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A review of advances in coaxial Electrospinning for drug delivery

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Review paper

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Abstract:

Nanofibrous scaffolds are employed as drug carriers in the healthcare industry. Coaxial Electrospinning is a method for preparing core–shell nanofibers cost-effectively and efficiently in which the drugs or bioactive components are encapsulated into a body covered by a shell layer. The coaxial electrospun nanofiber morphology is affected by solution properties, process parameters, and environment parameters. Therefore, Coaxial electrospun nanofibers have been developed for more sustained drug release due to their well-controlled drug release rate, low cost, and reduced toxicity. This paper provides a concise incursion into the application of coaxial electrospun nanofibers in drug delivery and cites pertinent processing parameters that may influence the performance of the nanofibers and drug release when applied to drug delivery. One of the critical challenges in producing nanofibers is finding methods that have sufficient speed for producing industrial textiles. Polymeric drug delivery systems can improve therapeutic efficacy, reduce toxicity, and increase patient compliance by delivering drugs at a controlled rate over some time in an active setting.

Keywords: Coaxial Electrospinning; Core-shell; Drug delivery

1. Introduction

Nanotechnology is one of the most promising and developed technologies with many potential medicinal applications. Recent research on nanotechnology in biomedicine shows that this technology may solve problems such as controlled release, various local administration, intestinal absorption, etc. Nanofibers mimic the porous topography of natural extracellular matrix (ECM), valid for tissue regeneration and sustained release of encapsulated drug or growth factor. Nanofibrous scaffolds' unique features and easy adjustability have made them a very flexible tool for drug delivery to treat various pathologies. Since there is an inherent difference in pathologies, each field of application requires release and specificity. It has the unique mechanical properties of nanofibers. Most real medical materials are derived from fossil fuel sources, thus exacerbating pollution and climate change, and require alternative and sustainable materials. For example, cellulose nanofibers have high specific surface area, mechanical strength, reactive surface, biocompatibility, biodegradability, non-toxicity, and low-cost [1, 2].

Polymeric delivery systems using electrospun nanofibers have been in focus due to their flexibility in surface functionalities, superior mechanical durability, and interconnected and readily controlled secondary structures, which allow them to be used as drug carriers. These systems employ some of the most effective methods used in the manufacturing of high-performance nanofibers with remarkable features such as large surface area per unit mass and high porosity under certain fabrication conditions [3–8]. Thus, fibrous drug carriers have been developed for more sustained drug release because of the well-controlled drug release rate, low cost, and reduced toxicity [9]. Electrospinning is a versatile technique that can produce nanofibers containing compatible drugs with designed structure and morphology [7, 10]. Over the years, drug-loading methods have been developed via blend electrospinning in which drug molecules are directly unified within the nanofibers. Several problems appeared in this method, such as the non-uniform distribution of drugs released from blended nanofibers, which is undesirable due to the medicines adsorbed on the surfaces

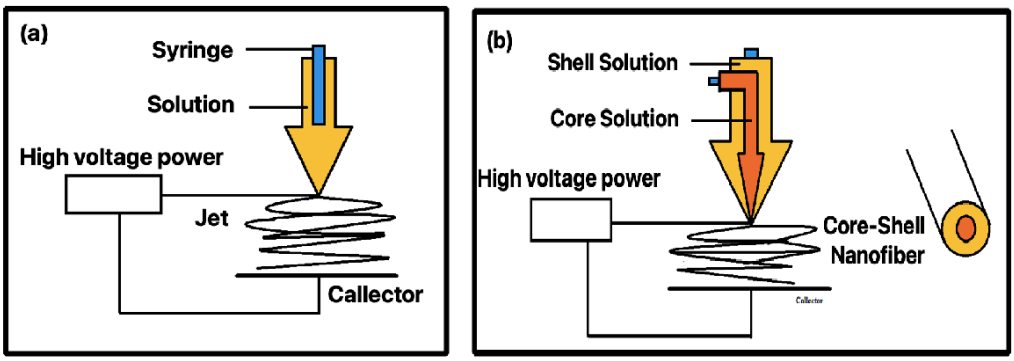

Figure 1. (a) A schematic diagram of electrospinning, (b) The schematic diagram of Coaxial electrospinning.

or in the interior of electrospun nanofibers. In 2003, the coaxial electrospinning process introduced a new class of nanofibers. In the coaxial electrospinning process, drugs or bioactive components can be encapsulated into the core, which is covered by the shell layer to mitigate the burst release of the drug to some extent [5, 7, 11]. In this review, we will concentrate on the coaxial electrospinning designs to obtain various core–shell structure nanofibres. Therefore, the general core–shell structure is examined, and electrospinning parameters, including the type of polymer, polymer concentration, solution feed rate, voltage, and class of drugs, are discussed. These parameters can significantly affect the core–shell nanofibers. The drug release mechanism was described in monolithic and blended core designs in drug delivery applications.

2. General Electrospinning Process

Different methods can be employed to create nanofibers, such as drawing [12, 13], template synthesis [14, 15], phase separation [16], self-assembly and Electrospinning [17, 18]. Among these, Electrospinning is a versatile technique that allows us to spin many synthetic and natural polymers onto polymer nanofibers with controllable morphology.

A schematic diagram of Electrospinning is illustrated in Figure 1a. Electrospinning consists of a polymer solution, or melt, placed in a syringe or pipette that is charged with a high-voltage source. A syringe pump forces the polymer solution through a small-diameter capillary [18, 19].

Although Electrospinning is a simple process, several processing variables must be controlled to produce nanofibers instead of droplets or bead morphologies [20]. The fiber morphology is affected by solution properties and operating conditions such as polymer molecular weight and concentration, the solvent of polymers, applied voltage, solution flow rate and tip-collector distance, and environmental parameters, including temperature and humidity. The optimization of these parameters to achieve desirable nanofiber morphology and properties is the main aim of the electrospinning process [21, 22].

3. Coaxial Electrospinning

The general setup of coaxial Electrospinning is similar to that of general Electrospinning [11, 22]. Coaxial Electrospinning was performed using a variable high DC voltage power supply and a programmable pump, which could be set from 1 kV to 30 kV. Two separate polymer solutions using coaxial nozzles were mounted on the pump with a multirack grip; the core and shell components' flow rates were identical during the tests [23, 24]. The schematic diagram of coaxial Electrospinning is illustrated in Figure 1b. The quality of the process and the morphology of the fibers are affected by several parameters, i.e., the solution, processing, and environment parameters [25]. In addition, the interactions between the core and shell polymer solutions and their flow rates can affect the morphology of nanofibers' properties [10]. The core-shell structure features two parts, with one outer part ('shell') and the inner part ('core') covered by the outer part. In addition, each core and shell can perform independent functions [11].

Core-shell nanofibers hold great potential for improving the loading of various drugs and bioactive agents. Antibiotics, DNA, proteins, growth factors, etc., can be directly incorporated into the core, protected by the shell layer, and could reveal a sustained release without any burst effect [5, 27]. The polymer of the shell layer provides a diffuse obstacle, minimizing surface enrichment [28].

The core-shell fibers can be fabricated by coaxial and emulsion electrospinning, allowing us to load two drugs while reducing the initial burst release and allowing for sustained release profiles. However, the emulsifier used in emulsion electrospinning is challenging to remove. Coaxial Electrospinning is extensively used and is simple to adopt. Materials not capable of forming electrospun fibers alone can be used in the core solution after removing the shell layer, and non-electrospinnable fibers can thus be obtained. These reasons contributed to our choice of electrospinning method [29–33]. In another study, present shell-core fibers were successfully prepared by using Eudragit S100 (ES100) and poly(vinyl alcohol) (PVA)/pectin (PEC) through coaxial electrospinning technology [34]. In another study, polylactic fibers were used to treat periodontitis using coaxial electrospinning [35]. In another study, Co-axial electrospinning of PLLA shell, collagen core nanofibers for skin tissue engineering was reported [29].

4. Effect of the Solution Parameters

Solution viscosity is one of the critical factors in determining the morphology of electrospun nanofibers [22]. The

Figure 2. Compound Taylor cone. Outer fluid: PVP–DMF (DMF: dimethyl formamide) melt. Inner solution: oil [26].

sheath solution's thickness must be adequate to produce enough viscous traction for the core solution to overcome the interfacial tension and thus allow a stable Taylor cone to be formed [36]. A sufficiently high viscosity of the shell fluid and a low value of the solution interfacial tension are essential for developing a compound cone in a steady state. By lowering the shell and core solution interfacial tension, the inner meniscus can be steadily dragged into a jet by the outer melt. Figure 2 shows the compound Taylor cone of core and shell fluids [26]. The viscosity of the core fluid should be kept low to allow for a stable Taylor cone [37]. The thickness of polymer solutions depends on the concentration, temperature, and molecular weight. Navaporn Kaerkitcha experimented on the core–shell nanofibers using PAN as the core polymer and PMMA as the shell polymer. When using a constant concentration of the core solution, the diameter of the obtained electrospun fibers slightly increased with the increase in the viscosity of the shell solution. In contrast, when using a constant concentration of shell solution, the average diameters of the electrospun fibers were not significantly different from one another when the viscosity of the core solution was increased, Figure 3.

The viscosity can be controlled by the concentration of the polymer solution [38]. When the polymer concentration is low, bead-only structures will be produced due to a lack of chain entanglements in the solution. When the concentration is too high, pumping the solution through the syringe needle will be difficult, and the answers may dry at the tip of the hand before the electrospinning Taylor cone can begin. Increasing the concentration of the core solution results in the formation of ultrafine fibers bead–less morphology [39]. Rui Chen observed an increase in the overall fiber diameter when a higher core concentration was used, with the shell solution concentration maintained at constant attention [40]. Moreover, the shell concentration could not be too high because a lower viscosity tended to facilitate the formation of more uniform fibers with a smaller fiber diameter [40]. Similarly, [11]. They observed increased overall fiber diameter when higher shell and core concentrations were used in the solution. The immiscibility of the two solutions is the critical factor for the successful fabrication of [37]. The Taylor cone becomes unstable if the core and shell solutions show high miscibility. The morphology of the electrospun nanofibers was sprayed during Electrospinning or showed blend types due to the blend of core and shell solutions during Electrospinning. Figure 4 shows the morphology of core–shell electrospun nanofibers [Figure 4 (b)] and their blended core and shell layer (Figure 4 (a and c)] [37]. However, several groups have demonstrated that coaxial electrospinning combinations can make polymeric core-shell nanofibers of miscible polymer solutions. Sun et al. [41] reported the formation of core-shell polymeric nanofibers using various concentrations of the same answer. On the other hand, in their study, Rahmani et al. [42] reported that core–shell fibers of polymethyl methacrylate (PMMA) and polystyrene (PS) had been successfully electrospun to assess the influence of the solvent on the final fiber morphology. Four organic solvents, such as N, N dimethylformamide (DMF), dichloromethane, toluene, and tetrahydrofuran (THF), were used in the shell solution while the core solvent was preserved. They demonstrated that DMF, THF, and toluene are considered suitable solvents for PS. Their differences in viscosity play a role in the fiber morphology, Figure 5. Moreover, In the DMF/toluene core–shell solvents, nanofibers have large diameters; this morphology is attributed to the low evaporation rate of the solvent in a partially dried electrospinning jet.

Moreover, Zeynep Kurban [43] showed that the shell solution must be more conducting and viscous than the core. They reported that it is possible to drive the interface between the body and the shell to instability and thus controllably create highly porous fibers by creating a case in which a highly conducting core and sufficiently low surface tension between the body and cover are both present.

The charge-carrying capacity of the polymer solutions with high conductivity is more significant than those with low conductivity. Therefore, it has been observed that an in-

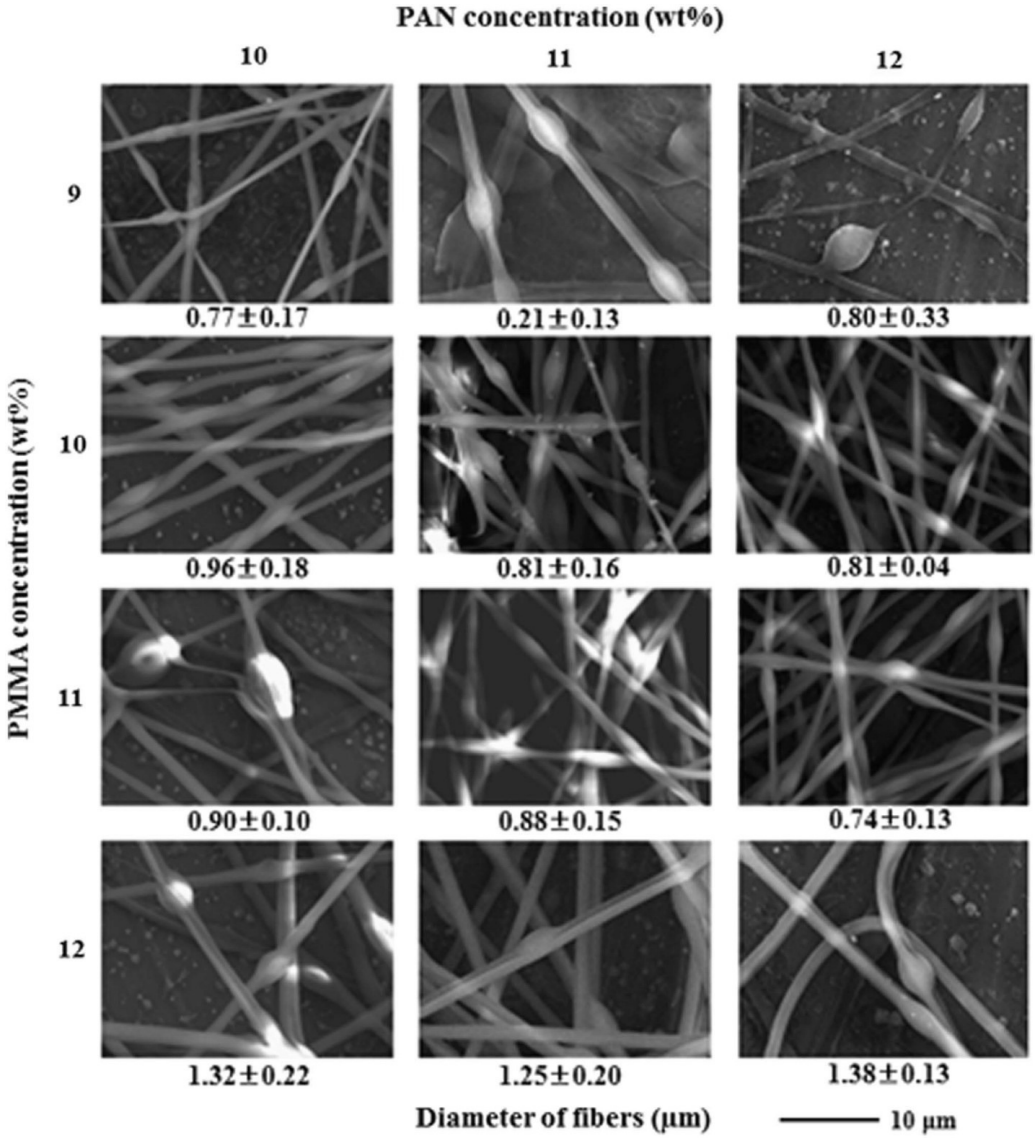

Figure 3. SEM images of core-shell nanofibers with different PAN(core) and PMMA (shell) concentrations [8].

crease in solution conductivity results in a substantial decrease in fiber diameter. It has also been shown that the radius of the nanofiber jet is inversely related to the cube root of the electrical conductivity of the solution [21]. The conductivity of the shell is necessary. The effects of the shell/core electrical conductivity ratio on the fiber diameter were evaluated by enhancing the electrical conductivity of the shell solution. This is probably due to the higher repulsive forces of the stretching jet, leading to smaller fiber yields [44]. In addition, Minoru Miyauchi [44] observed that fiber mat conductivity increased by increasing the ratio of the core solution. They reported that core–shell fibers of multiwalled carbon nanotubes (MWNT)-cellulose mats demonstrated excellent conductivity because of a conductive pathway of bundled MWNTs.

Mehdi Pakravan has reported that the core PEO solution helped the shell chitosan solution, which is a non-electro spinnable solution, by forming a stable Taylor cone and continuous jet ejection during the entire process. This could be attributed to a combination of parameters such as using the same solvent in both solutions, higher conductivity of the shell solution, and low solvent vapor pressure.

5. Polymers

Numerous materials, including hydrophobic and hydrophilic materials, have been successfully electrospuned into ultrafine coaxial fibers. The selection of appropriate materials and solvents is essential for the steady generation of core-shell nanofibers, especially those for drug delivery systems. Polymeric nanofiber carriers can be fabricated through both synthetic and natural polymers. However, natural polymers play a more critical role in drug delivery than synthetic polymers [22]. This may be due to good biocompatibility, biodegradable and toxicologically harmless, and more abundantly available than synthetic polymers. The Electrospinning of natural polymers has several problems, such as destructive mechanical properties and weak moisture resistance because of strong hydrogen bonding.

Furthermore, the electrospinning of these natural polymer blend solutions was difficult with the high polymer con-

Table 1. The List of studies using co-axial electrospinning to prepare core-shell nanofibers for biomedical applications.

Shell/core polymers	Drugs	Solvents		Fiber diameter (nm)	Objective of the study	Reference
		shell	core			
Thermoplastic carboxymethyl cellulose/poly(ethylene oxide)	Thiocarbohydrazide (TCH)	DMF	Chloroform	86.12	Drug delivery-demonstrate core-sheath fiber formation using bio-degradable materials to controlled drug delivery	11
Poly(lactic-co-glycolic acid) (PLGA)/gelatin(Gt)	Thiocarbohydrazide (TCH)	Poly(lactic-co-glycolic acid) (PLGA)	gelatin (Gt)	197	Controlled drug release-Periodontal regeneration	25
Polycaprolactone(PCL) /poly(ethylene oxide) /Polyvinyl alcohol(PVA)	basic fibroblast growth factor (bFGF)	methanol/chloroform	Polyvinyl alcohol (PVA)	—	wound healing -diabetic ulcers	64
Polycaprolactone(PCL) /Polyvinyl alcohol(PVA)	Liposomes /FITC-dextran	Polycaprolactone (PCL)	Polyvinyl alcohol (PVA)	233.4	coaxial nanofibers -tissue engineering and regenerative medicine	65
Polyvinyl alcohol (PVA)/Gelatin	—	Ethanol/de-ionized water	Ethanol /PBS	182	Coaxial electrospinning -tissue engineering	48
Aligned/Poly (ε-caprolactone)	—	Aligned	Poly (ε-caprolactone)	250	Delivering bioactive proteins	66
Polyvinyl alcohol PVA Polycaprolactone (PCL)	liposomes	PVA	PCL	—	Drug delivrey	65
SnO_2/ZnO	—	SnO_2	ZnO	Gas sensing properties		67
Starch/Cellulose	Doxorubicin	Starch	Cellulose	Drug delivery		68

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tent. The crude polymer is usually blended with synthetic polymers to provide sufficient mechanical properties and improve electrospinnability. In addition, coaxial Electrospinning can overcome these problems without changing the nature of the polymers [10, 23, 45, 46]. M. Merkle [47] reported a synthetic polymer, polyvinyl alcohol (PVA), as a shell polymer and natural protein gelatin as a core polymer used as a model system for core–shell nanofibers. PVA is a semicrystalline, hydrophilic, and biocompatible polymer that can be electrospuned into nanofibers in aqueous solution. Gelatin is often electrospun combined with synthetic polymers such as poly (ε-caprolactone) and PVA to improve the fiber's mechanical properties [47]. Table 1 lists studies using coaxial Electrospinning to prepare core-shell nanofibers for biomedical applications. Esmaeili et al. [48] has summarized the natural materials that have improved electrospun nanofibers' chemical and physical properties for biomedical applications. Mehdi Pakravan [23] used this method to prepare chitosan nanofibers by coaxial Electrospinning of PEO as a core solution for the chitosan shell. Then it removed the core phase by washing PEO to expose the chitosan nanofibers. In another study, composed of poly(γ-benzyl-α,L-glutamate) (PBLG) and poly(vinylidene fluoride) (PVDF) with significantly enhanced electromechanical properties was reported [50].

6. Effect of the processing parameters

It is accepted that voltage significantly influences nanofibers' morphology [51]. Increasing the applied voltage values leads to an increase in the standard deviation of fiber alignment. It can be observed that voltage in the range of 10-25 kV affects the morphology of nanofibers. On the other hand, applied voltage initially leads to an increase in the average fiber diameter until 20 kV. For higher voltage values, the fiber diameter did not increase further. This may be due to the high strength of the electrical field, which increased the instabilities of jet polymer fluid at high conducted voltage. Figure 6 shows the effect of voltage on the fiber diameter [45, 52]. Akbar Esmaeili [48] examined the effect of the applied voltage on coaxial Electrospinning of TCMC/PEO/TCH nanofibers. They showed that the applied voltage significantly impacts the fiber diameter, and increasing the voltage of Electrospinning in the range of 15–25 increased the fiber diameter.

In contrast, Kok Ho Kent Chan [53] reported that when the applied voltage was increased to 18 kV, the Taylor cone became unstable, with the surface of the fluid meniscus subsiding rapidly into the inner walls of the spinneret. All experiments were done with constant feed rates. This could be attributed to the fact that the electric field pulls the solution at the tip of the spinneret at a relatively fast speed, and when the feed rate of the pump is unable to supply enough answer to meet the rate at which the solution is drawn; the meniscus subsides and breaks down within the inner walls of the spinneret which knows it as the multijet mode. The feed rate adjusts the flow rate of the fluid exiting from the spinneret tip. It influences the nanofiber diameter in Electrospinning, as observed by Kok Ho Kent Chan [53] investigating the effect of feed rate. It has been reported

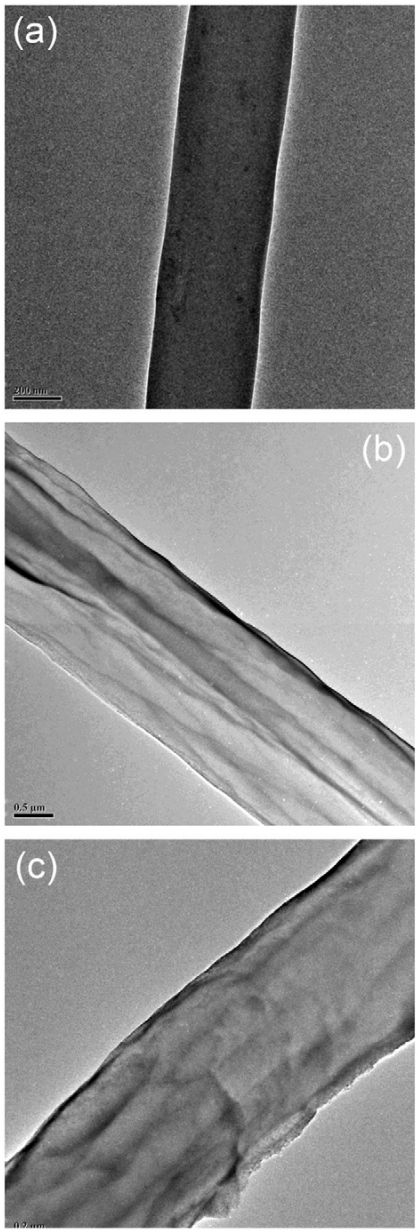

Figure 4. TEM images of the morphology of core-shell nanofibers electrospun with two miscible liquids, (a) morphology blend type,(b) indistinct core/sheath structure, and (c) Collapsed core/sheath structure [49].

that when the sheath flow rate is maintained at fixed values. In contrast, the core capillary feed rate is varied, the core flow rate is too low, and an insufficient solution is delivered. A continuous incorporation of the core into the shell does not occur. In addition, Ying Li [54] have determined that for the collagen-PEG heart–shell system, a core–shell flow rate combination of a higher rate of shell solution resulted in producing good quality core–shell nanofibers.

Moreover, higher flow rates with the same flow rate ratio produced fibers with beads-on-string morphology. From previous studies, we have gathered that the flow rate of the core plays a more critical role in preparing the coaxial fibers. Furthermore, the flow rate of the core solution is usually lower than that of the shell solution [36]. Gener-

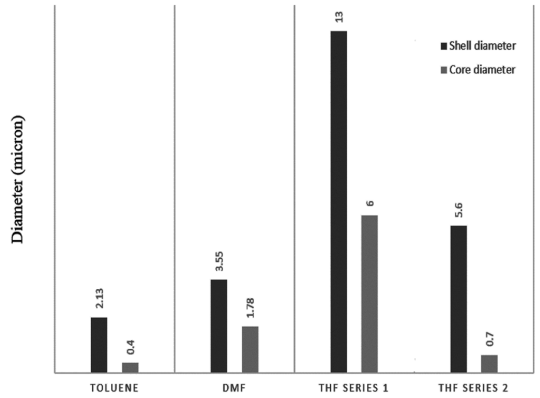

Figure 5. Size distribution of core-shell electrospun fibers (PMMA as core and PS as a shell solution) with different shell solvents [42].

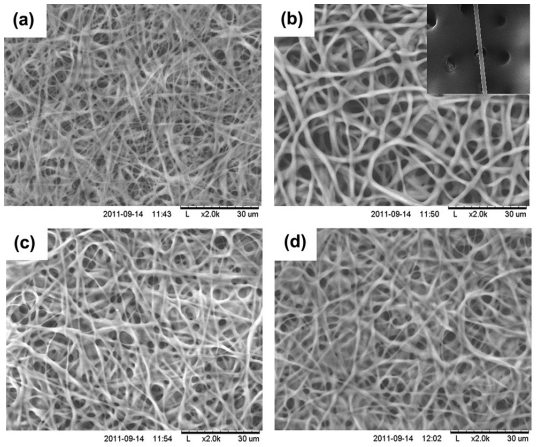

Figure 6. SEM images effect of voltage on the fiber diameter (a) 10 kV, (b) 15 kV, (c) 20 kV, (d) 25 kV. (flow rate = 1 mL/h, distance = 14 cm) [45].

ally, the tip-to-collector distance is one of the most critical parameters affecting the electrospinning process [36]. Solvent evaporation from the nanofibers is necessary to obtain defect-free electrospun nanofibers, and the collector distance determines this. Amir Houshang Hekmati [55] reported that increasing the collector distance will decrease the nanofibers' diameter.

7. Core-shell electrospun nanofibers for drug delivery

Since medical science is facing many problems in the prevention, diagnosis and treatment of various diseases, new technologies can be helpful as one of the most significant solutions to solve or reduce these problems. Today's nanotechnology has taken a big step towards reducing these problems. The pharmaceutical world needs suitable carriers and formulations to deliver the correct dose of medicine to the place of effect and avoid the side effects of drugs. In this regard, using colloidal carriers such as liposomes, nanoparticles, polymers, and lipid nanofibers is one of the most appropriate methods to achieve the aforementioned goal. Drug delivery systems designed based on nanotechnology will result in more therapeutic effects, less toxicity, more patient comfort and satisfaction from the treatment conditions, and more drug accumulation at the impact site. Skins produced from nanofibers are used as two-dimensional systems in skin drug delivery with a high surface-to-volume ratio. There are different methods for making nanofibers, among which electrospinning has been introduced as a simple and unique method for making nanofibers, so that the final product has a very high specific surface and according to the type of materials used, it has various applications in different fields, especially manufacturing. Drug delivery systems play. Among the main advantages of skin drug delivery systems, the following can be mentioned: Wide contact surface that leads to faster tissue wetting. The dose prescribed in them is more reliable compared to syrup and medicinal drops. The inherent flexibility of polymer nanofibers compared to other Medicinal forms increases their shelf life before consumption (during storage). Due to the lack of need for water, patients do not face the problems of retardation, swallowing, nausea, etc. They are convenient for patients at any time and place. The drug used in the nanofibrous layer enters the systemic circulation without the liver's first pass. For drugs with the first pass of the liver, it is very desirable because it reduces the dosage and side effects [56–58].

The coaxial electrospinning approach allows for the formation of core-shell fibers, which may result in burst release at the initial stage of drug delivery. One challenge is to obtain sustained release of a single drug to control the burst release of drugs [6]. The two main features of electrospun nanofibers that make them attractive as drug carriers are the large surface area to volume ratio of nanofibers and the control properties, such as the diameter, porosity, and morphology by varying the processing variables and type of materials, which can regulate the drug release profile [21]. The drug release mechanism is dominated by swelling followed by desorption from the nanofiber surface, diffusion through the channels and pores of nanofibers, or matrix degradation [36]. Loading the drug molecules in the shell solution will result in burst release in the initial stage, where the drug molecules are near the surface of the nanofibers. This will result in short-term release [59]. Coaxial Electrospinning can provide burst release from the sheath surface and a sustained release from the fiber core [59]. Various drug delivery systems, including hydrophilic drugs and proteins, are incorporated into nanofibers. One of the essential aims of coaxial Electrospinning is to achieve long-term hydrophilic drug release from nanofibers. Furthermore, some studies examined the different types of structures for drug control burst release. Two types of core–shell nanofibers with monolithic and blended bodies were investigated. The drug delivery strategy for long-term effect is realized with drug delivery systems [60].

8. Core-core-shell nanofibers with monolithic cores

The drug release mechanism was explored, and the drug release from blended simple and core-shell nanofibers with monolithic cores was examined and compared. Some studies noted that the core-shell nanofiber sample had a slower and more sustained drug release compared to the blend nanofibers. Akbar Esmaeili [11] reached the drug release of core–shell and blended simple nanofibers. They fabricated TCH-loaded blend and core-shell nanofibers from TCMC and PEO. They showed that the core-shell nanofiber sample containing TCH had a slower and more sustained drug release than the blend of simple nanofibers. Along the same lines, Marziyeh Ranjbar-Mohammadi [25] fabricated TCH-loaded blend and core-shell nanofibers from PLGA and GT for application-controlled drug delivery systems. The release rate in blend nanofibers increased with the enhanced hydrophilicity polymer and drug on the nanofiber surface, which is randomly distributed across the diffusion path and can significantly facilitate water uptake and swelling of the polymeric matrix of the electrospun nanofibers [25]. In addition, they showed the sustained drug release from the core shell nanofibers from PLGA and GT for 75 days.

In addition, Mahboubeh Maleki [27] successfully demonstrated the formation of core-shell nanofibers by coaxial electrospinning system and investigated based on tetracycline hydrochloride (TCH) as the core and poly(lactide-co-glycolide) as the shell materials. Comparison of drug release from blend electrospinning and core-shell structures showed that the blend fiber mats had more excellent releases than core-shell fiber networks with or without TCH in the shell, as there was no boundary within fibers to delay the migration of TCH to medium. This is attributed to the border thickness between TCH and shell diameter being different, which might influence the ability of drug molecules to reach the fiber surface. The critical factors changing the release patterns of blend and various core-shell fiber delivery with monolithic cores devices as the essential elements were drug concentration, delivery structure, and fiber morphology. Therefore, the release profile of the drug was controllable by adding TCH to the polymeric shell, which would also affect the release profile at low drug concentrations.

Despite all the positive and efficient features of nanofibers, a series of limitations have caused the use of these structures to face a significant challenge in the industry, and other types of scaffolds have more efficiency and supply in the market. One of the most important limitations is the complex and time-consuming preparation of these nanofibers. Devices are mainly capable of producing nanofiber sheets in laboratory sizes, but for industrialization, devices are needed that are the most devices of this type in the shortest time. It has been the focus of many companies. To compensate for this shortcoming, a new innovative method has been predicted and designed, but it has not yet reached industrial mass production. In this method, which Iranian researchers invented, a simple method is considered to produce these nanofibers, which eliminates the need for high voltage and allows the use of any natural source, even citrus juice, to make uniform nanofibers, and there is no need for synthesis. Polymers are not used [61–63].

9. Core-shell nanofibers with blend cores

Developing a novel composite fiber system allowing for core-shell nanofibers and burst release at the initial stage followed by an extended sustained release remains a significant challenge [6]. Spela Zupancic [5] compared drug release from core-shell Nanofibers with monolithic and blended core. They fabricated the core-shell nanofibers with poly (methyl methacrylate) (PMMA) shell and monolithic poly (vinyl alcohol) (PVA) core and core-shell nanofibers with blended (PVA and PMMA) core loaded with ciprofloxacin hydrochloride (CIP) as a drug model incorporated within these nanofibers. Core-shell nanofibers with lower amounts of PVA in the body could prevent burst release and achieve sustained drug release for four weeks. Moreover, core-shell nanofibers blend core (PVA: PMMA) and PMMA as a shell of nanofibers have supported drug release for more than 25 days. The formation of the interconnected pores spanning has affected the release mechanism, so core-shell nanofibers with blend cores can achieve more sustained drug release.

10. Conclusion

Nanofibrous scaffolds have been applied as drug carriers to improve human health. Electrospinning is one of the techniques used in drug carriers with high loading capacity, ease of operation, and cost-effectiveness. Core-shell nanofibers hold great potential for drug delivery and tissue engineering. The drug is often incorporated in blend nanofibers, which might result in low delivery efficiency and burst release. In contrast, core-shell nanofibers improve the loading of hydrophilic drugs and proteins and could reveal a sustained release without any burst effects. The coaxial electrospinning approach allows the formation of core-shell fibers, which can use some non-electrospinnable materials to form a fibrous structure with two separate polymer solutions (core and shell solutions). Electrospun nanofibers are affected by several parameters, such as the solution, process, and environmental conditions. In coaxial Electrospinning, the interactions between the core and shell polymer solutions and their flow rates can significantly affect the release mechanism. Therefore, more sustained drug release can be achieved. Presently, most studies of coaxial nanofibers regarding drug delivery have shown new methods of coaxial nanofibers with blend and monolithic cores. These achieve more sustained drug release. To fulfill the growing demand for drug delivery systems, novel methods for coaxial nanofibers in loading drugs and other bioactivities must be further explored.

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This manuscript does not report on or involve the use of any animal or human data or tissue. So the ethical approval does not applicable.

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