenges and limitations. Plant-based bioactive compounds can be sensitive to geographical locations and seasons, potentially causing allergic reactions and adverse effects.[334] One significant drawback is the insolubility of many plant materials, which limits their ability to be electrospun on their own. This issue is often mitigated by using copolymers.[259] Additionally, surface tension can hinder smooth fiber production, as demonstrated by Ali *et al.*, who utilized a cationizer to reduce the surface tension of the solution.[167] Poor mechanical properties are another concern; thus, several biopolymers are combined with plant extracts to enhance cellular uptake.[335] For example, soy-based scaffolds have low molecular weight, which complicates thorough characterization and optimization for biomedical applications.[336]

Although plant extracts are integrated into various biopolymers such as PVA, PLA, PCL, PGA, cellulose, and chitin, not all these biopolymers dissolve in water, necessitating the use of harmful chemical solvents like DMAc, HFEP, and HFP. These solvents, which evaporate during fiber manufacture, pose health risks and may leave residues that cause problems during applications.[336] Intensive research can overcome these obstacles. While plant extracts are brittle and cannot be electrospun alone, synthetic and natural biopolymers can mitigate this limitation. Additionally, green solvents, such as ionic liquids or deep eutectic solvents, can be employed to avoid using harmful organic solvents.[337,338]

This review highlights the significant potential of bioactive electrospun nanofibers derived from plant extracts for biomedical and food packaging applications. Various plant materials, including leaves, seeds, stems, flowers, and fruits, have been used to extract bioactive chemicals with antibacterial, antioxidant, anti-inflammatory, and anticancer properties. These bioactive chemicals are effectively integrated into nanofibers using biopolymers as carriers.

The electrospinning process offers a flexible method to customize the structure and size of nanofibers, enabling specific properties. The resulting nanofibers find use in various applications such as enhanced wound healing, regulated drug administration, scaffolds for tissue engineering, food packaging protection, and antibacterial filtering. However, challenges such as the natural fragility of plant extracts, insufficient mechanical strength, and the necessity for carrier polymers and organic solvents during manufacturing must be addressed.

Future developments should focus on improving the structural durability of nanofibers through novel composite architectures and ensuring the continuous release of bioactive substances. Comprehensive *in vivo* testing is crucial to assess the long-term safety and effectiveness of these nanofibers in living organisms. Additionally, employing environmentally friendly electrospinning processes to scale up manufacturing will facilitate the commercialization of these eco-friendly nanomaterials. In summary, bioactive electrospun nanofibers from plants represent a highly promising field that bridges nanotechnology and natural phytotherapy.

Future research on bioactive electrospun nanofibers must prioritize several key efforts. These include developing advanced multi-polymer composites and hybrid nanofibers to enhance mechanical strength, exploring synergistic combinations of plant extracts to boost therapeutic benefits, and creating carrier matrices for prolonged release of bioactive compounds. To ensure safety and efficacy, extensive testing in animal models should precede human trials. This focused trajectory involves scaling up electrospinning rigs for large-scale production, utilizing environmentally friendly solvents, and commercializing plant extract-based electrospun products.

Abbreviations

AA	Acetic acid
AcA	Acrylic acid
BC	Bacterial cellulose
CS	Chitosan
CECS	Carboxyethyl chitosan
CA	Cellulose acetate
DIW	Deionized water
DMAc/DMA	Dimethylacetamide
DMF	Dimethylformamide
DCM	Dichloromethane
DMSO	Dimethyl sulfoxide
EDC	*N*-Ethylenecarbodiimide
EDTA	Ethylenediaminetetraacetic acid
ECM	Extracellular matrix
FA	Formic acid
Gel	Gelatin
AuNPs	Gold nanoparticles
GT	Gum tragacanth
GO	Graphene oxide
HFIP	Hexafluoroisopropanol
ILs	Ionic liquids
PCL	Poly(caprolactone)
PVP	Poly(vinyl pyrrolidone)
PLGA	Polylactic-*co*-glycolic acid
PU	Poly(urethane)
PEO	Poly(ethylene oxide)
PS	Poly(styrene)
PLA	Poly(lactic acid)
PVA	Poly(vinyl alcohol)
PS	Poly(styrene)
PCL	Poly(caprolactone)
PAN	Poly(acrylonitrile)
AgNPs	Silver nanoparticles
THF	Tetrahydrofuran
TFE	Trifluoroethanol
ZnONPs	Zinc oxide nanoparticles

Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

Data availability

The data supporting the findings of this study are available within the article and its supplementary materials. Data can also be requested from the corresponding authors [Md Nur Uddin, Ayub Ali, and Abdur Rahman Bhuiyan at nur@duet.ac.bd, ayubali@duet.ac.bd, and arahman@duet.ac.bd, respectively], subject to reasonable request and any applicable privacy or ethical restrictions.

Conflicts of interest

The authors declare no potential conflict of interest.

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