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Review Article

Electrospun nanofibers and their potential in dental applications: an updated review

Fernando Rosas López Portillo[1], Aurea Elizabeth Valle Urias[2], Tonantzin González Arredondo[3], Marco Antonio Quiroz Beltran[4], Jose Aurelio Cortina Aguilar[5], Felix Manuel Manjarrez Guerrero[3], María del Rosario Cázarez Camacho[6], Karely Rojo López[7], Alfredo del Rosario Ayala Ham[8], Ramsés Eduardo Sandoval Castro[8], Cristhal Duque Urióstegui[9], Alan I. Valderrama Treviño[10]*

[1]Department of Graduate Clinic of Oral Rehabilitation, Autonomous University of Sinaloa, Mexico
[2]Department of Teaching Clinic, Autonomous University of Sinaloa, Mexico
[3]Department of Orthodontics, Autonomous University of Sinaloa, Mexico
[4]Department of Community and Preventive Area, Autonomous University of Sinaloa, Mexico
[5]Department of Dental Operative Clinic, Autonomous University of Sinaloa, Mexico
[6]Department of Community Dental Clinics, Autonomous University of Sinaloa, Mexico
[7]Department of Teaching Clinic, Autonomous University of Sinaloa, Mexico
[8]Department of Endodontics, Autonomous University of Sinaloa, Mexico
[9]Department of Orthodontics. NOVA, Mexico City, Mexico
[10]Department of Biomedical Research, UNAM, Mexico City, Mexico

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***Correspondence:**
Dr. Alan I. Valderrama Treviño,
E-mail: alan_valderrama@hotmail.com

ABSTRACT

The use of Electrospun nanofibers has proven to be an innovative technology with great potential in the field of dentistry, particularly in tissue engineering and the regeneration of oral and dental tissues. Their ability to mimic the extracellular matrix facilitates cell adhesion, nutrient transport, and cell proliferation, optimizing the biological response. However, despite their multiple benefits, some disadvantages have been reported, related to their structural composition or the difficulty in obtaining ultrafine fibers. Direct electrospinning techniques have been proposed to optimize parameters and incorporate biomolecules. The continuous advancement in biomaterials research will enable better clinical applications and the consolidation of dental tissue regeneration.

Keywords: Electrospinning, Nanofibers, Odontology, Nanotechnology, Tissue engineering

INTRODUCTION

Nanofiber scaffolds created using the electrospinning technique have been widely explored in the field of tissue engineering, demonstrating great potential in the field of regenerative medicine and dentistry.[1] Due to the various findings described about their structural characteristics that resemble the proteins present in the extracellular matrix, which favors cellular adhesion, migration, cell proliferation, and specific gene expression, making them promising materials for periodontal tissue regeneration and other dental applications.[2,3]

Electrospinning, initially described by Anton Formahls in 1930, has evolved significantly over time, allowing the fabrication of fibers with diameters on the nanometric and micrometric scale. This has consolidated the technique as an efficient method for producing biomimetic scaffolds with great potential in the field of regenerative dentistry, especially in the area of bone and periodontal regeneration, with extensive experimentation in the development of barrier membranes and controlled drug release.[4]

For the imitation of the natural extracellular matrix, various biomaterials have been developed and utilized, with nanofibrous scaffolds being particularly notable for promoting cell adhesion, proliferation, and differentiation. Three primary methods have been described: self-assembly, phase separation, and electrospinning, with the latter being the most widely used due to its simplicity, ability to modify fiber diameter, and versatility in material selection.

At a practical level, electrospun nanofibers have been shown to facilitate cell growth due to their porous structure and ability to align cells, which enhances nutrient and waste exchange and enables rapid integration with dental cells. Additionally, these nanofibers can withstand the challenges posed by bacterial exposure in the oral cavity and the high masticatory pressures they are subjected to several challenges have been noted, including limitations in cell infiltration and the precise fabrication of three-dimensional structures.[5]

Optimization and reproducibility remain complex issues. Despite their substantial potential, scaling up production remains a significant challenge.[4] This article aims to review recent advances in the fabrication and application of electrospun nanofibers in the field of dentistry, highlighting their advantages and challenges.

ELECTROSPUN NANOFIBERS: CHARACTERISTICS AND PROPERTIES

Nanotechnology has been likened to the Industrial Revolution due to its profound impact on both human-centric equipment and industrial processes, nanofibers are a prominent part of this nanotechnology group, playing a vital role in tissue engineering.

Their significance stems from the characteristics of nanofiber scaffolds, which are three-dimensional or two-dimensional structures characterized by high porosity, a large surface area, and excellent intercellular biocompatibility. These features stimulate growth factors and other essential components in tissue engineering.[6]

Electrospinning is an electrohydrodynamic process that employs a dry spinning technique, necessitating precision since the fibers produced for scaffolds must have a diameter within the range of 0.01 to 10 µm. To achieve this, electrostatic forces are applied, enabling precise control over fiber size.[7] The process involves using a drop of a polymeric solution that is electrified at high voltage to produce a jet. As the jet stretches and elongates, it forms fibers, resulting in the formation of the Taylor cone.

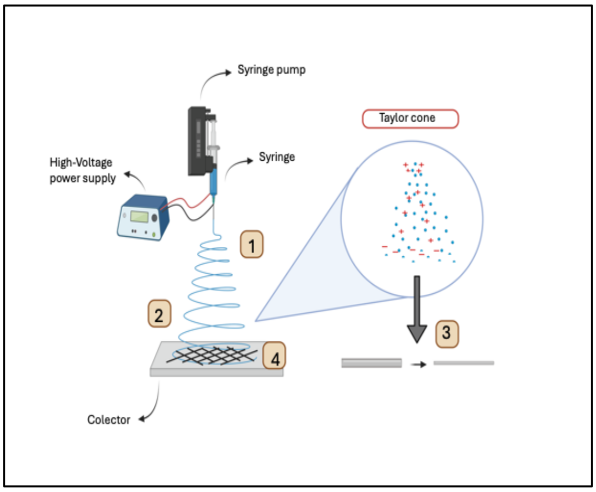

Figure 1: Description of 4 fundamental parameters in electrospinning: (1) Taylor cone formation; (2) charged jet extension; (3) curvature instability leading to thinning; (4) fiber solidification on the collector).

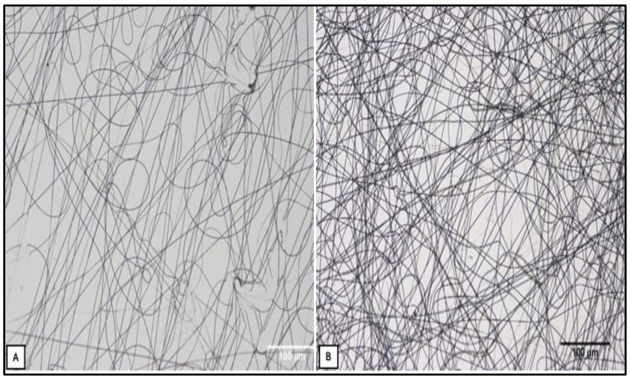

Figure 2: Optical microscopy for parameter optimization in electrospinning with a flat collector. (A) Illustrates broken and discontinuous fibers with bulbs, causing structural weakness and impaired cell adhesion; (B) demonstrates that adjusting electrospinning parameters, like injection speed and collector-voltage source distance, results in fibers with uniform morphology.

When the Taylor cone reaches a critical charge density, it becomes unstable, causing a jet to emerge from its tip, this jet is then deposited onto a collector, which can be either flat or tubular.8 The basic setup includes a high-voltage source, a syringe pump, a nozzle (typically a hypodermic needle), and a conductive collector. The process unfolds in four stages these are the formation of the Taylor cone, extension of the charged jet, curvature instability causing thinning, solidification of the fibers on the collector (Figure 1).[4] The morphology of the fibers depends on modifications in these steps. Three key parameters are involved: the characteristics of the polymeric solution, including conductivity, volatility, and viscosity, which are crucial for preventing defective fibers (Figure 2).

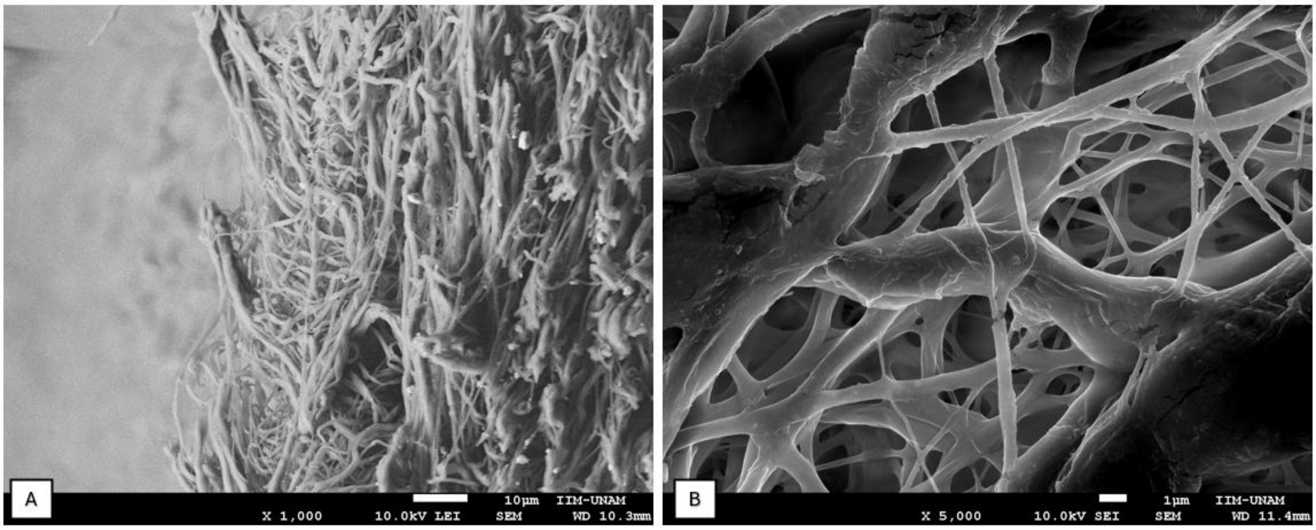

Figure 3 (A and B): SEM of an electrospun scaffold made from biodegradable copolymers.

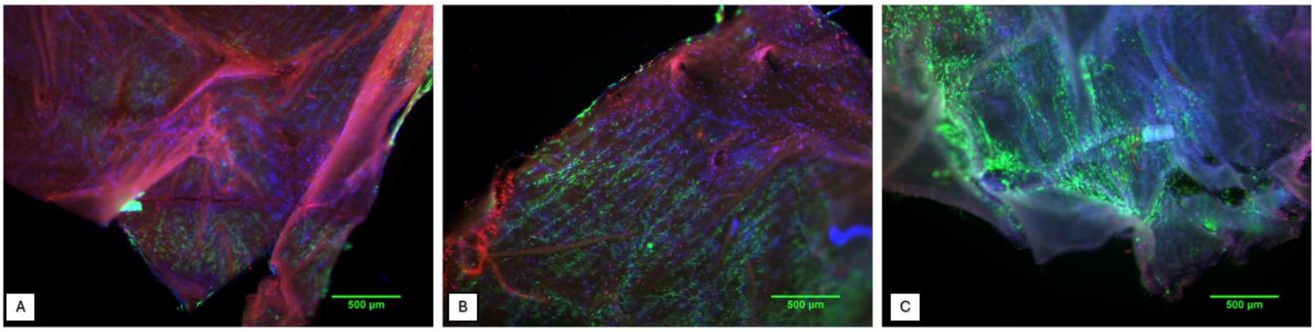

Figure 4: Calcein, ethidium homodimer, and DAPI cytotoxicity assay. (A-C) Shows different growth patterns of fibroblasts cultured on a PLGA-PCL-Gel scaffold at 6, 8, and 10 days, visualized by MERGE staining with calcein-ethidium homodimer and DAPI. Observe the cell proliferation and predominance of green (live cells).

Table 1: Types of biomedical polymers and characteristics.

Type of polymer	Name	Characteristics
Natural	Collagen	Structural support in ECM, biocompatibility, low immunogenicity.
	Hyaluronic Acid	Cartilage regeneration, high viscosity.
	Chitosan	Tissue regeneration, drug delivery.
	Alginate	Biocompatibility, used in tissue engineering.
	Phospholipids (Lecithin)	Formation of biological membranes, application in regenerative medicine.
Synthetic	Polylactic Acid (PLA)	Biodegradable, used in drug delivery and bone regeneration.
	Polycaprolactone (PCL)	High mechanical strength, slow degradation, used in tissue engineering.
	Polylactic-co-glycolic acid (PLGA)	Biodegradable, controlled drug release.
	Polyglycolic acid (PGA)	Biodegradable, used in absorbable sutures.
	Polyurethane (PU)	High elasticity, used in medical devices.
	Polyvinyl alcohol (PVA)	Used in cell culture matrices.
Copolymer	Collagen-Chitosan (CC)	Improves mechanical strength.
	PLGA with Chitosan (PEG-g-CHN)	Enhances controlled drug release.
	PLGA-PEG-PLA	Electrospun scaffolds for drug delivery.

The electrospinning method itself is another parameter, where factors like applied voltage and the distance between the nozzle and collector directly impact fiber diameter and uniformity. Lastly, environmental parameters such as temperature, air humidity, and air flow affect solvent evaporation, which is vital for fiber solidification (Figure 3).[9] Within the electrospinning process, various materials derived from biodegradable and natural polymers have been described (Table 1). Among natural polymers, collagen, hyaluronic acid, chitosan, alginate, and phospholipids have been noted. Synthetic polymers highlight the use of PLA, PGA, PLGA, and PCL, which have demonstrated mechanical properties and control over the degradation process.

Additionally, the use of copolymers has been described, where natural and synthetic polymers are combined, with primary investigations focusing on Collagen-Chitosan, PLGA with PEG-g-CHN, and PLGA with PEG-PLA (Figure 4).[10]

DENTAL APPLICATIONS

Electrospun nanofibers have demonstrated significant potential in biomedicine, encompassing tissue engineering, controlled drug delivery, and medical implants, with potential applications in dentistry. Tissue regeneration has become increasingly important for promoting cellular growth in bones, cartilage, and nerves by incorporating growth factors and antibacterial agents, or using scaffolds with silica nanofibers, which have shown effectiveness in animal models for bone regeneration in mandibular defects. Enhanced cell adhesion and reduced infection rates facilitate wound healing.

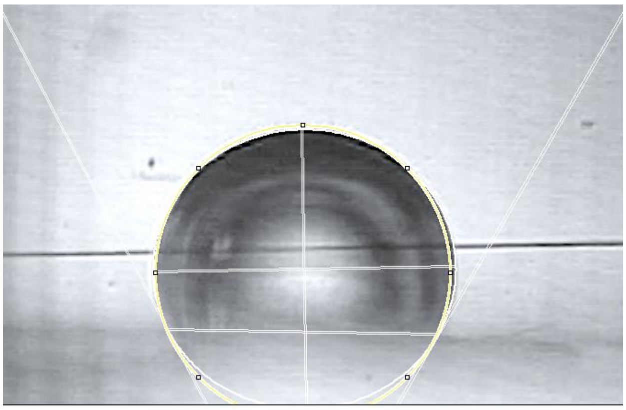

Figure 5: Contact angle measurement.

Moreover, improving mechanical properties can lead to greater strengthening and flexural resistance of materials used in dental restorations (Figure 5).[10,11] Figure 5 depicts the property of electrospun polymers is their contact angle, where a hydrophilic scaffold with a contact angle below 90° can enhance cell adhesion, migration, and proliferation. Additional applications in dentistry have been noted, especially in cases of dental trauma or extensive caries, where regeneration of the pulp-dentin complex has been observed. The use of antibacterial chitosan nanofibers combined with mangosteen extract has demonstrated a decrease in oral bacterial load, thereby preventing future caries.

Furthermore, a significant application in dentistry involves the controlled release of drugs via PLLA nanofibers loaded with nanodiamonds and growth factors, allowing for localized delivery of analgesics and antibiotics.[12] Electrospun nanofibers have become a crucial component in research involving both in vivo and in vitro studies, validated through clinical trials, particularly in patients with periodontitis. These studies have shown promise in regenerating bone, cementum, and periodontal ligament. Current research aims to optimize scaffolds to improve the organization of the regenerated periodontal ligament by combining electrospinning techniques with advanced biomaterials.[2]

ADVANTAGES AND DISADVANTAGES

Electrospinning presents a significant advantage due to its process versatility, allowing for scalability and facilitating the large-scale production of nanofibers. Nevertheless, difficulties remain in solvent removal at elevated volumes, underscoring the need for ongoing development of novel solutions to optimize industrial-scale fabrication.[13] During the electrospinning process, personnel safety is of paramount importance, given that the manipulation of solvents and the high voltage of the equipment pose critical risks that require the adoption of appropriate safety measures.[14]

The electrospinning technique offers a significant advantage due to its ability to modify fiber diameter and various parameters, including applied voltage, nozzle-to-collector distance, and solution concentration. Furthermore, a broad spectrum of biomaterials is available, encompassing both natural and synthetic biopolymers approved by the FDA. The characteristics of these scaffolds closely resemble the extracellular matrix, promoting cellular adhesion, proliferation, nutrient transport, and can be functionalized with biomolecules like proteins, growth factors, and DNA, thereby optimizing cellular response.[15]

Nevertheless, a significant challenge of the electrospinning technique arises from the non-woven nature of the electrospun membranes, which complicates cellular infiltration. Furthermore, efforts to enhance scaffold porosity require the involvement of mechanical structures, which can compromise mechanical strength, potentially weakening the structure. A reduced cellular migration into the scaffold's interior has been noted due to the higher concentration of nutrients on the surface.[12]

CONCLUSION

Electrospun nanofibers represent an innovative technology that has demonstrated potential in dentistry, with applications in tissue regeneration, bone growth, controlled drug delivery, and prevention of caries and infections. Their ability to mimic the extracellular matrix makes them appealing for tissue engineering. Despite these advantages, challenges persist, including difficulties in producing ultrafine fibers, reduced mechanical strength due to increased porosity, and limited cellular infiltration in some scaffolds. Nevertheless, developing new strategies-such as optimizing electrospinning parameters and incorporating molecules-could enhance clinical outcomes. Progress in biomaterial research will enable further refinement of scaffolds, leading to greater advancements in regenerative dentistry. Additional studies are needed to ensure more effective and safe procedures.

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