

Review Article

Electrospinning in Periodontology: "A Fine Line: Spinning Fibers for Flawless Healing!"; Applications in Tissue Engineering

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ABSTRACT:

Electrospinning is an old yet fascinating technique. It is a method of producing ultra fine fibers. It utilizes a high voltage to create an electric field which draws a polymer solution or melt into a jet, that dries due to evaporation of the solvent or solidifies to form fine fibers of nanometer range. Electrospinning enables the creation of scaffolds that closely mimic the natural extracellular matrix. These fibers have multiple applications in tissue regeneration. In the field of periodontology, electrospinning has attracted attention for its potential uses in tissue engineering, guided tissue regeneration (GTR), and drug delivery. The combination of electrospinning and 3D printing presents thrilling prospects for revolutionizing tissue engineering in periodontology. This cutting-edge approach has the potential to significantly boost the effectiveness of regenerative therapies, leading to improved patient outcomes. Continued research will be essential to fully harness the clinical possibilities of these technologies.

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INTRODUCTION

Electrospinning is a technique that employs an electric field to draw a polymer solution into fine fibers, in nanometer range, to create a non-woven mat. These mats have a high surface area as they're composed of nanofibers and they mimic the extracellular matrix (ECM) of natural tissues.

Electrospinning provides a simple and versatile method for generating ultrathin fibers from a rich variety of materials that include polymers, composites, and ceramics. (Li, D., & Xia, Y., 2004)

An electric field is used to create a charged jet of polymer solution. As this jet travels in air, the solvent evaporates leaving behind a charged fiber that can be electrically deflected or collected on a metal screen that is oppositely charged. Fibers with a variety of cross sectional shapes and sizes were produced from different polymers. The diameter of these fibers was in the range of 0.05 to 5 microns. (Doshi, J., & Reneker, D. H., 1995)

Periodontal disease affects millions worldwide, necessitating effective regenerative treatments.

Electrospinning has emerged as a promising technique in this field, enabling the creation of scaffolds that closely mimic the natural extracellular matrix.

Key Milestones

1. Late 1500s: Sir William Gilbert observed that a charged piece of amber caused a water droplet to form a cone and eject smaller droplets, marking the first recorded instance of electrospinning. (Chain, T. V., 2020)
2. Early 20th Century: In 1902, J.F. Cooley and W.J. Morton patented the use of electrical forces to create thin fibers from liquids, but the process remained underdeveloped. (Reneker, D. H., & Chun, I., 1996)
3. Mid-20th Century: Anton Formhals advanced the technology in the 1930s and 1940s by patenting electrostatic spinning devices, but it still lacked widespread use. (Formhals, A., 1934)
4. Modern Era (1990s-Present): A resurgence in the 1990s, led by Doshi and Reneker, demonstrated electrospinning's ability to create nanofibers with

high surface area and porosity, sparking renewed interest for use in various fields, such as biomedicine and filtration. This breakthrough renewed interest in electrospun nanofibers, especially for their unique qualities, such as: (Doshi, J., & Reneker, D. H., 1995)

- Extremely high surface area relative to volume,
- Porous structures,
- The ability to form non-woven mats.

PRINCIPLE OF ELECTROSPINNING

This method uses electrostatic forces to form nanofibers from a polymer. A high-voltage field creates a “Taylor cone”, and when electrostatic forces exceed surface tension, a fine jet is released. The jet solidifies into nanofibers (<100 nm), collected on a grounded collector.

MECHANISM OF ELECTROSPINNING

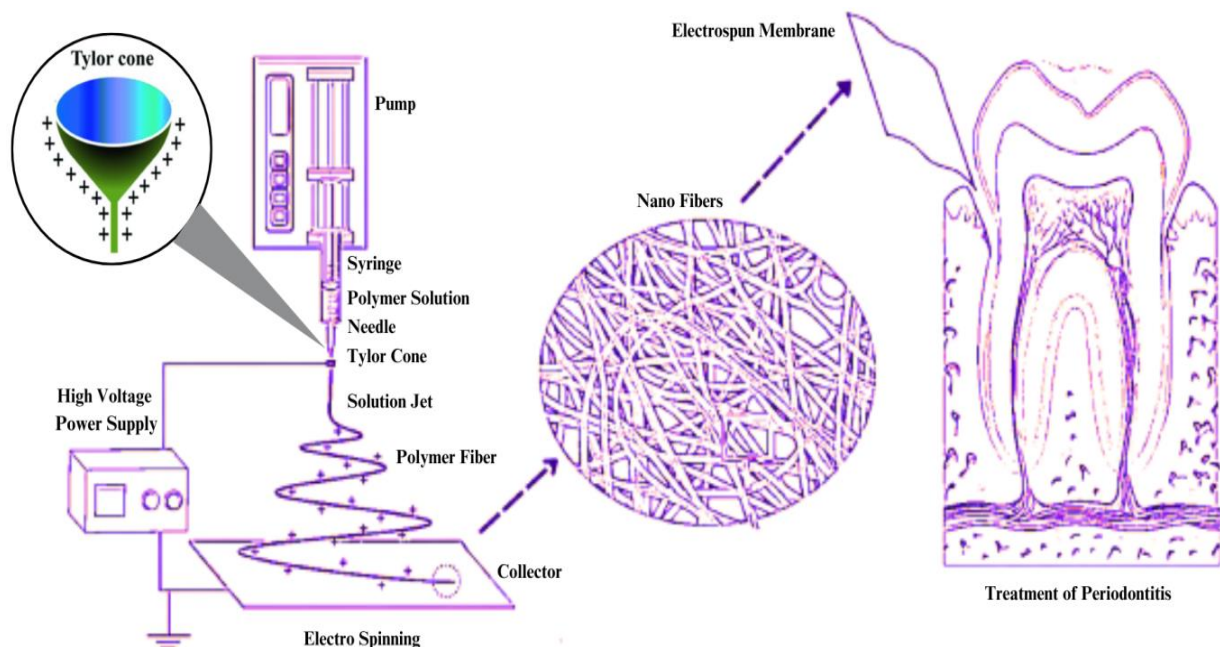
Process Description

This electrostatic processing method uses a high-voltage electric field to form solid fibers from a polymeric fluid stream (solution or melt) delivered through a millimeter-scale nozzle. Nanofibers are the ultra-fine solid fibers notable for their very small diameters (<100 nm), their large surface area/unit mass and small pore size.

- a) **Selection of the Polymer Solution/Melt:** A polymer is dissolved in a solvent or it is melted to create a solution that is capable of being stretched into fine fibers.

- b) **An Electric Field:** A high-voltage electric field is applied between a spinneret (a small needle or nozzle) and a grounded collector (metal screen) or oppositely charged collection plate. As the intensity of the electric field is increased, the hemispherical surface of the fluid at the tip of the spinneret elongates to form a conical shape known as the Taylor cone.
- c) **Formation of Jet:** When the polymer is discharged from the tip of the syringe it initially held by surface tension. The electric field creates a charge on the liquid surface, and when the electrostatic forces overcome the surface tension and visco-elastic components of the polymer, a thin jet of the polymer is ejected from the tip of the spinneret/nozzle (from a cone known as Taylor cone). The ejected polymer fluid form jet.
- d) **Formation of Fiber:** This jet thins and stretches as it travels toward the collector (oppositely charged metal screen). As it travels, it solidifies into thin fibers due to the evaporation of the solvent or cooling of the melt.
- e) **Deposition of Fibers:** The fibers are then collected on a grounded surface of the collector, in form of a mat or ordered structure.

Material Selection: Common polymers used include polylactic acid (PLA), polycaprolactone (PCL), gelatin, and collagen, which are chosen for their biocompatibility and mechanical properties.



MECHANISM OF ELECTROSPINNING

APPLICATION IN PEERIODONTOLOGY

Electrospinning plays a significant role in enhancing the periodontal healing through its innovative use in tissue engineering. The process is widely used to create nanofibers with a high surface area-to-volume

ratio, which makes them ideal for a variety of applications. Here’s how it contributes to this field:

- **Tissue Engineering Scaffolds:** Electrospun mats can be used as scaffolds to support the regeneration of periodontal tissues, including

bone and soft tissue. These provide a conducive environment for cell attachment, proliferation and differentiation. Here are some notable studies that investigate the use of electrospun mats for tissue regeneration in periodontology:

Zhang et al. (2014) demonstrated that electrospun PCL nanofibers support the adhesion and growth of periodontal ligament cells, enhancing tissue regeneration. **Mansouri et al. (2016)** found that gelatin/PCL composites improved biocompatibility and supported cell growth with favorable mechanical properties. **Ravi et al. (2018)** showed that chitosan scaffolds promoted the attachment and proliferation of human periodontal ligament stem cells, aiding in tissue regeneration. **Han et al. (2020)** developed PLGA/HA scaffolds that enhanced mechanical strength and osteogenic differentiation for bone regeneration. **Huang et al. (2021)** highlighted the potential of silk fibroin mats for promoting cell attachment and tissue growth. **Zhang et al. (2022)** found that polyurethane nanofibers with growth factors significantly improved cell migration and differentiation, offering promise for periodontal regenerative therapies.

These studies underscore the potential of electrospun mats to enhance biocompatibility, support cell proliferation, and facilitate tissue integration in periodontal treatment.

- **Controlled Drug Delivery Systems:** Electrospun mats can be infused with bioactive agents such as growth factors or antibiotics. This allows for localized, controlled release, reducing inflammation and promoting faster healing in periodontal pockets. Electrospun scaffolds mimic the extracellular matrix, promoting cell adhesion and growth. Their high porosity and surface area allow for efficient encapsulation and release of bioactive compounds, making them ideal for tissue regeneration applications.

Zhang et al. (2015) demonstrated successful incorporation of antibiotics into electrospun mats for localized periodontal treatment. **Tian et al. (2016)** investigated electrospun fiber mats loaded with growth factors to enhance periodontal tissue regeneration. **Mao et al. (2019)** explored electrospun mats infused with anti-inflammatory agents to reduce inflammation and promote healing.

These studies highlight the effectiveness of electrospun mats in enhancing drug delivery in periodontal therapy.

Bioactive Agents like platelet-derived growth factor (PDGF) and bone morphogenetic proteins (BMPs) are commonly used to enhance tissue regeneration. Localized delivery of **antibiotics** can reduce infection and inflammation in periodontal pockets.

The controlled release mechanism in electrospun scaffolds operates primarily through diffusion and degradation. In diffusion, bioactive agents embedded within the polymer matrix are gradually released,

influenced by fiber structure and polymer characteristics. Meanwhile, polymer degradation allows the scaffold to break down at a customizable rate, providing sustained and prolonged delivery of the bioactive agents over time, making it a powerful tool for targeted therapies.

Advantages

- **Localized Treatment:** Delivering bioactive agents directly to the site of interest minimizes systemic exposure and side effects.
- **Sustained Release:** Controlled release profiles can be designed to match the healing timeline of periodontal tissues, enhancing therapeutic efficacy.
- **Enhanced Bioactivity:** The electrospinning process can preserve the activity of sensitive bioactive agents, ensuring they remain effective upon release.

A. Guided Tissue Regeneration (Barrier Membranes): In guided tissue regeneration (GTR), electrospun fibers can serve as effective barrier membranes, preventing the migration of epithelial cells while allowing the regeneration of periodontal tissues, by allowing the periodontal ligament cells to populate the area.

Gottlow et al. (1984) established the importance of barrier membranes in GTR for preventing epithelial cell migration. **Rothamel et al. (2012)** evaluated electrospun collagen and polymeric membranes, showing effective facilitation of periodontal tissue regeneration. **Li et al. (2017)** investigated electrospun polycaprolactone (PCL) membranes, demonstrating inhibition of epithelial cell migration while promoting periodontal ligament cell proliferation. **Kang & Kim (2018)** studied silk fibroin nanofibrous membranes in GTR, showing effective support for periodontal tissue regeneration.

These studies highlight the effectiveness of electrospun fibers in GTR applications.

The mechanisms of action of electrospun membranes in periodontal therapies are twofold. First, their barrier function effectively restricts the migration of epithelial and connective tissue cells into the defect site, promoting the selective proliferation of periodontal ligament cells and osteoblasts. Second, the porous structure of these membranes facilitates nutrient diffusion and supports the migration of essential cells for tissue regeneration. This dual functionality enhances the overall effectiveness of periodontal treatments.

B. Periodontal Defects: Clinical research indicates that electrospun membranes can significantly enhance the healing of periodontal defects. Patients treated with these membranes show greater periodontal attachment levels compared to those who receive conventional treatments.

C. Bone Regeneration: Studies suggest that incorporating electrospun membranes with bone

grafts improves bone regeneration, creating a conducive environment that supports osteoconductive activity.

- D. Soft Tissue Healing:** Electrospun membranes are also effective in promoting soft tissue healing around dental implants and in gum recession procedures, resulting in reduced postoperative complications.

ADVANTAGES OF ELECTROSPUN SCAFFOLDS

- 1. Advantage over Conventional Fiber Spinning:** Unlike conventional fiber spinning techniques, which yield polymer fibers with diameters down to the micrometer range, electrospinning is capable of producing polymer fibers with diameters in the nanometer range.
- 2. Biocompatibility:** By adjusting the composition and structure of electrospun fibers, researchers can enhance their biocompatibility and bioactivity, both of which are vital for effective integration into the periodontal environment and reducing the risk of adverse reactions.
- 3. Customization:** Electrospinning enables customization of scaffolds' mechanical properties and degradation rates to meet the needs of periodontal tissues. Fiber morphology can also be adjusted by varying parameters like voltage, polymer concentration, and flow rate.
- 4. Promoting Cell Migration:** The large surface area and porosity of electrospun fibers and facilitates better cell migration.
- 5. Cell attachment and nutrient exchange:** One of the major advantages of electrospun scaffolds is their high surface area-to-volume ratio, which enhances cell adhesion, providing optimal attachment sites for cell growth. This feature facilitates better nutrient diffusion, making these scaffolds ideal for tissue regeneration and healing in periodontal applications.

LIMITATIONS OF ELECTROSPUN SCAFFOLDS

- Controlling fiber alignment and uniformity.
- Optimization of process conditions for specific materials.
- Long-term Studies^{**}: More research is needed to assess the long-term efficacy and biological behavior of these combined scaffolds in vivo
- Variability in fabrication methods can lead to inconsistent results, highlighting the need for standardized protocols.
- Material Selection^{**}: Finding suitable biocompatible materials that can be used in both electrospinning and 3D printing is crucial.
- Process Optimization^{**}: Developing optimized protocols for combining these techniques to ensure scaffold integrity and functionality.

- **Production Scalability:** While electrospinning is effective at a small scale, scaling up for clinical use can be challenging.

APPLICATION IN OTHER FIELDS

Electrospun nanofibers have diverse applications due to their unique properties:

- **Filtration:** With their small fiber size and high porosity, these nanofibers are highly effective in air and liquid filters. Their large surface area enhances particle capture, making filtration more efficient.
- **Wound Dressings:** Nanofiber mats, known for their biocompatibility and large surface area, promote wound healing by supporting cell attachment. They can also be infused with drugs or antimicrobial agents to accelerate the healing process.
- **Energy Devices:** In energy systems like batteries, fuel cells, and supercapacitors, nanofibers serve as separators or membranes. Their structure improves ion transport and provides a stable mechanical barrier for efficient energy storage and transfer.

FUTURE DIRECTIONS

Hybrid Systems like combining electrospun scaffolds with other delivery systems, such as hydrogels or 3D-printed structures, may enhance release profiles and functionality. **3D Printing:** This approach enables the precise deposition of materials to build intricate 3D structures. By enabling detailed customization of scaffold designs, it allows for the production of scaffolds that can be tailored to meet specific anatomical requirements with more complex tissue-engineered constructs. This adaptability is particularly beneficial in biomedical applications, as it ensures that the scaffolds can mimic the natural architecture of tissues, providing better integration and support during the healing process. Additionally, 3D printing can accommodate varying porosity and structural properties within the same scaffold, further enhancing its performance in tissue engineering and regenerative medicine.

Combining electrospinning with 3D printing represents a significant advancement in the field of tissue engineering, particularly for applications in periodontology. 3D printed scaffolds can be designed to fit irregular/ complex defect shapes, improving the precision of regenerative treatments. Here's an overview of this innovative approach: **Advantages of Combining Techniques:**

- 1. Enhanced Scaffold Design:** The combination allows for the creation of scaffolds with micro- and nano-scale features can be customized to fit periodontal defect. Customizable geometries can be produced, which can better match the anatomy of periodontal defects.
- 2. Improved Mechanical Properties:** 3D printing can create durable scaffolds with tailored mechanical

properties that can withstand the forces in the oral environment, while electrospun fibers enhance biocompatibility and cell adhesion.

3. Layered Structures: This approach allows for the development of multi-layered scaffolds that can provide different biochemical environments or support various types of cells (e.g., bone cells, periodontal ligament cells).
4. Controlled Release of Bioactive Agents: Both techniques can be utilized to incorporate growth factors or drugs directly into the scaffold, allowing for localized and sustained release, which is critical for enhancing healing in periodontal applications.

CONCLUSION

Electrospinning offers a promising avenue for enhancing periodontal healing, providing innovative solutions to improve regenerative therapies. Its ability to create effective scaffolds, deliver drugs, and promote tissue regeneration positions it as a valuable tool in modern periodontics. Continued research and development in this domain is anticipated to result in more effective and tailored periodontal treatments down the line. It's a versatile and promising technology for a wide range of scientific and industrial applications. Ongoing research and clinical trials will further clarify their role in periodontal regeneration and optimize their use in practice. In summary, the application of electrospun membranes in periodontal and implant treatments represents a promising approach to improve healing outcomes in both hard and soft tissues.

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