Electrospun Bead-on-String Fibers: Useless or Something of Value?

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Abstract

Bead-on-string fibers, which were initially thought to be a "by-product" of the electrospun fibers, are widely observed in electrospinning, which is a convenient method to produce nanofibers. The electrospun bead-on-string fibers were thought to have detrimental properties and were generally discarded, but recently they have gained attention since they are considered to have promising applications in many fields, including tissue engineering, drug delivery, and air/water filtration, among others. This chapter is a comprehensive and systematic literature review that summarizes the processes, methods, vital influencing factors, formation conditions, morphology changes, and applications of the electrospun bead-on-string fibers. It helps to understand the current research status and to further understand the mechanism by which these bead-on-string fibers are formed.

Keywords: electrospinning, bead-on-string fibers, instability, filtration, sustained drug

1. Introduction

Electrospinning is a powerful and effective technique to fabricate nanoscale fibers from polymer solutions or melts [1]. The electrospun nanofibers have been widely used as scaffolds in tissue engineering, drug delivery, industrial filter material, wound dressing, and composite applications owing to their porous and high specific surface area [2–6]. In 1934, Furmhals patented the experimental device for the preparation of polymer fibers via electrostatic power which is considered as the beginning of electrospun nanofibers [7]. Following several decades since the invention of experimental device, the development of electrostatic spinning was attended to improve the setup for producing polymer filaments [8–10]. However, recently, electrospinning technology has received wide attention together with the development of nanotechnology [11]. Electrostatic spinning technology has gradually become the most direct and effective method to prepare nanofiber materials.

Bead-on-string fibers have been widely observed in electrospun products. At first, bead-on-string fibers were considered as useless products in electrospinning which could affect the performance of nanomaterials since the beads would greatly reduce the surface area [12]. However, further studies showed that the incorporated beads in the micron range are effective for drug-loading purposes [13]. In this sense, spheres are able to solve the problem of having electrospun fibers that are too fine to incorporate high doses of drug in the tissue engineering scaffolds [14, 15]. The particular structure of bead-on-string fibers, mainly composed of micron-sized spheres and nanometer-sized fibers, presents some microporosity that can be used in air/water filter to solve the problem of low filtration efficiency and high air pressure resistance of highly efficient filtration materials [16–18]. In summary, bead-on-string fibers have potential applications in tissue engineering, drug delivery, as well as in air and water filters.

In recent years, the development of bead-on-string fibers has received a lot of attention. However, most studies focused on the influential factors of the formation of electrospun bead-on-string fibers [19, 20]. Until now, there have been few reviews about electrospun bead-on-string fibers. This chapter provides a detailed and systematic description on the processes, methods, influential factors, formation conditions, morphology changes, and applications of the electrospun bead-on-string fibers, which is based on in-depth literature survey of this technique in recent decades.

2. Preparation methods of electrospun bead-on-string fibers and the polymers used

Traditional electrospinning devices were mainly composed of high-voltage power supply (a few thousand voltages to tens of thousands of voltages), solution storage device (polymer solution or melt), spraying device (capillary needle with millimeter level) and collecting device (metal plate or aluminum foil) [10]. In order to overcome the low production efficiency, new spinning equipment have recently appeared, such as multi-nozzle electrostatic spinning, non-nozzle electrostatic spinning, and bubble electrospinning, which laid the foundation for the industrialization of the electrospinning nanofibers [21–23].

The fundamental principle of electrospinning is that the solution forms a liquid drop at the end of the spraying device under a high-voltage electric field. As the voltage increases, the shape of the droplet gradually changes to form the Taylor cone [9, 12]. When the electric field force of the solution or the melt overcomes the surface tension and the viscous force, the droplet of the polymer solution or melt is ejected from the tip of the needle in the form of a jet and solidified on the collecting device [24].

2.1. Traditional electrospinning

Almost all electrospinning methods can be used to produce bead-on-string fibers by adjusting the processing parameters. Although the electrospinning methods and devices used to prepare bead-on-string fibers have some differences, the working principle of electrostatic spinning and formation mechanism of bead-on-string fibers are the same.

Traditional electrospinning is the most common method to prepare bead-on-string fibers [25]. However, the polymer used in traditional electrospinning must be soluble in the solvent. Therefore, it is difficult to use polymers that cannot be dissolved in the solvent to form bead-on-string fibers. With the wide application of electrospun bead-on-string fibers in drug delivery, emulsion electrospinning and coaxial electrospinning have also emerged as interesting methods for preparing bead-on-string fibers [26].

2.2. Emulsion electrospinning

Polymers that do not have tendency to form nanofibers from its solution or melt can be dispersed in a carrier that can easily form nanofibers in order to prepare nanofibers by emulsion electrospinning [27]. In this way, water-soluble drugs can be dispersed inorganic solutions of polymers to form stable homogeneous oil in water (O/W) or water in oil (W/O) emulsions. Large droplets of O/W emulsion will burst into small droplets in the electrospinning process. Bead-on-string fibers can be obtained [28, 29]. However, the W/O emulsion is different. The formation mechanism of bead-on-string fibers is based on droplets in aqueous phase that move to the fiber center and combine, which is followed by the jet stretching and solvent evaporation, which cause demulsification, allowing the formation of the bead-on-string fibers [30]. During the preparation of drug-loaded bead-on-string fibers by the emulsion electrospinning, the drugs and polymers are not necessary to be solved in the same solvent. Furthermore, the water soluble drugs can be formed as floating droplets in the emulsions and embedded in the beads once the bead-on-string fibers are prepared. Qi et al. successfully prepared bead-on-string fibers and performed sustained release of drugs by adding calcium chloride in alginate aqueous solution to crosslink Ca ions and alginate to form calcium alginate microspheres encapsulating drug model Bovine serum albumin (BSA) [26].

2.3. Coaxial electrospinning

Nozzles for coaxial electrospinning consist of two capillary tubes, including the inner layer and the outer layer capillary tubes. The principle of coaxial electrospinning is that two kinds of solutions are injected into the inner and outer capillary tubes to join at nozzle tip. Before the solution is sufficiently mixed, the mixture is sprayed out to form a stratified polymer jet since the large electric field force droplets are subjected at the end of the spraying device, allowing solvent evaporation and the solution solidification, forming a core-sheath structure obtained on the collecting device [31, 32]. If the drug or the bioactive factor is encapsulated in the polymer cortex, the nanofibers can be used as a drug delivery carrier [32–35].

Coaxial electrospinning can overcome the shortcomings of uneven distribution of drugs due to poor spinnability of drugs or poor compatibility of drugs and polymers. Furthermore, durgs to be loaded are not necessary to be spinnable [36]. Tian et al. successfully prepared bead-on-string fibers by coaxial electrospinning. In this experiment, the outer fluid was a 20% (w/v) poly(ethylene glycol) (PEG) (M = 20,000) solution in a mixed solvent of N,N-dimethylformamide (DMF) and methylene chloride (MC v/v = 1:1), and the inner fluid was a 35% (w/v) polystyrene (PS, M_W = 350,000) solution in DMF. The study also showed that the bead region and the fiber part were constituted by outer fluid and inner fluid, respectively, through energy-dispersive X-ray spectroscopy [37].

Using different methods of preparation as mentioned above, there are a bunch of polymers that can be used to produce bead-on-string fibers, as shown in **Table 1**. The solvents and some of the additives that can promote the formation of bead-on-string fibers are listed.

Polymer	Solvent	Additives	References
Poly(hydroxybutyrate-co-valerate) (PHBV)	Chloroform (CF)	—	[38, 39]
Poly(ethylene oxide) (PEO)	Distilled water	—	[25, 30]
PEG + PS	DMF + MC	—	[37]
Poly (L-lactic acid) (PLLA)	Dichloromethane (DCM)	Alginate, sodium bis (2-ethylhexyl) sulfosuccinate	[26]
Poly-(methyl methacrylate) (PMMA)	DMF	Titanium, tetrachloride ($TiCl_4$) hydrolyzed nanoparticles	[40]
Poly (butylene succinate) (PBS)	CF, DCM, 2-chloroethanal (CE), isopropanol (IPA)	LiCl	[41]
Silk fibroin + gelatin	Formic acid	—	[42]
PS	1,2-Dichloroethane, DMF, ethylacetate (EA), methylethylketone (MEK), Tetrahydrofuran (THF)	—	[19, 43]
Chitosan	Glacial acetic acid + deionized water	—	[44]
Poly (Ɛ-caprolactone) (PCL) + gelatin	Acetic acid + EA + water	—	[4]
Poly (lactic acid) (PLA)	N,N-dimethylacetamide (DMAC) + DCM	—	[45]
Silk-like polymer with fibronectin functionality (SLPF)	Formic acid	—	[46]
Poly (vinyl alcohol) (PVA)	Distilled water	Ethanol, NaCl	[47]
Polyvinylpyrrolidone (PVP)	Ethanol + water	LiCl, NaCl, $MgCl_2$	[48]

Table 1. Polymers used for producing bead-on-string fibers.

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3. Influencing factors of electrospun bead-on-string fibers and their formation conditions

Electrospinning is a process in which the polymer solution forms a Taylor cone at the end of the spraying device under high electrostatic voltage. In parallel, there is competition between viscous resistance, surface tension, and electric field force suffered by the polymer solution. When the electric field force reaches a certain critical value, the liquid drops overcome the effect of the viscous resistance and surface tension, and are then ejected from the tip of the needle in the form of jet. Finally, the jet is solidified to form fibers on the collecting device [9, 24, 49]. In the initial stage of jet sprayed from the tip, the path of the jet has linear acceleration motion. Due to the existence of the viscous resistance, the acceleration decreases continuously, when the acceleration is zero or constant, making the presence of any disturbance change the linear motion of the jet forming the instability of the jet [24, 50, 51].

Instability of jet is a transport phenomenon where it may be originated from a particular disturbance or fluctuation and extended at different rates with time. There are three modes of instabilities in electrospinning process. The first one is the Rayleigh mode, which is the axisymmetric extension of the classical Rayleigh instability when electrical effects are important, and then the axisymmetric conducting mode, and the whipping conducting mode. The latter are dubbed "conducting modes" because they are sensitive to the surface and conductivity of electrospinning solution at high electric field [51, 52]. Among three types of jet instability that are related to the instability modes, the Rayleigh instability is driven by the surface tension, the varicose instability and whipping instability are caused by the nature of electricity. One or more different instability modes may occur in electrospinning process, which depends on the basic processing parameters such as the velocity, radius, and surface charge density of the jet [53–55].

The formation of beads is related to the three types of instability in electrospinning process. It is generally accepted that Rayleigh instability and varicose instability are favorable for the formation of beads, while whipping instability inhibits bead formation [38, 51, 52]. In electrospinning process, jet instability caused by capillary waves will lead to burst of cylindrical jet and then breakup of liquid droplet gradually shrinks into the ball to get the smallest surface area due to surface tension [24]. Owing to the existence of instability, spherical small droplets produce deformation, which will lead to an increase in the surface area and surface energy, which causes instabilities of jet to continue. Finally, bead-on-string fibers are collected on the collection device [25]. Similarly, varicose instabilities are caused by the nature of electricity in which the charges on the jet repel each other and jet is stretched and refined under the force of an electric field. When the charges on jet suddenly decrease, cylindrical jet will collapse to form droplets and will be stretched due to the charge repulsion. Ultimately, bead-on-string fibers are formed [56, 57]. Whipping instability is caused by the excessive charges on the surface of cylindrical jet which can generate fluctuation. When the fluctuation is big enough, jet will split into many small branches. If the whip continues to exist, the jet will split into smaller branches to form nanoscale fibers [24]. When the Rayleigh instability and varicose instability dominate jet instabilities, bead-on-string fibers will form. If the whipping instability is dominant in jet instabilities, smooth fibers will be obtained [56–59].

The aforementioned analysis intends to show which is in a dominant position among the Rayleigh instability, varicose instability and whipping instability determines whether bead-on-string fibers can be formed. Surface tension, viscosity, and charge density of spinning solution have a great impact on the three instabilities above. Therefore, influencing factors of bead-on-string fiber formation can be discussed from three aspects of surface tension, viscosity, and charge density of the spinning solution.

3.1. Surface tension of spinning solution

The surface tension of solution is the cohesive force between the molecules of the same kind, which makes the surface molecules of the liquid close to each other, and the liquid shows automatic shrinking to obtain the minimum surface area. Rayleigh instability, one of axisymmetric instability, is driven by surface tension that the vertical jet often suffers by surface tension to form a symmetrical waveform in the free-falling process [60, 61]. Therefore, surface tension has an important effect on the formation of bead-on-string fibers [62]. In recent years, there are many researchers working on the effect of surface tension on the formation of bead-on-string fibers. Most works have focused on the effect of the surface tension on the formation of bead-on-string fibers by changing the type of solvent or the mixing ratio of spinning solutions and comparing the morphology of fibers. Fong et al. studied the variation of water and alcohol ratio to obtain different surface tension of poly(ethylene oxide) (PEO) solutions, showing that the increase in surface tension of polymer solution was favorable to the formation of bead-on-string fibers [25]. Zuo et al. and his colleagues studied the effect of surface tension of added PHBV solution on the formation of bead-on-string fibers. The results showed that greater surface tension of spinning solution was more likely to obtain bead-on-string fibers. The reason is that the surface tension of the polymer solution attempts to obtain smaller mass unit area by shrinking jet into a sphere when the jets are broken, which leads to the increase of Rayleigh instability and the formation of bead-on-string fibers [38]. Therefore, it is reasonable that controlling surface tension of spinning solution is crucial for the preparation of the desired bead size and morphology.

3.2. Viscosity of spinning solution

The viscosity of the solution determines the ability of a solution to flow under external force, where the internal friction force is generated at the interface due to the flow of solution being limited by entanglement of molecular chains. This property of polymer solution is characterized by viscosity. All factors that cause the increase of entanglement density can make the movement of molecular chain more difficult and increase the viscosity of solution. The number of molecular weight per unit volume characterized by the concentration of the solution and the length of the molecular chain can affect the viscosity of solution and hence the formation of bead-on-string fibers [63]. Generally speaking, the greater the concentration and molecular weight of solution, the stronger the entanglement degree and the cohesion molecular chains, which leads to a greater concentration of spinning solution. Many research works have indicated that the greater the viscosity is, the stronger viscous resistance the jet has, which is more conducive to resist surface tension. In this case, the Rayleigh instability and varicose instability are limited, and the whipping instability is dominant in the jet instability, inhibiting the formation of the beads [53, 64–66]. There are many studies about the effects of molecular weight, viscosity, and concentration of polymer solution on the formation of bead-on-string fibers. Gupta et al. explored relationships between fiber formation, viscosity, molecular weight, and concentration of linear homopolymers of poly(methyl methacrylate) (PMMA) ranging from 12,470 to 65,700 g/mol Mw in a proper solvent. The researchers experimentally determined the critical chain overlap concentration, c*, the crossover concentration between the dilute and the semidilute concentration regimes, which was in good agreement with the theoretically determined value, estimated by the criteria $c^* \sim 1/[\eta]$ ($[\eta]$ is the intrinsic viscosity; c* is the critical chain overlap concentration), where the intrinsic viscosity was estimated from the Mark-Houwink parameters, K and a (at 25 8°C in DMF) obtained from the literature [20]. The experiment indicated that the value of the zero shear viscosity with the c/c* had a certain relationship with morphology of the fibers. As the concentration was increased (semidilute untangled regime $1 < c/c^* < 3$), polymer droplets and some bead-on-string fibers were observed. Upon further increase in concentration (semidilute entangled regime), bead-on-string fibers were obtained at $3 < c/c^* < 6$. Uniform fiber formation was observed at high concentration (semidilute entangled regime $c/c^* > 6$) [20]. Furthermore, it was found that the lower molecular weight polymer showed greater critical chain overlap concentration solution, increasing the solution concentration needed to form corresponding fibers described above [20]. Zhang et al. further explored the effect of various concentrations of PEO solutions on the morphology of bead-on-string fibers. The results showed that there were obvious changes in the morphology of bead-on-string fibers, showing increased fiber diameter and the main diameter of beads changed from 300–600 nm to 900–1500 nm, when concentration of PEO solution changed from 2.5 to 7.5% [67]. Overall, viscosity of polymer solution had an important effect on the formation of bead-on-string fibers, which can be inhibited by increasing the viscosity of the polymer solution.

3.3. Charge density of spinning solution

In general, the charge density of solution is usually characterized by density of charge distribution. Electrospinning is a process where the jet is stretched under an electric force. The greater charge density the solution has, the easier charge fluctuations take place, which makes jet bend in the axis of the electric field causing the occurrence of whipping instability, allowing jet to split into small branches to form nanoscale fibers [24]. When the fiber can be properly obtained, lower charge density polymer and smaller electric force jet makes harder the jet slender, making easier bead-on-string fibers fabrication. As the charge density of jets increase, the diameter of beads become smaller, making the morphology of the beads change from spherical to spindle. Geng et al. proved this theory [44]. The results showed that the morphology of fibers had significant change at different electric fields strengths. When the electric field strength was 1 kV/cm, the product contained spindle-shaped beads, presenting a crude fiber. As the electric field was strengthened to 3–4.5 kV/cm, uniform fibers were observed. However, when the values exceeded 4.5 kV/cm, many bead-on-string fibers were obtained. Fong et al. also studied the relationship between charge density and morphology of fiber [25]. The results indicated that the size of beads became smaller, the number of beads decreased, and the shape of beads changed from spherical to spindle with increasing charge density. When the charge density increased to a certain value, charge neutralization of jet due to corona discharge phenomenon occurs. It led to the decrease of charge density and then the jet cannot be drawn efficiently to form bead-on-string fibers. Therefore, the charge density of polymer solution is key to the formation of bead-on-string fibers without taking into account the surface tension and viscosity of the polymer solution.

The main influencing factors of charge density of polymer solution are the electrical conductivity of the polymer solution and the electrospinning parameters. Therefore, bead-on-string fibers can be obtained by adjusting electrical conductivity and electrospinning parameters.

In general, solution charge density is used to characterize the electrical conductivity which characterizes ability to conduct current. The greater electrical conductivity the solution has, the higher unit charge density the jet solution has, which allows better conductive solution and allows the jet to be drawn to form smooth electrospun fibers within certain range. Electrical conductivity can be changed by adding salt ions. Nartetamrongsutt et al. studied the effect of salt ions on the morphology of bead-on-string fibers through added salt ions in the same polyvinylpyrrolidone (PVP) solutions to change electrical conductivity of spinning. Data showed electrical conductivity became larger with the increase of salt ions in the PVP solution. The results indicated that the greater electrical conductivity and viscosity the polymer solution had, the easier Rayleigh instability was limited, which was favorable for the formation of uniform fiber [48]. On this foundation, Liu et al. added 0.5 wt% and 1.0 wt% LiCL solution in 14 wt% poly(butylenes succinate)/(chloroform/2-chloroethanol), respectively, and electrospun under same condition [41]. The results were consistent with Fong. This is because the electrical conductivity of the solution became larger by adding salt ions that can increase electrical density to draw jet easily under same voltage. The morphology of the beads changed from spherical to spindle at the same voltage [41].

The applied voltage is the most influential factor to the charge density of the jet in the electrospinning parameter. Only under the function of applied voltage the liquid drop at the end of the spraying device can be ejected to form fiber, when the electric field force is larger than the viscous resistance and the surface tension. The charge on the surface of jet and the electrical force jet suffered increases with increasing the applied voltage. This theory has been proved by many experiments [19]. A previous report by Jarusuwannapoom et al. [43] explored the effect of voltage on the number of beads with polystyrene (PS)/1,2-dichloroethane spinning solution at various voltages. The results showed that when the concentration of the spinning solution was 10 wt%, the number of beads increased as voltage changed from 15 to 25 kV. The reason is that low concentration and viscosity solutions led to lack of molecular chain entanglement, which caused jet to be drawn sharply to produce instability of jet with increasing electric density and repulsion between charges. Owing to low viscous resistance of polymer solution, viscous resistance cannot compete with surface tension, and therefore, jet split into smaller drops and shrunk into spheres, forming bead-on-string fibers. However, when concentration increased to 20 wt%, the number of beads decreased with increasing voltage. Under high concentration, the viscosity increased and the electric density of the jet also increased, increasing the repulsion between charges and allowing the jet to be drawn. Meanwhile, surface tension could not overcome the viscous resistance, making jet to break and shrink due to high viscosity. Therefore, the jet continuously moved in the form of cylinder to eventually form fibers [43].

3.4. Other factors

Collecting distance, spinning rate, solvent evaporation rate, environmental temperature and humidity also can affect the formation of beads. The collecting distance is characterized by the distance from the nozzle to the collecting plate. When the motion and movement time of the jet became longer and the time for solvent evaporation became longer in the electric field, the number of beads decreased and the diameter of beads became smaller. Meanwhile, the increase of collecting distance reduced electric field force to weaken stretch jet suffered, which was favorable to decrease number of beads. The final morphology of fiber depends on the contribution of both aspects [46]. Generally speaking, the faster speed at which the jet moves, shorter the residence time of the jet in air. On the one hand, molecule chains of polymer solution cannot draw enough under electric field force. On the other hand, there is no time to completely evaporate the solvent, therefore forming the bead-on-string fibers. Environmental parameters, including temperature humidity and air velocity, can also affect the formation of bead-on-string fibers. The effect of environmental factors on spinning is not easy to control and adjust. Therefore, keeping the external environmental factors stable and not interfering with the movement of jet process are also important [47, 68].

4. Characterization and morphology of the beads within bead-on-string fibers

To characterize the bead-on-string fibers, normally electron microscopes, optical microscopes are used [18, 26, 44]. Through the images obtained from those microscopes, it can be seen that the morphology of beads within the bead-on-string fibers were not always the same. Generally, spherical- and spindle-shaped beads are taken the most part. However, there are also some heteromorphic ones, such as concave beads [19]. According to the formation conditions of bead-on-string fibers, the morphology of beads can be tuned by changing various processing parameters, such as polymer concentration, which can determine the viscosity of the electrospinning solution, applied voltage and solution electrical conductivity, which are related to the charge density of the solutions, and collecting distance [19, 48]. An increase in the viscosity of the solution leads to a less likely formation of the beads. Higher charge density decreases the possibility of beads formation. Longer collecting distance was favorable to decrease numbers and diameters of beads. According to our recent study, the silk fibroin/PEO bead morphology and aspect ratio can be tuned by changing solution properties, applied voltage, and collecting distances. Our results are consistent with the previous studies [19, 48].

5. Applications of electrospun bead-on-string fibers

5.1. Drug delivery

It is generally believed that the smaller size of the capsules, the larger surface area the capsule and drug occupy, presenting a faster decomposition rate of the drug and making easier the drug to be absorbed by the body. Electrospun fibers have many outstanding advantages as drug carriers due to their nanoscale, which allow drugs that are generally difficult to be absorbed by the body to present a slow delivery and hence enhance the absorption and produce better treatment effect. Furthermore, biodegradable materials that are used as drug carriers can be broken down into small molecules that are absorbed or expelled from the body to accomplish treating function with the release of the drug [68]. However, there are some shortcomings, such as for instance, the drugs often found on the fiber surface and cannot be coated completely causing drugs to be partially exposed, which can lead to burst release [14, 69, 70]. Therefore, the achievement of sustained release must overcome the problem of drugs' burst release.

The characteristics of the alternating distribution of sub-nanofiber and sub-micron beads of the electrospun bead-on-string fibers meet the demand of drug loading and sustained release. Bigger beads not only can complete coat water-soluble drugs or solid particles, but also can realize the function of easy absorption and fast decomposition of material to achieve drug sustained-release. Many researchers have studied the function of electrospun bead-on-string fibers in drug sustained release. The initial report was performed by Qi et al. that first dissolved AOT (sodium bis(2-ethylhexyl)sulfosuccinate) in dichloromethane, where BSA was then added after crosslinking, and then fiber-forming materials poly(L-lactic acid) (PLLA, Mw = 500,000) was added to form water in oil emulsion, with which bead-on-string fibers loading BSA was successfully prepared [26]. The experiment compared the release effect within 120 h of smooth electrospinning fibers and bead-on-string fibers with the same amount of drug loading. The results showed that the smooth nanofibers showed a drug release rate of up to 80% in 10 h and the phenomenon of burst release of drug was significant. However, when the drug was loaded on the bead-on-string fibers, the release amount of drug was below 50%, which indicated that the defect, burst release of drug of smooth fiber as drug carrier, can be improved by bead-on-string fibers to realize sustained release and control of drug. He further studied the storage locations of BSA in bead-on-string fibers by the vapor etching. It was found that most drugs were coated on the beads. Somvipart et al. also proved that bead-on-string fibers can be used to achieve sustained drug release [42]. In the experiment, methylene blue was added into the spinning solution to prepare both smooth and bead-on-string fibers. The test of drug delivery *in vitro* showed that the released amount of methylene blue from smooth fiber reached 80%; however, the release amount of methylene blue from bead-on-string fibers was only 50% which achieved sustained drug release. To summarize, bead-on-string fibers can be used as drug carrier to achieve sustained drug release.

5.2. Filter material

With the rapid development of the society, environmental pollution leads to poor air quality which results in frequent occurrences of respiratory diseases and lung diseases that bring great harm to people's life and health. Therefore, the development of high-efficiency air-filtrating materials has become a pressing requirement. According to previous studies, traditional nonwoven fiber materials have been widely used in the field of air filtration, such as glass fiber or melt-blown fiber, which have been used as indoor air filter or the core filter media of N95 respirators. However, the filtration efficiency is relatively low for fine particles since the micron-sized pore of the material are not small enough [71].

The electrospinning nanofibers that are characterized by small size, large specific surface area, high porosity and good connectivity are considered as the most promising materials for air filtration media [72, 73]. However, electrospinning nanofibers used as air filter material have higher packing density, hindering the flow of air [74, 75]. Porous bead-on-string fibers that have high specific surface area and porosity, and beads covered with micropores not only can improve packing density but also benefit air flow and adsorption for the solid particles in the air [76]. Yun et al. studied the filtration properties of the fiber mat with different morphologies by preparing bead-on-string fiber mat and particle/nanofiber composite. The results showed that the quality factor of the bead-on-string fiber mat and composite fiber mat was higher than nanofiber mats [76]. Wang et al. studied the filtration of bead-on-string fibers and found that the existence of beads could greatly improve the efficiency of air filtration. In this experiment, the bead-on-string fibers formed from 5 wt% poly(lactic acid) solution and solvent mixture containing dichloromethane (DCM)/N,N-dimethylacetamide (the ratio is 1:10) exhibited excellent filtration efficiency (99.997%) and a low pressure drop (165.3 Pa), which are promising characteristics for the membranes' application as filters for respiratory protection, indoor air purification, and other filtration applications [45].

6. Conclusions

Electrospun bead-on-string fibers have been successfully prepared by adjusting the concentration, surface tension, and charge density of the spinning solutions and electrostatic spinning parameters. Bead-on-string fibers characterized by alternating distribution of sub-nano fiber and sub-micron beads have shown great potential for the application of sustained drug release and air filtration systems. Recently, with the increase of the applications of bead-on-string fibers, much research has been performed on the formation mechanism of bead-on-string fibers. It is hoped that morphology and number of bead-on-string fibers can be controlled accurately to achieve particular applications. These research results have great significance for drug-sustained release, administration of air pollution, and improvement of water quality.

The mechanism of bead-on-string fibers formation has been proved to be caused by axisymmetric instability of jet. However, there has been few theoretical and fundamental research and no systematic summary has been prepared. Furthermore, the effective formulas and models to theoretically study and predict bead-on-string fibers have not yet been established. Therefore, the establishment of systematic theoretical, effective models, and formulas of bead-on-string fibers is essential for its research and applications.

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