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Review Article

AN OVERVIEW ON RECENT ADVANCEMENT METHODS AND CHARACTERIZATION OF NANOFIBER TECHNOLOGY

Arun Kumar Mantha, Latha Kukati*, Naseeb Basha Shaik, Arshiya Sheerin, Manasa Devasari, Shirisha Adepu

Department of pharmaceutics, G. Pulla Reddy College of Pharmacy, Osmania University, Hyderabad, India

**Corresponding author: lathakukatil@gmail.com*

ABSTRACT

This paper highlights the unique features and a brief introduction to the Nanofiber production methods, characterization and their potential applications. Nanofibers are made from various materials and have been used for a wide range of applications such as reinforcement fibers in composites, protective clothing, filtration, biomedical devices, electrical and optical applications, and nanosensors. Nanofibers with controlled diameters range from Nanometer to Micrometer which possess unique properties like a high surface area- to-volume ratio, low density and high pore volume. These properties make nanofibers more advantageous. The most widely used techniques are electro spinning and electro spunning methods. The potential uses for the different nanofiber technology was identified and many of the techniques are still in the developmental stage, but some of them are already fulfilling fledgy roles in the fields of biomedical and industry. Other issues encounters in the technology limitations, research challenges, and future trends are also discussed in the article.

Keywords: Nanofibers, Nanometer, Electro spinning, Electro spunning, Nanosensors.

1. INTRODUCTION

The nanomaterials and nanotechnology have known spectacular development devices to be fabricated at the nanoscale recently [1]. The processing of materials into the nano-sized materials based on physical and mechanical properties of polymers/polymer composite possess as compared to bulk materials [2]. Nanofibers have been used for a wide range of applications in the field of Biomedical and Industrial process. Nanofibers have attained a great attention because of their remarkable properties. Compared to standard fibrous structures nanofibers area have unit light-weight with tiny diameters, governable pore structures and high surface-to-volume quantitative relation, creating them as ideal for use [3].

Nanofibers are the fiber which ranges in diameter of 1 to 100 nanometers. Nanofibers are one-dimensional nano-materials which have a huge applications in the field of research and commercial applications owing to their unique physico-chemical properties and characteristics [4]. Nanofibers are widely used in various biomedical applications such as drug delivery, gene delivery, cell therapy, cancer therapy, tissue engineering, and regenerative medicine. In fact, the nanofibers have been proven to be much more efficient systems for cellular and molecular applications as compared to their micro- or macro-scale counterparts, owing to their functional properties such as large surface area, high aspect ratio, superior surface properties, quantum confinement effects, and fast-absorbing ability of biomolecules, which provides abundant binding sites to cell receptors and thus allowing a strong cell-matrix interaction to take place while engineering cells, tissues, and organs. By the close matching with extracellular matrix (ECM) fibers, can also used as a biomimemtic scaffolds because of their high surface area to volume ratio the drug loading is in higher rates of protein adsorption as compared to the macro-surfaces. Polymers/polymer composite Nanofibers are defined as Nanofibers composed of two or more poly-mers such as nanoparticles, polymeric inorganic salts [4].

Nanofibers are currently investigating in different techniques like self-assembly and thin films, quantum dots, Nanofibers, Nanorods, Nanotubes, Nanowires, Nanocrystals and Nanofoams. Future applications are tried to be broadened and efforts are focused on up-scaling and also improving the Nanofiber properties.

2. METHODS USED IN THE FABRICATION OF NANOFIBERS

Nanofiber composites can be prepared using different techniques such as Electrospinning, Self-assembly, Template synthesis, and Phase-separation. Among all the techniques Electrospinning is the most widely used method [5].

2.1. *Electrospinning*

It is quite simple and low cost process as compared to the other techniques and has an intermediate production rate the properties of the resultant fibers being suitable for various biomedical applications. Besides the conventional electrospinning technique, several variations of this method are developed. They include multi needle, needleless, and co-electrospinning or co-axial electrospinning. Mostly multi needle and needleless techniques are used in the enhancement of the productivity. The co-axial electrospinning is developed to synthesize core-shell and multi-layer composite nanofibrous structures with additional functionalities and improved quality [6]. Electrospinning is a process for submicron scale polymer-based filament production (usually called nanofibers) by means of an electrostatic field. Due to these forces, liquid flowing out of a capillary nozzle elongates and forms a fine jet gets atomized into fine droplets. The droplets produced in the method are electrically charged particles. A basic electrospinning setup consists of three elements: 1) A capillary jet source 2) A high voltage electrical generator 3) A metal collector

Electrospinning is usually conducted at room temperature with atmosphere condition. There are basically two electrospinning set-ups; vertical and horizontal. In electrospinning method (fig. 1) a high voltage is applied to a liquid polymer, leading to the ejection of a continuous jet flow of the polymer solution from the spinneret towards the collector then surface tension of the polymer droplet is affected by the applied electric field [7]. The droplet gets elongated in a cone known as "Taylor cone" and extruded to fiber jet. When the solvent expels out, it will travel through the atmosphere and gets evaporated followed by deposition on the metal collector in the form of fine threads as non-woven web.

Based on the polymer preparation process, the electrospinning method can be classified into two groups *i.e.* 1) Solution electrospinning and 2) Melt electro-spinning Solution electrospinning is restricted principally by its low productivity, further solvent extraction method, and demand of noxious solvent. In the melt electrospinning the polymer melt is higher in the viscosity hence electrical discharge issues of high voltage may become a problem [8].

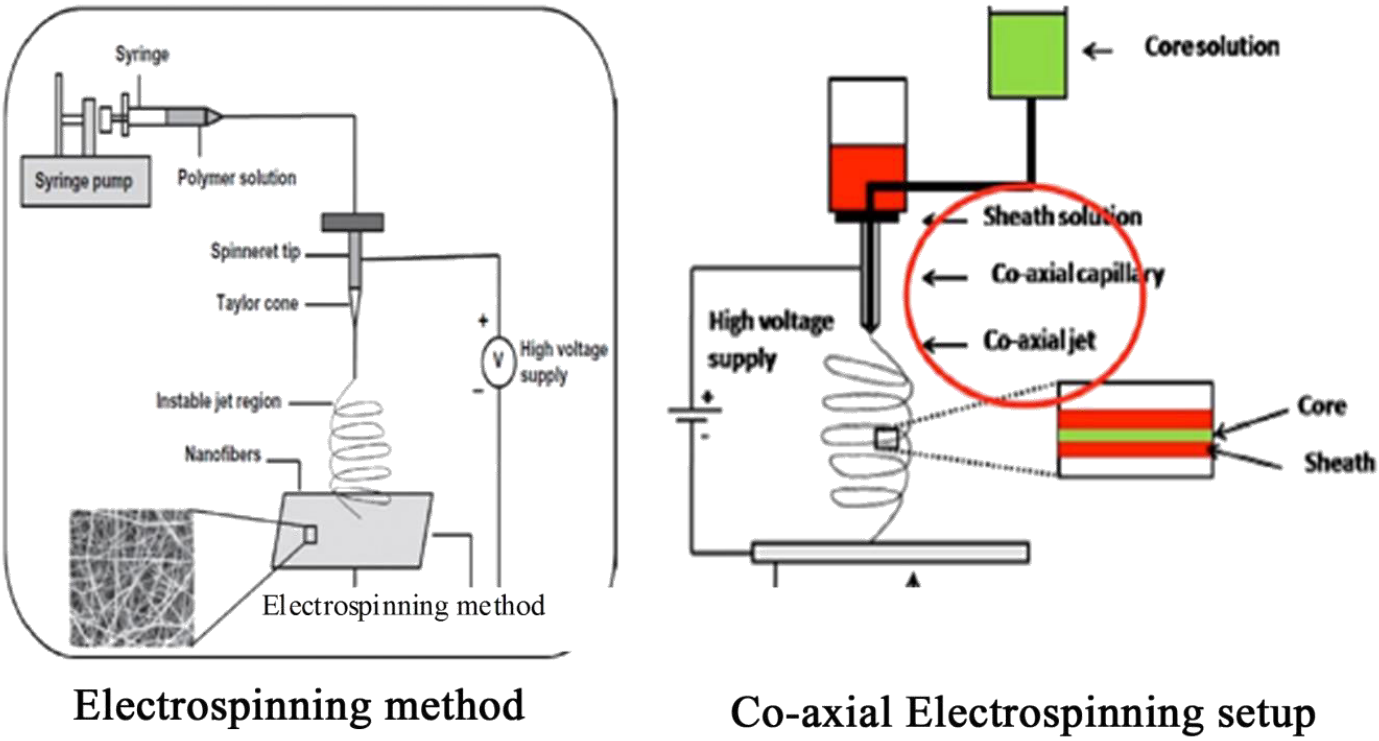

Fig. 1: Electrospinning method and Co-axial Electrospinning setup

2.1.1. Drug incorporation techniques via electro-spinning

Drug and therapeutic agents are incorporated into electrospun nanofibers through various techniques like blend electrospinning, chemical immobilization, co-axial electrospinning, physical adsorption and emulsion electrospinning.

2.1.2. Factors affecting electrospinning process

- Spinning solution concentration and viscosity.
- Applied voltage.
- Spinning solution temperature.
- Surface tension.
- Electrical conductivity.
- Molecular weight of polymer.
- Spinning distance between the spinneret and metal collector.
- Spinning angle.
- Orifice diameter.
- Solvent boiling point.
- Humidity of electrospinning chamber
- Dielectric constant.
- Feeding rate of polymeric solution.

2.2. Freeze-Drying

Freeze drying can produce fibers structures with controllable size directly from the usage of polymers by without usage of other structure directing materials as compared to other techniques [4]. In addition, other high temperature pretreatments as required for other techniques, are not required in the freeze drying technique. The principle involved in the freeze drying is sublimation of solvent directly in to the atmosphere which produces fibers. Therefore, it's drawn increasing attention within the fabrication of nanofibers.

2.3. Phase separation

Phase separation methodology has accustomed produce porous chemical compound fibers and scaffolds by causing the separating of a compound resolution into a polymer-poor part and a polymer-rich part. Recently, this method has been used to produce polymeric nanofibrous constructs from aliphatic polyesters. In this method Higher gelling temperatures leads to formation of microfiber formation, but with lower gelling temperatures the diameter was reduced to nanofiber dimensions [5]. The disadvantage of this method is defining of the gelling temperature was difficult. As similarly the fiber diameter is not influenced by polymer concentration. Increasing the polymer concentration has been found to increase in the tensile modulus and tensile strength of the constructs, without affecting fiber diameter. However, this process can perform with limited number of polymers and would be difficult to scale-up to a commercial setting.

2.4. Template synthesis method

The template synthesis method is used for the synthesis of new nanofiber structures, which can make conductive polymers, metals, carbon and other nonmaterials of tubular structure or fibrous structure. Usually in this technique metals and metal oxide template fibrous nanomaterials are produced by relied on chemical reactions such as electrochemical deposition, electro-chemical polymerization, chemical polymerization and chemical vapor deposition etc., [5]. Nanomaterials produced in this process are unevenly distributed, higher porosity and the pore size is non-uniform in nature. Although the template synthesis method is simple, it can only synthesize nanoscale short fibers or brush-like fibers with one end connected to the membranes, and cannot obtain a continuous nanofibrous filament.

2.5. Self-assembly

It is a bottom-up approach to fabricate nanofiber of weak non-covalent interactions to build nanofibers from small molecules, proteins, peptides, and nucleic acids. Several approaches have been demonstrated [8], but all rely on intermolecular forces to assemble small units into fibers with diameters of approximately 10 nm, arranged into networks with a very high water content (> 99.5%).On Further, this technique can be used to assemble the nanofibers *in-vivo* to create an injectable scaffold for tissue repair [5]. Nanofibers fabricated by this method are of the smallest scale (5-8 nm), the fabrication process is a challenging technique, limited to a few polymers, and can only create short fibers with lengths of one to several mm.

2.6. Centrifugal spinning or Force spinning

It is a recently developed nanofiber forming method and it draws extensive interest mainly due to its high production rate, which is 500 times faster than traditional electrospinning. Rather than electrostatic force, centrifugal spinning develops centrifugal force to realize the high-rate production of nanofibers.

Centrifugal spinning (fig. 2) is accustomed fabricate nanofibers by exploitation compound solutionsor com-

pound melts, whilenot the nonconductor constant restrictions and also the involvement of high voltage field of force [9]. Electrospinning is definitely the preferred method for nanofibers fabrication; nevertheless it faces some drawbacks for instance high electric field necessities, solutions with superior dielectric properties, low production rate, high production cost and plenty of different safety related to topics, electrospinning could not be suitable for mass production of certain materials.

3. CHARACTERIZATION OF NANOFIBERS

Different methods are used to characterize the nanofibers and nanofiber composites after the fabrication and drug loading [10]. Mainly two types of characterizations are done for Nanofibers they are physical characterization and mechanical characterization are described in table 1 and table 2 respectively.

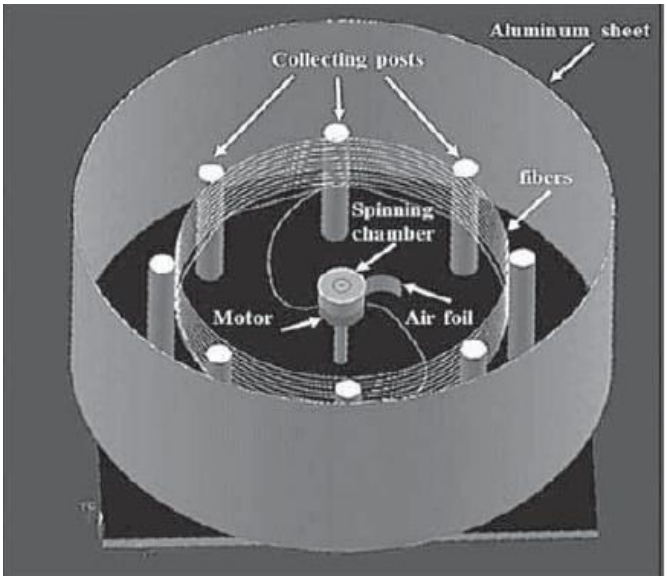

Fig. 2: Schematic representation of Centrifugal spinning

Table 1: Physical characterization of Nanofibers

Characterization techniques	Properties analyzed
Scanning electron microscopy	Fiber diameter, orientation, structure, and morphology
Transmission electron microscopy	Internal structure (core-shell structure, for example)
Atomic force microscopy	Surface roughness
Fourier Transform Infrared spectroscopy (FTIR)	Chemical functional groups
Thermogravimetric analyzer and Differential scanning calorimetry	Thermal behavior
X-ray diffractometer	Crystallographic structure and phase analysis
Mercury porosimetry	Porosity and pore size distribution
Rheometer	Rheological properties, such as viscoelasticity
Universal testing machine and nano-indentation	Mechanical properties

Table 2: Mechanical characterization of Nanofibers

Test methods	Instruments and techniques
Tensile test	(a) Atomic force microscope cantilevers (b) Commercial nano tensile tester (c) Custom made in situ TEM tester (d) AFM-based nanoindentation system
Bend test	(a) Three-point bend test using AFM (b) Lateral displacement of free-end of fiber using AFM tip (c) Buckling of fiber using AFM
Nano-indentation	(a) Elastic–plastic indention using AFM-based nanoindentation system (b) Elastic–plastic indention using AFM (c) Elastic indention using AFM
Others	(a) Electrically induced deflections in TEM (b) Resonating wire bridged across prongs of microfabricated tuning fork (c) Resonant contact AFM

4. MERITS AND DEMERITS OF NANOFIBERS METHODS

Merits and demerits of nanofibers methods were described in table 3.

4.1. Naturalpolymers accustomed acquire nanofibers with medical applications

Collagen fibers, Fibrinogen, Cellulose derivatives, chitosan, hyaluronic acid [1].

Table 3: Merits and demerits of nanofibers methods

Process	Can the process be scaled up	Control on fiber dimensions	Advantages	Disadvantages
Electrospinning	yes	yes	Cost effective. Long, continuous nanofibers can be produced	Jet instability
Template synthesis	No	yes	Fibers of different diameters can be easily achieved using different templates	-
Phase separation	No	No	Minimum equipment requirement. Process can directly fabricate a nanofiber matrix. Batch-to-batch consistency is achieved. Mechanical properties of the matrix can be tailored by adjusting polymer concentration.	Limited to specific polymers
Self-assembly	No	No	Good for obtaining smaller nanofibers	Complex process

4.2. Synthetic polymers to obtain nanofibers with medical applications

Polydioxanone, poly anhydrides, polyorthoesters, poly-trimethylene carbonate, poly ethylene acetate, poly lactide-co-glycolide, poly-L-lactide-co-ε-caprolactose, polyglycolic acid.

4.3. Biomedical applications of nanofiber composites

Nanofiber composites have been widely used in various biomedical applications, which include the key applications of drug delivery, tissue engineering, stem cell therapy, cancer therapy, and wound healing [11].

4.3.1. Drug delivery

The main goal of developing drug delivery systems is to efficiently deliver the drug molecules, within the recommended therapeutic level, to the target cell, tissue, or organ for a defined period of time [13]. Remarkable properties such as high loading capacity, high encapsulation efficiency, target-specific, prolonged delivery of drugs, and ease of operation.

4.3.2. Tissue engineering

Tissue engineering, in particular scaffold-based tissue engineering, involves the culturing of isolated cells from the patient or donor into a scaffolding system that could support the growth and function of the isolated cells into a specific tissue which could be grafted back to the defective site of the patient where tissue regeneration is required.

Bone tissue engineering, cartilage tissue engineering, tendon and ligament tissue engineering, neural tissue engineering, cardiovascular tissue engineering.

4.3.3. Stem cell therapy

Stem cells are considered an integral part of regenerative medicine. The fate and functions of stem cells, which are responsible for tissue organization, can be regulated by providing an appropriate culture system that mimics the native cellular microenvironment [12]. The nanofibers can be designed to mimic the structural and chemical compositional aspects of native ECM, and have been shown to influence the fate and functions of stem cells.

4.3.4. Cancer therapy

Cancer is one of the deadliest diseases, which has shown continuously increased incidence and mortality rates worldwide. Although cancers are now being diagnosed and treated at an early stage with the help of surgery, chemotherapy, and radiation therapy, the prevention or complete eradication of cancer cells without damaging the rest of the body remains a challenging task. Due to technological advances, nanofiber composites are emerging as an alternative strategy for cancer prevention and treatment. The nanofiber composite mediated drug delivery technology significantly improves the targeting ability of drugs, the prolonged exposure of the drug to the cancerous cells, and it also improves solubility of water-insoluble drugs

4.3.5. Wound healing

Wound healing could be a complicated and dynamic method by that skin or alternative body tissue repairs itself when injury. However, the prevalence of chronic wounds necessitates the event of recent wound healing product that aids within the quicker healing of wounds and therefore the correct functioning of human organ systems [13]. Among the various choices, the electrospun nanofiber composites have shown more choice of promise for formulating wound healing products.

4.3.6. Immobilization of enzymes

Enzymes are usually immobilized on inert nonsoluble material for improving the durability and maintaining the properties of the enzymes such as bioprocessing and controlling reaction for longer duration [13, 14]. Various methods have been implemented for the preparation of an enzyme carrier, such as gel matrices, porous particles, and porous membranes [14]. Among these, the unique properties of electrospun nanofibers can efficiently relieve the hurdles that usually hinder the catalyzing ability of an enzyme immobilized on a carrier material [15].

5. APPLICATIONS IN OTHER FIELDS USING NANOFIBERS

Applications of nanofibers in other fields were described in Fig. 4.

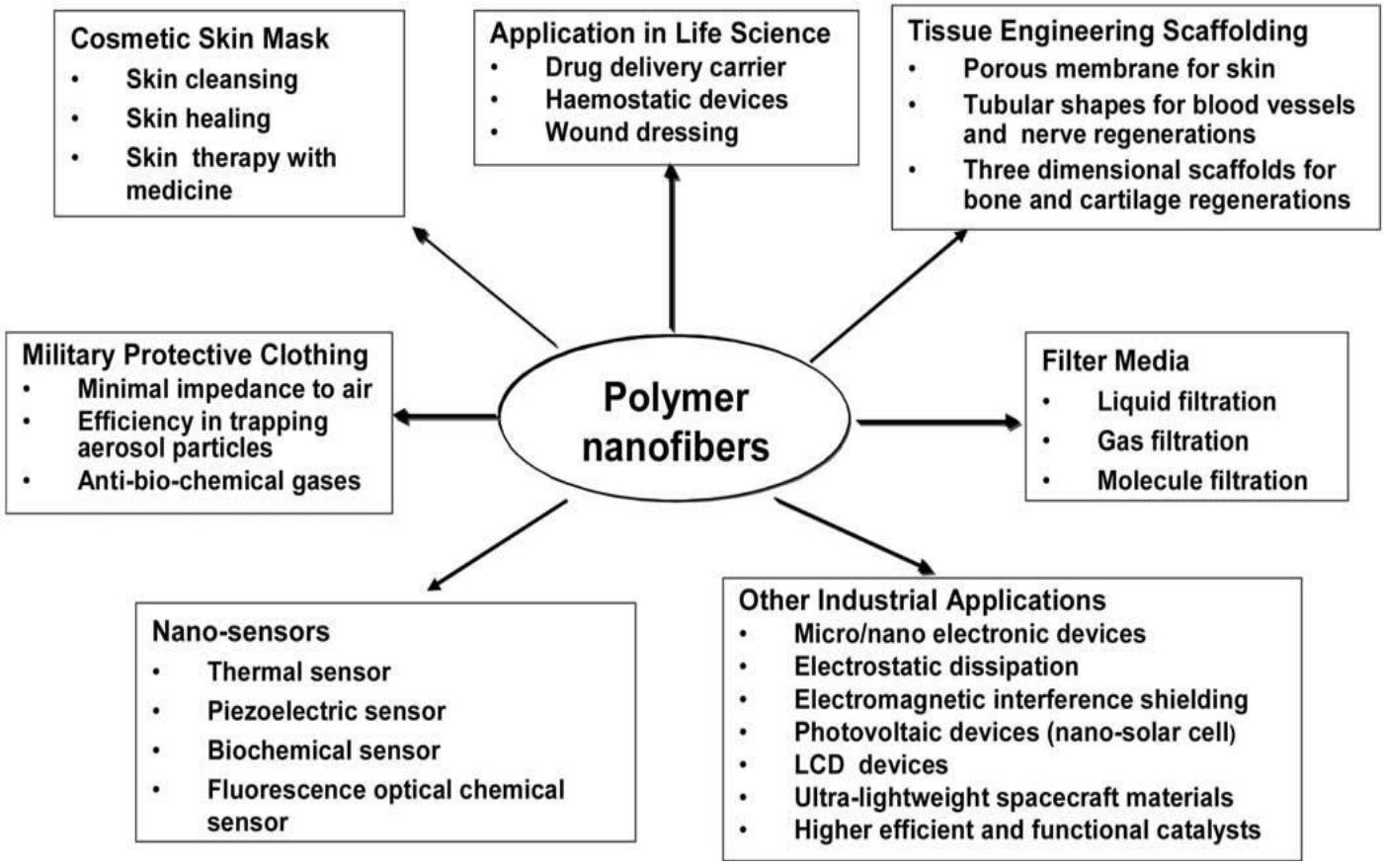

Fig. 4: Applications of Nanofibers

6. SUMMARY AND OUTLOOK

In this review paper, definition, production techniques, and properties of nanofibers were illustrated in details. Nanofibers could be fabricated using different methods for instance bicomponent extrusion, self assembly, template synthesis, phase separation, melt blowing, drawing, electrospinning and centrifugal spinning. Electrospinning technique could be a versatile, efficient, and low cost method for fabrication of Nanofibers of a rich variety of materials. The critical parameter of electrospinning were concentration and viscosity of spinning solution, applied voltage, surface tension, electrical conductivity, molecular weight of the polymer, spinning distance and angle, orifice diameter,

feeding rate and relative humidity. These parameters were found to have a huge significant influence on nanofiber properties and morphology. In the last decade the amount of researches regarding this methodology and its applications has augmented and this demonstrates the importance of electrospinning. To introduce the desired functionalities and com-plexities into nanofibers as well as to enhance their physical properties for more intricate and specific applications, selection of suitable materials coupled with novel approaches in manipulating nanofiber structures, including smaller fiber dimension, inter fiber adhesion, and fiber surface functionalization, are necessary.

Conflict of interest

The authors declare no conflict of interest.

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