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# Nanofibers In Pharmaceuticals - A Review

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## ABSTRACT

Unique properties of Nanofibers have attracted for the designing of controlled drug delivery systems due to high surface area to volume ratio, porosity so only we can applied in advance application such as Biodegradable and controlled drug delivery systems. The benefits of the fibrous carriers are site specific delivery of drugs to the body. Nanofibers are an exciting new class of material produced using an innovative manufacturing process technology. These fibers are produced from a variety of polymers in geometrical shapes ranging from Nonwoven web, yarn, and bulk structures. The Synthetic polymer Nanofibers are made from Nylon, Acrylic, Polycarbonate, Polysulfones, and Fluro polymers among other polymers. The biological polymer nanofibers are made from materials such as Polycaprolactum, Chitosan, Polylactic acid, and Copolymer of Polylactic/glycolic acid among other biopolymers. At present, there are three techniques available for the synthesis of Nanofibers: Electro spinning, self-assembly, and phase separation, out of these Electro spinning is the most widely used technique. Mostly , the bioactive molecules like anti-cancer drugs, enzymes. Cytokines, and polysaccharides can be entrapped within the interior or physically immobilized on the surfaces of nanofiber for controlled drug delivery. The advanced approach for creating Nanofibers made of proteins developed, greatly improve drug delivery methods for the treatment of cancers, heart, and Alzheimer's diseases, as well as aid in the regeneration of human tissue, bone and cartilage. This review paper reports on fabrication of nanofibers and its characteristics and high tech application in drug delivery, tissue engineering and filter medium.

**Keywords:** Electro spinning, controlled drug delivery, Fabrication, characterization, applications.

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## INTRODUCTION

Nanofibers are defined as fibers with diameters less than 50-500 nanometers. National Science Foundation (NSF) defines nanofibers as having at least one dimension of 100 nanometer (nm) or less. Recently nanofibers are used in the healthcare systems, as a tool for drug delivery system in various diseases. The use of nanofibers proves the importance and convenience of them as drug carriers. There smaller size plays an important role in delivering the drug to the appropriate site in the body[1]. Delivery of drugs or pharmaceutical agents to patients in a most physiologically acceptable manner has always been an important concern. The objective of drug delivery systems is to deliver a defined amount of drug efficiently, precisely and for a defined period of time. The new technologies and materials will have a profound impact on drug delivery. Either biodegradable or non-degradable materials can be used to control whether drug release occurs via diffusion alone or diffusion and scaffold degradation. Additionally, due to the flexibility in material selection a number of drugs can be delivered including: antibiotics, anticancer drugs, proteins, and DNA. Using the various electro spinning techniques a number of different drug loading methods can also be utilized: coatings, embedded drug, and encapsulated drug (coaxial and emulsion electrospinning). These techniques can be used to give finer control over drug release kinetics[2] .Some properties of nanofibers which are useful for drug delivery are as follows

### Properties of Nanofibers

Nanofibers exhibit special properties mainly due to extremely high surface to weight ratio compared to conventional nonwovens.

Low density, large surface area to mass, high pore volume, and tight pore size make the nanofiber nonwoven appropriate for a wide range of filtration applications [67].

Figure: 1 shows how much smaller Nanofibers are compared to a human hair, which is 50-150 μm and Figure: 2 shows the size of a pollen particle compared to Nanofibers. The elastic modulus of polymeric Nanofibers of less than 350 nm is found to be 1.0 ± 0.2 Gpa.

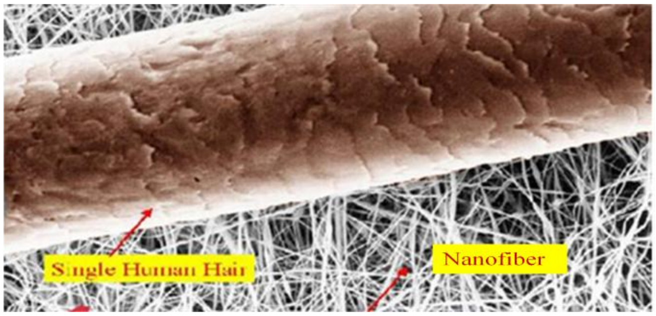


**Figure:1 Comparison between human hair and nanofiber web[3].**

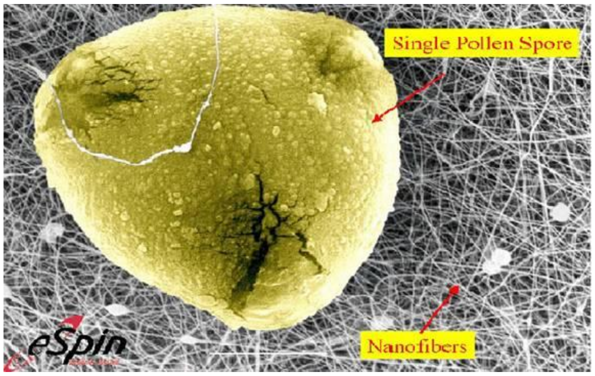


**Figure 2. Entrapped pollen spore on nanofiber web [3].**

A major upsurge in research on nanofibers has taken place most recently due to its high surface area and nanostructure surface morphologies that enable a myriad of advanced applications. Nanofibers have been reported to have marked differences in their thermal and mechanical properties compared to regular fibers and bulk polymers.

## Thermal properties

There are a few published reports on the thermal properties of nanostructured materials. Thermal analysis has been carried out on a number of electrospun polymeric materials to understand the relationship between nanostructure and thermal properties. DSC studies have indicated that electrospun PLLA fibers have lower crystallinity, glass transition temperature ($Tg$), and melting temperature ($Tm$) than semicrystalline PLLA resins. Zong et al. attributed the decrease in the $Tg$ to the large surface to volume ratio of nanofibers with air as the plasticizer. The high evaporation rate followed by rapid solidification at the final stages of electrospinning is expected to be the reason for the low crystallinity. The $Tg$ and the peak crystallization temperature ($Tc$) of the electrospun polyethylene terephthalate (PET) and poly- ethylene naphthalate (PEN) decreased significantly, while the heat of crystalline melting increased. The decrease in $Tg$ and Tm, and the increase in the heat of melting were attributed to the increase in the segmental mobility. The melting temperature of the PET and PEN electrospun fibers remained almost constant, without any significant variations compared to that of regular fiber forms. PEO Nanofibers have shown a lower melting temperature and heat of fusion than the PEO powder, which is attributed to the poor crystallinity of the electrospun fibers[7].

## Mechanical properties

Electrospun fibers have nano structured surface morphologies with tiny pores that influence mechanical properties like tensile strength, Young's modulus, etc. Gibson et al. have found that there is no significant change in the Young's modulus of electrospun Pellethane thermoplastic elastomers. When compared with cast films, electrospun elastomers have shown a 40% reduction in the peak tensile strength and 60% reduction in elongation at maximum applied stress. The decrease in the tensile strength has also been reported by Buchko et al. with SLPF fibers. Nanofiber reinforced polymer composites have shown more highly enhanced mechanical properties than the unfilled or carbon/glass fiber filled composites. Young's modulus of a nanofiber composite has been found to be 10-fold greater than the pure Styrene-Butadiene rubber. As is evident, there is less information available on the mechanical properties of nanofibers and nanofiber composites. Research on the mechanical properties of nanofibers and their composites from a variety of polymers is essential for a greater understanding on the contributions of nanofibers to the mechanical and performance related characteristics of nanofiber composites[7].

## Physical properties

The simplest comparison between eletrospun Nanofibers , meltblown fibers and spunbonded fibers size. The differences in basic web properties such as fiber area ,basis weights, thicknesses, permeability, and strength. Electrospun Nanofibers have diameters that are 1to 2 orders of magnitude corresponding increase in fiber surface area and decrease in basis weight.

## Filtration properties

As the fibers themselves have a small diameter, the thickness of the nanofiber web can likewise be quite small , with a thickness of four nanofiber diameters approaching only one micron. The thin web has limited mechanical properties that preclude the use of conventional web handling. As a result nanofiber web have been applied on to various substrates. Substrates are selected to provide complementary functionally to the nanofiber web. In the case of nanofiber filter media, substrates have been selected for pleating , filter fabrication,durability in use , and filter cleaning. Figure: 3 is a photomicrograph showing a cross-section of Nanofibers electronspun onto a polyester spun bond substrate. The substrate is chosen to provide mechanical properties , while the nanofiber web Domionates filtration performance.

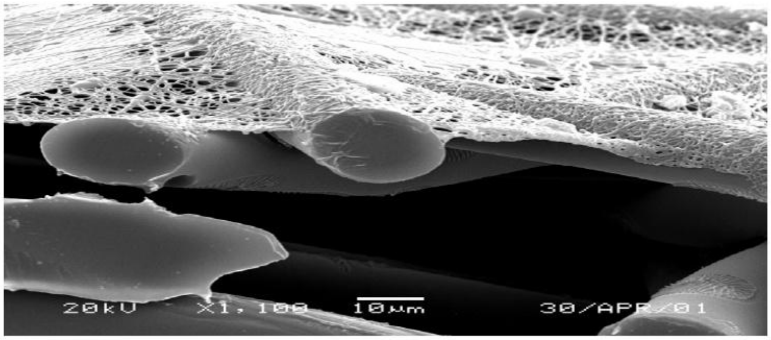


**Figure 3: Cross section view of nanofibre web on spunband substrate**

Controlling parameters of electrospinning allows the generation of Nanofibers webs with different filtration characteristics. Different fiber sizes can be made, some as small as 40 nm. Fibers can be put on one side or on both sides of a substrate. Additionally figure shows a comparison between a light layer of Nanofibers and a heavier layer of Nanofibers . Nanofibers have been electrospun on to a variety of substrates, including glass polyester , nylon, and cellulose filter media substrates.

## FABRICATION OF NANOFIBRES

### Principle

Drug delivery with polymer nanofibers is based on the principle that dissolution rate of a drug particulate increases with increased surface area of both the drug and the corresponding carrier if necessary. For controlled drug delivery, in addition to their large surface area to volume ratio, polymer nanofibers also have other additional advantages. For example, unlike common encapsulation involving, Controlled delivery systems are used to improve the therapeutic efficacy and safety of drugs by delivering them to the site of action at a rate dictated by the need of the physiological environment. A wide variety of polymeric materials have been used as delivery matrices, and the choice of the delivery vehicle polymer is determined by the requirements of the specific application[61]. Polymeric nanofibers have recently been explored for their ability to encapsulate and deliver bioactive molecules for therapeutic applications.

Three distinct techniques have proven successful in routinely creating nanofibrous tissue structures: self assembly, phase separation, and electrospinning[50-52]. The electrospinning method is the most simple and efficient. Electro spinning as a polymer-processing technology has been known for more than 70 years[53].

### Self-assembly

Self-assembly involves the spontaneous organization of individual components into an ordered and stable structure with preprogrammed non-covalent bonds[54,55]. Self-assembly, that is, the autonomous organization of molecules into patterns or structures without human intervention, are common throughout nature and technology[56]. Self-assembly of natural or synthetic macromolecules produces nano scaled supramolecular structures, sometimes nanofibers[57]. Compared with electrospinning, self-assembly can produce much thinner nanofibers only several nanometers in diameter, but requires much more complicated procedures and extremely elaborate techniques. The low productivity of the self-assembly method is another limitation.

### Phase separation

Phase separation is a method frequently used to prepare 3-D tissue-engineering scaffolds. Phase separation of a polymer solution can produce a polymer-rich domain and a solvent-rich domain, of which the morphology can be fixed by quenching under low temperature. Removal of the solvent through freeze-drying or extraction can produce porous polymer scaffolds. Phase separation can be induced by changing the temperature or by adding non solvent to the polymer solution, thus called thermal induced or non-solvent-induced phase separation, respectively. Polymer scaffolds obtained by the phase separation method usually have a sponge like porous morphology with microscale spherical pores[58,59].

Unlike self-assembly, phase separation is a simple technique that does not require much specialized equipment. It is also easy to achieve batch-to-batch consistency and tailoring of scaffold mechanical properties and architecture is easily achieved by varying polymer/porogen concentrations. However, this method is limited to being effective with only a select number of polymers and is strictly a laboratory scale technique[60].

### Electrospinning process:

The nanofibers can be manufactured by Electro spinning process. Electro spinning is a process that was originally developed in the early 1930s, but did not receive much attention until recent decades. Most likely the increased interest is due to the refocusing of more research groups on nanotechnology. Although electro spinning has existed for a significant period of time and is relatively easy to execute, the physics of electro spinning nanofibers is only understood to a limited extent.

A typical electro spinning process involves dissolving the drug of interest and a polymer in an appropriate solvent. The solution is then placed in a syringe, and a high voltage is applied. A small amount of the polymer solution is drawn out of the syringe, forming a Taylor cone. Increasing the applied voltage further results in the initiation of a charged fluid jet, which follows a chaotic trajectory of stretching and bending until it reaches the grounded target. A stable jet is formed when the charge is increased above a critical voltage, and there is a balance between the surface tension of the fluid and the repulsive nature of the charge distribution on the surface of the fluid. The presence of molecular entanglements in the polymer solution prevents the jet from breaking into droplets (electro spraying), and when combined with the electrical forces results in a whip-like motion of the jet, known as bending instability. This process typically results in the drawing of a virtually endless fiber with a nanometer-sized to micrometer sized diameter. The final product is a three-dimensional nonwoven mat of entangled Nanofibers with a high surface-area-to-volume ratio.

A schematic diagram of electro spinning is as shown in Figure 4. The process makes use of electrostatic and mechanical force to spin fibers from the tip of a fine orifice or spinneret. The spinneret is maintained at positive or negative charge by a DC power supply. When the electrostatic repelling force overcomes the surface tension force of the polymer solution, the liquid spills out of the spinneret and forms an extremely fine continuous filament. It has the misleading appearance of forming multiple filaments from one spinneret nozzle, but current theory is that the filaments do not split.

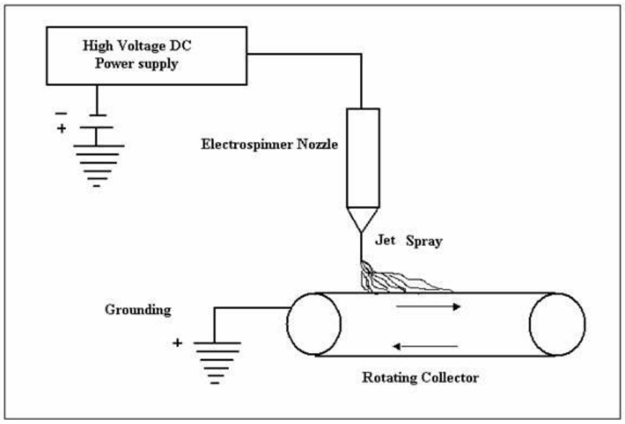


**Figure 4. Schematic representation of electrospinning process[3].**

These filaments are collected onto a rotating or stationary collector with an electrode beneath of the opposite charge to that of the spinneret where they accumulate and bond together to form nanofiber fabric.

The distance between the spinneret nozzle and the collector generally varies from 15 –30 cm. The process can be carried out at room temperature unless heat is required to keep the polymer in liquid state. The final fiber properties depend on polymer type and operating conditions. Fiber fineness can be generally regulated from ten to a thousand nanometers in diameter [3].

Electrospun nanofibers with a high surface area to volume ratio have received much attention because of their potential applications for biomedical devices, tissue engineering scaffolds, and drug delivery carriers. In order to develop electrospun nanofibers as useful nanobiomaterials, surfaces of electrospun nanofibers have been chemically functionalized for achieving sustained delivery through physical adsorption of diverse bioactive molecules. Surface modification of nanofibers includes plasma treatment, wet chemical method, surface graft polymerization, and co-electrospinning of surface active agents and polymers. A variety of bioactive molecules including anti-cancer drugs, enzymes, cytokines, and polysaccharides were entrapped within the interior or physically immobilized on the surface for controlled drug delivery. Surfaces of electrospun nanofibers were also chemically modified with immobilizing cell specific bioactive ligands to enhance cell adhesion, proliferation, and differentiation by mimicking morphology and biological functions of extracellular matrix. This review summarizes surface modification strategies of electrospun polymeric nanofibers for controlled drug delivery and tissue engineering.

**Polymer-solvents used in electrospinning.**

The polymer is usually dissolved in suitable solvent and spun from solution. Nanofibers in the range of 10-to 2000 nm diameter can be achieved by choosing the appropriate polymer solvent system[4]. Table 1 gives list of some of polymer solvent systems used in electrospinning.

**Table 1. Polymer solvent systems for electrospinning**

| Polymer | Solvents |
|---|---|
| Nylon 6 and nylon 66 | Formic Acid |
| Polyacrylonitrile | Dimethyl formaldehyde |
| PET | Trifluoroacetic acid/Dimethyl chloride |
| PVA | Water |
| Polystyrene | DMF/Toluene |
| Nylon-6-co-polyamide | Formic acid |
| Polybenzimidazole | Dimethyl acetamide |
| Polyramide | Sulfuric acid |
| Polyimides | Phenol |

**Drug Loading**

One method to incorporate therapeutic drugs into nanofibers involves solubilizing the drug into the polymer solution to be spun[62]. Using this method, a loading efficiency of 90% into PDLA nanofibers was reported for the antibiotic drug Mefoxin. Covalent conjugation to polymers represents another method to modulate drug release[63]. It has also been suggested that the high porosity of nanofibers allows for rapid diffusion of degradation by products[64]. However, the burst release may also be indicative of the drug being attached only on the surface. As the drug and carrier materials can be mixed together for electrospinning of nanofibers, the likely modes of the drug in the resulting nanostructed products are[65]:

1. Drug as particles attached to the surface of the carrier which is in the form of nanofibers,
2. Both drug and carrier are nanofiber-form, hence the end product will be the two kinds of nanofibers interlaced together,
3. The blend of drug and carrier materials integrated into one kind of fibers containing both components, and
4. The carrier material is electrospun into a tubular form in which the drug particles are encapsulated.

## MECHANISM OF DRUG DELIVERY

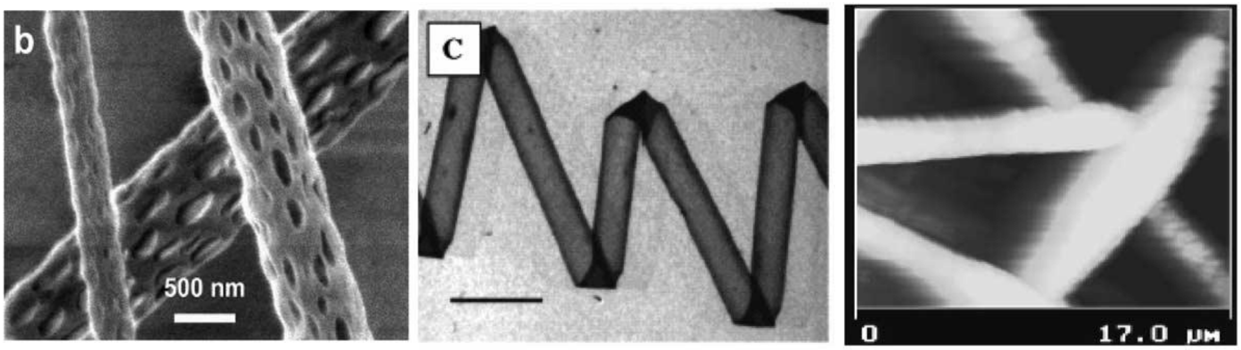
Nanofiber drug delivery systems may provide insight into the direct incorporation of bioactive growth factors into scaffolds. Additionally, drug delivery systems can be combined with implantable tissue engineering scaffolds to prevent infection while repair and regeneration occur. Biodegradable polymers release drug in one of two ways[66]: erosion and diffusion. Release from biodegradable polymers in vivo is governed by a combination of both mechanisms, which depends on the relative rates of erosion and diffusion.

Most biodegradable polymers used for drug delivery are degraded by hydrolysis. Hydrolysis is a reaction between water molecules and bonds in the polymer backbone, typically ester bonds, which repeatedly cuts the polymer chain until it is returned to monomers. Other biodegradable polymers are enzymatically degradable, which is also a type of chain scission. As water molecules break chemical bonds along the polymer chain, the physical integrity of the polymer degrades and allows drug to be released. The different mechanisms were given below[66].

## CHARACTERIZATION

### Geometrical characterization

Geometric properties of nanofibers such as fiber diameter, diameter distribution, fiber orientation and fiber morphology (e.g. cross-section shape and surface roughness) can be characterized using scanning electron microscopy (SEM), field emission scanning electron microscopy (FESEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM) [20,21,22,23]. The use of TEM does not require the sample in a dry state as that of SEM. Hence, nanofibers electrospun from a polymer solution can be directly observed under TEM. An accurate measurement of the nanofiber diameter with AFM requires a rather precise procedure. The fibers appear larger than their actual diameters because of the AFM tip geometry [24]. For a precise measurement, two fibers crossing to each other on the surface are generally chosen. The upper horizontal tangent of the lower fiber is taken as a reference, and the vertical distance above this reference is considered to be the exact diameter of the upper nanofiber [25]. **Figure 5:** shows the nanofiber structures observed through SEM, TEM and AFM. AFM can also be used to characterize the roughness of fibers. The roughness value is the arithmetic average of the deviations of height from the central horizontal plane given in terms of millivolts of measured current [20].



(a) (b) (c)

**Figure 5: (a) SEM of PLLA nanofibers [10], (b) TEM of elastin-mimetic peptide fibers (bar represents 3.3 mm) [71], and (c) AFM of polyurethane nanofibers [20].**

Another geometric parameter is porosity. The porosity and pore size of nanofiber membranes are important for applications of filtration, tissue template, protective clothing, etc.[21,25,33]. The pore size measurement can be conducted by, for example, a capillary flow porometer [21,25,26]. Schreuder-Gibson et al. compared the pore sizes of membranes electrospun from Nylon 6,6, FBI (polybenzimidazole), and two polyurethanes, Estane1 and Pellethane1. They found thatNylon 6,6 could be electrospun into a very fine membrane with extremely small pore throat sizes (with a mean flow pore diameter of 0.12 mm) which were much smaller than the average fiber diameters. FBI also exhibited pore sizes (0.20 mm) smaller than the electrospun fiber sizes. However, the Estane1 and Pellethane1 exhibited mean pore sizes which were significantly higher, with average flow pore diameters of 0.76 and 2.6mm, respectively[25].

## Chemical Characterization

Molecular structure of a nanofiber can be characterized by Fourier transform infra red (FTIR) and nuclear magnetic resonance (NMR) techniques [27,25]. If two polymers were blended together for the fabrication of nanofibers, not only the structure of the two materials can be detected but also the inter-molecular interaction can be determined. In the case of a collagen and PEO blend used for electrospinning of nanofibers, the NMR spectrum showed a new phase structure which was caused by the hydrogen bond formation between the ether oxygen of PEO and the protons of the amino and hydroxyl groups in collagen [29]. Supermolecular structure describes the configuration of the macromolecules in a nanofiber, and can be characterized by optical birefringence [30,31,32], wide angle X-ray diffraction (WAXD), small angle X-ray scattering (SAXC) and differential scanning calorimeter (DSC) [30,33]. Fong & Reneker [34] studied the birefringence of the styrene–butadiene–styrene (SBS) triblockco polymer nanofibers with diameters around 100 nm under an optical microscope. The occurrence of birefringence reflects the molecular orientation. Zong et al. [33] noticed that the electrospun PLLA fibers quenched below 0 c resulted in amorphous fiber structure. After drying the electrospun nanofibers at room temperature, they found that melting point transitions appeared at two peaks by DSC. It was explained that during electro spinning of this polymer molecule had no time to crystallize and hence it could only have an amorphous super molecular structure. It should be noted that polymer crystallization does occur during electro spinning when the polymer is in a molten form, see a subsequent discussion. Since the supermolecular structure changed during the electro spinning the transition points of the polymers also changed. One of them was lower than the normal melting point due to defects existing in crystallization while drying.

Surface chemical properties can be determined by XPS, water contact angle measurement, and FTIR– ATR analyses.[34] measured the atomic percentage of fluorine in PMMA-TAN blend. It was shown that the atomic percentage of fluorine in the near surface region of the electrospun fibers was about double the atomic percentage in a bulk polymer. Surface chemical properties of nanofiber can also be evaluated by its hydrophilicity, which can be measured by the water contact angle analysis of the nanofiber membrane surface.

**Physical characterization**

Air and vapor transport properties of electrospun nanofibrous mats have been measured using an apparatus called dynamic moisture vapor permeation cell (DMPC) [35,60]. This device has been designed to measure both the moisture vapor transport and the air permeability (convective gas flow) of continuous films, fabrics, coated textiles and open foams and battings. Schreuder-Gibson & Gibson compared electrospun nanofibrous nonwovens of thermo plastic polyurethane with the corresponding meltblown nonwovens. Average pore size of the electrospun nonwovens was 4– 100 times smaller than that of the meltblown nonwovens, resulting in an increase in air flow resistance by as much as 156 times. However, no significant difference has been found for the ‘‘breathability’’, or moisture vapor diffusion resistances of the two nonwovens [37]. Crosslinking the fibers of the electrospun membrane significantly decreases liquid transport through the membrane. Electrical transport properties of electrospun nanofibers were investigated by [38,39]. Norris et al. measured the conductivity of the electrospun nonwoven ultra-fine fiber mat of polyaniline doped with camphorsulfonic acid blended with PEO (polyethylene oxide). As the non-woven mat was highly porous and the ‘‘fill factor’’ of the fibers was less than that of a cast film, the measured conductivity seemed to be lower than that of the bulk [30]. Wang et al. measured the conductivities of PAN (polyacrylonitrile) nanofibers before and after carbonized using a digital electrometer with two neighboring contacts of 4 mm distance. The electrospinning was conducted carefully and briefly so that there was only one continuous fiber deposited across the two neighboring contacts. The PAN fiber (before carbonized) exhibited a resistance which was beyond the upper limit of the electrometer, whereas the graphitization of the PAN nanofiber led to a sharp increase in conductivity to around 490 S/m [39].

Kim & Lee [40] characterized the thermal properties of nanofibers of pure PET [poly (ethylene terephthalate)] and PEN [poly(ethylene naphthalate)] polymers and PET/PEN blends obtained in melt form. They found that the electrospinning of polymers resulted in increase of crystallinity and decrease of Tg (glass transition temperature) and Tc (crystallization peak temperature) of PET and PEN. The crystalline melting peaktempe ratures (Tm) of PET and PEN were almost the same before and after electrsopinnning. On the other hand, not only Tg and Tc but also Tm of the electrospun PET/PEN nanofibers were lower than those of the bulk. The change in thermal properties of electrospun neat polyesters was primarily resulted from decrease of molecular weight after the electrospinning by thermal as well as mechanical degradation. However, the change in those of PET/PEN blends was attributed to exchange reactions of PET and PEN in melt blends[40].

**Mechanical characterization**

Mechanical tests of nanofibrous nonwoven membrane can be performed using conventional testing techniques [41,42,21,43,25]. When the membranes are collected on a static collector screen, no anisotropy in the in-plane tensile behavior seems to have been reported. Figure 6 shows typical stress–strain curves of a PLLA nanofibrous mat obtained by [21] for tissue engineering applications. It has been found the tensile strength of nanofibrous mat was similar to that of a natural skin. However, when the membranes were obtained from a rotating drum, Lee et al. found that the electrospun nonwoven mats had different properties in different directions [42,44]. The fiber orientation depended on the linear velocity of the drum surface and other electrospinning parameters.

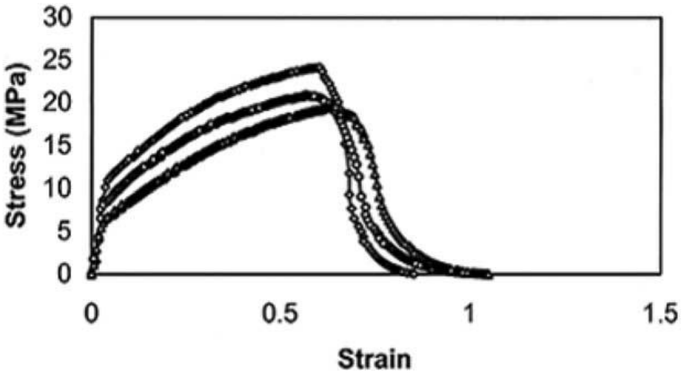


**Figure 6: Tensile stress–strain curves of nanofibrous membranes electrospun from PLGA**

Due to very small dimension, the mechanical characterization of an individual nanofiber is a challenge for the existing test techniques. The established methods and standards for determining the mechanical behavior of conventional fibers are inadequate in the case of manipulation or testing of nanofibers. This is probably one of the main reasons why articles addressing the mechanical tests of single nanofibers are rare in the literature. [45] described a cantilever technique to measure the tenacity of a single electrospun PAN (polyacrylonitrile) ultrafine fiber. A cantilever consisting of a 30 mm glass fiber was glued at one end onto a microscope slide and a 15 mm nylon fiber was attached at the free end of the glass fiber. The electrospun test fiber was glued with epoxy resin to the free end of the nylon fiber. A part of the same fiber was cut and deposited on a SEM specimen holder for diameter measurement using SEM. As the sample fiber was stretched with a computer controlled Instron model 5569, the deflection of the cantilever was measured under light microscopy using a calibrated eyepiece. A chart was used to convert the deflections into actual values of fiber tenacity. The elongation-to-breakof electrospun PAN fibers was estimated using a caliper. It was reported that the electrospun PAN fibers with a diameter of 1.25 mm and length of 10 mm exhibited failure at 0.4 mm deflection at 41 mg of force and the resulting tenacity was 2.9 g/day. The mean elongation at breakof the same fiber was 190% with a standard deviation of 16%.

No report in the open literature has been found on the tensile test of a single polymer nanofiber yet. On the other hand, significant efforts have been made to characterize the mechanical specifically tensile properties of single carbon nanotubes. The methods used wherein can also be applicable for the measurement of tensile properties of single electrospun polymer nanofibers.

Due to nanometer specimens, the mechanical measurements for carbon nanotubes reported so far were conducted in terms of AFM, SEM, or TEM. [46] obtained the bending strength and Young's modulus of a carbon nanotube by deflecting one end of the tube with an AFM tip while keeping the other end fixed. Yuet al. [47] successfully used AFM cantilever tips to measure the tensile properties of individual multi-wall carbon nanotubes via a SEM. They designed a nanomanipulator so that the carbon nanotube could be manipulated in three dimensions inside the SEM, and was attached to the tips of the AFM [48]. Very recently, Demczyket al. [49] directly measured the tensile strength and elastic modulus of multiwalled carbon nanotubes under TEM by using a tensile testing device fabricated through a microfabrication technique. It is expected that the similar techniques can be applied to understand themechanical properties of single nanofibers.

## APPLICATIONS OF NANOFIBERS

### Filtration

Nanofibers have significant applications in the area of filtration since their surface area is substantially greater and have smaller micropores than melt blown (MB) webs. High porous structure with high surface area makes them ideally suited for many filtration applications. Nanofibers are ideally suited for filtering submicron particles from air or water.

Electrospun fibers have diameters three or more times smaller than that of MB fibers. This leads to a corresponding increase in surface area and decrease in basis weight. **Table 2** shows the fiber surface area per mass of nanofiber material compared to MB and SB fibers [9].

**Table 2: Fiber surface area per mass of fiber material for different fiber size [8].**

| Fiber Type | Fiber size, in Micrometer | Fiber surface area per mass of fiber material m2/g |
|---|---|---|
| Nanofibers | 0.05 | 80 |
| Spunbond fiber | 20 | 0.2 |
| Melt blown fiber | 2.0 | 2 |

Nanofiber combined with other nonwoven products have potential uses in a wide range of filtration applications such as aerosol filters, facemasks, and protective clothing. At present, military fabrics under development designed for chemical and biological protection have been enhanced by laminating a layer of nanofiber between the body side layer and the carbon fibers [9]. E-Spin Technologies, Inc has produced a prototype of activated carbon nanofiber web. PAN-based nanofibers were electrospun. Then these webs were stabilized, carbonized, and activated. These activated PAN nanofibers gave excellent results for both aerosol and chemical filtration[11,12].

Electrospun nanofiber webs are used for very specialized filtration applications. Donaldson is making and marketing filter media that incorporate electrospun nylon fibers for gas turbines, compressor and generators [13].

### Medical Application

Nanofibers are also used in medical applications, which include, drug and gene delivery, artificial blood vessels, artificial organs, and medical facemasks. For example, carbon fiber hollow nanotubes, smaller than blood cells, have potential to carry drugs in to blood cells [14, 15]. Nanofibers and webs are capable of delivering medicines directly to internal tissues. Anti-adhesion materials made of cellulose are already available from companies such as Johnson & Johnson and Genzyme Corporation [16]. Researchers have spun a fiber from a compound naturally present in blood. This nanofiber can be used as varieties of medical applications such as bandages or sutures that ultimately dissolve in to body. This nanofiber minimizes infection rate, blood lose and is also absorbed by the body [17].

To meet these varied requirements a layered composite structure is used. The bulk of the filter is generally made of one or multiple MB layers designed from coarse to fine filaments. This is then combined with a nanofiber web. The MB layer provides fluid resistance while the outer nanofiber layer improves smoothness for health, wear and comfort.

Nanofibers greatly enhance filtration efficiency (FE). Scientists at the U.S. Army Natick Soldier Center studied the effectiveness of nanofibers on filter substrates for aerosol filtration. They compared filtration and filter media deformation with and without a nanofiber coating of elastic MB and found that the coating of nanofiber on the substrate substantially increases FE [18].

With most of the nanofiber filter media, a substrate fabric such as SB or MB fabric is used to provide mechanical strength, stabilization, pleating, while nanofiber web component is used to increase filtration performance [16,19].

**Nanofiber Composite Construction:**

Nanofibers were applied to 0.6 ounces per square yard (osy) nylon SB material and to 1.0 osy nylon SB as shown in Figure 8 [8].Then two such layers were laminated Then two such layers were laminated together. Figure9 shows three different types of nanofiber composite fibers designed by altering the thickness and weight of base cloth.

The performance and the durability of the composite structure depends on the finished fabric architecture. The final nanofiber fabric architecture is as shown in **Figure 10**. The two types of constructions are;

1. The Nanofibers /SB layer between outer shell layer fabric and chemical filtration layer.
2. Nanofibers /SB layer is impregnated over the shell fabric and free floats against chemical filtration layer.

Polymeric nanofiber composites can provide enhanced protection against chemical agent micro droplets, biological aerosols, radioactive ducts, etc.

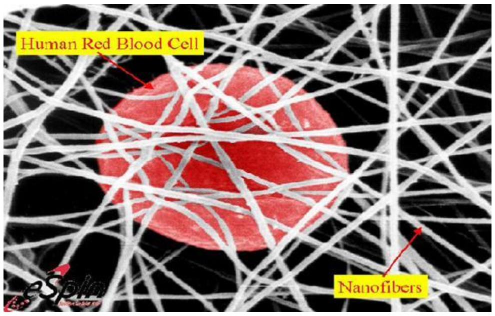


**Figure 7: Comparison of red blood cell with nanofibers web[20].**

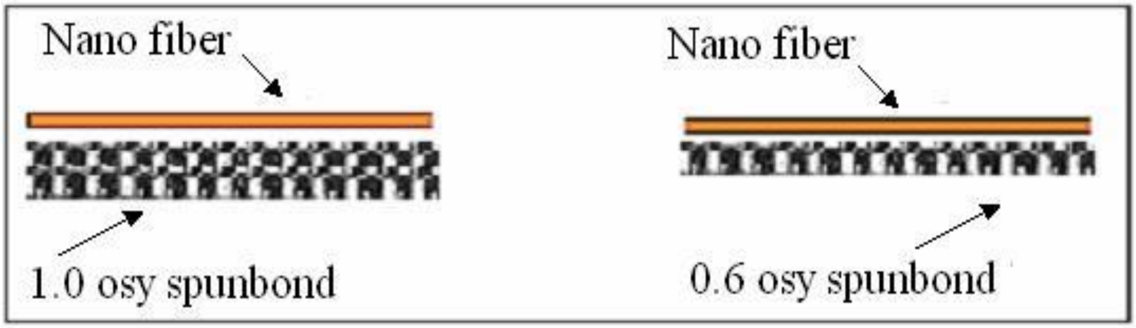


**Figure 8: Nanofiber impregnation to Spunbond layers** [8]

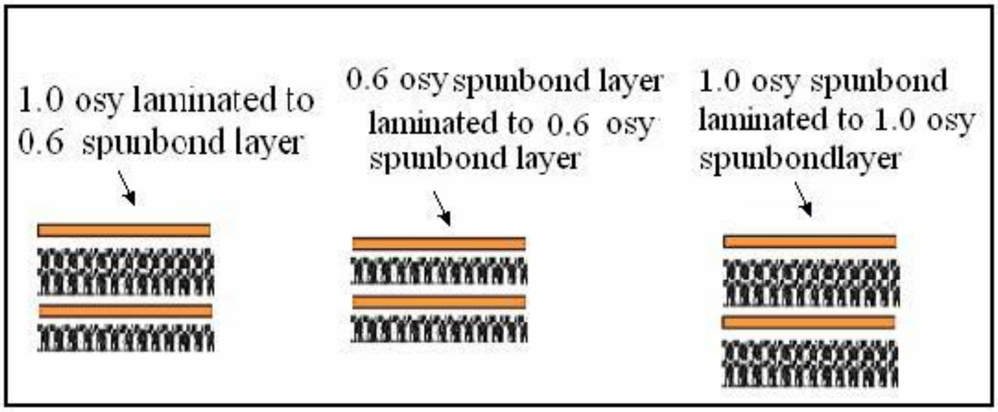


**Figure 9: Nanofiber composite fiber layer options** [8]

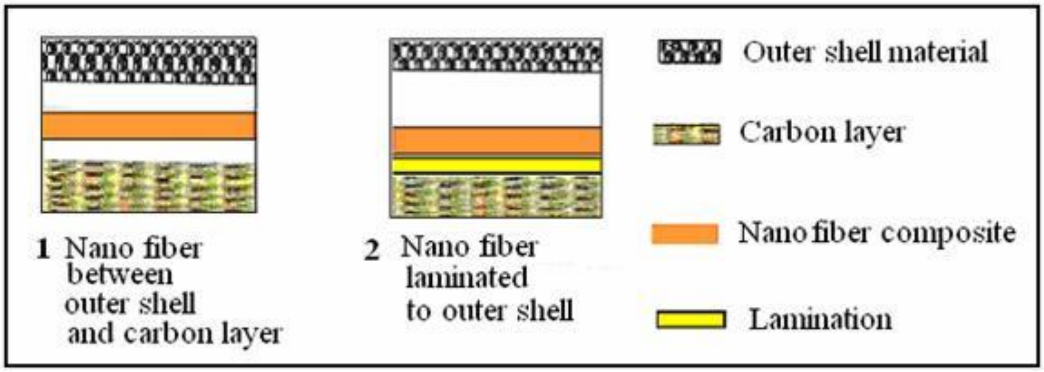


**Figure 10: Nanofiber composite fabric Designs** [8]

**Figure 11: Nanofiber wound fiber**[84]

## NANOFIBERS IN ADVANCED WOUND CARE[84]

In contrast to traditional wound care, advanced wound care dressings operate in moist environments, require less frequent changing and help reduce the pain of dressing changes and lessen scarring. **Figure 11** shows nanofiber wound pad.

**Nanofibers may help in the improved care of:**

- Acute wounds, including those caused by burns, surgical or traumatic wounds
- Chronic wounds, such as ulcers, not proceeding through the normal stages of healing
  - Permeability of gases and liquids
  - High absorption capacity of liquids (exudate)
  - High filtration efficiency for bacteria resulting in decreased infections
  - Possibility to add drugs – haemostatic or antimicrobial dressing
  - Swelling and gel forming capability to keep moist environs
  - Anti adhesive effect to the derma - painless removal of the dressing without destroying newly formed tissue

**Polymers in nanofibers in advanced wound care**

Polyvinylalcohol, Chitosan, Carboxy Methylcellulose, Gelatine, Collagen Hyaluronic acid, Polyurethane

**Applications of Nanofibers as Drug Delivery System:**

Desired properties of Nanofibers for application as drug delivery Protect the drugs in the case of systemic application from decomposition, e.g., in the blood circuit. They should allow controlled release of the drug at a release rate as constant as possible over a longer period of time, adjusted depending on the field of application. Permeate certain membranes or barriers, e.g. BBB. They are supposed to concentrate the drug release only on the targeted body. Nanofibers have potential medical applications, which include, drug and gene delivery, artificial blood vessels, artificial organs, and medical facemasks. For examples carbon nanofiber, hallow Nanofibers are smaller than blood cells, have potential to carry drugs in to blood cells[72].

Nanofibers are capable of delivering medicines directly to internal tissues. This nanofiber can be used as varies of medical applications such as bandages or sutures that ultimately dissolve in to body. This Nanofiber minimizes infection rate, blood lose and is also adsorbed by the body. Employing electrospun Nanofibers as drug delivery vehicles has been based on their unique functionally and inherent nanoscale morphological characteristics.

A rich variety of therapeutic agents such as antibiotics[73], anticancer drugs[74], polysaccharides[75], proteins[76] ,and growth factors[77] have been physically or chemically formulated within the bulk

Phase of electrospun Nanofibers or on their surface for accomplishing controlled topical within the defined period of time. Such medicated Nanofibers could be could be applied to various purposes including tissue engineering scaffolds. Recently introduced surface modified designs for drug loading open up the new possibility of constructing more sophisticated drug delivery platforms. Table 3: shows Marketed Nanofibers products available.

**Table 3: Markedly available Nanofiber products**

| **Product** | **Description** | **Manufacture** |
|---|---|---|
| Integra | Nano fiberoys bovine type1 collagen/glycosaminoglycons/synthetic polysiolxane based dermal analogue | Integra life sciences |
| Nanocell | Nanofibrous microbial cellulose masks | Thaionano cellulose |
| Apligral | Bovine collagen nanofibrous sponge with neonatal foreskin fibroblasts and keratinocytes | Novartis |
| Kerlix AMD | Nanofibrous PHMB gauge | Kendall |
| Dermafuse | Bioactive borate glass nanofibrous dressing | Mo-sci corporation U.S.A |
| Trans type | Eletrospun nylon Mesh/Collagen/Silicone dermal substitute embedded with allogenic fibroblasts | Advanced Tissue Sciences |
| Tegaderm | Eletrosun poly(caprolactone) (PCL)/gelatin/polyurethane/scaffold | 3M company |
| Chito flex | Fabricated chitosan nanofiberous dressing | Hemcon Med Tech.Inc. |
| Permacol | Dermal matrix of procine nanofibers | Covidien |
| Allo Derm | Condaners a cellular matrix Nanofibers autograft | Life cell corporation |

## Topical drug delivery

Electrospun Nanofibers for drug and gene delivery application have been used for tissue engineering to improve therapeutic efficacy. in addition, the fibrous surface structure shows strong adhesiveness to mucous layers because their nano-porous structures instantly absorb moisture at mucous layers through nano-void volumes[78]. The superior adhesiveness to word biological surfaces allows Nanofibers to be an ideal candidate for topical drug delivery devices.

## Vitamins[79,80]

Electrospun Nanofibers can be used as carriers for delivery of some vitamins to the skin. Usually, vitamins are applied to the skin in the form of topical creams, lotions, or ointments. Here vitamin – E and vitamin-A, were selected as the model vitamins, due to their benefits in cosmetics. Vitamin –A is naturally occurring, and lipid soluble substances, known to be used for the treatment of leukemia, acne, and other skin disorders. Vitamin-E is also lipid soluble vitamin, it shows potent antioxidant ability, owing to the presences of a hydroxyl group on its chromanol ring which can readily donates a proton to reduce free radicals.

## Protein delivery

Nanofiber to regulate the release of the encapsulated proteins in core. A near Zero order release of platelet derived growth factor-bb (PDGF-bb) can be produced with no associated burst release. In addition, aligned PDGF-bb loaded Nanofibers are fabricated. These aligned drug loaded fibers may simultaneously provide biochemical and topographical cues to the seeded cells, provisions that should prove beneficial for many tissue engineering applications.

### Nucleic acid

Luu et al. describe the encapsulation of plasmid DNA in a PLA-PEG block co-polymer nanofibrous natrix for tissue engineering purposes[81]. Approximately 80% of the β-galactocidase receptor gene is released in 20 days. Transfection experiments performed on the osteoblastic cells line MC3T3-E1 demonstrate increased transfection efficiency of the fiber-encapsulated DNA over naked plasmid added to the medium, but lower than that with a commercial transecting reagent. For improving stability of DNA during the electrospinning processes Liang et al. have incorporated solvent-induced compacted DNA in PLA-PEG-PLA triblock co-polymer[82].

### Delivery of chemotherapeutic agents

Nanfibers have been used sparingly as an anti-neoplastic drug delivery. This has to do with the nature of fibrous scaffolds, which permit delivery only after tumor-resection and surgical implantation of the device. The majority of nanofiber anti-neoplastic agent delivery systems have been envisioned for the treatment of malignant gliomas. The current DDS of choice is post tumor-resection implantation of a drug-eluting wafer. Thus, all these studies have tried to elucidate the benefits of implantation of a drug-eluting wafer. Doxorubicin Hcl , a hydrophilic anti-neoplastic agent is electonspun as an aqueous emulsion in a solution of PEG-PLLA copolymer[83]. This method affords uniform distribution of the drug within the fiber and a administered burst release.

## CHALLENGES IN NANOFIBERS

The process of making nanofibers is quite expensive compared to conventional fibers due to low production rate and high cost of technology. In addition the vapors emitting from electrospinning solution while forming the web need to be recovered or disposed of in an environmental friendly manner. This involves additional equipment and cost. The fineness of fiber and evaporated vapor also raises much concern over possible health hazard due to inhalation of fibers. Thus the challenges faced can be summarized as[10]:

Expensive,

Health hazards,

Solvent vapor,

Packaging, shipping& handling,

## CONCLUSION

Today Nanofibers are at the forefront of nanotechnology. Their unique porous structures and large surface to volume area make them suitable for a wide variety of applications. Nanofiber controlled drug delivery system is becoming the flash news in pharma field . Nano structure delivery architecture are promising candidates that will enable efficient in Targeted and Novel drug delivery. Electrospinning provides the most versatile process to produce nanofibers with a wide range of properties. Potential medical applications include efforts to fabricate electrospun polymer nanofiber scaffolds for nerves, tissues, skin and bone. Still several problems must be resolved for further applications such as the drug loading, the initial burst effect, the residual organic solvent, the stability of active agents, and the combined usage of new biocompatible polymers.

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