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REVIEW ARTICLES

Advances and challenges in nanofiber production: techniques and applications in nanotechnology

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Abstract

This article presents a concise review of nanofiber production techniques, materials obtained by innovative technologies to produce nanofibers. The use of nanofibers has evolved significantly due to their unique properties, allowing maximization at the nanometric scale. The large-scale production capacity, simplicity in manufacturing and versatility have increased interest in several areas, especially in pharmaceuticals, for controlled drug release. Different nanofiber manufacturing techniques were explored and how each one can improve medical-pharmaceutical devices, biomaterials, nanotechnology, textile industries, air and water filters, human tissue engineering, among others. It was observed that interest in nanofibers has grown worldwide in research. Despite the advances, challenges remain to optimize production and expand knowledge in the pharmaceutical sector. Future research should focus on more economical and sustainable manufacturing processes, in addition to exploring biodegradable and biocompatible polymers to solve problems in pharmaceutical formulations.

Keywords: *nanofibers, electrospinning, centrifugal spinning, melt blowing spinning, pharmaceutical applications.*

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1. Introduction

Nanotechnology is a field of science that focuses on the study of materials with dimensions ranging from 0.1 to 100 nanometers. Over the decades, this area has had a notable impact on improving the properties of biodegradable and non-biodegradable polymeric materials. Nanofibers, structures obtained from innovative one-dimensional, two-dimensional and three-dimensional nanomaterials, have attracted considerable attention from researchers around the world due to their large contact surface[1-5].

In the present work, it was possible to compile different nanofiber manufacturing techniques, such as melt blowing technology, electrospinning technology, supersonic CO_2 laser stretching technology, solution blow spinning technology and, last but not least, roto-spinning/centrifuge spinning technology. We highlight the properties resulting from these techniques, including the high surface area/volume ratio[6-10].

Furthermore, it was possible to present an analysis of the most widely used pharmaceutical applications for nanofibers, which include the efficient delivery of different drugs and their controlled release, the diagnosis of different diseases, such as different cancers, and the treatment of open wounds of different etiologies for the release of anti-inflammatories and antibiotics.

2. Different Ways of Obtaining Polymeric Nanofibers

In the manufacture of nanofibers, several factors are carefully considered to optimize their properties. Furthermore, production parameters represent a crucial aspect, which vary significantly between different techniques. To this end, the techniques covered in this review include:

2.1 Fusion blowing technology

Nanofiber production by melt blowing emerged as an evolution of polymer processing techniques, aiming to obtain ultrafine fibers with improved properties. Although the melt blowing technique has its roots in older industrial processes, the specific application for nanofiber production

has gained prominence in recent decades, driven by advances in nanotechnology[11-17].

The development of the technique has enabled the production of nanofibers from a variety of thermoplastic polymers, with precise control over the fiber diameter and the morphology of the fibrous mat. This has opened doors to diverse applications in areas such as filtration of different fluids, medicine, textile industry and composites, where the unique properties of nanofibers have proven advantageous[18,19].

Melt blowing technology consists of the production of fibers in a single step, through the extrusion of a given polymer, which may be biodegradable or not, which is melted through one or more holes in a given injection die, previously heated to the melting temperature of the chosen material, which is followed by stretching the material to be extruded with hot air[20,21].

The air exerts a drag force on the molten material, reducing the molten extrudate to micrometric and nanometric fibers, which are subsequently collected in the form of a non-woven mat in a cylindrical collector that winds the nanofiber produced. Melt blowing technology allows the use of thermoplastic polymers, representing an economically viable spinning process option (Figure 1).

2.1.1 Advantages

Melt blowing technology, used in the production of nanofibers, has significant advantages over other techniques, boosting its application in various sectors[22-24].

The production of nanofibers using melt blowing technology is often used in the manufacture of high-performance filters because it has a filtration efficiency of approximately 99%, resulting in greater purity of the fluid to be filtered in the nanofiber structure, elimination of pollution from water bodies and air treatment systems, reduction of corrosion, superior mechanical resistance to other available techniques, greater miscibility after treatment and modification of fluids subject to filtration, as is the case of separation of compounds and sterilization of medicines by filtration at 0.22 µm.

One of the main advantages is the high production rate, which allows the manufacture of nanofibers on an industrial scale, meeting the demand for large volumes of material. This continuous and efficient process reduces production costs and increases the commercial viability of nanofibers.

Material versatility is another strength of melt blown technology. It enables the production of nanofibers from a wide range of thermoplastic polymers, including high-performance and biodegradable polymers. This flexibility makes it possible to create nanofibers with tailored properties for a variety of applications[11-21].

Control over fiber morphology is also an important advantage. Melt blowing technology allows parameters such as temperature, pressure, and air speed to be adjusted to control the diameter, orientation, and structure of nanofibers. This controllability enables the production of nanofibers with optimized mechanical, thermal, and electrical properties.

Furthermore, melt blowing technology is a relatively simple and low-cost process compared to other nanofiber production techniques. The absence of solvents and the lower complexity of the equipment contribute to the reduction of production costs and the sustainability of the process.

Finally, melt blowing technology enables the production of nanofibers with high porosity and specific surface area, which is advantageous for applications such as filtration, adsorption, and controlled drug release. The porous structure of nanofibers increases the efficiency of these processes and enables the creation of materials with unique properties.

2.1.2 Disadvantages

The melt blowing technique, despite its ability to produce nanofibers on an industrial scale, has some disadvantages that limit its applicability in certain situations[25,26].

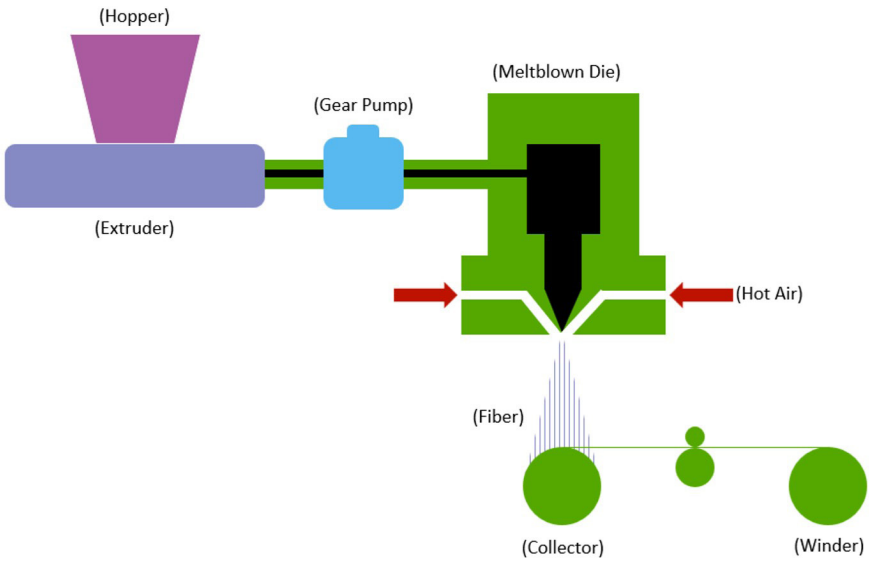

Figure 1. Representation of melt blowing technology. Source: Own file.

One of the main disadvantages is the difficulty in controlling the morphology of nanofibers. Obtaining nanofibers with uniform diameter and precise alignment can be challenging, especially in large-scale melt blowing processes. Non-uniform diameter distribution and random fiber alignment can affect the mechanical, electrical, and other properties of nanofibers, limiting their applications in some areas that require specific properties.

Another disadvantage is the limited choice of materials. The melt blowing technique is best suited for thermoplastic polymers with high melt viscosity. Polymers with low viscosity or high thermal sensitivity may be difficult to process by melt blowing, limiting the range of materials that can be used.

High processing temperature is also a common disadvantage of the melt blowing technique. The need to heat the polymer to the melting temperature can lead to thermal degradation of some materials, affecting the properties of the nanofibers. In addition, high processing temperature can increase energy consumption and production costs.

The formation of defects in nanofibers is another disadvantage of the melt blowing technique. The presence of defects such as beads, knots and breaks in the fibers can affect the mechanical and other properties of the nanofibers. The formation of defects can be influenced by several factors such as polymer viscosity, processing temperature and blowing air velocity.

Finally, safety is a major concern in melt blowing due to the high processing temperature and high velocity of the blowing air. The need for appropriate protective equipment and stringent safety measures can increase the costs and complexity of the process.

2.2 Electrospinning technology

The electrospinning technique is based on some parameters, without which it is impossible to produce quality nanofibers. Among the determining parameters for the electrospinning process, it is possible to mention the use of a polymer solution that must respect some physical-chemical parameters such as polymer concentration, conductivity, viscosity of the solution, molecular weight of the polymers used, volatility of the solvents used in the formulation and molecular structure of the components. Other parameters of relevant importance include the application of high voltages ranging from 10 kV to 50 kV, distance between the collector and the polymer injection needle, constant flow of the polymer solution that is carried out by means of an infusion pump and an appropriate collector. The electrospinning system has collectors that can be fixed or rotary, equipped with distance adjustment to eliminate possible imperfections in the structure of the nanofibers and/or formation of beads. Figure 2, below, shows details of the electrospinning process, taking into account solution variables, environmental variables and electrospinability variables[27,28].

Before being electrospun, the polymer solution must have an adequate pH to favor the electrical potential differential between the injection needle and the collector. The distance between the injection needle and the collector is crucial and facilitates fine adjustment of the final conditions of the nanofiber obtained. In cases where the drug incorporated into the polymer solution is thermolabile, it must have temperature and humidity control and be equipped with an exhaust fan to eliminate organic solvent vapors, which may be harmful to health[29,30].

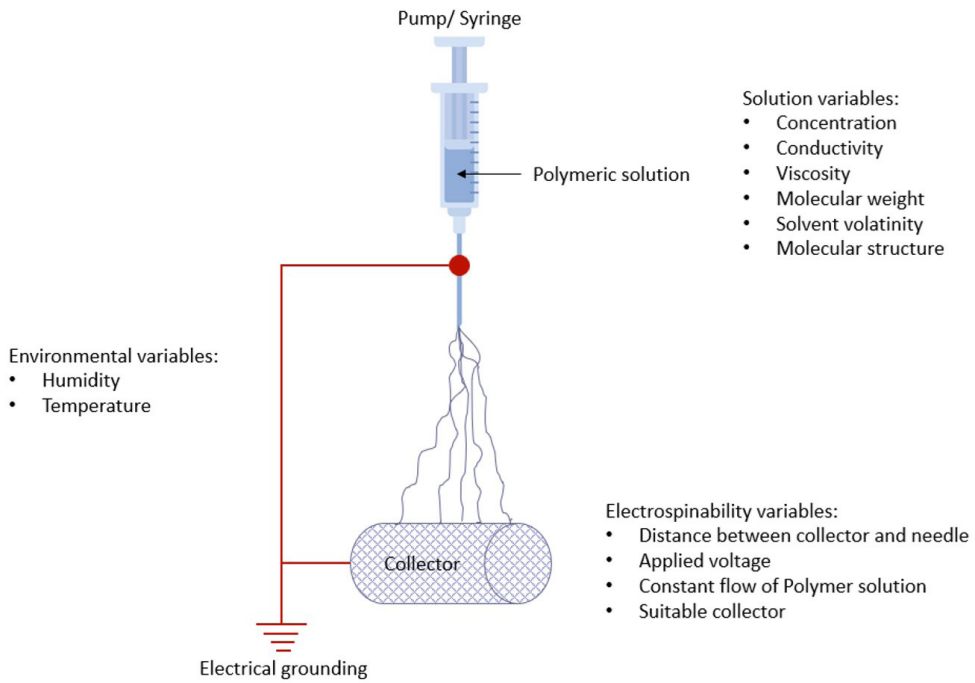

Figure 2. Representation of electrospinning technology. Source: Own file.

2.2.1 Advantages

Electrospinning stands out as a versatile and efficient technique for the production of nanofibers, offering significant advantages in various fields. The main advantage lies in the ability to produce fibers with diameters on the nanometric scale, which imparts unique properties to the resulting materials[31,32].

Another major advantage of electrospinning is the precise control over the morphology of nanofibers. By adjusting parameters such as applied voltage, solution flow rate, and the distance between the emitter and the collector, it is possible to control the diameter, alignment, and porosity of the fibers. This precision allows for the production of tailored materials for specific applications, ranging from biomedical devices to high-efficiency filters[33].

The versatility of electrospinning also manifests in the wide range of materials that can be processed. Synthetic polymers, natural polymers, and mixtures of both, ceramics, metals, and even composites can be electrospun, opening doors to the creation of materials with combined properties and innovative functionalities[34].

Additionally, electrospinning stands out for the simplicity of the equipment and ease of operation. The process can be carried out under controlled or uncontrolled environmental conditions, without the need for vacuum or high temperatures, which reduces costs and simplifies production. This characteristic makes electrospinning an accessible technique for research laboratories and industrial-scale production[35,36].

The ability to produce nanofibers with high surface area is another important advantage of electrospinning. This characteristic is particularly useful in applications such as catalysis, sensors, and energy storage devices, where the high surface area increases the efficiency of processes.

Finally, electrospinning allows for the production of complex structures, such as hollow nanofibers, multilayer fibers, and even three-dimensional fabrics. This ability to create customized structures opens up new possibilities for the development of advanced materials with innovative functionalities.

2.2.2 Disadvantages

Despite its versatility and ability to produce nanofibers with unique properties, the electrospinning technique has some disadvantages that limit its applicability in certain situations[37].

One of the main disadvantages lies in the low production rate, which makes it difficult to scale the process for large-scale industrial applications. Electrospinning is a relatively slow process, which can increase production costs and limit its feasibility for mass manufacturing of nanofibers[38].

Another negative point is the complexity of controlling the process parameters. The morphology of nanofibers, such as diameter, alignment, and porosity, is highly sensitive to variations in electrospinning parameters, such as applied voltage, solution flow rate, distance between the emitter and the collector, and properties of the polymer solution. Small variations in these parameters can lead to significant changes in the morphology of nanofibers, requiring precise and constant control of the process[39].

The non-uniform distribution of nanofiber diameter is also a common disadvantage of electrospinning. Achieving nanofibers with uniform diameter throughout the fibrous mat can be challenging, especially in large-scale electrospinning processes. The non-uniformity of diameter can affect the mechanical, electrical, and other properties of the nanofibers, limiting their applications in some areas[39].

Additionally, electrospinning can be limited by the viscosity and electrical conductivity of the polymer solution. Some polymer solutions may not be suitable for electrospinning due to their high viscosity or low electrical conductivity, which can hinder the formation of uniform nanofibers[39].

Finally, safety is an important concern in electrospinning due to the high electrical voltage involved in the process. The need for appropriate protective equipment and strict safety measures can increase the costs and complexity of the process[39].

2.3 CO_2 laser supersonic stretching technique

The CO_2 laser supersonic stretching technique stands out as a promising alternative for the production of nanofibers, especially in applications that require the absence of chemical solvents. In this process, a CO_2 laser is used to fuse precursor fibers, generally with diameters in the range of 100 to 200 μm. The laser provides controlled thermal energy, allowing precise fusion of the material without compromising its properties[40].

After melting, the fibers are subjected to a supersonic air flow. This flow, generated by a high-speed nozzle, exerts a drag force on the molten material, inducing stretching and consequently the formation of nanofibers. The supersonic air speed ensures fast and efficient stretching, resulting in fibers with nanometric diameters and high uniformity[8].

One of the main advantages of this technique is its continuous process nature. Melting and stretching occur in sequence, allowing the production of long-chain nanofibers with high productivity. In addition, the absence of chemical solvents eliminates the need for drying and purification steps, reducing the time and cost of the process[41].

The supersonic CO_2 laser stretching technique is widely applied in the processing of thermoplastic polymers such as polyglycolic acid (PGA), polyethylene terephthalate (PET) and polylactic acid (PLLA). These polymers are biocompatible and biodegradable, making the nanofibers produced by this technique suitable for various pharmaceutical applications, tissue engineering, controlled drug delivery and medical devices[42,43].

The synthesis of *nylon-66* nanofibers by this technique tends to result in a high melting point, close to the equilibrium melting point. Additionally, the technique enables the production of polymeric nanofibers with extended chains, which contributes to the improvement of mechanical properties[41].

2.3.1 Advantages

The CO_2 laser stands out for its high power and comparative efficiency, making it an immediate choice for sectors that require material processing. In addition to offering a low cost per watt of energy consumption and adequate beam quality, the CO_2 laser has an output power ranging from a few watts to 15 kW. Its effectiveness surpasses that of He-Ne and argon lasers[8,44,45]

Although less widespread compared to other nanofiber production techniques, it presents some promising advantages when compared to other nanofiber fabrication methods. Among the advantages, it is possible to mention precise control of fiber morphology, material versatility, production of aligned nanofibers, non-contact process, potential for high-scale production, improved material strength, and use in the manufacture of electronic devices[45].

The use of the CO_2 laser allows for precise control of heating and stretching of the material, enabling the production of nanofibers with controlled diameter and alignment. Additionally, the high speed of the supersonic jet contributes to the efficient stretching of the fibers, resulting in ultrafine and uniform nanofibers[31,46].

The technique can be applied to a variety of materials, including thermoplastic polymers, ceramics, and composites. It also allows for the processing of materials with high melting temperatures, expanding the range of materials that can be used[47,48].

The supersonic jet and precise laser control enable the production of nanofibers with a high degree of alignment, which is advantageous for applications requiring anisotropic properties[49].

The use of the laser eliminates the need for physical contact with the material, reducing the risk of contamination and damage to the fibers[49-51].

The technique has the potential to be scaled up for mass production of nanofibers, which is important for industrial applications. Due to precise control and the ability to process various materials, the technique is promising for specific applications in areas such as the medical-pharmaceutical field for the production of scaffolds for tissue engineering and controlled drug release, electronics for the production of conductive nanofibers for flexible electronic devices, and composites for reinforcing materials with aligned nanofibers[50].

It is important to note that the technique is still under development and requires further research to optimize the process parameters and fully explore its potential[50].

2.3.2 Disadvantages

The CO_2 laser supersonic stretching technique, although promising in certain applications, has some disadvantages that limit its applicability. Among the disadvantages, the divergence of the CO_2 laser is inferior to that of He-Ne and argon lasers. The divergence ranges from 1 to 10 milliradians. The beam width varies from 3mm to 100mm. The optical cavity has considerable thickness and reduced length[52].

The technique requires sophisticated and expensive equipment, including high-power CO_2 lasers and precise control systems for the supersonic flow. The process demands extremely precise control of various parameters, such as laser power, gas flow speed, and stretching rate, which increases the complexity and cost of the operation[52].

The technique is more effective for materials that absorb CO_2 laser radiation well. Materials with low absorption may require higher power lasers or pre-treatments, increasing the cost and complexity[52].

Heat-sensitive materials can be damaged by the laser, limiting the application of the technique. Additionally, the large-scale application of the technique remains a challenge due to the complexity of the process and the cost of the equipment[53].

Ensuring the uniformity of material properties over large areas can be challenging due to variations in laser power and gas flow. Additionally, high-power laser radiation poses a significant safety risk to operators, requiring stringent protective measures[54].

The supersonic gas flow can also pose risks, such as excessive noise and particle generation. Additionally, the high cost of regular preventive maintenance can be a disadvantage, and in some cases, the combination of these factors discourages the adoption of the technique[55].

The technique produces an irregular surface finish on some materials, requiring additional processing steps that are more time-consuming[56].

In summary, the CO_2 laser supersonic stretching technique is a powerful tool for material processing, but its disadvantages in terms of complexity, cost, material limitations, scaling challenges, and safety must be carefully considered[56].

2.4 Solution blow spinning technique.

The solution blow spinning technique was developed to overcome the limitations of the conventional electrospinning technique, which include the need for high electric potential and the *in situ* synthesis of nanofibers. In solution blow spinning, these restrictions are minimized[57-60].

Being innovative, this technique is used for the production of microfibers and nanofibers in different size variations. Although the setup for this process is costly, it offers significant advantages and allows for the production of nanofibers with unique and stable properties[61].

This technique primarily requires three components: a polymer solution at a known concentration, a standard commercial airbrush with adjustable flow, and a source of compressed gas, preferably N_2, as O_2 is flammable. With these components, the technique can be employed for the *in situ* deposition of nanofiber mats and scaffolds, providing uniform coverage of non-conductive targets. The applications of this technique span various fields of tissue engineering and surgery[62] (Figure 3).

2.4.1 Advantages

The solution blow spinning (SBS) technique offers several advantages in the production of nanofibers, making it a promising alternative to other techniques such as electrospinning and rotary spinning. Notable points include its versatility, simplicity, low cost, high productivity rate, and the fact that it does not require an electric field in the nanofiber manufacturing process[63].

SBS allows the processing of a wide range of materials, including polymers, ceramics, and composites, offering flexibility in material choice for different applications[64].

Compared to electrospinning, SBS generally requires simpler and less expensive equipment, facilitating the implementation of the technique on an industrial scale and allowing for large-scale production of nanofibers, with significantly higher production rates compared to electrospinning[65].

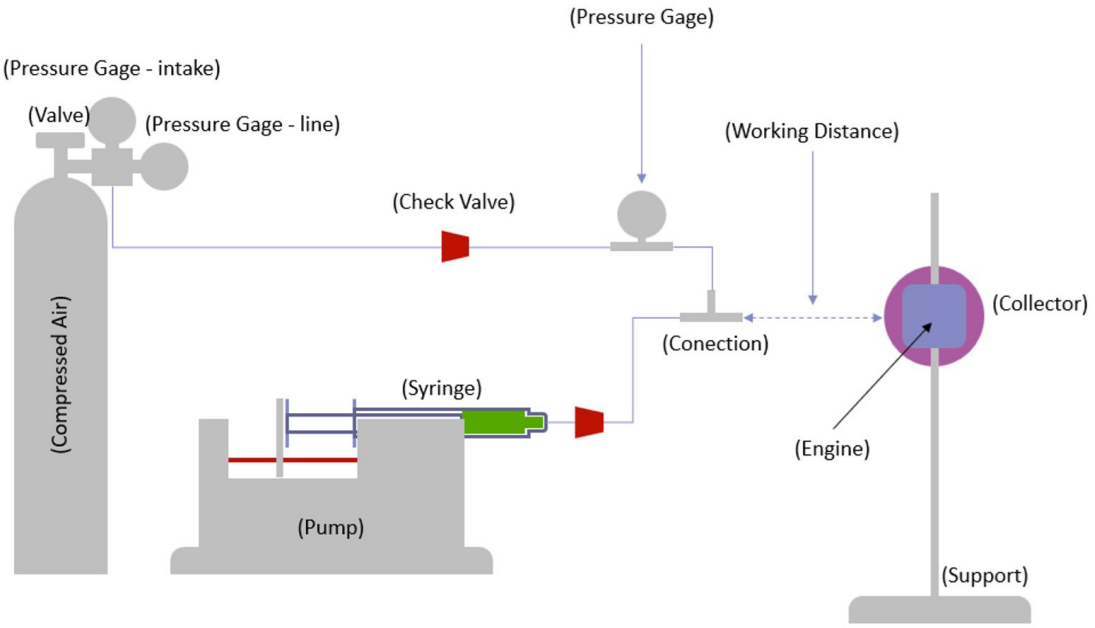

Figure 3. Representation of solution blow spinning technology. Source: Own file.

One of the greatest advantages, if not the most important, is that SBS does not require the application of an electric field, as is the case with electrospinning, which simplifies the process and reduces associated safety risks[66].

In summary, solution blow spinning stands out as a promising technique for large-scale nanofiber production, offering material versatility, simplicity, low cost, and high production rates[67].

2.4.2 Disadvantages

Although promising for nanofiber production, the solution blow spinning technique has some disadvantages that deserve attention. Among the disadvantages are the complexity of the process, the use of solvents, limited control over nanofiber morphology, variation in fiber distribution, and scalability, which remains a challenge and presents processing difficulties for some materials[67].

Solution blow spinning involves various parameters that need to be precisely controlled, such as solution viscosity, temperature, air pressure, and fiber collection speed. This makes the process complex and challenging to optimize[68].

The technique requires the use of solvents, which can be toxic and harmful to the environment. The need to handle and dispose of these solvents demands safety precautions and increases production costs[69].

Compared to other techniques, such as electrospinning, solution blow spinning may offer less control over the diameter, alignment, and orientation of nanofibers. This can limit the application of nanofibers in some areas that require specific properties[70].

The technique can result in a wider distribution of fiber diameters, which can affect the uniformity of the final material's properties[70].

Large-scale production using solution blow spinning is still a challenge, which limits its industrial application on a large scale[71].

Some materials can be difficult to process using solution blow spinning due to their viscosity or other rheological properties. Therefore, it is important to consider these disadvantages when choosing the most suitable nanofiber production technique for each application[71].

2.5 Rotary jet spinning/centrifugal spinning

Rotary Jet Spinning, or centrifugal spinning, is a nanofiber production technique that uses the centrifugal force generated by a rotor attached to the shaft of a Brushless Spindle motor, which spins at high speed and is capable of stretching and solidifying polymer solutions, thus forming ultrafine fibers[72].

Its operating principle is based on the centrifugal force that expels the polymer solution from the rotor's reservoir compartment through orifices of known diameters. The polymer solution is poured into the rotor's reservoir compartment during the equipment's operation, which spins at high speeds between 2,000 and 24,000 rpm[73].

The technique generally requires the use of highly volatile solvents, making it mandatory to use fume hoods to protect the equipment operator from the gases emitted by the solvents[6].

Rotary Jet Spinning has been widely used in the medical-pharmaceutical field for the production of dressings, controlled drug release, tissue engineering, air and water filter manufacturing, fabrics with enhanced properties, and material reinforcement[74-77] (Figure 4).

2.5.1 Advantages

The Rotary Jet Spinning technique, also known as 'centrifugal spinning,' offers several advantages in nanofiber production, making it an interesting alternative compared

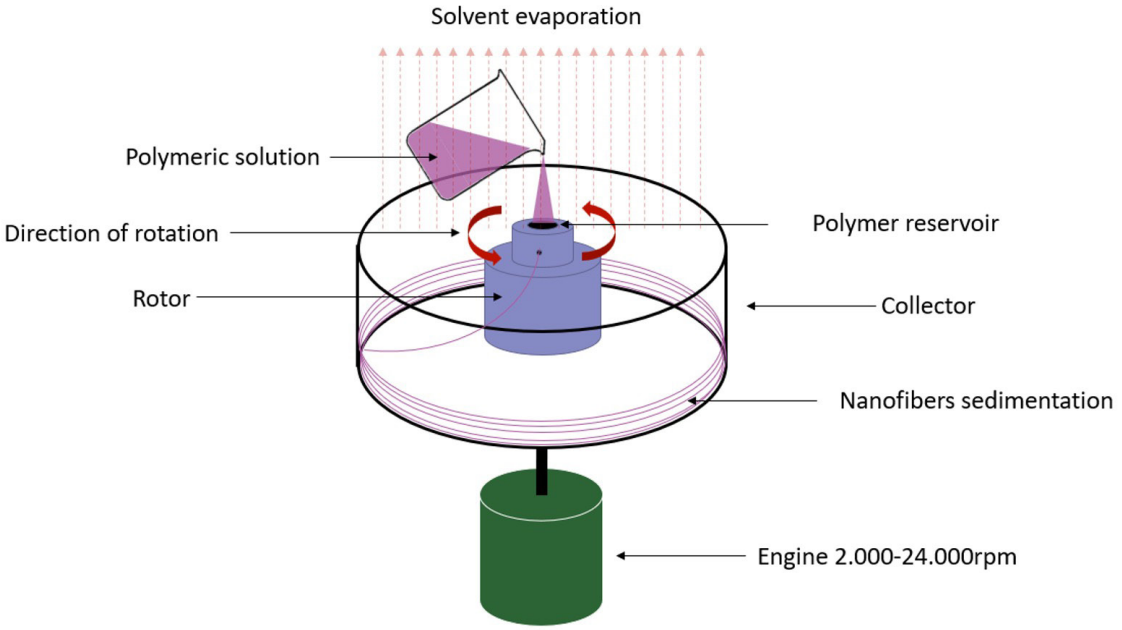

Figure 4. Representation of centrifugal/rotary spinning technology. Source: Own file.

to other conventional techniques. Here are some of the main advantages:

Rotary Jet Spinning allows for large-scale production of nanofibers, with significantly higher production rates compared to electrospinning. This is due to the centrifugal force used in the process, which enables the simultaneous ejection of multiple fibers in a short period of time[78].

The technique is compatible with a wide range of materials, including polymers, ceramics, metals, and composites. This makes it suitable for various applications in different fields, such as pharmaceuticals, engineering, and the textile industry[79].

Control of morphology is a noteworthy point, as Rotary Jet Spinning allows precise control over the diameter, alignment, and orientation of nanofibers, enabling the production of structures with specific properties for each application[80].

Compared to electrospinning, Rotary Jet Spinning generally requires simpler and less expensive equipment, facilitating the implementation of the technique on an industrial scale and can be easily adapted for continuous production processes, which is advantageous for mass production of nanofibers[81].

In some cases, rotary spinning may require a smaller amount of solvents compared to electrospinning, which is beneficial from an environmental standpoint. Additionally, it has the capability to produce hollow nanofibers. The technique allows the production of hollow nanofibers, which have specific applications in areas such as drug microencapsulation and controlled substance release[82].

In summary, rotary spinning stands out as a promising technique for large-scale production of nanofibers, with a high production rate, material versatility, and control over fiber morphology[83].

2.5.2 Disadvantages

Although rotary spinning offers significant advantages in the production of nanofibers, it also presents some disadvantages that should be considered, such as the limited control over fiber alignment. Unlike electrospinning, which allows for more precise fiber alignment, rotary spinning tends to produce nanofibers with random orientation. This can be a disadvantage in applications that require specific fiber alignment[84].

Another feasible point of attention is the distribution of fiber diameter, as rotary spinning can present greater variation in fiber diameter compared to electrospinning. This can affect the uniformity of the final material's properties[72].

Another relevant point is the difficulty in processing certain materials, as some materials can be more challenging to process through rotary spinning due to their viscosity or other rheological properties. This can limit the range of materials that can be used with this technique[85].

Precise control of the porosity of nanofiber mats can be more challenging in rotary spinning compared to electrospinning or other available techniques. Additionally, it is less suitable for the production of complex nanofiber structures, such as hollow or multilayer nanofibers[86].

Safety is a determining factor in some cases, as the high rotation speed used in rotary spinning can pose safety risks, requiring appropriate protective equipment and strict safety measures[87,88].

It is important to emphasize that the choice of nanofiber production technique directly depends on the specific needs of each application. Rotary spinning can be an excellent option for large-scale production of nanofibers with random orientation, while electrospinning may be more suitable for applications that require precise control of fiber alignment

and morphology[85,89]. Considering the different approaches discussed for nanofiber production, it is important to concisely summarize their main characteristics. Table 1 below presents a comparative overview of the five techniques discussed, highlighting the operating principle, advantages, limitations, and most common applications of each method. This summary contributes to a critical analysis in choosing the most appropriate technique, depending on the desired application.

3. Regulatory Challenges in Nanofiber Production

Nanofibers have gained increasing attention in materials engineering, particularly for biomedical, pharmaceutical, and environmental applications. However, the transition of these technologies from bench to market faces substantial regulatory hurdles. The various nanofiber production techniques such as electrospinning, centrifugal spinning, self-assembly, and solution spinning pose specific challenges that hinder the standardization and validation processes required by regulatory agencies like the FDA (Food and Drug Administration) and EMA (European Medicines Agency)[90-93].

One of the primary obstacles is related to scaling up manufacturing processes. While electrospinning is efficient at the laboratory scale, its low throughput and sensitivity to environmental conditions make it less suitable for large-scale production. Techniques like rotary jet spinning or melt-electrospinning writing demonstrate greater scalability potential but still lack standardized systems that ensure reproducibility across industrial batches[91-94].

Material reproducibility represents another critical challenge. Parameters such as solution viscosity, ambient humidity, surface tension, collection speed, and temperature directly affect nanofiber morphology, porosity, and diameter. Minor variations in these factors can lead to inconsistencies in physicochemical and functional properties, complicating efforts to meet strict quality and safety standards imposed by international regulations[92-94].

In addition, comprehensive characterization of nanofibers remains inadequately regulated. Methods to evaluate uniformity, stability, mechanical integrity, release kinetics, and behavior in biological systems are diverse and sometimes lack consensus. The absence of universally accepted protocols complicates harmonization among researchers, manufacturers, and regulatory bodies, making the approval process longer and less predictable[91-93].

In the pharmaceutical field, regulatory demands are even stricter. Nanofibers used for drug delivery or tissue engineering must demonstrate not only safety and efficacy but also interbatch reproducibility, long-term stability, absence of impurities, and biocompatibility. Manufacturing in Good Manufacturing Practice (GMP) environments is mandatory, yet not all current production methods are compatible with GMP requirements without significant technological adaptation[91-93].

Another major regulatory consideration is the need for robust preclinical and clinical testing. Although many nanofiber-based technologies show promising results in vitro and in animal models, translating these findings to human use requires extensive data on toxicokinetics, biodistribution, immunogenicity, and metabolic fate. Many devices or formulations fail at this stage not due to inefficacy, but due to a lack of comprehensive regulatory data[91-93].

The lack of international standardization in nanotechnology regulation further complicates product development. Each regulatory agency may use different criteria for evaluation, forcing developers to tailor regulatory dossiers for each jurisdiction. This increases costs and extends timelines, particularly impacting academic groups and startups with limited resources[91-93].

Consequently, despite the high innovation potential of nanofiber production techniques, their regulatory viability still depends on overcoming both technical and structural barriers. Advancements in automated manufacturing

Table 1. Comparison of the main nanofiber production techniques regarding operating principle, advantages, disadvantages, and typical applications.

TECHNIQUE	WORKING PRINCIPLE	ADVANTAGES	DISADVANTAGES	TYPICAL APPLICATIONS
Melt Blowing	Extrusion of molten polymer with hot air to form nanofibers	High production rate, no solvent use, relatively low cost, high porosity	Limited morphology control, high temperature, limited materials, defect formation	Filtration, textile industry, industrial composites
Electrospinning	Application of high electric field to a polymer solution to eject a jet	Precise control of morphology, wide range of materials, simple equipment	Low production rate, complex parameter control, electrical safety risks	Controlled drug delivery, tissue engineering, sensors
Supersonic CO_2 Laser Stretching	Melting with CO_2 laser followed by stretching with a supersonic jet	Solvent-free, continuous production, high uniformity, precise morphology control	Expensive equipment, complex process, thermal risks, challenging scale-up	Medical devices, tissue engineering, flexible electronics
Solution Blow Spinning	Spraying polymer solution with compressed gas (e.g., N_2)	High productivity, no need for electric field, versatile and low cost	Less control over morphology, solvent use, fiber diameter variation	Wound dressings, tissue engineering, nanofibrous films
Rotary Jet Spinning	Ejection of polymer solution by centrifugal force from a rotating rotor	High production rate, simple equipment, control over diameter and porosity	Limited fiber alignment, diameter variation, mechanical safety risk, porous structure control	Wound dressings, drug release, tissue engineering, filters

Source: Own file.

platforms, validated characterization protocols, and stronger collaboration among academia, industry, and regulatory bodies are essential to convert these promising technologies into accessible, approved products[91-93].

4. Applications

Nanofibers demonstrate vast potential in various engineering fields; however, their application in the medical-pharmaceutical field has stood out as a true revolution. The ability to provide more effective treatments, coupled with the concern for reducing healing time and the side effects of conventional medications, highlights the significant impact of this technology[90-93]. The applications discussed in this article will be presented below in a simple flowchart (Figure 5), followed by a detailed analysis later.

4.1 Controlled drug release

The control and efficient delivery of drugs to the site of action have been one of the greatest and main applications of nanofibers. The proper delivery of active pharmaceutical ingredients (API) and diagnostic agents to the receptor or desired site mainly depends on the choice of drug carrier[95-97].

The main purpose of the drug carrier in this field of knowledge is to ensure that the API has the maximum effect upon reaching the desired area, maintaining all its properties from the initial stage to the point where it reaches the target organs, thereby promoting proper drug release for better patient recovery[98-100].

Given this, nanofibers effectively meet all criteria for drug delivery. The use of polymers in nanofibers, such as gelatin, has proven to be a choice that provides better performance of the API, as it offers biodegradability and efficient compatibility with the human body, thus not causing damage to target organs nor allowing the fixation of toxins in the human body[101].

Drug delivery in wound treatment, when using conventional treatments, faces the problem of side effects caused by medications due to their low surface contact and inadequate uniformity. However, with the aid of nanofibers with drugs incorporated into them, it is possible to help partially or completely reduce the side effects[101,102].

From another perspective, nanofibers act as a protective shield against enzymes and external agents that may settle and, in some way, hinder the ongoing healing process. When all these factors are considered and understood, it becomes evident that nanofibers are efficient drug carriers[96,99,103-105].

4.2 Cancer treatment and diagnosis

Nanofibers, structures with nanometric dimensions, emerge as promising tools in the fight against cancer, offering innovative applications in both diagnosis and treatment. In terms of diagnosis, nanofibers enable the creation of highly sensitive biosensors capable of detecting tumor biomarkers at minimal concentrations, allowing for early and precise disease diagnosis. Additionally, the ability to functionalize nanofibers with antibodies or other specific ligands allows for the creation of targeted imaging systems, which facilitate the visualization of tumors at early stages[101,106,107].

Cancer has been a type of problem for the natural entity that has weakened everyone due to its limitations in curing. However, nanofibers have shown impressive performance in cancer diagnosis. Currently, for example, pathological examination is the technique used to detect tumors present in the body in general. However, single sample testing cannot fully provide the genomic character of a given tumor[108-110].

To counter this, Liquid Biopsy is being strongly preferred and involves collecting a blood sample to identify Circulating Tumor Cells (CTCs) that are directly injected into the bloodstream by solid tumors. Given this, nanofibers are very useful in regulating or delivering these CTCs much more easily[111,112].

In cancer treatment, nanofibers offer several advantages. Their high surface area and porosity allow the incorporation of anticancer drugs, therapeutic agents, or genetic material, enabling controlled and targeted release of these compounds to tumor cells. This approach minimizes the side effects associated with conventional chemotherapy and increases treatment efficacy. Additionally, nanofibers can be used in photothermal therapy, where they are functionalized with nanomaterials that absorb light and generate heat, selectively destroying cancer cells[113].

Cancer cells can also be efficiently cured and treated using magnetic nanofibers, which work in such a way that the magnetic nanoparticles present in the nanofibers heat the tumor from the inside and then it is destroyed. This heat is generated with the help of an external alternating magnetic field (AMF). Although heat regulation here is still a major concern. Thus, this proves that nanofiber is an effective technique for cancer diagnosis and treatment[114-116].

Additionally, biodegradable nanofibers can be used in the regeneration of tissues damaged by cancer or conventional treatments, promoting patient recovery. The versatility of nanofibers allows for the creation of personalized devices

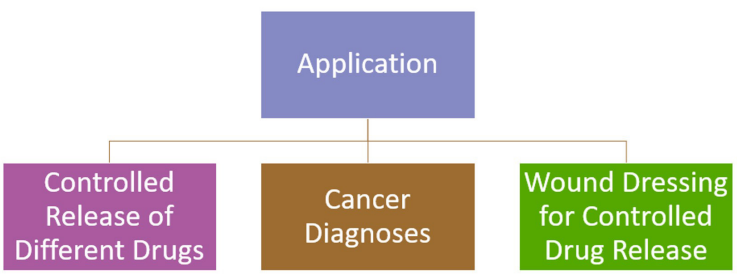

Figura 5. Flowchart of different nanofibers application. Source: Own file.

tailored to the specific needs of each patient, opening new perspectives for cancer treatment and diagnosis[117,118].

4.3 Wound dressings/coverings

Nanofibers have shown extraordinary potential in the development of wound dressings and coverings, offering several advantages over traditional materials. Their nanometric structure provides a high surface area, which facilitates interaction with cells and tissues, promoting healing. Additionally, nanofibers can be designed to gradually release therapeutic agents, such as antibiotics and growth factors, accelerating the tissue repair process and preventing infections[119-121].

The ability to control the composition and morphology of nanofibers allows for the creation of customized dressings for different types of wounds, ranging from superficial injuries to chronic ulcers. The flexibility and conformability of nanofibers also ensure a perfect adaptation to the wound surface, minimizing patient discomfort and promoting tissue regeneration. Additionally, the biodegradability of many nanofibers eliminates the need for dressing removal, reducing the risk of damage to newly formed tissue[122-124].

Continuous research in this area has explored the use of different polymers and manufacturing techniques to optimize the properties of nanofibers and expand their clinical applications. The combination of nanofibers with other technologies, such as photodynamic therapy and controlled gene release, has also shown promising results in the treatment of complex wounds. With the advancement of nanotechnology, nanofibers are expected to play an increasingly important role in regenerative medicine, offering innovative solutions for wound treatment and improving patients' quality of life[125-127].

5. Conclusion and Future Perspectives

In summary, the production of biodegradable nanofibers through the techniques explored in this article represents a significant advancement for pharmaceutical applications. Each method, from electrospinning to rotary jet spinning, offers unique advantages in terms of controlling the morphology, composition, and properties of nanofibers, allowing customization for different therapeutic needs. The diversity of techniques presented demonstrates the potential for innovation and the adaptability of nanotechnology to overcome challenges in drug delivery and regenerative medicine.

The choice of the ideal technique will depend on the specific application, the materials used, and the desired properties of the nanofibers. Continuous research and the development of new methodologies are crucial for improving the production of biodegradable nanofibers, optimizing drug release, interaction with biological tissues, and biodegradability. Additionally, the combination of different techniques and the incorporation of innovative materials can open new frontiers for the development of more effective and safer drug delivery systems.

Finally, biodegradable nanofibers represent a promising platform for the future of medicine, with the potential to revolutionize the treatment of various diseases and improve patients' quality of life. Continuous research and development in this area are essential to explore the full potential of this technology and ensure its benefits are accessible to everyone.

The future prospects for nanofiber production techniques are promising and diverse. With the continuous advancement of nanotechnology, it is expected that new production methodologies will be developed, focusing on more economical and sustainable processes. The exploration of biodegradable and biocompatible polymers will be crucial to overcoming current challenges, especially in the pharmaceutical sector, where controlled drug release can be enhanced. It can be inferred that research should also focus on optimizing existing techniques, aiming to increase the efficiency and quality of the nanofibers produced, which can lead to significant improvements in medical-pharmaceutical devices, biomaterials, and other industrial applications.

Additionally, the versatility of nanofibers will continue to expand their use in various fields. Human tissue engineering, air and water filter manufacturing, and the textile industry are just a few sectors that can benefit from the unique properties of nanofibers. The ability for large-scale production and the simplicity of manufacturing are factors driving continuous interest and global research. With increased investment in nanotechnology, it is likely that new applications and technological improvements will emerge, solidifying nanofibers as essential components in various industries and promoting significant advancements in science and medicine.

6. Author's Contribution

- **Conceptualization** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Data curation** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Formal analysis** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Funding acquisition** – NA.
- **Investigation** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros.
- **Methodology** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Project administration** – Roberto da Silva Gusmão.
- **Resources** – NA.
- **Software** – Roberto da Silva Gusmão.
- **Supervision** – Roberto da Silva Gusmão; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Validation** – Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.

- **Visualization** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.
- **Writing** – **original draft** – Roberto da Silva Gusmão.
- **Writing – review & editing** – Roberto da Silva Gusmão; Erandi Mendes Maciel; Walquíria Cubíssimo Frattini; Eliton Souto de Medeiros; Francisco Antonio Helfenstein Fonseca; Henrique Tria Bianco.

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