Electrospun Polymer Materials with Fungicidal Activity

Subjects: Polymer Science

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There has been special interest in innovative technologies such as polymer melt or solution electrospinning, electrospraying, centrifugal electrospinning, coaxial electrospinning, and others. Applying these electrokinetic methods, micro- or nanofibrous materials with high specific surface area, high porosity, and various designs for diverse applications could be created.

Keywords: electrospinning ; biopolymers ; Phaeomoniella chlamydospora

1. Electrospinning

The first description of the electrospinning process was given in 1902 when J.F. Cooley applied for a patent entitled "Apparatus for electrically dispersing fluids" [1]. In his patent (US 692631), he described a method using high-voltage sources to obtain fibers. The next significant scientific development was achieved by Zeleny [2], who published his work on the behavior of liquid droplets at the end of metallic capillaries. His work marked the beginning of efforts to mathematically model the behavior of liquids under the action of electrostatic forces In the 1930s, Formhals patented his invention for industrial production of artificial filaments plastics [3]. Between 1964 and 1969, Taylor laid the theoretical foundation of the electrospinning process [4]. His publication contributes to the understanding of the process by mathematically modeling the shape of the cone formed by the drop of liquid under the action of electrostatic forces. This characteristic droplet shape is still known as the Taylor cone.

Nowadays, electrospinning has established itself as one of the most promising and effective methods for obtaining continuous micro- and nanofibers [5]. Interest in the method of electrospinning in the period 2000–2021 grew many times over. According to ScienceDirect®, the number of scientific publications in the database for the year 2000 when searching for the keyword "electrospinning" is eight, and in 2021 this number increases to 5695.

Depending on the viscosity of the solutions, two processes are distinguished: electrospraying or electrospinning. When using diluted polymer solutions, electrospraying is observed—obtaining micro- or nano-sized particles. When an electric field is applied to concentrated polymer solutions (solutions with sufficiently high viscosity), a fiber formation process is observed. This process is known as electrospinning. Polymers have flexible chains in solution. They form the so-called "random coils". In highly concentrated solutions of such polymers, the statistical globules are interpenetrating and form a physical network of intertwined segments of the polymer chains. This entanglement is essential for forming an elastic network and forming a micro- or nanoscale fiber (diameters in the micro- or nanoscale and hundreds of meters in length) [6].

In both processes, under the action of electrostatic forces, the surface of the drop is deformed and acquires a conical shape (Taylor's cone) [4]. When the applied voltage is high enough (inducing enough repulsion of the charges to overcome the surface tension of the polymer solution), a jet of liquid is ejected from the tip of the needle. Initially, the trajectory of the jet is straight and stable, then it undergoes separation processes in electrospraying and stretching and bending to obtain a long and thin filament in electrospinning [7].

Fiber formation by electrospinning is a process that is affected by a number of factors such as spinning solution parameters and electrospinning process parameters. When using a polymer with a high molar mass, the viscosity of the solution increases. In order to observe an electrospinning process which will lead to defect-free fiber formation, it is necessary for the polymer solution to be sufficiently viscous, since at lower viscosity values, fibers with defects are obtained. Shenoy et al. reported that complete, stable fiber formation occurs at >2.5 entanglements per chain [6].

The viscosity of a solution is closely related to its concentration. Increasing the viscosity or the solution concentration results in a more uniform fiber formation and narrow distribution of the mean fiber diameter [8]. In solutions with low viscosities, the surface tension is the determining factor and then only spheres or fibers with spherical defects are obtained, while above a certain critical concentration, a continuous fibrous structure is obtained and its morphology is affected by the concentration of the solution [9].

The parameters of the electrospinning process, which influence the morphology of the fibers, are the electric voltage, the feeding rate of the spinning solution, the distance between the tip of the capillary and the collector, the collector rotation speed, the type of collector used, etc. The applied voltage is a major factor without which the process cannot be carried out. Typically, a positive or negative voltage of over 6 kV is required for the jet to form a Taylor cone [10]. Uniform defect-free fibers are obtained above a certain critical value of solution feed rates. Increasing the velocity above the critical one leads to the formation of particles [11]. Another key parameter for fiber formation is the distance between the tip of the capillary and the collector. It was found that when this gap is reduced, the time of flight of the jet is shortened. In brief, if the distance is too short, the solvent evaporation time is insufficient and the fibers fail to dry before reaching the collector. In this case, solvent-containing fibers are deposited [12][13]. For this reason, it is necessary to find an optimal gap for the solvent to evaporate and dry fibers to be deposited on the collector. Environmental parameters such as temperature and air humidity also influence fiber morphology and diameter. It was found that with increasing temperature, fibers with smaller diameters are obtained, which is due to a decrease in the viscosity of the polymer solutions at high temperatures [14]. Predominantly, electrospinning of polymer solutions is carried out in air.

The use of different types of collectors and focusing devices can affect the jet trajectory and hence the morphology and orientation of the resulting fibers. The simplest collector used in electrospinning is a stationary metal plate or foil located at a certain distance from the needle. When using this type of collector, the fibers are usually deposited randomly on the metal plate. It has been established that a certain control of the orientation of the resulting mat is achieved with the rotary movement of the collector. Different types of collectors used in electrospinning are solid cylinder, solid cylinder with a wire, a disc, blades, etc. The advantage of using a drum or disc collector is that oriented fibers can be prepared, and long oriented bundles can be obtained. The disadvantages of their use, however, are that the degree of fiber orientation decreases with increasing layer thickness. By using a wire-wrapped or wire-built collector, highly oriented fibers can be obtained. Very good fiber ordering is obtained when blade-type collectors are used [15]. Needle electrodes were also made with the aim of self-organizing the fibers into bundles and yarns. Comb-type electrode with a different number of interchangeable needles, from one to five, has been developed as well. The body of the comb is made of solid wood, and the electrode needles are made of stainless steel [16].

2. Applications of Electrospinning

In recent years, the interest in the production of micro- and nanofibrous materials by the electrospinning method has been continuously increasing. This is due to the possibility of imparting desired properties to the obtained fibrous materials, such as biodegradability, biocompatibility, mechanical strength, etc. Electrospun fibrous materials are known to possess a large specific surface area (10^3 m^2/g) and small pore size and spatial structure [17]. The potential applications of these materials as filter media [18][19], tissue engineering scaffolds [20][21], carriers of active substances [22][23], protective clothing [24], and sensors [25] are the subject of increasing interest.

Polymers are all around us, as polymer products have widely entered our lives. Natural polymers such as cellulose and starch are widely used in the food industry and for the production of paper and packaging. Obtaining polymers from renewable sources changes production and recycling technologies, providing opportunities to create environmentally friendly materials that do not pollute the environment, degrading significantly faster than synthetic polymers. Therefore, research in the field of polymers is necessary not only for the development of such branches of industry as the production of products based on polymers, but they are an important and key component of interdisciplinary research related to the development of high technologies, nanotechnology, biotechnology, medicine and pharmacy, and environmental protection.

Over the past few decades, there has been a continued scientific and industrial interest in biocompatible and biodegradable polymers, especially in saturated polyesters. This is due to the fact that they can be obtained from renewable sources and also to their valuable physicomechanical properties. One of the most attractive synthetic polymers are the aliphatic polyesters such as poly(lactic acid), poly(glycolic acid), and their copolymers. Aliphatic polyesters are characterized by one main advantage—they degrade in the human body and in the environment through the hydrolysis of their ester bond. In addition, they are compatible with human organs and tissues. That is why these synthetic polymers are considered to be one of the most promising for obtaining polymer products for the needs of medicine and pharmacy [26][27]. These polymers are used to produce absorbable sutures, controlled drug release systems, and orthopedic fixation devices (implants) such as pins, screws, and plates [28][29]. Their wide application to make suitable polymeric products for the needs of tissue engineering is known as well [30].

Fibrous materials obtained by applying the method of electrospinning/electrospraying solutions of aliphatic polyesters are characterized by a set of desirable properties such as biocompatibility, degradability, similarity to the extracellular matrix of natural tissues, and excellent physicomechanical properties. In the literature, there are quite a few studies related to the influence of the various parameters of the electrospinning process on the diameters and morphology of the obtained polylactic acid (PLA) fibers. Micro- and nanofibrous materials based on homo- and copolymers of PLA are promising candidates for application in cell and tissue engineering [31][32] to create new drug carriers [33], for the restoration of bone tissue [34], for water purification [35], etc.

In the last ten years, there has been a growing interest in PLA electrospinning, as evidenced by the growing number of scientific publications. The number of scientific publications on PLA electrospinning according to ScienceDirect data in 2011 was 143, reaching nearly 1000 in 2021. In 2007, Spasova and co-authors successfully electrospun poly(L-Lactic acid) (PLLA) and PLLA/polyethylene glycol (PEG) mixed solutions [36]. Increasing the amount of PEG in the solution resulted in thinner and more hydrophilic fibers with average diameters of 330 nm. The thinnest fibers were obtained when using a PLLA/PEG spinning solution with a concentration of 5 wt% and a PLLA to PEG ratio of 70/30. The process takes place at a constant value of the applied voltage of 11 kV. Electrospinning under these conditions, however, leads to the appearance of defects along the fiber length. Two types of cells—fibroblasts and osteoblasts—were used to conduct biological tests to establish the cellular compatibility of the obtained materials. It was found that the osteoblasts began to organize into tissue-like structures, especially in the materials with a higher content of the water-soluble polymer.

By using electrospinning, the valuable properties of polylactic acid and its copolymers are combined with natural polymers such as chitosan, which has its own biological activity [37][38]. PLLA/PEG fibers were obtained which were coated with chitosan [37]. The presence of chitosan coating was demonstrated by SEM and fluorescence microscopy. The behavior of the obtained hybrid fibrous materials when placed in contact with human blood was investigated. Chitosan-coated materials have been found to induce blood clotting. The microbiological tests carried out against *Staphylococcus aureus* show that the chitosan coating imparts antibacterial activity to the obtained mats. Combining hemostatic with antibacterial properties makes these materials suitable for treating wound surfaces.

Toncheva and co-authors created PLLA and PLLA/PEG membranes containing one or more drug substances, such as diclofenac sodium, lidocaine hydrochloride, benzalkonium chloride, or combinations thereof. The incorporation of low-molecular-weight salts contributes to the improvement of the conductivity of the spinning solutions and the preparation of oriented fibers with antimicrobial properties [16][39]. In addition, Ignatova et al. found that fibers based on PLA and 8-hydroxyquinoline-2-carboxaldehyde possess antitumor activity against HeLa cancer cells [40].

There are two main approaches to electrospinning drug-loaded materials. In one approach, a mixed spinning solution containing the polymers and drugs is prepared [16][39]. In the other approach, electrospinning is performed from two polymer solutions loaded into two syringes, with a separate drug incorporated into each solution [41][42]. The advantages of the electrospinning method when using two syringes containing solutions of different biologically active substances is that they do not ionically interact with each other. The obtained new materials can find applications in biomedicine and pharmacy.

Electrospraying is a technique that can be used to produce micro- and nanoparticles. Virsovska and co-authors first compared the application of the electrospinning technique with the simultaneous electrospinning/electrospraying technique on PLLA and nanosized ZnO mats [43]. To obtain the “in” type materials, ZnO was added to a PLLA solution and the resulting suspension was subjected to electrospinning. The “on” type materials were obtained by simultaneous electrospinning and electrospraying, using two separate pumps to deliver the two solutions. One syringe contains a concentrated PLLA solution and the other a suspension of ZnO in a dilute PLLA solution. It was found that combining the two methods leads to the preparation of hybrid fibrous materials with improved photocatalytic and antibacterial activity. New self-cleaning hybrid fibrous materials based on PLLA decorated with nanosized ZnO and expanded graphite or fullerene (C60) were also obtained [44].

By using the electrospinning method, biologically active substances of natural origin can easily be incorporated into fibrous materials. Curcumin is a polyphenolic compound extracted from the roots of the turmeric plant (*Curcuma longa* L., family Zingiberaceae). It has antitumor, antioxidant, anti-inflammatory, and antimicrobial properties [45][46]. Yakub and co-authors successfully incorporated curcumin into fibers of PLLA and PVP or PEG [47][48]. Curcumin incorporated into the fibers is protected from photodegradation. The presence of polymers that can form hydrogen bonds with curcumin facilitates its extraction. The obtained new materials, based on PLLA, possess both good mechanical properties and antibacterial, antioxidant, and anticoagulant activities.

By exploiting the property of PLA to form stereocomplexes, novel fibrous materials of PLLA and PDLA [49][50] and PLLA and PDLA-*b*-PBS [51][52] have been obtained, which have an increased melting temperature and therefore are suitable for biomedical applications. Moreover, PLA fibrous materials were prepared, on which a polyelectrolyte complex of *N*-carboxyethyl chitosan and polyoxyethylene-*b*-quaternized poly-2-(dimethylamino)ethyl methacrylate was formed, which possesses hemostatic properties and reduces the adhesion of pathogenic microorganisms [53].

Incorporation of metal oxide nanoparticles into fibers by electrospinning is a promising method for preserving their properties and imparting specific properties to hybrid fibrous materials such as antibacterial, antifungal, antitumor, antioxidant, anti-inflammatory, self-cleaning, and other activities [54][55].

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