

Electrospinning and Characterization of Nanofibers: Emerging Applications in Pharmaceutical Formulations

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ABSTRACT

Effective delivery of therapeutics is frequently limited by poor aqueous solubility and stability, low oral absorption and bioavailability, rapid clearance, narrow therapeutic windows, and multiple biological barriers (e.g., mucilage layers, membranes, enzymatic degradation, and clearance). Advanced nanostructured delivery systems can mitigate these constraints, and electrospun nanofibers are particularly attractive due to their high surface area-to-volume ratio, interconnected porosity, tunable morphology, and drug-incorporation capacity, enabling improved wettability, dissolution, and controlled release. This study provides a comprehensive, integrative review of electrospinning through a process–structure–property lens, synthesizing how electrospinning parameters (polymer concentration/molecular mass/viscosity, conductivity, surface tension; applied voltage, flow rate, tip-to-collector distance; temperature, humidity, airflow) govern jet formation (Taylor cone, initiation, whipping instability), solvent evaporation, deposition, and the resulting morphologies (beads, smooth/fine/thick/ribbon-like/porous/fused/aligned or random mats). The review traces key technological evolution from the Taylor cone concept to nanoscale fiber development and, subsequently, coaxial/aligned/needleless systems, roll-to-roll manufacturing, and recent AI-, PAT-, and 3D-enabled smart electrospinning platforms. Material-driven design strategies are discussed across polymeric fibers (including core–shell, hollow, porous, crosslinked, and nanoparticle-filled systems), calcined metal-oxide and composite fibers, carbon nanofibers derived from PAN via stabilization and carbonization, and advanced architectures such as nanotubes, nano shell-functionalized fibers, nanocrystal-loaded fibers, and nanobots. Characterization workflows spanning SEM/TEM/AFM, XRD/Raman/FTIR, DSC/TGA, contact angle, roughness, and zeta potential are linked to drug loading/entrapment efficiency and in vitro release modeling (e.g., Higuchi and Korsmeyer–Peppas), including burst and diffusion/degradation-controlled phases. Electrospun systems show broad pharmaceutical utility (oral, buccal, transdermal, ocular, vaginal delivery; wound healing; tissue engineering; oncology; vaccination), while scalability, reproducibility, solvent toxicity, and standardization remain key barriers that emerging QbD, PAT, automation, modeling, and greener, AI-assisted manufacturing may help overcome.

Keywords: Electrospinning, Nanofibers, Drug delivery, Nanostructured delivery systems, Bioavailability, Core-shell, Process-structure-property relationship

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1. INTRODUCTION

The effective delivery of many kinds of therapeutics to their target sites continues to be a challenge because their limited water solubility, poor stability, poor oral absorption or bioavailability, rapid clearance or narrow therapeutic window are significant difficulties in achieving their desired effects. In addition, biological barriers, such as mucilage layers, cell membranes, enzyme degradation and clearance, have a significant effect on drug absorption and bioavailability at its sites of action[1]. Given such challenges, development of advanced nanostructured delivery systems, such as nano bombs, nanoparticles, liposomes, nanorods, nano ballons, nanocrystals, nanotubes, nanosheets and nanofibers etc, which could

significantly improve solubility, stability, loading and release of drugs and facilitate the targeted delivery of therapeutic agents toward disease sites. Over these many systems, electrospun nano fibres attracted the attention because of their high surface area to volume ratio, interconnectivity with porosity, adjustable fibre morphology and capacity to incorporate drugs[2]. Electrospinning is a procedure that can yield micro or nano structural fibres that have extended in length from polymer solutions or melts. However, the topography and morphology of electrospun fibers depend on concentration of polymer, voltage, flow rate of polymer solution and distance between the electrodes to a different extent. Electrospun nanofibers' complex pore architecture offers

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some beneficial features including good wettability, higher dissolution rate and drugs-controlled release. Novel fibres architecture such as core-shell, coaxial, multilayer, aligned fibres and Janus fibres are also developed. Many researches on electrospinning processes, selecting the appropriate polymer, drugs delivery and tissue engineering exist, but there is still a weak comprehensive review to address the whole aspects for process-structure-property relationship of electrospinning, the structure and performance in the drug delivery via nanofibers and the efficacy in different treatments. In the current study, the relationships have been demonstrated including process parameters of electrospinning process, morphology of the nano fiber structures, physical and chemical properties, analytical results, the efficacy of the drug, respectively. In especial, focuses on electrospun advanced Nanostructures[3].

2. HISTORICAL DEVELOPMENT OF ELECTROSPINNING

The development of electrospinning has progressed from the fundamental understanding of electrohydrodynamic jet formation to sophisticated, scalable, and digitally

controlled nanofiber manufacturing platforms. The major technological milestones are summarized in TABLE 1. Principles forming a foundation for electrospinning emerged from Taylor's discovery of the Taylor cone which exhibited the deformation of a liquid droplet due to an electric field[4]. Interest in electrospinning re-emerged in the 1990s and with growing recognition of the potentials of generating continuous, large surface area, morphology-controlled nanofibers. New techniques emerged over the 2000s-such as coaxial electrospinning, electrospinning, aligned electrospinning, dual nozzle electrospinning and needle-less electrospinning-that built on the established principles. Electrospinning can produce fibers on demand at a range of scales using roll-to-roll procedures and alternative large-scale electrospinning technology within the last decade[5]. A range of disciplines including artificial intelligence (AI), process analytic technologies (PAT) automated control, 3-D structuring and the manufacture of high precision electro-spinning solutions, enable efficient process replication and controllable structuring, enabling the device to turn a room sized set of equipment into an electrospinning fiber-based tool kit for multiple disciplines[6].

Table 1. Historical evolution of electrospinning technology

year	Major milestone	Key significance
1960s	Taylor cone	Fundamental electrohydrodynamic concept[7]
1990s	Nanofiber development	Establishment of electrospinning for nanoscale fibers[8]
2000s	Coaxial, aligned & needleless systems	Greater control of architecture and productivity[9]
2010s	Roll-to-roll production	Scale-up and continuous manufacturing[10]
2020s	AI, PAT, 3D & smart systems	Intelligent optimization and precision manufacturing[11]

3. PRINCIPLES AND MECHANISM OF ELECTROSPINNING

3.1 Basic Components

3.1.1. High Voltage Power Supply

High voltage power supply is an important part of electrospinning setup. It generates an electrostatic potential difference of 5-30kV between the spinneret and the collector. Such potential difference leads to deformation of the droplet generated at the needle tip as a result of electrostatic repulsion[12]. Eventually a Taylor cone is formed and a charged jet of polymer melts or solution extrudes out toward to the collector and eventually solidifies by either loss of solvent (melts) into fibers. Applied voltage level play a very important role in jet emission, jet diameter, beading and Fiber morphology[13].

3.1.2. Syringe Pump

The syringe pump guarantees the controlled and continuous pumping of the polymer solution/melt into the spinneret with a fixed flow rate. A steady flow rate is necessary to provide an unvarying Taylor cone and a

continuous jet. If the flow rate is excessively high, then bead formation, insufficient solvent removal, and large fiber diameter can occur. If the flow rate is too small, then the jetting process can be interrupted. The flow rate typically varies between 0.1 to 5 mL h[14]

3.1.3. Spinneret

Spinneret is the part through which the polymer solution is fed into the electric field. Normally, it is made up of a stainless-steel needle that is attached to the high voltage power source and syringe. The geometry of the spinneret including the diameter, length, and shape influences the properties of the nanofibers formed during electrospinning. In order to achieve the desired fiber structure, there are various types of spinnerets such as non-axial, coaxial, tri-axial, multi-jet, and needleless spinnerets[15].

3.1.4 Collector

The collector is the grounded or oppositely charged electrode which collects the charged polymer jet and helps in the formation of fibers. Solvent evaporation or solidification of the polymer takes place during the movement of the jet between the spinneret and the

collector, and the resulting solid nanofibers are formed. There are different types of collectors which affect the alignment of fibers. The random alignment of nanofibers takes place with the help of a stationary flat collector, while aligned fibers are formed using a rotating collector. There are some specialized collectors including parallel electrode, wire collector, and patterned collector[16].

3.2 Electrospinning Process

Electrospinning is being electrohydrodynamic method which fabricated the ultrafine fibers from polymer solution/melt by means of electric field with high voltage. These procedures comprise of five basic steps of: Taylor cone formation, jet ejection, jet whipping instability, solvent evaporation and fibre deposition[17].

3.2.1 Taylor Cone Formation

The first stage of electrospinning is the formation of a Taylor cone. A strong electric voltage between the spinneret and grounded collector forces positive or negative charge to accumulate on the surface of the polymer solution dropped at the tip of the spinneret needle. Electrostatic pressure develops with time, until the electrostatic repulsion force begins to outweigh the effect of the surface tension of the solution[18]. When the electrostatic force is found to be equal or stronger than the surface tension, a pointed conic fluid drops are formed, named Taylor cone, which is formed with semi-vertical angle of 49.3 degrees. The Stability condition and parameters are the electrical conductivity, viscosity, surface tension, polymer concentration and applied voltage[19].

3.2.2 Jet Initiation

The process of jet initiation starts when the electrostatic forces due to the applied electric field overcome the surface tension forces present on the Taylor cone. The result is the formation of a small jet of charged liquid that shoots out of the apex of the Taylor cone towards the grounded collector. In the early stages of jet initiation, the jet is observed to follow a straight line, and the major cause of jet stretching is the electrostatic repulsion forces among the charges present on the surface of the jet. Solvent evaporation begins during this period as well as

alignment of the polymer chain along the electric field[20].

3.2.3 Whipping Instability

When the charged jet is propagating away from the end of the needle, it experiences an effect called whipping instability. This instability is caused by the interaction between like charges on the jet's surface. Thus, the initially straight jet starts bending, whipping, and spiraling in the air. This leads to significant elongation of the travel path of the jet and stretching of the polymer chain. Such large-scale elongation significantly decreases the diameter of the fibers down to the nano meter range while providing molecular orientation in the fibers. Despite the fact that the whipping instability causes the production of ultrafine fibers, over-whipping can result in bead formation or fiber breakage[21].

3.2.4 Evaporation of Solvent

The solvent present in the polymer jet constantly evaporates while the polymer jet flies from the spinneret towards the collector due to the extensive surface area and stretching of the polymer jet. As the solvent molecules diffuse into the atmosphere, the polymer concentration in the jet increases and leads to solidification of the polymer jet into continuous nanofibers. The solvent evaporation rate depends on solvent volatility, ambient temperature, humidity, airflow rate, and the distance between the spinneret and the collector. Solvent evaporation needs to be complete for the production of dry and mechanically stable fibers. Otherwise, flattening of the fibers, fusion of fiber intersections, porosity, or solvent entrapment may occur[22].

3.2.5 Fiber Deposition

The deposition of the fibers is the last step of the electrospinning process when the fully polymerized fibers are collected by using a grounded collector. Fiber deposition can be either random or aligned according to the structure of the collector used. Fibers deposited on flat stationary collectors tend to form randomly oriented nonwoven nanofiber mats, while rotating drum collectors, parallel electrodes, and structured collectors are used to form well-aligned fibers. The structure of the fibers affects their strength, porosity, surface area, and functionality[23].

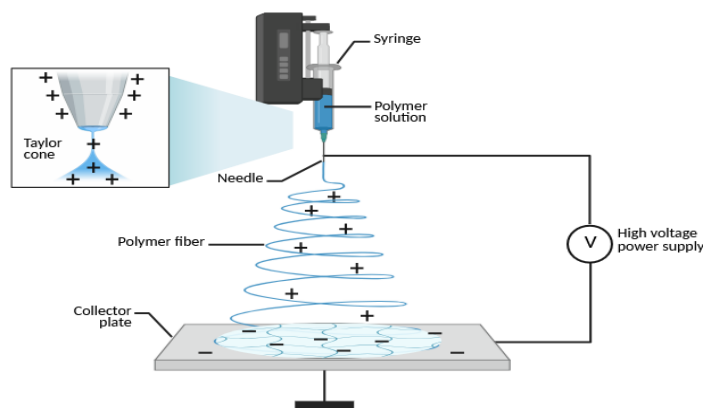


Figure 1: Schematic Representation of Electrospinning Mechanism[24]

4. FACTORS AFFECTING ELECTROSPINNING

4.1 Solution Parameters

Some parameters of the solution were among the most important parameters for electrospinning because they strongly effect on shape, size and homogeneity of the electro spin nanofibers[25].

4.1.1 Polymer Concentration

One important electrospinning process parameter is the concentration of polymer. This is because the viscosity of the solution and entanglements of molecular chain are strongly dependent on polymer concentration and both of these can affect the nanofiber morphology. For low polymer concentrations, there is lack of chain entanglements in the solution causing electrospray and formation of droplets or bead-on-string shapes, instead of continuous fibers[26]. At the optimal concentration, good chain entanglements and appropriate viscosity will give uniform and smooth nanofiber morphology without any defect. For high polymer concentrations, high solution viscosity can obstruct solution flow, forming thick fibers, plugging needle, and creating an unstable jet to produce fibers of abnormal morphology[27].

4.1.2 Molecular Mass

The molecular mass of the polymer dictates the amount of chain entanglements and also controls the electrospinning jet stability. If you have a low molecular mass, you will likely have beads or broken fibers due to poor inter-chain interactions. A high molecular mass, and you get good chain entanglements so that jet stability is reached and nanofibers will form. Polymers of very high molecular mass will have a high solution viscosity[28].

4.1.3 Viscosity

Viscosity is a measure of the resistance of the polymer solution to flow, and it has close correlation with polymer concentration and molecular weight. Viscosity is one of the key parameters that determine whether an electrospinning jet can exist or not. Solutions with low viscosities form beads since the electrostatic forces dominate over cohesive forces. Higher viscosity causes formation of fibers due to better chain entanglements, while too high viscosity could inhibit jet elongation and cause needle clogging[29].

4.1.4 Conductivity

The general electrical charge on the electrospinning jet is controlled by the electrical conductivity of the liquid solution. Increased electrical conductivity results in greater charge density on the jet, giving increased electrostatic repulsion forces and, consequently greater stretching of the jet producing fibres with smaller diameter. The conductivity can be increased by adding salts, an ionic surfactant, or a conductive polymer[30].

4.1.5 Surface Tension

Surface tension is the cohesive force at the surface of the polymer solution. For electrospinning process, the electric field should exceed the surface tension for the creation of the unique Taylor cone and production of jets. High

surface tension prevents jet formation but favors beads formation, while low surface tension allows jet formation. The surface tension is manipulated by selecting appropriate solvent and/or addition of surfactant to the polymer solution[31].

4.2 Process Parameters

4.2.1 Applied Voltage

The electrospinning process is initiated by an applied voltage. An electrostatic charge generated at the needle tip is produced by using a high electrical potential between the tip of the spinneret and the collector. When the electrostatic charge on the tip of the needle exceeds the surface tension of the solution, a stable Taylor cone is formed and a charged polymer jet is ejected from the tip of the cone[32]. It is necessary to apply an optimal voltage level in order to achieve the desired effect and produce uniform nanofibers without beading. Too low a voltage leads to insufficient charge accumulation on the needle tip thus causing formation of the droplet, whereas too high a voltage causes the instability of the jet, hence whipping, beading, branching and non-uniformity in fiber diameter may arise[33].

4.2.2 Flow Rate

Flow rate is the rate at which the polymer solution is delivered from the syringe to the spinneret. It directly affects jet formation, solvent evaporation, and fiber morphology. Low flow rate is used because a small flow rate helps complete evaporation of solvent, which leads to a formation of smooth and uniform continuous nanofibers with small diameters. High flow rate provides a larger quantity of solutions, but solvent cannot complete evaporating under such conditions; as a result, beads and ribbon-like structures with larger diameters and inter fiber overlay phenomenon appear[34].

4.2.3 Effect of distance between needle and collector

The distance between the needle tip (spinneret) and collector affect the flight time, elongation and evaporation of solvent from the solution. With small distance incomplete solvent evaporation, leads to form wet, beaded and collapsed as well as bound fibre. At long distance the electric field is not so potent to stretching and consequently breaking of fibres. The optimum distance of needle and collector favour optimum nanofiber formation[35].

4.3 Environmental Parameters

4.3.1 Temperature

It controls viscosity of the solution, surface tension and solvent evaporation rate, which play important role in stretching of jet, formation of fibers and their solidifications, surface roughness, porosity. Increasing the temperature reduces viscosity and surface tension. Low viscosity is favorable for extending of the jet into thin filaments and in formation of thin fibers and their solidification with higher rate by faster evaporation of the solvent at a high temperature. But excessively high temperature may induce premature evaporation of solvent

near the tip of the needle, causes clogging of the needle. An optimum range of 20-30°C is preferred[36].

4.3.2 Humidity

The humidity of the surrounding medium during electrospinning is an important environment factor especially if we are using volatile and/or hydrophilic solvent. The solvent evaporation rate and fiber formation are dependent on humidity. When humidity is low, solvent evaporation speed is fast, this can result in fiber without bead, uniform and dry fiber[37]. However, under certain range of humidity (medium humidity, such as ~50-60%) can lead to the separation of phases which could enhance the surface porosity of the fiber (such as, for the applications in tissue engineering and drug delivery) But the speed of solvent evaporation is slower in high humidity, then fiber can become wet and form ribbon

structure, ribbon or bead can occur due to the inadequate dryness. The relative humidity around 30-50% would be suitable to provide the steady jet and uniform nanofiber[38].

4.3.3 Air Flow

Airflow within the electrospinning chamber plays an important role in solvent evaporation, Taylor cone stability, and fibre deposition. Appropriate airflow can help with complete evaporation of the solvent, stabilized Taylor cone, and rapid solidification of fibers. The polymer jet is easily perturbed by a very high airflow velocity resulting in random distribution of the fibers in the collector with variability in diameter and alignment. Too low airflow will result in incomplete removal of the solvent leading to fused fibers or flattening of fibers on the collector[39].

Morphological Feature	Parameters
Bead Formation	Low polymer concentration, low viscosity, high surface tension, high flow rate[40]
Smooth Continuous Fibers	Optimum concentration, viscosity, voltage, flow rate, humidity, and temperature[41]
Thick Fibers	High polymer concentration, high viscosity, low conductivity, large needle diameter[42]
Fine Fibers	High conductivity, optimum voltage, moderate temperature, controlled flow rate[43]
Ribbon-like Fibers	High humidity and incomplete solvent evaporation[44]
Porous Fibers	Moderate to high humidity with volatile solvents (phase separation)[45]
Fiber Fusion	High flow rate, short tip-to-collector distance, incomplete solvent evaporation[46]
Aligned Fibers	High-speed rotating collector[47]
Random Fiber Mats	Static or low-speed collector[48]
Branched/Split Fibers	Excessively high voltage or very high solution conductivity[49]

5. MATERIAL-DRIVEN DESIGN STRATEGIES FOR FUNCTIONAL ELECTROSPIN NANOFIBERS

5.1 Polymer Nanofibers

The most extensively used materials for electrospinning are polymers, because of their variable composition which is accessible by appropriate polymer-solvent pairing, thus giving the possibility of using a multitude of NFs. The NFs fabricated by the technique of electrospinning exhibit consistent fibre diameter and high aspect ratio which leads to homogeneous structural and macroscopically scalable materials. Their mechanical property can be regulated by varying conditions of polymer concentration and solution viscosity as well as voltage, flow rate, tip to substrate distance and collection procedure[50]. Porous NFs can be obtained from either phase separation process or after treatment as in this study providing high surface for efficient interfacial interactions. Coaxial electrospinning of NFs produces materials with core shell structures containing more than one kind of functional materials into a single fibre and hollow NFs, obtained by utilizing templates of sacrificial materials or dual solvent systems provides light weighted structures with unique transport behaviours. After-spinning processing like chemical and

physical crosslinking leads to improved mechanical and thermal and chemical stability. Blends of polymers and NFs filled with nanoparticle exhibit synergic effects from the combining components to increase performance and functionality[51].

5.2 Metal oxides and composite nanofibers

The metal oxide nanofibers by electrospinning coupled with calcination technique are received considerable attention due to its high stability with thermal and chemical and control on the structure and composition. A significant technique to prepare the metal oxide nanofibers using desired metals through controlled process parameters, combined with a thermal treatment procedure is electrospinning method. During conventional electrospinning procedure, metallic precursors such as, metal alkoxides and metal salts are dispersed in a polymer solution and subsequently electrospun to provide continuous polymeric nanofibers. Under subsequent high temperature treatment, the polymer matrix is degraded via pyrolysis and accordingly metal oxide nanofibers are achieved as the desired morphology and porosities[52]. These variations in the crystallinity, specific surface area and structural stability of metal oxides can be achieved by varying the compositions of precursors, solution condition

and calcination condition. For the case of the preparation of composite metal oxide NFs, the pre-prepared metal nanoparticles (NPs) and metal precursors are added to the electrospinning solution so that interfaces can be formed between oxide and these metal in the matrix. During calcination process, the polymer matrix will be decomposed; Meanwhile the metal precursors will be decomposed into nanoparticles and can be uniformly dispersed in the metal oxide NF matrices. Essentially, this method uses the inherent versatility of electrospinning in loading various materials to control phase distributions in the NFs[53].

5.3 Carbon Nanofibers (CNFs)

During production the electrospinning of precursors followed by carbonization, leading to CNFs, the structure and adjustable character give numerous advantages. Initially the producing of CNFs follows electrospinning procedure of suitable polymers generally the preferred material is polyacrylonitrile (PAN) because of its higher content and uniform morphology after electrospinning[54]. After obtaining that, high aspect ratio NFs can form nonwoven mats usable as precursors. The most popular two-stage transformation from PAN NFs by thermal treatment of the CNFs has two stages: stabilization of polymer (by carrying out 200-500 °C and under oxygenated atmosphere) in order to improve mechanical characteristics and make chemical changes, and carbonization carried out from 600 to 3000 °C under an inert gas[55].

5.4 Nanotubes

The electrospin nanotubes are structural analogues of common electrospin nanofibers, with tubular hollow interiors instead of a solid core. This novel architecture features increased specific surface area, lower density, higher porosity, improved mass transfer property, which make it suitable for diverse application fields including biomedical, pharmaceutical, environment and energy. The internal hollow lumen can be considered as an internal container which could be employed to store drugs, biomolecules and nanoparticles and achieve high loading capacity, controlled drug release compared to solid nanofibers. Many strategies were designed to synthesize electrospin nanotubes. Coaxial electrospinning is the most common strategy; which uses a pair of concentric nozzles for fabricating core-shell fibers, followed by the etching out of the core to yield hollow nanotubes of the desired inner diameter and thickness of the wall[56]. Emulsion electrospinning is a method that yields hollow nanostructures via phase separation due to the solvent evaporation using single nozzle. Hollow nanotubes were formed using templates with sacrificial templates that are dissolved after the formation of electrospin membranes with hollow interiors and by the extraction of one polymer phase in blended fibers. Besides, preformed fiber is chemically or thermally converted to carbon or ceramic nanotube with great mechanical, electrical, and thermal stability. Compared with electrospin nanofibers (1, 2), electrospin nanotubes exhibit several beneficial features:

Hollow structures significantly enlarge drug-loading capability and prolong/stimulus-responsive drug release rates. High specific surface area is beneficial for cell adherence, protein immobilization, absorption and catalysis activities; porosities can also ensure fast mass transport; Wall thickness control results in tuning of mechanical property and release rates[57]. With this regard, electrospin nanotubes have shown great promise for targeted or controlled drug delivery and tissue engineering. The hollow lumen of electrospin nanotubes can act as an internal space to accommodate co-delivered hydrophilic and hydrophobic therapeutic agents (drugs, nanoparticles, growth factors, imaging agents) for sequential or combined therapy. Porous structure can enhance cell infiltration, vascularization and tissue integration, making it promising in regenerative medicine and personal medicine[58].

5.5 Nano shell

Electrospin nanofibers incorporating nano shells are another example of a functional architecture in which the increased surface area and porosity of nanofibers are combined with special optical, magnetic, and therapeutic characteristics of nano shells. Nano shells are core-shell nanoparticles made up of a core material, which is usually dielectric or polymeric, coated by metallic shells like gold or silica. These particles can be applied to the surface of electrospin fibers or incorporated into them to impart multiple functions. These particles are attached to the surface of fibers either via surface functionalization or incorporation of the particles in the polymeric matrix through electrospinning. Functionalization of the fibers with targeting ligands, antibodies, peptides, or stimuli responsive polymers increases the specificity of the nanofiber scaffold[59]. In response to various external stimuli such as near infrared (NIR) light, magnetic fields, ultrasound, or pH, these nanofiber architectures can release drugs or generate heat at tumour site for therapeutic purposes. The functional design starts with the manufacturing of the nanofiber scaffold via electrospinning technique that gives a highly porous structure and high surface area for drug delivery and cell interaction[60]. Nano shells made of gold, silica, or any other material are introduced to or onto the nanofibers to make them multifunctional by giving the ability of drug delivery, imaging, and phototherapy. Then the nano shells on nanofibers are functionalized with certain biomolecules such as targeting ligands, antibodies, etc., to ensure high selectivity of the drug delivery. When the system is delivered to the targeted site in the body, it responds to the external stimuli, such as near-infrared (NIR) light, pH change, or magnetic field, that activates the nano shells inside the nanofibers. As a consequence of this, the controlled release of drugs occurs, and, if it is gold nano shells, photothermal effect will be provided. Thus, the targeted drug delivery and responsive therapy together provide the targeted treatment and effective tissue regeneration[61].

5.6 Nanocrystals

Incorporation of drug nanocrystals (NCs) in electrospin nanofibers is an innovative approach for the fabrication of nanofibrous structures with improved pharmaceutical properties. Drug nanocrystals are highly pure crystalline drug particles having sizes between 10-1000 nm, stabilized with surfactants or polymers. The combination of drug nanocrystals and electro spin nanofibers offers the advantages of both drug nanocrystals (high loading capacity) and electro spin fibres (large surface area and porosity). The electrospinning of nanocrystals-loaded nanofibers has been introduced in order to improve the solubility of many drugs that belong to the BCS Class II and IV due to their low solubility[62]. The nanofibrous system is used in order to inhibit aggregation of nanocrystals and increase physical stability of nanocrystals as well as for controlled or immediate drug release depending on selected polymers. Hydrophilic polymers such as PVP, PVA, PEO, and HPMC have been widely used in order to prepare nanocrystal-loaded fibers using electrospinning. The structural design of these hybrid materials can be developed using different types of fibers such as monolith nanofibers, core-shell nanofibers, multi-layered nanofibers, and aligned nanofibers. It should be noted that the core-shell electrospinning technology provides a number of advantages as nanocrystals are protected from the external environment in the core and drug release is controlled by the shell. The surface modification of nanocrystals can increase mucoadhesive properties and cell uptake[63]. Electro spin nanofiber-nanocrystal composites have shown significant potential in the fields of oral drug delivery, buccal films, transdermal patches, wound dressings, ocular implants. The combination of electro spin nanofibers with nanocrystals not only increases dissolution rates and bioavailability but also improves the stability and effectiveness of drugs while retaining the scalability of the production process. Therefore, this dual system has proved to be an innovative delivery method[64].

6. TYPES OF ELECTROSPINNING TECHNIQUES

6.1 Blend Electrospinning

Combined electrospinning is considered the simplest and most commonly used electrospinning method that is used for producing functional nanofibers. In combined electrospinning, at least two types of polymers or one type of polymer along with some bioactive compounds like drugs, nanoparticles, proteins, and nanocrystals are mixed together in the same solvent system to produce a homogeneous solution. The spinning of such a solution under an electrical field results in the production of continuous nanofibers containing all these components in a uniform fashion in their matrices. The composition of the blend has a considerable effect on the physicochemical characteristics of the produced nanofibers, such as the fiber size, morphology, mechanical properties, porosity, wetting, biodegradability, and drug release mechanism[65]. The combination electrospinning technology has special significance for loading drugs into nanofibers due to the following reasons. It is widely used

in the fields of pharmacy and biomedicine in applications such as wound healing, tissue engineering, regenerative medicine, antimicrobial bandages, cancer treatment, and drug delivery systems. However, for successful production, the blending of the materials and solvent selection are crucial. If the materials do not blend well or if there is phase separation in spinning, then beads or uneven fibers can be produced[66].

6.2 Coaxial Electrospinning

The process of two or more polymer solutions simultaneously electrospin to fabricate multi-functional nano-fibers known as co-electrospinning technique. There are various configuration in co-electrospinning like coaxial electrospinning, side-by-side electrospinning, dual-nozzle electrospinning. The co-electrospinning can fabricate the nano-fibers that comprises of multi-polymers and combines different properties in single fiber. Co-axial electrospinning process using two concentrically arranged double capillaries produces core-shell nano-fibers where core solution is fed by inner nozzle and shell solution by the outer nozzle[67]. Due to the presence of electric field at higher potential the compound Taylor cones of the two solutions were produced and stretched to form continuous core-shell fibers. The advantage of using core-shell structure lies in the spatial arrangement of the materials in order to design drug delivery or protection of biological agents for the sustained release. Side-by-side electrospinning is a special case of co-electrospinning used to fabricate Janus nano-fibers, when two immiscible polymer solutions are fed through two adjacent nozzles or capillaries[68]. Janus fibers are different from the core-shell fiber where the two polymers will be laterally separated since they have a different surface tension or the electrical force, and will have different compartment on single fiber. Janus nano-fibers are capable to exhibit dual functionalities like dual response sensors, filters, tissue regeneration, drug delivery systems, etc[69].

6.3 Emulsion electrospinning

The process of emulsion electrospinning, compared with others electrospinning techniques, is more complex. The water in oil (W/O) emulsions for encapsulation of hydrophilic drugs and oil in water (O/W) for encapsulating of hydrophobic chemicals are employed, so this technique leads to production of the core shell fibers. The mechanism of emulsion electrospinning depends upon the choice of solvent for the production of electrospun nanofibers[70]. Droplets of another polymer which cannot be dissolved in the solvent of dispersed phase, is within an emulsion, this happened at polar-nonpolar interface. A low molecular weight drug, will readily diffuse through the nanofibrous material, or the core-sheath fibrous system. The difference in emulsion and blending electrospinning is there is not a common solvent, because either the polymer or drug must dissolve in a given solvent[71]. Hence, a variety of hydrophilic drugs are easily loaded with a hydrophobic polymer, and there is no deleterious organic solvent effect on the electrospinning process. A number of polymeric systems can be incorporated into emulsion

electrospinning procedures, these include natural polymeric systems such as those which are protein- and polysaccharide-based, and synthetic polymers such as PVA, PEO, PCL[72].

6.4 Melt Electrospinning

It is a solvent-free electrospinning technique that allows for production of micro and sub-micron-diameter fibers which are greatly applicable for tissue engineering and biomedical use. This technique makes use of melts of the polymer to obtain fibers whereas, solution electrospinning involves polymers dissolved in a solution, so as to avert all solvent related issues and toxins, affecting the environment. Higher viscosity of the polymers used allows generation of stable jet and hence Fibers are fabricated using melt electrospinning writing (MEW). This technique facilitates the formation of scaffolds with precisely controlled architecture, porosity, thickness and geometry on layer-by-layer basis. With interconnected porosity, cell attachment, proliferation, and formation of matrix occur in a scaffold produced using MEW technology, which eventually leads to cell infiltration[73]. Processing temperature of the melt solution, voltage applied, flow rate, distance between the spinneret and collector, and speed of the collector dictate the fiber diameters and morphology. Fabrication of ordered fibrous structures with enhanced mechanical properties depends on a proper control of the processing variables. Melt electrospinning has proven to be a versatile technique that has been extensively explored for a number of applications in tissue engineering, regenerative medicine, biomedical engineering, filtration and additive manufacturing. Most applications are focused on processing biodegradable thermoplastic polymers like polycaprolactone (PCL), polylactic acid (PLA), polyethylene oxide (PEO), and polyethylene (PE)[74]

6.5 Aligned Electrospinning

Aligned electrospin nanofibers are really good because they let us control the direction of the fibers the way the pores are arranged and some other special properties. We can also pack the fibers together tightly. The usual ways of aligning fibers need tools or outside forces.. A new method is simpler and can be used on a large scale. It works by controlling the field near the nozzle where the fibers come out. We put two blocks that do not conduct electricity between the nozzle and the collector. This changes the way the electric field is distributed. It makes the fibers move in a two- wave instead of a three-dimensional spiral. This gives us fibers that are all aligned in the direction. We used computer simulations to check if this method works. It does. We can also rotate the collector to make fibers that cross each other or form a rhombus shape[75]. This method can make pieces of aligned nanofiber membranes. They are stronger have pores that're all the same size and are more porous than membranes with randomly arranged fibers. The cross-aligned membranes are more stable. They still have pores that are connected and evenly distributed. This makes it easier for things to move through them. All these good things about nanofiber membranes make them

perfect for things like energy storage, filters and special materials. They are also more durable and work better for tasks. Aligned electrospin nanofibers are very useful, for things because of their special properties and controlled pore architecture[76].

6.6 Yarn Electrospinning

Compared with electrospin two-dimensional (2D) nanofiber mats, electrospin nanofiber (NF) yarns provide a one-dimensional (1D) fibrous structure that enhances mechanical properties, mechanical stability, and flexibility. More importantly, electrospin NF yarns are compatible with the knitting and weaving of conventional textile fabrication and are useful

for smart textiles, wearable electronics, biomedical textiles and other functional applications. The yarns retain the high surface area and the breathability that are similar to conventional electrospin nanofibers while being more capable of processing and strength. There have been several electrospinning techniques for the fabrication of NF yarns[77]. Stable yarn electrospinning is performed by spinning and then twisting electrospinning aligned nanofibers into continuous yarns. Water bath electrospinning involves collecting electrospinning nanofibers on a liquid surface in which flow direction aligns nanofibers to form yarn structures. However, neither of these techniques leads to enhanced mechanical strength and compatibility with various polymer systems, and the fibers often result in poor alignment, random twisting and insufficient strength. Continuous conjugated yarn electrospinning was developed, in which oppositely charged nozzles produce electrospinning jets which are directed toward a central core fiber on a cone shaped rotating collector. This method creates alignment and twisting of the electrospinning nanofibers around the core fiber, which results in a continuous yarn with improved orientation, tensile strength and structural integrity[78]. Fiber alignment, twisting, and uniform winding can also be improved using a rotating collector. Some challenges in this technique, including alignment consistency, twist control, the high rate of production, and scale up of manufacture need to be overcome. It is expected that improvements of electrospinning machines, collector design and process automation would bring about a mass production and various applications of electrospinning NF yarns in the textile and biomedical industry[79].

6.7 Roll-to-Roll Electrospinning

The innovative concept is about how Roll-to-Roll electrospinning will solve the production throughput limitation issue raised in the classical single needle electrospinning. For classical electrospinning, on a static collector the fibers can be collected forming the membrane with limited size. For Roll-to-Roll Electrospinning production fibers and collector motion are integrated, enabling continuous deposition over larger areas and sizes. In such technique, a solution/melt is continually supplied from one or more nozzles, while simultaneously, a moving substrate travels in the direction of electrospinning, guided with one or other types of collectors such as a rotating

drum, belt or even alternatively by placing numerous collectors along the electrospinning path[80]. High voltage makes possible the deformation of solution forming a Taylor cone, subsequent jet stretches out into nanofibers. Among all the great advantages Roll-to-Roll electrospinning process offers, the production speed and controllable large-scale uniform nanofiber membrane production capability with fixed fiber morphology and

thickness appear to be the most significant benefits. Key parameters for fine-tuning fiber diameter, porosity, alignment, and membrane thickness-such as applied voltage, concentration of polymer solution, solution flow rate, speed of collector rotation, distance between spinneret and collector and external environment condition can be systematically varied[81].

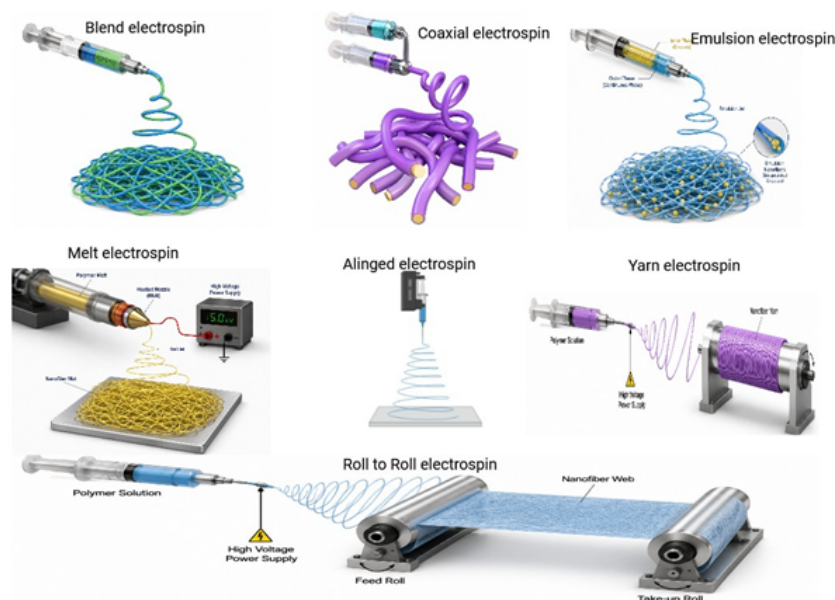


Figure 2: Schematic illustrations of coelectrospinning and corresponding NF membranes: a) Blend Electrospin b) Coaxial Electrospin c) Emulsion Electrospin d) Melt Electrospin e) Aligned Electrospin f) Yarn Electrospin g) Roll to roll electrospin[82]

7. CHARACTERIZATION OF ELECTROSPIN NANOFIBERS

7.1 Scanning Electron Microscopy

Scanning electron microscopy is the method that is most frequently employed to analyse the morphology of electrospun nanofibers. In SEM images it is possible to evaluate the fiber diameter, their surface morphology, pore size distribution and fiber alignment and whether they are defective or agglomerated. SEM is important to evaluate effects of electrospinning on the fiber's morphology. Specimens require conductivity, therefore must be coated, usually with platinum or gold, prior to viewing[83].

7.2 Transmission Electron Microscopy

Transmission Electron Microscopy technique is used to study the internal structure and ultrastructure of electrospun nanofibers in nanometer scale resolution. TEM gives valuable information about core shell structure, hollow structure, particle loading and distribution of additives in the nanofibers. TEM analysis is very helpful to characterize the composite and coaxial electrospin nanofibers because of their internal morphology that has significant influence on drug release and mechanical strength properties[84].

7.3 Atomic Force Microscopy:

Atomic force microscopy is an advanced method for characterizing surfaces, enabling the formation of 3D

images of electrospin nanofibers with nanometer accuracy. This microscopy technology differs from electron microscopy in that it does not need electrical conductivity and can perform studies at room temperature. AFM enables researchers to obtain data about roughness, fiber height, mechanical properties, adhesion forces, and stiffness. Atomic force microscopy is commonly used to study nanofibers, since their properties largely determine cell adherence, proliferation, and release of medications[85].

8. STRUCTURAL CHARACTERIZATION

8.1 X-Ray Diffraction (XRD)

X-ray diffraction (XRD) is a commonly employed technique in the characterization of the crystalline structure of electrospin nanofibers. XRD offers data regarding the crystal structure, composition of the phases, degree of crystallinity and crystal size of the fiber. In XRD, x-rays get diffracted by atomic planes of the sample according to Bragg's law. Well-defined diffraction peaks imply a crystalline nature of the structure while less defined peaks reflect the amorphous state. XRD is especially beneficial in confirming the presence of nanoparticles or crystalline drugs in electrospin nanofibers and structural change following heating and other post-treatments[86].

8.2 Raman Spectroscopy

Raman spectroscopy is an analytical technique employed for characterizing molecular structure, bonding, and structural defects of electrospun nanofibers. Raman scattering occurs when the laser photon interact and inelastic scattering produce characteristic vibrational modes of the molecule. Thus, information with regards to the functional groups, interactions between chains and/or graphene sheets or carbon nanomaterials like carbon nanotubes. A typical Raman spectrum of carbon nanofibers that shows characteristics D and G bands were obtained with this method and structural defects & the degree of graphitization can be studied[87].

8.3 Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared (FTIR) spectroscopy is frequently used for the determination of the chemical composition and functional groups within electrospun nanofibers. This method involves the measurement of infrared radiation absorbed by molecular bonds which result in the formation of spectra representing different chemical functionalities. The method can be used to determine the polymer composition, successful drug, nanoparticles, or bioactive molecules incorporation, and intermolecular interactions such as hydrogen bonding. The method is also used for the identification of changes that may occur in the course of electrospinning process, crosslinking, or surface modification. These changes include shifts in peaks position and/or intensity or appearance of new absorption bands which indicate the presence of molecular interactions and structural changes[88].

9. THERMAL CHARACTERISTICS

9.1 Differential Scanning Calorimetry

Differential Scanning Calorimetry is one of the most common thermodynamic methods employed in thermal properties analyses of electrospun nanofibers. The principle of DSC is to detect the heat flow variation caused by physical, as well as chemical transformations of a nanofiber sample during the heating procedure. The method is often used for assessment of various thermal properties such as the glass transition temperature, melting temperature, crystallization of amorphous and semicrystalline polymeric materials, and thermal stability. With DSC, the influence of electrospinning on the degree of crystallization in a polymer, and, subsequently, on the relationship and interaction between the polymers, drugs, and other additives in nanofibers may be also evaluated[89].

9.2 Thermogravimetric Analysis

Thermogravimetric analysis is one of the most important thermal analysis techniques employed for the characterization of electrospun nanofibers with respect to their thermal stability and decomposition process. TGA is a technique where weight loss is recorded of nanofibers as the temperature is increased in a controlled environment such as nitrogen or air. Information about moisture content, solvent content, degradation temperature, and overall thermal stability of nanofibers can be derived from

TGA. For electrospun nanofibers, the main role of TGA is that it allows assessment of the effect of additives, drugs, nanoparticles, or fillers on the thermal stability of electrospun nanofibers. Weight loss onset and rates give information about the decomposition process of nanofibers and material purity[90].

10. SURFACE CHARACTERIZATION

10.1 Contact angle

Contact angle, which is a crucial parameter used to determine the wettability of electrospun nanofiber, could generally be measured by applying a water drop on to electrospun nanofiber and measuring the angle created by the droplet and the substrate. A contact angle of $<90^\circ$ corresponds to the hydrophilicity, whereas an angle $>90^\circ$ signifies hydrophobicity. The wetting ability will significantly affect the cellular adsorption on the substrate, or even influence the protein adsorption and drug loading within/on to the substrate[91].

10.2 Surface Roughness

Surface roughness is the term that describes the irregularity and topological variations present in the surface of electrospun nanofibers. This feature is typically assessed through techniques such as Atomic Force Microscopy, Optical Profilometry and Scanning Electron Microscopy. Surface roughness in nanofibers is influenced by several variables including polymer concentration, speed of solvent evaporation, electrospinning parameters and the diameter of the fibers. A high degree of surface roughness may be advantageous when there is a requirement for increased surface area for protein adsorption, cell attachment and catalysis. In contrast, it may be desirable to minimise surface roughness in applications such as when control of fluid flow and minimal friction are important[92].

10.3 Zeta Potential

Zeta potential is the electrical potential at the slipping plane of a colloidal particle suspended in a liquid. It measures the magnitude of electrostatic repulsion or attraction between particles and is a key indicator of suspension stability. Zeta potential is normally

measured through electro kinetics and streaming potential measurements. High zeta potential values, either positive or negative, represent better stability of surface charges, whereas low zeta potentials, near zero, suggest that the particles can aggregate easily. The charge present on the surface determines the interaction with proteins, cells, microorganisms, and other charged drugs. The significance of zeta potential in electrospun nanofibers is that it affects drug loading, antimicrobial properties, tissue engineering, biosensing, and target drug delivery systems[93].

11. DRUG LOADING AND ENTRAPMENT EFFICIENCY

11.1 Drug Loading

Drug loading is defined as the amount of active ingredient that is incorporated in the nanofiber matrix with respect to the weight of nanofibers used. This is an important factor which dictates the dose capability of the drug delivery system based on nanofibers. The drug loading depends on the following parameters: the ratio of drugs to polymers; the concentration of the polymer used; the drug solubility; type of electrospinning (blend, coaxial or emulsion), and the electrospinning process parameters[94]. High drug loading results in high drug release duration and reduction in the amount of carrier required for effective drug delivery. But very high drug loading can cause drug crystallization, bead formation, poor fiber structure, and burst drug release which affects the performance of the nanofibers. The determination of drug loading can be done by dissolving a certain weight of nanofibers in a specific solvent and then measuring the amount of the drug using UV-visible spectroscopy and HPLC methods[95].

11.2 Entrapment Efficiency

Entrapment efficiency (EE) is the percent amount of the starting drug molecule which is effectively entrapped in the electro spin fibres. EE depends on the suitability of the electrospinning technique in ensuring that the drug is retained inside the polymeric matrix during the fabrication process. It is important that there be high entrapment efficiency since it is an assurance of proper dosing of the drug, reduced drug waste, and continuous drug release. Factors that affect entrapment efficiency include the physiochemical characteristics of the drug and polymer, drug-polymer interaction, solvent system, electrospinning conditions, and environment[96]. The better the compatibility of the drug molecule within the polymer matrix, the higher the efficiency of entrapping the drug. Entrapment efficiency is usually estimated through extraction of the entrapped drug from a specific weight of nanofibers and then comparison of the concentration obtained with the theoretically predicted one. The most common analytical technique used is UV-Visible spectroscopy or HPLC[97].

12. IN VITRO RELEASE STUDIES

To evaluate the characteristics of drug release from nanofiber-based drug delivery systems, *in vitro* studies were performed under controlled experimental conditions. These *in vitro* drug release studies were carried out in order to assess the rate and extent of drug release along with the underlying mechanism of drug release, which could be related to the *in vivo* performance of the drug delivery system. Nanofiber mats were exposed to buffers such as PBS or SBF at $37 \pm 0.5^\circ\text{C}$. Aliquots of the release media were taken at specified intervals, and fresh buffers were added in equal volumes[98]. The cumulative percentage release of the drug was determined at the various time intervals. The release kinetics were determined by analyzing zero-order, first order, Higuchi, Korsmeyer-Peppas, Hixson-Crowell models. There is

usually an initial burst in release if drugs are embedded in an electrospun nanofiber as a result of excess drug that might be physically adsorbed to the fiber surface, following subsequent release governed by diffusional or polymeric degradation mechanism. The nature of the polymers, diameter of nanofibers, drug concentration, porosity of the nanofibers, crosslinking, and nature of the release medium pH, would control the mechanism of release[99].

13. CHARACTERIZATION OF ADVANCED NANOSTRUCTURED SYSTEMS

13.1 Nanotubes

Nanotubes are analyzed in order to find out more about their hollow shape, structure, and functionality. SEM and TEM methods are employed in order to study such properties as fiber diameter, wall thickness, and hollow cavity formation. AFM is used to determine surface roughness. FTIR reveals information about chemical bonds. XRD shows whether the material is crystalline or amorphous. Thermal stability is studied using DSC and TGA techniques, and mechanical analysis studies strength and flexibility[100].

13.2 Nanobots

Nanobots are smart nanomaterials used for site-specific drug delivery and responsive therapy. Properties of electrospin nanobots regarding structure and morphology are determined through SEM and TEM to validate size, shape, and surface modification. Dynamic Light Scattering is often used to measure particle size distribution and colloidal stability. Zeta potential is used for determination of surface charge and interaction potential[101]. FTIR and Raman spectroscopy are used for determination of composition and functional group modification. Electrospin nanobots with magnetic properties must be characterized through Vibrating Sample Magnetometry (VSM) to determine their magnetic response[102].

13.3 Nanoshells

Nanoshells prepared by electrospinning method are characterized by core-shell or hollow-shell types that have the ability to entrap the drug and provide sustained drug release mechanism. SEM and TEM are very important techniques in studying the shell thickness, core-shell configuration, and structural integrity. EDS analysis is very useful in analyzing the elemental composition and confirmation of shell formation[103]. The FTIR spectroscopy studies the interaction of the polymer and the drug and the chemical stability, while XRD analyzes the change in the crystallinity after the entrapment of the drug. Thermal stability and degradation are analyzed using DSC and TGA methods[104].

13.4 Nanocrystals

Drug nanocrystals electrospin are nanometer crystalline particles formed within electrospin fibers to enhance rate of dissolution and bio-availability of the drug. The Nanocrystals are analysed with Scanning electron microscopy, Transmission electron microscopy, atomic force microscopy[105]. Crystal identification was done by

XRD technique. DSC was performed to analyse the process of melting and polymorphic transition. FTIR spectroscopy reveals about the molecular interactions

between drug and the carrier polymer. DLS is performed for determining the particle size. The rate of dissolution is evaluated by the performed dissolution tests[106].

Technique	Information	Application
SEM	Fiber diameter and morphology	Surface analysis[107]
TEM	Internal structure	Core-shell fibers[108]
FTIR	Functional groups	Drug-polymer interactions[109]
DSC	Thermal transitions	Drug crystallinity[110]
XRD	Crystalline nature	Amorphization studies[111]
TGA	Thermal stability	Degradation profile[112]
AFM	Surface topography	Roughness analysis[113]

14. PHARMACEUTICAL APPLICATIONS OF ELECTROSPUN NANOFIBERS

14.1 Oral Drug Delivery

Electrospin nanofibers find extensive application in oral fast dissolving films, gastro-retention dosage forms, and sustained release drug delivery systems. These nanofibers enhance the solubility and bioavailability of water-insoluble drugs by virtue of their large surface area and amorphous nature[114].

14.2 Buccal Drug Delivery

Buccal patches made from nanofibers help in achieving Mucoadhesion, prolonged retention and controlled release of the drug, and hence offer efficient systemic delivery of the drug without undergoing the first pass effect[115].

14.3 Transdermal Drug Delivery

Electrospin nanofibers act as transdermal drug patches with controlled release and improved skin permeation properties. Nanofibers have been studied in applications involving delivery of hormones, anti-inflammatory agents, antimicrobials, and treatment of various chronic diseases[116].

14.4 Ocular Drug Delivery

Ocular inserts and contact lenses have been developed using nanofibers as coatings to provide sustained drug release on the eye surface[117].

14.5 Vaginal drug delivery

Nanofiber materials in the form of vaginal inserts or drug delivery patches are used for local administration of medications with antifungal, antibacterial, antiviral, and contraceptive properties[118].

14.6 Wound Healing systems

The most sophisticated applications are nanofiber wound dressings, which ensure moisture regulation, porosity, antimicrobial action, and release of bioactive molecules that facilitate tissue healing and decrease chances of infection[119].

14.7 Tissue Engineering

As an artificial substitute of the extracellular matrix (ECM), electrospun nanofibers stimulate cell attachment, growth, and differentiation. They are widely used for engineering skin, bone, cartilage, vascular, nerve, and cardiac tissues[120].

14.8 Cancer

Electrospinning nanofibers allow localized chemotherapy and combination therapy with minimal systemic toxicity. Electrospin nanofibers are also studied as a means of preventing cancer recurrences after surgery[121].

14.9 Vaccination

Electrospin nanofibers are increasingly being used as carriers for vaccines, allowing sustained release of antigens and strengthening immune response. They are studied for application in mucosal, transdermal, oral, and heat-stable vaccines[122].

15. RECENT INNOVATIONS IN ELECTROSPINNING

15.1 Smart Nanofibers

The latest research in intelligent electrospin nanofibers emphasizes multifunctional nanofibers which can sense and respond to physiological stimuli. Intelligent nanofibers integrate conductive polymers, nanoparticles, biosensors, and bioactive molecules that facilitate real-time sensing, antimicrobial action, tissue regeneration, and controlled drug delivery. Intelligent nanofibers have demonstrated much promise in wound dressings, wearables, and regenerative medicine[123].

15.2 Stimuli-responsive Systems

The stimuli-responsive electrospin nanofibers are engineered for the controlled release of therapeutics in response to external or internal stimuli like pH, temperature, enzymes, light, magnetic field, ultrasound, and electrical stimulus. The latest trend in the field involves the development of dual-responsive nanofibers that have multiple stimuli for triggering drug release. These systems help achieve high therapeutic efficiency and low side-effects, particularly in cancer treatment and targeted drug delivery[124].

15.3 Core-Shell Nanofibers for Drug Delivery

Core-shell electrospin nanofibers synthesized by means of coaxial electrospinning have been recognized as an effective tool to deliver drugs. In this regard, the shell is used to preserve the sensitivity of the active ingredient, and the core is used as a reservoir of drug-loaded nanoparticles. Modern research is devoted to protein, peptide, nucleic acid, and growth factor encapsulation while maintaining their biological function[125].

15.4 AI-Based Formulation Development

The use of Artificial Intelligence (AI) and Machine Learning (ML) for electrospinning formulation development has become more important lately. It allows predicting compatibility of polymers, processing parameters optimization, and predicting morphology and drug release behaviour of electrospun nanofibers[126]. Optimization of formulations with the help of AI saves time and provides an efficient way to develop formulations according to QbD approach. Recent developments include creation of digital twins and predictive models[127].

15.5 3D Electrospinning

Three-dimensional electrospinning is a relatively new process which addresses some shortcomings of traditional 2D nanofiber meshes by manufacturing spongy and layered constructions. Some latest developments in 3D electrospinning include cryogenic electrospinning, layer by layer deposition, near field electrospinning and electrospinning using 3D-printing[128]. These innovative 3D nanofibrous scaffolds very much resemble the extracellular matrix which makes them ideal for application in the field of tissue engineering, organogenesis, stem cell culture and advanced drug delivery systems[129].

16. CONCLUSION

Electrospinning is a very flexible technique to develop many kinds of functional nanofibers having controllable morphology, composition, and physical and chemical properties of electrospun materials. Being associated with high surface area to volume ratio, porosity and interconnectivity, Mechanical controllability and functional ability of surfaces, the electrospun nanofibers have demonstrated a great promise in the area of drugs delivery and biomedical applications. The following work will review the basic principle of electrospinning, electrospinning of solutions depending on process parameters and variations of electrospinning under special environment together with the current progress made during process developments, including classical single monoaxial method towards coaxially spun (double-, triple-, concentric triple- and co-axially) fibers, emulsion electrospinning, melt electrospinning, aligned nanofibers production, yarn spinning and roll to roll electrospinning. Also included in the discussion are advanced nanostructures like carbon nanofibers, nanotubes, fiber with embedded nanocrystals, nano-shells, and nanobots. Electrospinning technology has proved itself useful in developing functional nanofibers for application in drug delivery, wound dressing, tissue engineering, regenerative medicine, and oncology. However, despite the many difficulties involved in terms of scalability, reproducibility, toxicity of solvents, and lack of standardization associated with the technology, there is hope that future developments in Quality by Design (QbD), Process Analytical Technology (PAT), automation, and modeling will overcome all these hurdles. The incorporation of artificial intelligence, machine learning, green

manufacturing, and next generation electrospinning technologies will facilitate the process.

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