Application of Nanofibers in Drug Delivery

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ABSTRACT

The growing interest in polymeric nanofibers for drug delivery systems is attributed to their exceptional micro and nanostructural characteristics, which include a high surface area, small pore size, and the ability to form three-dimensional structures. These properties enable the development of advanced materials with diverse applications in biomedicine. Electrospinning is recognized as a straightforward and cost-effective method for fabricating nanofibers. The electrospinning setup comprises a syringe with a nozzle, an electric field source, and a grounded target, along with a pump to facilitate the flow of polymer solutions. The electrospinning process is influenced by various parameters, categorized into solution, process, and ambient parameters, all of which significantly affect the morphology and characteristics of the resulting nanofibers.

Characterization methods for nanofibers include imaging techniques such as optical microscopy, scanning electron microscopy, and atomic force microscopy, as well as porosity measurement methods like mercury porosimetry. The chemical properties of nanofibers can be analyzed through Fourier transform infrared spectroscopy and nuclear magnetic resonance. The multifaceted applications of nanofibers in drug delivery encompass the delivery and detection of vitamins, DNA and siRNA delivery, growth factor delivery, and approaches for oral mucosal and peroral drug delivery, alongside their roles in biosensors, tissue engineering, regenerative medicine, and wound dressings. This comprehensive review focuses on recent advancements in nanofiber technology and its profound implications for enhancing clinical outcomes in drug delivery.

Keywords: Nanofibers, Drug delivery, Vitamins delivery, Biomedical applications

1. *INTRODUCTION*

In the last decade, the field of nanomedicine has witnessed remarkable advancements driven by the extraordinary potential of nanofibers in various biomedical applications. The vast interest in polymeric nanofibers for drug delivery is fueled by their unique micro and nanostructural characteristics, which include high surface area, small pore size, and the capability to generate three-dimensional structures. These properties facilitate the creation of sophisticated materials that can address a range of medical challenges. According to estimates, the global market for nanofiber products is expected to grow significantly in the coming decades, with numerous companies worldwide likely to engage in their production.

The National Science Foundation (NSF) defines nanofibers as materials with at least one dimension measuring 100 nm or less. These solid fibers possess a high surface area-to-mass ratio, exceptional porosity, flexibility, and remarkable mechanical properties. In healthcare, nanofibers serve as tools for drug delivery, improving the efficacy and safety of therapeutic agents by precisely controlling the rate, duration, and site of drug release.

Three primary techniques are employed for the consistent creation of nanofibrous structures: self-assembly, phase separation, and electrospinning. Among these methods, electrospinning has gained prominence due to its simplicity, cost-effectiveness, and scalability. The process allows for the production of nanofibers from various polymers, enabling the incorporation of a wide range of therapeutic agents, including antibiotics, anticancer drugs, proteins, vitamins, and DNA.

This work aims to provide a comprehensive review of the advancements in nanofibers for drug delivery systems. The examples highlighted herein demonstrate the significant impact that these innovative systems have on clinical outcomes, emphasizing the transformative potential of nanofiber technology in modern medicine.

2. Materials and Methods

2.1 Electrospinning Setup

The electrospinning setup utilized in this study consists of several key components essential for producing nanofibers. The primary apparatus includes:

1. Syringe with a Nozzle: A typical syringe (usually a 10 mL or larger size) is used to hold the polymer solution. The nozzle, typically made of metal or plastic, is connected to the syringe and is responsible for ejecting the polymer solution under the influence of an electric field. The nozzle's diameter can vary, influencing the diameter of the resulting nanofibers.

2. Electric Field Source: A high-voltage power supply is employed to generate an electric field between the nozzle and the collector. The applied voltage usually ranges from 10 kV to 30 kV, depending on the nature of the polymer solution and the experimental setup. The electric field creates a charged jet of the polymer solution that stretches and thins as it travels toward the collector.

3. Collector: The grounded target, or collector, is typically made of conductive materials such as aluminum foil, conductive paper, or metal plates. The distance between the nozzle and the collector is adjustable and significantly affects the fiber morphology and diameter.

4. Pump: A syringe pump is used to control the flow rate of the polymer solution being fed into the nozzle. The flow rate is a critical parameter that influences the fiber formation process and the morphology of the nanofibers produced.

2.1.1 Electrospinning Process

The electrospinning process involves several stages:

1. Solution Preparation: The polymer is dissolved in a suitable solvent to create a solution with a specific concentration, viscosity, and conductivity. The choice of solvent and polymer concentration is crucial for successful electrospinning and affects the morphology of the nanofibers.

2. Application of Electric Field: After the polymer solution is loaded into the syringe and the flow rate is set, the electric field is applied. The solution at the nozzle tip forms a Taylor cone due to the electrostatic forces. As the field strength increases, the cone elongates, and a thin jet of solution is ejected.

3. Formation of Nanofibers: As the charged jet travels toward the collector, the solvent evaporates, resulting in the formation of solid nanofibers. The properties of the nanofibers are influenced by various parameters, including the solution properties (viscosity, conductivity, surface tension), processing parameters (applied voltage, flow rate, tip-to-collector distance), and environmental conditions (temperature, humidity).

2.1.2 Nanofiber Characterization

Characterization of the electrospun nanofibers is crucial for understanding their structural and functional properties. Various characterization techniques are employed, including:

1. Morphological Analysis: Scanning Electron Microscopy (SEM) is often used to observe the fiber morphology, diameter, and surface characteristics. Optical microscopy and Atomic Force Microscopy (AFM) can also be utilized for detailed surface analysis.

2. Geometrical Properties: The fiber diameter, diameter distribution, and orientation are analyzed using image processing software to quantify the geometric characteristics of the produced nanofibers.

3. Porosity and Pore Size Measurement: Techniques such as mercury porosimetry and capillary flow porosimetry are employed to measure the porosity and pore size of the nanofibrous mats, which are critical for applications in filtration and tissue engineering.

4. Chemical Characterization: The molecular structure of the nanofibers is analyzed using Fourier Transform Infrared Spectroscopy (FTIR), Nuclear Magnetic Resonance (NMR), and Differential Scanning Calorimetry (DSC) to understand the chemical properties and interactions of the polymeric materials.

2.1.3 Methods for Drug Incorporation

Several methods for incorporating drugs into the polymeric solution for electrospinning were explored:

1. Blending: The most common method involves dissolving or dispersing the drug in the polymer solution before electrospinning. The drug's compatibility with the polymer is critical for achieving high encapsulation efficiency and preventing burst release.

2. Surface Modification: Drugs can also be conjugated to the surface of the nanofibers post-electrospinning to enhance bioactivity and control the release profile.

3. Emulsion Electrospinning: In this method, the drug solution is emulsified within the polymer solution. The distribution of the drug in the nanofibers can modulate the release profile and maintain the bioactivity of the encapsulated biomolecules.

4. Multi-drug Delivery Systems: This innovative approach combines multiple drugs within the same electrospun fiber mat to achieve a synergistic therapeutic effect.

5. Multilayer Coating: The electrospun fibers can be coated with additional layers of polymers or drugs to create a controlled release system that enhances the stability and bioactivity of the encapsulated substances.

2.2 Self-Assembly and Phase Separation

In addition to electrospinning, other techniques for nanofiber production include:

- Self-Assembly: This method involves the spontaneous organization of molecules into structured nanofibers through non-covalent interactions. Although it can produce thinner fibers, the process is complex and less scalable than electrospinning.

- Phase Separation: This technique produces porous nanofibrous structures by removing solvents through freeze-drying or extraction methods. It is effective with a limited number of polymers and is generally conducted at the laboratory scale.

These methodologies contribute to the diverse applications of nanofibers in drug delivery,

3 Results and Discussion

Recent years have seen a surge in research focused on nanotechnology, particularly in the context of nanofibers and their unique properties. Nanofibers, characterized by their high surface area-to-volume ratio, tunable porosity, and flexibility in composition, have emerged as promising materials in various biomedical applications such as drug delivery, biosensing, tissue engineering, and regenerative medicine (1, 2).

3.1 Delivery and Detection of Vitamins

Vitamins are essential organic compounds required in small amounts for various physiological functions. Their stability and delivery mechanisms are crucial, and researchers have demonstrated the successful incorporation of vitamins A, E, and D into nanofibrous scaffolds using electrospinning techniques. For instance, gelatin nanofibers loaded with vitamin A palmitate and vitamin E TPGS displayed a sustained release over 60 hours, effectively maintaining the bioactive properties of these vitamins (3). Additionally, *vitamin D detection has been enhanced through the development of electrochemical biosensors using polyacrylonitrile nanofibers, improving sensitivity and detection range (4).*

3.2 Tissue Engineering and Nanofibers

The application of electrospun nanofibers in tissue engineering dates back to the late 1980s when they were first utilized as substrates for cell growth. Due to their high porosity and structural similarity to the natural extracellular matrix, nanofibers are ideal for supporting cell attachment and proliferation (5). For instance, poly(lactide-co-glycolide) nanofibers were engineered to release β-carotene, promoting osteogenesis and facilitating bone tissue engineering (6).

3.3 Tissue Engineering and Regenerative Medicine

In the field of regenerative medicine, nanofibers serve as versatile scaffolds that can be tailored to support the growth and differentiation of various cell types. Research has shown that electrospun gelatin nanofibers enhance the formation of myotubes, improving muscle tissue regeneration (7). Additionally, functionalized PLGA nanofibers have demonstrated improved adhesion and contraction of cardiomyocytes, showcasing their potential in cardiac tissue engineering (8).

3.4 Polymeric Nanofibers in Tissue Engineering

Polymeric nanofibers have gained significant attention for their tunable drug loading and release capabilities. By mimicking the extracellular matrix, they can modulate stem cell differentiation and promote tissue regeneration (9). Notably, chitosan/silk fibroin nanofibrous membranes have shown promise in enhancing the proliferation of mesenchymal stem cells, indicating their suitability for bone tissue engineering applications (10).

3.5 Wound Dressings with Nanofibers

Electrospun nanofibers have been increasingly utilized in wound dressing applications due to their ability to provide a moist environment conducive to healing while also demonstrating antibacterial properties. Research indicates that nanofibrous dressings can enhance innate immunity and promote wound healing through the sustained release of antimicrobial agents such as 1α,25-dihydroxyvitamin D3 (11).

3.6 Electrospun Membranes in Wound Dressing

The unique structural properties of electrospun nanofibrous membranes make them ideal for wound dressings, offering high surface area and porosity that support cell adhesion and proliferation. They can be engineered from various biodegradable polymers, such as chitosan and polyurethane, to enhance their antibacterial efficacy and promote healing (12).

3.7 DNA and siRNA Delivery

Nanofibers have also been explored as carriers for nucleic acids like DNA and siRNA, which are vital for gene therapy applications. The high surface area and porosity of nanofibers facilitate cell adhesion and enable efficient delivery of nucleic acids, with studies demonstrating successful encapsulation of siRNA in PCL nanofibers leading to enhanced cellular uptake (13).

3.8 Growth Factor Delivery

The controlled release of growth factors from nanofibers has the potential to enhance tissue regeneration. Techniques such as coaxial electrospinning and surface modification allow for the effective incorporation of growth factors, providing sustained release profiles that are critical for promoting cellular activities essential for tissue repair (14).

3.9 Nanofiber Scaffolds for Oral Mucosal Drug Delivery

Fast-dissolving formulations utilizing nanofibers offer a novel approach to oral drug delivery, particularly beneficial for pediatric and geriatric patients. These scaffolds can be designed to provide sustained release of drugs, ensuring therapeutic levels are maintained over extended periods (15).

3.10 Self-Assembled Peptide Nanofibers (SAPNs)

SAPNs represent an innovative category of materials with autonomous self-assembling capabilities. These peptide-based nanofibers have shown promise as "smart" drug delivery systems, capable of responding to environmental cues such as pH changes to release therapeutic agents (16).

3.11 Nanofibers in Per Oral Drug Delivery

Electrospun nanofibers have been used to develop various oral drug delivery systems, including immediate and modified-release formulations. The incorporation of active pharmaceutical ingredients into nanofibers allows for tailored release profiles that can enhance drug bioavailability and therapeutic efficacy (17).

Conclusion

In summary, electrospinning is a powerful and versatile technology for producing nanofibers that have a multitude of applications in drug delivery, tissue engineering, and regenerative medicine. The ability to control the physical and chemical properties of nanofibers opens new avenues for the development of advanced therapeutic systems, enhancing the efficacy and safety of various biomedical applications (18).

REFERENCES

[1] *Sunil CU., et al. (2015). Nanofibers in drug delivery: an overview. World Journal of Pharmaceutical Research, 4(8), 2576-2594.*

[2] *Alijaniha, M. (2024). Preparation of eugenol nanoemulsion by the spontaneous method. Conferences Proceedings, 1(1).* https://doi.org/10.5281/zenodo.14575211

[3] *Hassan, M., Alijaniha, M., Jafari, S., & Ghafari, A. (2024). Physicochemical properties and antimicrobial efficacy of eugenol nanoemulsion formed by spontaneous emulsification. Chemical Papers.* https://doi.org/10.1007/s11696-024-03847-y.

[4] *Chauhan D., et al. (2018). Electrochemical immunosensor based on magnetite nanoparticles incorporated into electrospun polyacrylonitrile nanofibers for vitamin-D3 detection. Materials Science and Engineering C, 93, 145-156.*

[5] *Zong X., et al. (2002). Structure and process relationship of electrospun bioabsorbable nanofiber membranes. Polymer, 43(16), 4403-4412.*

[6] *Li T., et al. (2017). Engineering BSA-dextran particles encapsulated bead-on-string nanofiber scaffold for tissue engineering applications. J Mater Sci, 52, 10661–10672.*

[7] *Ostrovidov S., et al. (2014). Myotube formation on gelatin nanofibers – multi-walled carbon nanotubes hybrid scaffolds. Biomaterials, 35, 6268–6277.*

[8] *Yu J., et al. (2014). Electrospun PLGA fibers incorporated with functionalized biomolecules for cardiac tissue engineering. Tissue Eng Part A, 20, 1896–907.*

[9] *Chen FM., et al. (2010). Toward delivery of multiple growth factors in tissue engineering. Biomaterials, 31(24), 6279–6308.*

[10] *Lai GJ., et al. (2014). Composite chitosan/silk fibroin nanofibers for modulation of osteogenic differentiation and proliferation of human mesenchymal stem cells. Carbohydr Polym, 111, 288–297.*

[11] *Jiang J., et al. (2018). 1α,25-dihydroxyvitamin D3-eluting nanofibrous dressings induce endogenous antimicrobial peptide expression. Nanomedicine (Lond), 12(1417-1432).*

[12] *Zhao R., et al. (2014). Electrospun chitosan/sericin composite nanofibers with antibacterial properties as potential wound dressings. Int J Biol Macromol, 68, 92–97.*

[13] *Cao H., et al. (2010). RNA interference by nanofiber-based siRNA delivery system. J Control Release, 144(2), 203–212.*

[14] *Volpato FZ., et al. (2012). Preservation of FGF-2 bioactivity using heparin-based nanoparticles, and their delivery from electrospun chitosan fibers. Acta Biomater, 8(4), 1551–1559.*

[15] *Sudhakar Y., et al. (2006). Buccal bioadhesive drug delivery--a promising option for orally less efficient drugs. J Control Release, 114(1), 15–40.*

[16] *Gazit E. (2007). Self-assembled peptide nanostructures: the design of molecular building blocks and their technological utilization. Chem Soc Rev, 36(8), 1263–1269.*

[17] *Yu DG., et al. (2013). Electrospun medicated shellac nanofibers for colon-targeted drug delivery. Int J Pharm, 490(1-2), 384-390.*

[18] *Alijaniha, M., Riahi, S., & Rigi, A. (2024). AI Chatbots and Telemedicine in Cancer Care: Supporting Patients and Enhancing Communications. Book Series 4* , https://doi.org/10.5281/zenodo.13777221