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A Review On Electrospun Nanofibers In Drug Delivery

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ABSTRACT:

Electrospun nanofibers have emerged as a powerful and versatile tool in drug delivery systems, offering unique structural and functional properties that contribute to enhanced therapeutic outcomes. These nanofibers are characterized by their ability to enable high drug loading, controlled and sustained drug release, and improved biocompatibility, making them highly suitable for a wide range of applications. Their versatility is particularly evident in areas such as transdermal patches, wound care management, and targeted cancer therapy. By definition, nanofibers are typically classified as fibers with diameters below 100 nm, which provides them with unique physicochemical advantages over conventional drug delivery carriers. This review paper aims to examine the core aspects of the electrospinning process, including critical process parameters and material selection, while also exploring how these factors influence the drug release mechanisms of electrospun nanofibers. Furthermore, this article delves into the current challenges associated with the electrospinning process and its application in drug delivery systems. It also considers the future perspectives of this technology in advancing therapeutic interventions. In conclusion, while certain obstacles remain to be addressed, ongoing research and innovation in the field of electrospinning technology continue to expand its scope, promising significant advancements in drug delivery and other biomedical applications. This review provides a comprehensive overview of the current state of electrospun nanofibers, highlighting the challenges and opportunities for their development and application in drug delivery.

Keywords: Electrospinning, Nanofibers, Drug Delivery Systems, Polymeric Nanofibers, Controlled Release, Biomedical Applications

INTRODUCTION:

The delivery of therapeutic agents in precise doses over prolonged periods remains a critical challenge in modern medicine. Electrospun nanofibers, with their unique structural and functional properties, have emerged as promising tools to address these limitations. Electrospun nanofibers enable high drug loading, controlled release and enhanced interaction with biological tissues, making them ideal candidates for applications such as transdermal patches, wound healing and targeted cancer therapy.

Novel drug delivery systems aim to achieve controllable, programmed, sustained or targeted drug release, addressing challenges inherent in conventional methods such as premature degradation, first-pass metabolism, discomfort or pain during administration and systemic toxicity. Among these innovative approaches, polymeric nanofibers stand out as exceptional drug delivery vehicles due to their high surface-area-to-volume ratio, tunable porosity and the ability to encapsulate drugs with precision, enabling enhanced control over drug release profiles and targeting.

Electrospinning is the process of spinning fibers with the help of electrostatic forces. Fibers with diameter typically below 100 nm are categorized as nanofibers according to fiber science-related literatures. These fibers have enormous application in nanocatalysis, tissue scaffolds, protective clothing, filtration and optical electronics because of their small pores and higher surface area.

A high voltage electric field is applied to create electrically charged jets from polymer melts or solutions, which are then dried by the solvent evaporation to generate nanofibers. The oppositely charged collector, which may be a revolving drum or a flat surface, receives the highly charged fibers that are directed towards it. In pharmaceutical applications, the electrospinning procedure is useful because it creates low-energy, nanoscale drug particles in a single step. This review explores the fundamental aspects of electrospinning, its impact on drug release mechanisms and its recent applications in pharmaceuticals.

ELECTROSPINNING: Principle, Mechanism and Procedure:

The principle of electrospinning has evolved through centuries, with significant contributions shaping its current understanding. A timeline of key milestones in the development of this technique is summarised below:

Year	Contributor(s)	Milestone/contribution(s)
1600	William Gilbert	Observed electrostatic attraction of a liquid.
1846	Christian Friedrich Schönbein	Produced highly nitrated cellulose, a precursor for polymer-based materials.
1887	Charles Vernon Boys	Described the process of nano-fibre manufacture.
1900	John Francis Cooley	Filed the first patent for electrospinning.
1914	John Zeleny	Published work on fluid droplet behaviour at the ends of metal capillaries.
1931-1944	Anton Formhals	Filed multiple patents on electrospinning, advancing practical applications of electrospinning.
1938	N.D. Rozenblum and I.V. Petryanov-Sokolov	Successfully generated electrospun fibres.
1964-1969	Sir Geoffrey Ingram Taylor	Modeled the Taylor cone, providing a theoretical foundation for electrospinning.
1990	Reneker and various research groups	Popularized the term "electrospinning" and demonstrated its nanoscale potential.

Table 1: Key milestones in the historical development of electrospinning technology.

The electrospinning process involves 4 main components:

- syringe pump
- power source
- needle
- collector

Basic mechanism

The process is governed by the following steps: -

- Jet formation
- Taylor cone formation and jet thinning
- · Fiber solidification and collection

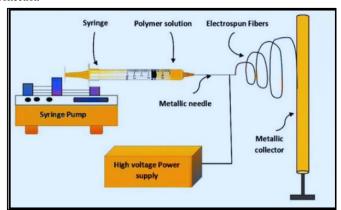


Fig 1. Basic setup of electrospinning

In this process drug of interest and a polymer is dissolved in an appropriate solvent. The resulting solution is put in a syringe and a high voltage is applied. As the voltage is increased, the solution at the needle forms a cone-shaped structure known as the Taylor cone.

Once the voltage surpasses a certain threshold, a charged polymer jet is ejected from the apex of the Taylor cone. This jet moves toward the collector, undergoing rapid stretching and bending due to the electrostatic forces acting on it. The jet's path becomes increasingly chaotic as it travels through the air, with electrostatic repulsion causing it to whip in various directions.

When the charge is raised above a certain voltage, a steady jet is created. The molecular entanglements in the polymer solution prevent the jet from fragmenting into droplets and their interaction with electrical forces induces a whip-like motion in the jet, referred to as bending instability.

Upon reaching the collector, the polymer solidifies and forms a nonwoven, three-dimensional mat of entangled nanofibers. This mat is highly porous and exhibits significant surface area, making it particularly suited for applications such as drug delivery, where enhanced drug loading, controlled release and tissue interaction are critical.

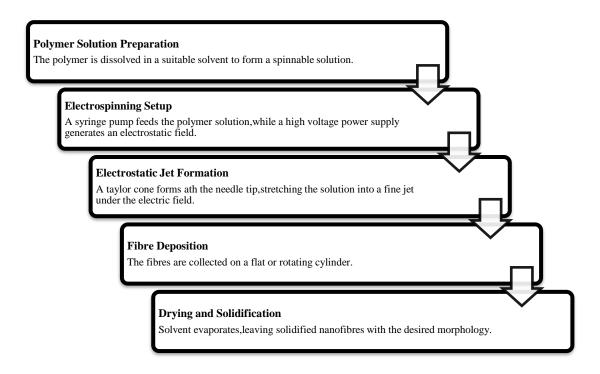


Fig 2: Flowchart of the electrospinning process for nanofibre production.

PARAMETERS GOVERNING ELECTROSPINNING PROCESS:

The various parameters that govern the electrospinning process are polymer solution parameters, process parameters and ambient parameters. **i.Polymer Solution Parameters**

Concentration of the polymer solution: For the formation of uniform nanofibers optimum concentration of polymer solution is required.

Molecular weight: Polymers with a high molecular weight result in greater chain entanglement, leading to increased viscosity and production of smooth nanofibers during electrospinning.

Viscosity: There is an optimal viscosity for electrospinning, as very low viscosity solutions cannot produce continuous, smooth nanofibers, while very high viscosity solutions make it difficult to eject jets from the solution.

Surface charge density and conductivity: Increasing the conductivity of the electrospinning solution enhances its charge-carrying capacity, which stretches the polymer jet and promotes higher bending instability. This leads to a decrease in fibre diameter and an increase in the area of deposition. Conductivity can be improved by adding ionic salts, such as potassium dihydrogen phosphate or sodium chloride, to reduce surface tension or by using organic acids as solvents to enhance charge density, both of which promote uniform fibre formation.

Surface tension: Decreasing the surface tension of the polymeric solution at a fixed concentration promotes the formation of smooth, continuous nanofibers by allowing the solution to stretch more easily during electrospinning, reducing bead formation.

ii. Process Parameters

Applied voltage: Higher the voltage, more will be the polymer ejection.

Feed flow rate: Smooth fibre production is influenced by a slow flow rate. A low feed flow rate is required to allow sufficient time for polarization of the polymeric solution.

Distance from syringe tip to substrate collector: The distance between the syringe tip and substrate collector in electrospinning is crucial for fiber quality, as an optimal distance ensures proper solidification, dryness and desired fibre morphology.

iii. Ambient parameters

Temperature: High temperature promotes thinner fibres due to faster solvent evaporation and increased polymer jet stretching.

Humidity: Low humidity, accelerates solvent evaporation, leading to faster solidification and potentially larger fibre diameters whereas high humidity, slows polymer elongation due to water condensation, resulting in thicker fibres, but for some polymers, it can decrease fibre diameter due to reduced concentration.

ADVANTAGES OF ELECTROSPUN NANOFIBERS:

- A wide range of solutions of natural polymers (such as chitosan, fibronectin, gelatin, collagen, silk, and ethyl cellulose) and synthetic polymers
 (such as polylactic acid, polyglycolic acid, poly(lactic-co-glycolic) acid, tyrosine-derived polycarbonates, polycaprolactone, polyurethane,
 poly(vinyl pyrrolidone), poly(vinyl alcohol)), or combinations of these, can be used to create nanofibers through the electrospinning process.
- Another important benefit is their high surface-area-to-volume ratio, which significantly enhances the loading capacity of drugs. This
 characteristic ensures effective administration of both hydrophilic and hydrophobic medications.
- The porous structure of these nanofibers enables controlled and sustained drug release. This property not only improves patient compliance
 by reducing the frequency of administration but also minimizes the risk of dose-related side effects. For instance, in chronic conditions
 requiring long-term therapy, the controlled release mechanism can maintain therapeutic drug levels over an extended period.
- By reducing the frequency of topical treatment, electrospun fibre mats can offer prolonged release, improving patient compliance.
- Nanofiber meshes are malleable, making them suitable for topical drug delivery applications.
- · Fiber mats can be incorporated into wound dressings, as part of a drug-releasing wound treatment technology.
- Electrospinning is a cost-effective method, enabling large-scale fabrication without compromising the quality of the nanofibers. This efficiency
 positions electrospun nanofibers as a viable solution for both research and clinical applications.

APPLICATIONS

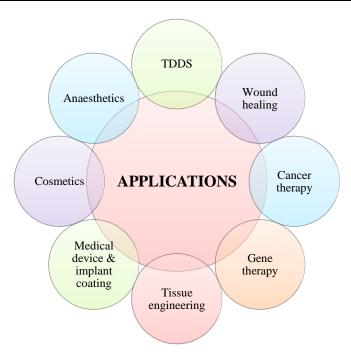


Fig 3: Applications of Electrospun nanofibres

Transdermal Drug Delivery Systems (TDDS): Electrospun fibres are used to bypass first-pass metabolism and gastrointestinal degradation, ensuring efficient drug delivery through the skin. Studies have shown that, compared to solvent-cast films, electrospun fibres provide prolonged and controlled drug release, enhancing patient compliance.

Wound Healing: Nanofibers made from biocompatible polymers like polylactic acid, poly(lactic-co-glycolic) acid and polycaprolactone are widely used for wound dressings. These fibres deliver antibiotics or growth factors in a controlled manner, promoting faster wound healing, preventing infections, and minimizing scarring. The incorporation of silver nanoparticles further enhances their antibacterial properties. Studies have shown that poly(lactic-co-glycolic) acid nanofibers may be loaded with the antibiotic cefazolin using a conventional electrospinning process.

Cancer Therapy: Electrospun fibres are effective carriers for chemotherapeutic drugs like doxorubicin, paclitaxel, and cisplatin. By facilitating targeted delivery and controlled release, these fibres reduce systemic toxicity and improve the therapeutic index of anticancer agents.

Gene Therapy: Bioactive molecules such as Ribonucleic acid (RNA), Deoxyribonucleic acid (DNA), and growth factors can be encapsulated within electrospun fibres for controlled release. This approach is particularly useful in gene therapy, where sustained release preserves the stability and bioactivity of therapeutic agents over time.

Tissue Engineering and Regenerative Medicine: Electrospun scaffolds mimic the extracellular matrix, providing structural support for cell growth and differentiation. These fibres are used in regenerative medicine for applications such as cartilage repair, vascular grafts and skin regeneration. Their tunable properties allow precise control over cellular responses, enhancing tissue regeneration.

Medical device and implant coating: Medical implants can be coated with electrospun nanofibers to increase biocompatibility and add features like medication administration. They alter the surface of the implant to direct cellular interactions and can incorporate bioactive substances for a variety of uses. For example, porous coatings enhance cell adhesion and deliver drugs to prevent infections. Nanofibers are used in coated stents, such as PK Papyrus, to increase flexibility and allow for prolonged drug release, which promotes anticoagulation and quick healing. Furthermore, nanofibrous coatings address problems like prosthesis failure by reducing stiffness mismatches between implants and tissues.

Cosmetics or skin care: The ability of electrospun fibre mats to adapt to the topography of the skin has driven their development as cosmetic skin care masks. Recent advancements include the development of silk fibroin (SF) nanofibrous mats loaded with a water-soluble vitamin E derivative (VE TPGS) using aqueous electrospinning. The fibre morphology was found to vary with VE TPGS content, forming ribbon-like shapes at lower doses and round shapes at higher doses. Ethanol vapor treatment improved the mats' water resistance, enhancing their practicality. In vitro studies demonstrated sustained release of VE TPGS and better growth and spreading of mouse skin fibroblasts on the mats compared to standard surfaces. Additionally, the mats protected cells from oxidative stress, indicating their potential in skincare, tissue regeneration and related applications.

Anaesthetics: Local anaesthetics such as lidocaine hydrochloride and bupivacaine are commonly used to manage pain during surgical procedures, typically requiring multiple injections to infiltrate the targeted area. Recent advancements have led to the development of electrospun fibres incorporating bupivacaine, which provide sustained local analgesia. This approach significantly reduces the need for repeated injections, improving patient comfort and procedural efficiency.

CHALLENGES AND FUTURE PERSPECTIVES:

Electrospinning faces several challenges, including the requirement for high voltage, needle clogging, and limited control over fiber alignment and quality. Low-conductivity polymer solutions can cause charge accumulation, leading to jet instability and poor-quality nanofibers. It also involves significant safety and environmental risks due to the use of high voltages and hazardous solvents. High voltages increase the risk of operator electrocution, necessitating strict safety protocols. Additionally, solvents such as chloroform, tetrahydrofuran, dichloromethane, and hexane, often used for dissolving polymers, are toxic and pose health risks. These substances are classified as carcinogens, requiring careful recovery and extensive cleaning of nanofibers intended for human contact. The recovery process for these solvents is complex. To address these concerns, eco-friendly alternatives like dimethyl carbonate and ethanol are under investigation.

Challenges also persist in achieving uniformity in fiber quality and scaling up production. While conventional single-needle electrospinning is inefficient for large-scale production due to its low yield, needleless electrospinning methods, such as rotary systems, double-ring slits, coil-based setups and foambased techniques, have emerged to enhance production rates. However, these methods often introduce new challenges, such as uneven electric field distribution and variable fibre quality.

In recent years, electrospinning has become a fast and efficient method for creating smart drug delivery systems that can be precisely controlled. The flexibility of electrospinning allows for easy adjustments to the drugs and polymers used, making it possible to customize drug delivery for various applications. By modifying the mechanical properties or drug release rates, electrospun nanofibers can be tailored to deliver medications in a more targeted and controlled way. One of the major challenges in drug delivery is ensuring that the right drug reaches the right place in the right amount, at the right time. This review highlights the potential of nanofibers as drug carriers for controlled release, with customizable properties suited for specific needs. There is still much to explore in the use of nanofibrous scaffolds, especially in areas like diabetes, hormone therapy and immune disorders. With careful planning, the challenges of electrospinning can be overcome, leading to improved drug delivery systems that combine tissue engineering with controlled release, minimizing side effects. In the future, customizable nanofibers may play a key role in personalized medicine, offering flexible solutions for individual patient needs.

CONCLUSION:

Electrospun nanofibers represent an exciting and innovative advancement within the field of drug delivery systems, offering numerous unique features that distinguish them from conventional methods. These nanofibers are characterized by their remarkably high surface area, tunable porosity, and the capacity to enable controlled and sustained drug release. These attributes contribute significantly to their versatility and effectiveness in various medical applications. Notably, they have been successfully employed in creating transdermal patches, wound dressings, and targeted therapies designed to treat complex diseases such as cancer. Furthermore, their compatibility with a wide range of both natural and synthetic polymers offers remarkable flexibility in designing drug delivery systems tailored to address specific medical needs and challenges.

Despite these impressive benefits, the field of electrospinning is not without its challenges. One significant hurdle is the requirement for specialized equipment to carry out the electrospinning process effectively. Additionally, the difficulty in scaling up production from laboratory settings to industrial levels presents a major obstacle for broader application. Another pressing concern relates to environmental safety, as many commonly used solvents in

the process pose ecological risks. Addressing these issues has become a primary focus of ongoing research efforts, which are exploring innovative solutions such as the use of eco-friendly solvents and the development of more efficient and scalable production techniques.

In conclusion, electrospun nanofibers hold immense potential for transforming drug delivery systems and advancing biomedical applications. Continued research and technological advancements are expected to enhance the practicality, scalability, and affordability of this technology, making it more accessible for widespread use in healthcare settings. With sustained innovation, the challenges currently associated with electrospinning can be addressed effectively, paving the way for improved therapeutic interventions and significantly enhancing patient outcomes in the future.

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