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REVIEW ARTICLE

A Review on Electrospun Nanofibres for Drug Delivery

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Abstract

Electrospinning is most widely used technique for fabrication of nanofibres. It is cost effective, simple and versatile process. The resulting nanofibres possess unique properties such as a high surface-area-to-volume and aspect ratio, low density, and high pore volume. These properties make the nanomaterials more advantageous than conventional materials in energy harvesting, conversion, and storage devices. There are different aspects of electrospinning, but the current discussion is based on the use of electrospun fibrous matrices for drug delivery. The article explains about all the available approaches to incorporate drugs onto or within electrospun fibrous matrices, along with their release mechanisms and about the applications of such drug carrying fibrous matrices for regeneration of various tissues, such as neural, vascular, cardiac, skin, and bone.

Keywords: *Electrospinning, Adsorption, Controlled release, Fibrous matrices, Synthetic polymers.*

Introduction

Based on the various evidences on the unique structural, physical, chemical, and biological properties of nanoscale materials, identifying, controlling and manipulating various parameters has become a great interest for discovery and development of next generation of materials.

In case of biomedical research, the primary aim for the use of nanoscale materials is based on the evidence that the native extracellular matrix (ECM) conducts some instructive physical and biological signals to cells at a similar scale [1].Thus, the creation of an *in vitro* micro environment that can recognize the key physicochemical features of native ECM would lead to predictable cell responses *in vivo*.

It revealed that the cells can respond to stimuli at different length scales, varying from nanometer to millimeter [2]. Scaffold fabrications, are useful for the incorporation of physical or chemical cues at varying scales. Sophisticated micro- and nanopatterning techniques, originally intended to be used for the semiconductor industry, have been then adopted for generating 3D structures with controlled topology to modulate cellular functions without any biological input [3, 4, 5]. The biological cell behaviors on isotropic and nonisotropic substrates imply that cells can sense the topography of their surrounding microenvironment and respond accordingly. However, the morphological changes possessed by such 3D structures than that of the native ECM would cause different cell responses.

To overcome this, fibrous matrices with sub micrometer dimensions can be used. Along with these morphology and dimension, fibrous matrices possess other definite properties, such as high surface-to-mass ratio, low density, high porosity, and interconnected pores, desirable for tissue formation.

Meanwhile, in the native ECM, a large amount of biomolecules are stored via physical adsorption or chemical immobilization with spatiotemporal release to instruct the development of residing cells. Based on this it would be highly desirable to develop ECM-like matrices with the capability of releasing various drugs.

Preparation Techniques

Several techniques are available to fabricate fibrous matrices [6], including phase separation [7], self-assembly [8] and electro spinning [9, 10, 11]. Among all these methods, electrospinning has been widely adopted because it is easy to operate, available at low cost, high production rate, and good reproducibility.

Apart from these, a variety of materials, including synthetic polymers (e.g., polycaprolactone [PCL], polylactide [PLA]), natural polymers (e.g., collagen, gelatin), or hybrids (e.g., PCL blended with collagen), can be electrospun into sub micrometer fibers with various fiber spatial arrangements (e.g., aligned, random, or cross aligned), which can have the capability to capture the major features of native ECM, which includes composition, morphology and spatial organization. As a result, substantial efforts have been made to explore the potential utilization of electrospun nanofibers for biomimetic engineering of various tissues [12].

Electro spinning

Electro spinning, is a widely used technology which utilizes high voltage electric fields for electrostatic fiber formation and produces polymer fibers with a diameter ranging from several nanometers to several micrometers [13].A typical electro spinning apparatus includes high voltage power supply system, spinneret system and collecting system as shown in (Figure 1). Electrospinning is also known as electrostatic spinning. It has been used extensively for over three decades, and its usefulness in the fields of science and technology is still on the increase.

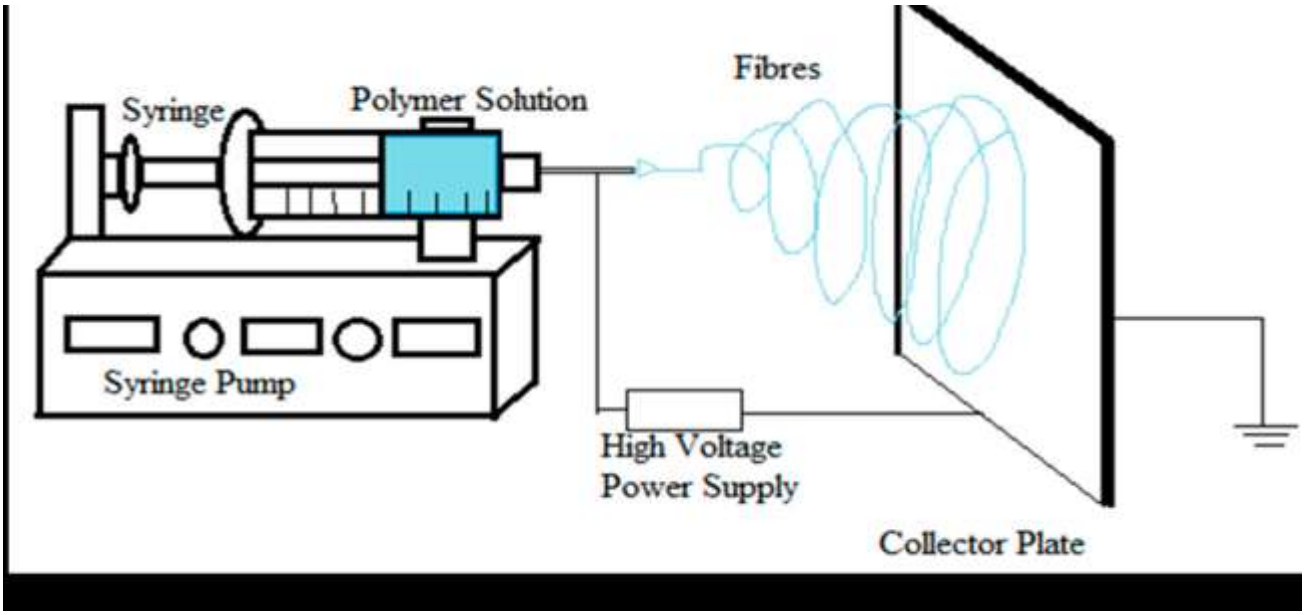

Figure 1: Schematic representation of electro spinning apparatus: The system consists of polymer solution/melt in a syringe, mounted on a syringe pump, operating at a constant slow speed. High voltage direct current supply is connected to the needle of the syringe to charge the fluid. With sufficient voltage, the fluid forms a Taylor cone and then jet erupts from the cone towards the collector plate with whipping instability

Process of Electro Spinning

The electrospinning process utilizes a very high voltage source (of either positive or negative polarity) to charge the polymer solution or melt, fixed with a grounded collector, and a syringe pump (Figure 1). The electrospinning process should be performed in a closed compartment in order to serve as a safety precaution for fibres production and personnel. When a sufficient repulsive charge is accumulated and when the repulsive force is equal to the surface tension, the drop surface on the conducting tube starts to form a cone called a Taylor cone. Under the influence of electric field the polymer solution/melt forms the equilibrium cone at an angle of 49.3^0 [14]. Whenever the electric field is increased further, the repulsive force overcomes the surface tension. As a result a liquid jet is formed from the Taylor cone because there is a sufficient attraction between the molecules in the solution melt. If the molecules of solution do not have sufficient cohesive attraction, then the jets break and the resulting particles are sprayed onto a collector plate.

The fiber originating from the Taylor cone travels through the air towards the collector plate, and during this process, the solvent gets evaporated, leading to deposition of a solid fiber onto the collector plate [14, 15]. After travelling through air for a short distance the jet starts to whip, thus increasing the path distance to the collector. This process assists in fiber thinning and solvent evaporation.

There are multiple theories proposed on the reason behind jet instability. Some of the prominent theories include: repulsive interaction of charges in the polymer jet [16]; increase in charge density during jet thinning, thus increasing radial charge repulsion to cause jet splitting at a critical charge density [17]; and, "whipping" instability (spiraling loops) [18], causing the fiber to turn, bend [19] and/or spray [20].

Types of electrospinning

The type of electrospinning process can have a significant impact on fiber formation in addition to the process and solution parameters. Two main aspects to deal within the type of electrospinning; are solution vs. melt electrospinning and nozzle configuration [15].

Solution vs. Melt vs Emulsion Electrospinning

In general, electrospun fibers can be obtained from polymer solutions or melts or emulsions. Melt spinning has some advantages like high-throughput rate and process safety and solutions have the advantage of using a large variety of polymeric materials suitable for the drug, lower energy consumption and superior mechanical, optical and electrical properties of prepared fibers.

On other hand emulsion electrospinning is needed for high melting polymers to prepare flame-retardant fibers. A comparison of different spinning methods using poly (lactic acid) (PLA) as a model polymer has been reported by Gupta *et al.*, [21].The melt of the polymer with other additives is forced out through the capillary, resulting in a thin fiber that cools and solidifies rapidly during its time in the air before depositing onto the collector.

The structural and tensile properties of the obtained fiber depend upon the take up speed drawing temperature and draw ratio.

Draw ratio is defined as the amount of stretching that the material undergoes during the drawing stage of electrospinning. The increase in draw ratio [22] and take-up speed [23] increases the molecular chain orientation along the fiber axis as well as the overall crystallinity of fibers formed from the melt. The solution spinning method is specifically suitable for polymers or blends of polymers that are thermally unstable or degrade upon melting.

It is of two types based on the method of using solvent namely, dry spinning and wet spinning. In dry spinning process, hot air or inert gas is passed through the polymer jet which supports for the evaporation of solvent and gradually solidifies the fibre. For example, a solvent combination of chloroform and toluene is used to produce PLA fibers of high strength by using dry spinning and hot-drawing processes.

They were able to obtain an optimal tensile strength of 2.2 GPa by electrospinning at 25^0C [24]. Whereas, wet-spinning process involves the usage of viscous coagulation bath containing the liquid, which is miscible with the spinning solvent but not with the polymer. The interaction between the polymer solvent and non-solvent leads to phase separation and then solvent removal from the jet.

In the emulsion electrospinning process, polymers are finely ground and mixed with another polymer containing catalyst and emulsifying agents to form an emulsion. The formed emulsion is then electrospun by either the dry or the wet spinning method. This technique has been used in preparing fibers from fluorocarbons with high melting points, ceramics, and polymer blends with flame-retardant properties [25].

Nozzle Configuration

Nozzle configuration indicates the number and the arrangement of capillary tubes from which the jets of fibers emerge. A single nozzle configuration is the simplest and most common configuration, in which the charged solution flows through a single capillary. This particular configuration has been used to electrospin different polymeric fibers either singly [26, 27] or in combination [28] or solvent systems. Co-electrospinning of polymer blends in the same solvent or a

mixture was the first and most common modification in the process.

Sometimes polymer blends are used to obtain the final properties of fibers. In case the polymers are not miscible in a common solvent, or when a homogeneous solution of polymers cannot be obtained, thermodynamic and kinetic aspects should be considered for electrospinning i.e to modify the nozzle configuration, where different polymer solutions are electrospun from different capillaries, side-by-side. In this type of configuration, two polymer solutions pass through separate capillaries arranged side-by-side, which are connected to a high voltage supply and never come into contact until they reach the end of the capillary. A single Taylor cone is formed, which ejects the jet with a non-uniform mixture of both polymer solutions and, after drying, is deposited in the collector. In this special type of modification, combined properties of two different polymers can be achieved. But both the polymeric solution used should have similar conductivity such that a single Taylor is formed.

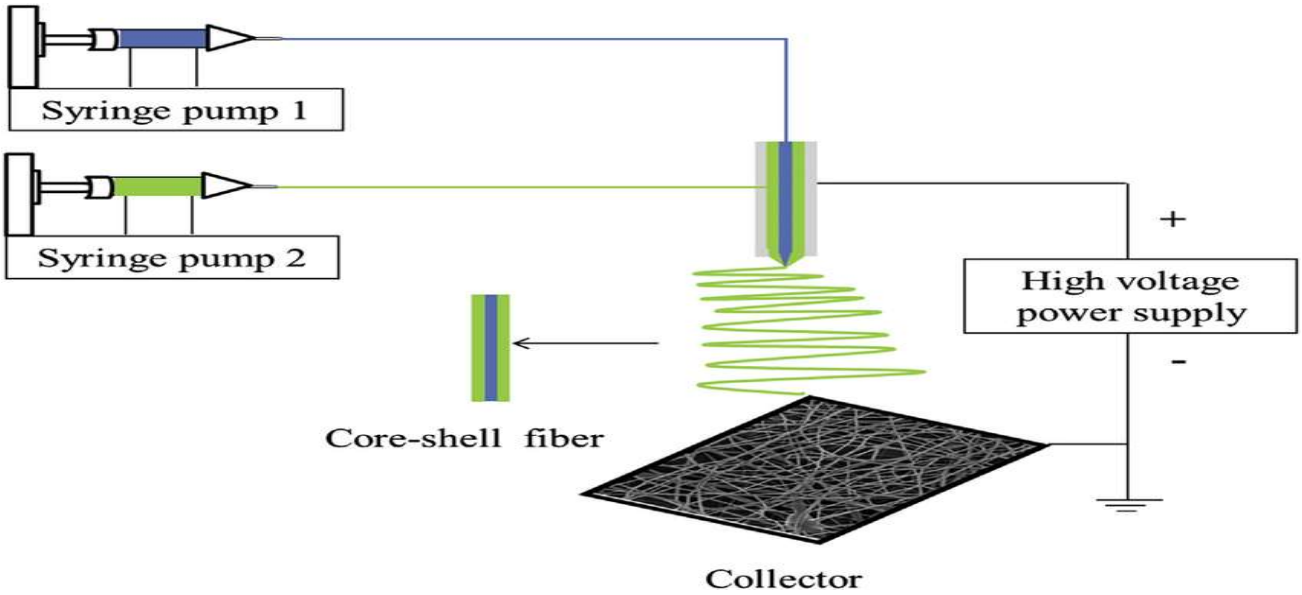

Figure 2: Coaxial electrospinning schematic diagram: Polymer solution 2 is passed through the inner capillary tube, while polymer solution 1 is passed through the outer capillary tube. The Taylor cone is formed where the inner solution (polymer solution 2) is surrounded by the outer solution. The jet erupts from the Taylor cone, and during that process, the polymer in the inner layer is coated with the polymer in the outer layer. The dried fiber with a core-shell design is then deposited on the collector.

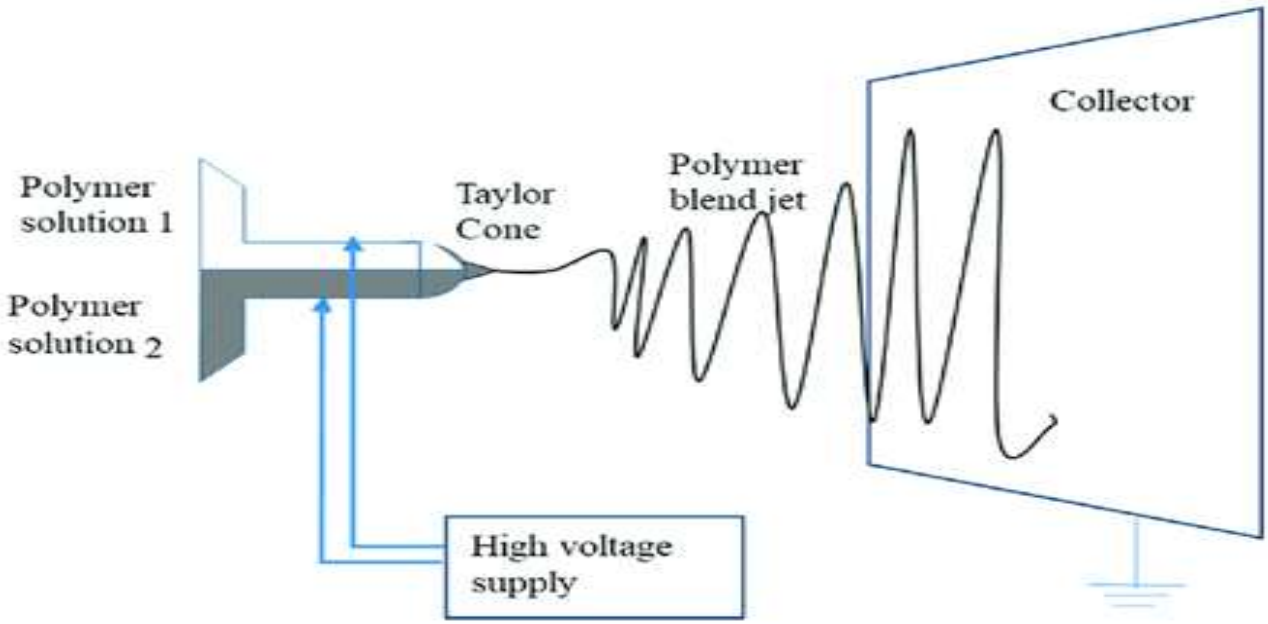

Figure 3: Side-by-side electrospinning schematic diagram: Polymer solutions 1 and 2 pass through separate capillaries, which are connected to the same high voltage supply, at either the same or different rates. A single Taylor cone is formed, which ejects the jet with non-uniform mixture of both the polymer solutions and, after drying, is deposited on the collector

The apparatus can be manipulated accordingly to obtain required morphologies and structures of fibers. The designs of the spinneret promote the production of coaxial electrospinning as shown in Figure 2 and in side-by-side electrospinning as shown in Figure 3. Polymer solution pass through 2 separate capillaries, which are connected to the same high voltage supply, at either the same or different rates. A single Taylor cone is formed, which ejects the jet with non-uniform mixture of both the polymer solutions and, after drying, is deposited on the collector. Figure 4 represents different structures of electrospun fibers, such as core-shell, hollow, nanowire-in-micro tube and three-dimensional fiber scaffold produced by tuning the configuration of the spinning apparatus.

Figure 4: Different structures of nanofibres

Techniques for Incorporation of Drug into nanofibres

Blending: Two common methods exist to incorporate drugs into electrospun fibers

- Dissolving the drug into the electrospinning solution [29,30,31]
- If the drug is not soluble and will maintain its crystal structure, the drug will be mixed with the electrospinning solution [32, 33, 34].

In either way, the electrospun nanofibers degrade or swell and then the drug inside of the fiber will be released. Due to ease of fabrication and effective surface area electrospun nanofibres are useful in sustained release of drug. Sustained release property of electrospun nanofibers is based on drug polymer compatibility [35].

Drug polymer compatibility refers to the physical interactions between drug molecules and polymer chains, which will influence the drug distribution in the final solid drug dispersion. This compatibility further depends on drug solubility in the polymer solvent system. The choice of polymer is the first step in developing a sustained release system because a polymer's hydrophobicity and glass transition temperature (Tg) considerably influence drug-release kinetics. Another parameter which influences sustained release of drug is drug compatibility with the polymer solvent system. Low solubility of drug in the polymer solvent system can cause preferential localization of the drug to the surface of the fibers during electrospinning even at low loading which leads to burst release.

Drug loading and ionization state can also influence the encapsulation of drugs into fibers. Higher drug loading and ionic content have been shown to lead to surface localization of drugs. Processing parameters can also affect the structural features of finished fibers, which can affect drug release.

The complexity of these parameters has limited the use of sustained release for a wide variety of drugs, especially at high dose, and consequently, most of the sustained-release nanofibers have been prepared with low loadings of hydrophobic molecules.

By optimizing the above mentioned design parameters, ideal sustained release could be achieved for both hydrophilic and

hydrophobic small-molecule drugs at high loadings.

Adsorption

Drug loading through the encapsulation of drugs within electrospun nanofibers using blending has often led to some drug molecules to denature due to exposure to high temperature which subsequently involves extra processing, thereby increasing the cost of manufacturing.

In addition, this can lead to batch-to-batch variation in terms of drug release and concentration characteristics. And also not all the drugs are suitable for encapsulation in such a way because of their lack of solubility in the electrospinning solutions [36] which could lead to accumulation of the drug onto the fiber surface leading to burst release.

To overcome such disadvantages, nanofibers, after electrospinning, can be immersed into drug solutions to let the drug molecules physically, chemically, or biomimetically get adsorbed onto the electrospun nanofibers. Physical adsorption has been utilized to load drugs onto the surface of nanofibers.

Types of Adsorption

Physical Adsorption

Physical adsorption often utilizes forces like electrostatic interactions, hydrogen bonding, hydrophobic interactions, and van der Waals interactions [37]. Nanofibers, due to their large surface area are able to adsorb many drug molecules. Some examples of physically adsorbed drug molecules include proteins, nucleic acids, and bioactive macromolecules, these drugs cannot be readily dissolved in the polymer solution and their charges make it extremely difficult to electrospin them along with fibers.

Physical adsorption leads to immediate-release profile and dosage control, applicable in the prevention of bacterial infection, which often occurs within a few hours of surgery. Drug loaded nanoparticles can also be adsorbed on the surface of nanofibers, which allows unique drug-release profiles and also high drug-loading capacities. There are three different modes that can be used to physically load drug molecules onto the surface of electrospun nanofibers Figure 5 [38].

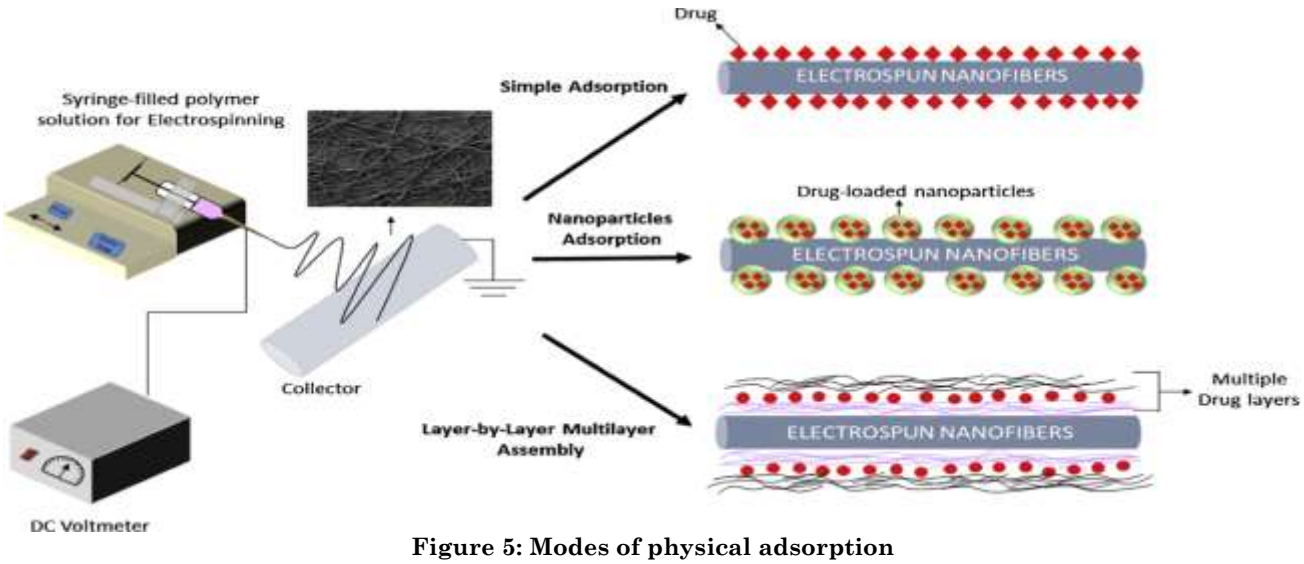

Figure 5: Modes of physical adsorption

Simple Physical Adsorption

Simple physical adsorption is the direct approach for loading drugs onto the surface of nanofibers. By considering the unique morphological features of electrospun fibers, a very direct and effective method for simple physical adsorption is to drop the drug solution onto the nanofiber mesh and leave it in order to allow the drug to get completely adsorbed. This method has been used to create postsurgical anti-adhesion barriers (e.g., Biteral adsorbed on PCL nanofibers) [39] and to avoid postsurgical bacterial infections [38].

Nanoparticle Assembly on the Surface

The principle behind this method is that the nanofibers and therapeutic or biologically active nanoparticles themselves, e.g., silver or hydroxyapatite, or encapsulate such agents exhibit attractive forces due to the opposite charges generated by electrospinning and electrospraying.

Essentially, the only condition for such approach is that the polymer used should be electrospinnable and the nanoparticles should be electrosprayable.

Layer-by-Layer Multilayer Assembly

Layer-by-layer (LbL) multilayer assembly is nothing but a adaptable surface modification method that, which precisely controls, allows multifunctional surface coatings from a few nanometers to several micrometers to easily be applied to nanofiber (and other) substrates.

Chemical Adsorption

Apart from physical adsorption, drugs can be adsorbed on nanofibers through chemical immobilization and released through the cleavage of the linking bonds. In this method, the nanofiber surface is initially activated to adsorb functional groups, and then subsequently biomolecules are allowed to conjugate with the nanofiber surface. Several approaches are used to create functional groups on the nanofiber surfaces including surface activation, bioactive molecule immobilization, and click chemistry [37].

Surface Activation

There are a variety of ways to activate the surface after electrospinning, such as ultraviolet (UV) or plasma treatment; plasma treatment is capable of generating functional groups like primary amine and carboxyl groups.

Another method for surface modification is chemical etching, and this is commonly used for polymers containing polyesters. Acid or base treatment leads to the removal of ester bonds, so that carboxyl or hydroxyl groups are exposed on the surface, thereby allowing drug molecules to chemically conjugate to such groups.

Bioactive Molecule Immobilization

Depending on the type of functional groups present certain types of conjugation techniques has been used to link drug molecules to the surface of nanofibers. Primary amine, carboxyl, thiol, and hydroxyl groups are all functional groups that are generally used for conjugation. Primary amine and carboxyl groups are frequently targeted sites which react in molecules for conjugation, and such reactions are often accelerated by using 1-ethyl- 3- (3-dimethylaminopropyl) carbodiimide /N-hydroxysuccinimide (EDC/NHS) chemistry. Hydroxyl groups are also often used via treatment with NaIO4 or Ce (IV), which activates the surface sites for drug conjugation.

Click Chemistry

The term “click chemistry” was introduced by K.B. Sharpless and coworkers to describe high yielding reactions, stereospecific, and simple to perform; that create by-products that replaced the need for chromatography; and that can be conducted in easily removable or benign solvents. Generally speaking, these reactions should proceed rapidly under mild reaction conditions, be tolerant to a wide variety of chemical groups, produce stable products, and be insensitive to moisture and oxygen.

Owing to these characteristics, click reactions are widely used in biomaterials and drug delivery. Click reactions include nucleophilic ring-opening reactions of epoxides and aziridines, non-aldol-type carbonyl reactions, addition of carbon-carbon multiple bonds, Michael additions, and Huisgen 1, 3-dipolar cycloaddition reactions (Table 1). Azide-alkyne cycloadditions are also commonly used to chemically adsorb drug molecules on the surface of nanofibers [40].

Table 1: Examples of polymers and corresponding click reactions that have been used for adding drug molecules

Polymers	Type of Click Reaction	Peptide/Drug Molecule
PEG	Azide-alkyne cycloaddition	RGD peptide [41]
pHEMA	Azide-alkyne cycloaddition	Gene delivery (DNA)[42]
PCPLG	Azide-alkyne cycloaddition	Water-soluble mannose[43]
PNIPAM	Azide-alkyne cycloaddition	BSA proteins[44]
Polyester ureas	Azide-alkyne cycloaddition	Drug molecules[45]
PCL	Condensation reaction	PEO[46]
PEG	Condensation reaction	Protiens[47]

*BSA, bovine serum albumin; PCL, polycaprolactone; PCPLG, poly(g-chloropropyl-L-glutamate); PEG, polyethylene glycol; PEO, polyethylene oxide; pHEMA, polyhydroxyethylmethacrylate; PNIPAM, poly(N-isopropylacrylamide); RGD, arginylglycylaspartic acid

Biomimetic Adsorption

Biomimetic adsorption plays a very significant role in the delivery of small proteins, growth factors, and other signaling molecules to sites that are only invasively accessible. Such molecules include bone morphogenetic protein (BMP)-2, transforming growth factor-b (TGF-b), vascular endothelial growth factor (VEGF), and plasmids containing genes.

Not only are these cues limited by in vivo accessibility, but they are also very expensive and thus cannot be administered orally or intravenously; delivery needs to be in situ. Therefore, to deliver such agents, biomimetic nanofibers provide the perfect scaffold. Biodegradable nanofibers can have such molecules adsorbed on the surface and, upon enzymatic activation; these molecules would be released and utilized by the tissue microenvironment. The adsorption can be either physical or chemical depending on the target drug [48].

Characterization of the Nanofibers

- *Scanning electron microscopy (SEM) studies:* Scanning electron microscopy with a QUANTA 400F field emission was used to obtain images of electrospun fibers. For this the nanofibers were coated with gold/palladium and images were taken in different parts of the nanofibers in 2000, 8000, 60000 magnification. Then the average fiber diameters were determined by measuring fibers randomly selected from SEM images. The thickness of nanofibers was measured by cross-sectional SEM images.

- *Mucoadhesion studies:* Texture Analyzer (TA.XT. PlusTexture Analyzer, Stable Micro Systems, London, UK) with a 50 N load cell equipped with a mucoadhesive holder was the instrument used for the determination of mucoadhesion properties of the nanofibers. Freshly excised animal mucosa (sheep cheek) was used as the model tissue, and it was frozen at -20^0. From this frozen mucosa a 2 mm thick cross section was taken and attached to lower end of probe using cyanoacrylate glue which is present in the instrument. The mucosa was dipped into a pH 6.8 simulated saliva solution and allowed to stand for 10 min prior to the experiment. The contact time of the probes was 150 sec and the force applied by them on the tissue surface was 0.2 N. The experiments were carried out at the rate of 1 mm/s. The tensile force was observed, while the probe was leaving the tissue surface and the performed mucoadhesion work, were measured and calculated by the device.

- *Mechanical properties:* The mechanical properties such as tensile strength and elongation at break values of the electrospun mats were evaluated on Texture Analyzer (TA.XT. PlusTexture Analyzer, Stable Micro Systems, London, UK) equipped with Tensile Grip with a 50 kg load cell and an extension rate of 5.0 mm/min. Six specimens were cut into a rectangular shape (3 cm x 1 cm) and tested. Tensile strength (mPa) and elongation break (%) values of the nanofibers were calculated from the strain-stress graphics.

- *Drug content:* The nanofibers were cut into a one cm diameter pieces and mixed in the simulated saliva solution. The amount of drug loaded in nanofibers was assayed.

- *Disintegration time:* Nanofibers were cut into 3cm x 3cm pieces, then they were placed on a watch glass and a one mL of simulated saliva solution was dropped. The period during which it completely disintegrated was measured

- *In vitro diffusion studies:* Franz type diffusion cells were used. The diffusional cross sectional area was 1 cm^2. A dialysis membrane (Sigma®, USA) with a pore size of 12,000 Da was used. The stirred (800 rpm) receptor phase (2.5 mL) containing the simulated saliva solution (pH 6.8) was thermostated at 37^{0}C. The donor compartment contained nanofiber formulation (circular pieces with 1 cm diameter) and one mL of simulated saliva solution. Samples (2.5 mL) were taken periodically from the receptor phase and replenished with the same volume of fresh buffer.

- *Contact angle measurements:* The contact angle measurements were performed on Attension Theta Lite optical tensiometer (Biolin Scientific, Finland). The nanofibers were stretched on a convex sample holder.

A volume of distilled water was dropped on nanofibers. The software of the instruments estimated the contact angle for 15 seconds. Finally, six replicate measurements were carried out.

- *Stability studies:* Stability studies were carried out on the nanofibers containing glutamine at 4°C, 25°C/60% relative humidity and 40°C/75% relative humidity conditions for a period of 30 days. The samples were analyzed at the end of this period.

- *Data analysis:* The data were evaluated for statistically significant difference by one-way ANOVA.

Applications

- Filtration: In air filtration applications, materials such as high efficiency particulate air (HEPA) filters are used to remove particulates and other debris from the air. The recent advances in nanomaterials have driven the study on the use of nanofibers in combination with materials such as textiles or fiberglass. The use of nanofibers on filters can be expected to significantly improve their performance, with increased filtration efficiency accompanied by only a slight rise in the pressure drop [49]. Filters are used in households and industry for removing substances from air or liquid, to remove pollutants from air or water (50, 51).

- Affinity membranes and recovery of metal ions: The functionalized nanofibers may be able to collect small molecules or metal ions from a solution. The functionalized nanofiber membrane was even able to directly covert metal ions collected into elemental metal (electroless recovery). Nanofiber membrane was surface coated with a thin layer of conducting polymer, polypyrrole, used to collect gold ions from aqueous solution and converts the gold ions into elemental gold particles [52, 53].

- Tissue engineering scaffolds (muscles, bones, cartilage): Multiple strategies have evolved and the application of nanotechnology can only improve the field of skin tissue engineering. Tissue engineering and regenerative medicine is an interdisciplinary field of research and clinical application focusing on the repair, replacement or regeneration of cells, tissues or organs to restore impaired function because of congenital defects, disease, trauma and ageing. Tissue regeneration is induced by supplying cells or drug or growth factor loaded matrix when tissues or organs lose their functions or are damaged. The biomimetic scaffolds for tissue regeneration have been produced by using natural and synthetic polymers having a certain strength and form, which includes sponge type or fibrous matrix or gel type cell culture scaffolds [54].

- The main aim is to repair, replace, maintain, or enhance the function of a particular tissue or organ. These technologies are organized into three areas: cell technology, scaffold construct technology, and technologies for *in vivo* integration. The scaffold construct technology focuses on designing, manufacturing and characterizing three-dimensional scaffolds for cell seeding and *in vitro* or *in vivo* culturing [55].

- Wound healing: Electrospun nanofiber membrane is used as good wound dressing aid because of its highly porous membrane structure with well interconnected pores are particularly important to discharge fluid from the wound; the small pores and very large surface area inhibits the exogenous microorganism invasions, and assist the control of fluid drainage; in addition, the electrospinning process provides a simple way to add drugs into the nanofibers for any possible medical treatment and antibacterial purposes as shown in Table 2. [56].

- Catalyst and enzyme carriers: In chemistry and biology fields, a carrier is used to catalyze high catalysis activity it increases the stability for catalyst is used to preserve high catalysis activity. Using an electro spun nanofiber mat as catalyst carrier, the extremely large surface could provide a huge number of active sites, thus enhancing the catalytic capability [66]. On the other hand chemical reactions using enzyme as catalysts have high selectivity and mild reaction conditions. The enzymes are immobilized on the carrier for easy separation from the reaction solution. The immobilization efficiency mainly depends on the porous structure and enzyme-matrix interaction. Nano-structured materials are recently used as enzyme carriers because of

their large surface area and porous nature.

Table 2: Polymeric nanofiber composites used as wound healing materials

Polymeric material	Electrospining condition	Fibre diameter	Material incorporation	Study cell(type)
PLGA	Two syringe pumps for two solutions	310 nm	Chitin nanocomposite	Human keratinocytes (NHOK and NHEK) and fibroblasts [57].
PLGA	Blend in HFIP solvent	200 to 450 nm	Collagen	Human fibroblasts [58].
Cellulose acetate, PLLA, PLGA	Drug loaded polymer	300 to 700	Alkannin and shikonin	*In vitro* release profile [59].
Recombinant human tropoelastin	Tropoelastin in HFIP and crosslinked with GA	2000 to 4000 µm	-	Primary human dermal fibroblasts [60].
Collagen/chitosan	Collagen/chitosan along with PEO in AcOH, GA cross-linking	100 to 450 nm	-	Wound healing with SD rats [61].
PCL and poly (oxyethyleneb oxypropylene-b-oxyethylene)	Lutrol F127 and PCL mixtures spun with acetone/ methanol	550 to 1600 µm	Acetazolamide and timolol Maleate	*In vitro* release profile [62].
PLGA	Freeze drying of inverted emulsion technique	-	Mafenide acetate, ceftazidime hydrate or gentamicin sulfate	*In vitro* release profile [63].
Tyrosine-PEG-derived poly(ethercarbonate)	Composite copolymer xerogel films	-	Bupivacaine HCl or mepivacaine HCl	*Invitro* release profile [64].
Diclofenac sodium	Spun in ethanol/ DMAc	200 to 600 nm	Eudragit L 100-55	*Invitro* release profile [65].

- Sensors: These are widely used to detect chemicals for environment protection, industrial process control, medical diagnosis, safety, security and defense applications. Nanofibers are used as a good sensor because they fulfill some requirements like small dimension, low fabrication cost and multiple functions, selectivity and reliability [67].

Conclusion

The electro spinning process plays a major role in various medical applications with various advantages and generated a lot of interest due to its ease of use, adaptability and flexibility in controlling the fiber diameter from the micrometer down to the nanometer range. The equipment used in the electrospinning process is constantly changing according to the desired formulations. Electrospinning began with a single nozzle configuration and evolved into multi-nozzle configurations through coaxial and emulsion spinning configurations. Further studies are being carried out to modify the nozzle configuration and collector design in order to significantly improve fiber properties and simplify the manufacturing process.

This review summarizes several important aspects of electrospinning in the use of electro spun fibers in drug. Various applications of electrospun nanofibers are also discussed. By careful selection of polymers, it is now possible to deliver various antibacterial agents and anticancer drugs in a required manner using electrospun nanofibers. In order to make further progress, particularly in the field of drug delivery, it is necessary to identify ways that allow large-scale fabrication of nanofibers with desired morphological and mechanical properties in a reproducible manner.

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