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Revolutionizing Drug Delivery: The Role of Nanofibers - A Review

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Abstract

The field of drug delivery has experienced a paradigm shift with the emergence of nanofibers as an innovative carrier system. This comprehensive review aims to delve into the multifaceted role of nanofibers in drug delivery, highlighting their unique properties and diverse applications in therapeutic interventions. Nanofibers, characterized by their high surface area-to-volume ratio and tunable properties, offer an exceptional platform for targeted and controlled drug release. Their versatile nature allows for precise engineering of size, morphology, and surface functionalities, enabling tailored drug delivery systems catering to specific therapeutic needs. This review encompasses a detailed analysis of the various fabrication techniques employed in producing nanofibers, encompassing electrospinning, self-assembly, and other advanced methodologies. Furthermore, the review presents an extensive survey of the diverse range of materials utilized in nanofiber production, such as polymers, proteins, and inorganic compounds, emphasizing their distinct advantages in drug encapsulation, protection, and release kinetics.The application spectrum of nanofibers in drug delivery is explored, spanning across various medical domains including cancer therapy, tissue engineering, wound healing, and infectious disease treatment. The review delves into recent advancements, challenges, and future prospects in this burgeoning field, underscoring the potential for nanofibers to revolutionize drug delivery strategies and improve therapeutic outcomes.In conclusion, this review underscores the pivotal role of nanofibers as a novel and promising carrier system in drug delivery, presenting a compelling case for their continued exploration and utilization in advancing medical treatments.

***Keywords:** Polymer nanofibers, Therapeutic applications, Biomedical engineering, Targeted delivery*

1. INTRODUCTION:

It was discovered several decades ago that a drug's therapeutic efficacy is dependent on its route of distribution, which can change a number of elements include distribution, toxicity, metabolism, pharmacokinetics, and Pharmacodynamics [1]. Alongside the creation of innovative medication delivery techniques like nanogels and microspheres micelles, nanoparticles, and nanofibers A fresh and promising instrument was acquired by the pharmaceutical business [2]. One can employ nanocarriers. medicines that are too toxic, unmanageable, rapidly removed, or unstable when molecules are free should be wrapped and

distributed using either an active or passive targeted method, depending on the final formulation [3, 4]. Using cells and occasionally their byproducts, such as stem cells, red blood cells, extracellular vesicles, and thrombocytes as nanocarriers, is one recently developed method for delivering medications. Several industries have lately begun using these carriers [5]. Of all these alternatives, biodegradable and biocompatible polymer-based nanofibers have garnered the greatest attention due to their remarkable physiochemical properties, which include a large surface area, tiny diameter, and high aspect ratio, as well as their extensive flexibility and efficiency [6, 7]. Additionally, a controlled and sustained release of the drug at the site of action will maximise its pharmaceutical effects, whereas the use of electrospun nanofibrous scaffolds in situ may lessen the disadvantages of systemic transfusion with free drugs or alternative delivery methods [8]. To give an example, A nanofiber can facilitate the dose-specific, site-specific, and timed release of several medications. reduce the possibility of antibiotic-resistant bacteria and multi-drug tolerance in cancer treatment [9–11].There are several ways to create nanofibers, such as electrospinning, self-assembly, template synthesis, and heat-induced phase separation [12–14]. But out of all of them, electrospinning technology is the most alluring due to its capacity to create nanofibers into 2D and 3D structures as well as its simple, straightforward, fast, and affordable manufacturing process [15]. The most efficient way to create composite fibres with synergistic qualities for new applications is through electrospinning, which combines multiple polymers with distinct functions in the solution phase [16].

1.1 Non-electrospinning

1.1.1 Methods Interfacial Polymerization

This method makes use of two different monomeric units that can further dissolve into two different phases, such water and oil stages. When the two monomers come into touch with the emulsion droplet, they will dissolve and then polymerize. For example, once the diamine has dissolved in the water phase, the oilsoluble diacid chloride is added to the solution. This reacts with the original precursor at the point of contact to form the wall material. The homogeneous nucleated growth of this approach allows for the creation of nanofibers. By Several forms of polymers can be created by selecting dissimilar monomers, however polyamide membrane is mentioned in the majority of articles [17, 18]. Sketching Drawing is another method used to generate fibresl ike dry spinning, that is.The main advantage of this method is that it only requires a micropipette or a sharp tip. With this method, a droplet of a polymeric solution that has already been deposited is pulled as wet fibres using a pointed tip. The wet fibres then harden as a result of the solvent evaporating due to the increased surface area. To avoid mass shrinkage, which limits the consistent tugging of the fibres and affects their size, cylindrical-shaped capillary tubes can be used in place of the tip of a sharp end with continuous polymer administration [18]. By employing this method, It is possible to produce continuous nanofibers in any arrangement. Furthermore, it is feasible to obtain precise control over drawing's key parameters, like viscosity and drawing speed, to enable reproducibility and control over the size or shape of the fibres generated [20]. This technique is easy to use, but it is limited to lab-scale production because single nanofibers can only be produced one at a time. It is also feasible to control the diameters of these fibres using this technique, albeit it is an interrupted technique with low yield. In order to withstand the strain caused by squeezing, only viscoelastic materials may be used. Additionally, depending on the size of the orifice, only fibres with dimensions By employing this method, it is possible to produce continuous nanofibers in any arrangement. Furthermore, it is feasible to obtain precise control over drawing's key parameters, like viscosity and drawing speed, to enable reproducibility and control over the size or shape of the fibres generated [20]. This technique is easy to use, but it is limited to lab-scale production because single nanofibers can only be produced one at a time. It is also feasible to control the diameters of these fibres using this technique, albeit it is an interrupted technique with low yield. In order to withstand the strain caused by squeezing, only viscoelastic materials may be used. Additionally, depending on the size of the orifice, only fibres with dimensions.

1.1.2 Phase Separation

It is possible to produce continuous nanofibers in any arrangement. Furthermore, it is feasible to obtain precise control over drawing's key parameters, like viscosity and drawing speed, to enable reproducibility and control over the size or shape of the fibres generated [20]. This technique is easy to use, but it is limited to lab-scale production because single nanofibers can only be produced one at a time. It is also feasible to control the diameters of these fibres using this technique, albeit it is an interrupted technique with low yield. In order to withstand the strain caused by squeezing, only viscoelastic materials may be used. Additionally, depending on the size of the orifice, only fibres with dimensionsIn the phase separation procedure, a polymer is treated with a solvent before it undergoes the gelation process. Stages as a result of physical interference,

separate. The other phase is removed once the solution has been extracted from it. Particular advantages like bulk homogeneity and minimal equipment needs are attained using this method. The polymer composition affects both fibre diameter and thickness in addition to determining the mechanical properties of nanofibers [21]. This method is frequently used to create nanocomposites for three-dimensional tissue engineering. Additionally, such that the method has certain drawbacks, such as the wide range of polymers that can be used and the fact that it is only an experimental process [22]. In tissue engineering, phase separation techniques could be used to produce a variety of chemically synthesised polymeric nanocomposite materials factors to take into account [23].

1.1.3 Template Synthesis

Using this method, nanofibers are produced in the tubular channels of polymeric or spongy ceramic materials. First, you need to fill the monomeric spongy template. In the small spaces of the spongy template, the monomers are then chemically or electrochemically transformed into polymer nanofibers. Nanofibers are separated once the template is etched or dissolved. The synthesised polymer's tendency to deposit onto the interior wall of the void passageways is why nanofibers created using this method usually have a hollow structure. Polymer solutions can also be directly fed into the hollow tubes to generate nanofibers without the need for monomers.

where, upon removal of the solvent, they harden into nanofibers. Instead of using monomers to make the nanofibers, this approach makes use of polymer solutions. Polymeric solution-made nanofibers often have larger diameters than monomer-made ones because the increased viscosity of polymeric solutions makes it difficult to use entirely tubular passages with low diameters [24, 25].

1.1.4 Self-Assembly

Using a process known as self-assembly, which is defined as the spontaneous assembly of materials into forms or forms without the need for human intervention [26, 27]. This technique is highly effective in producing comparatively thin nanofibers, typically measuring a few micrometres in diameter. It achieves this by creating supramolecular hydrogels through the self-assembly of smaller chemical compounds through non-covalent interactions such as hydrogen bonding and hydrophobic interactions. The fundamental process depends on these kinds of intermolecular interactions to bind smaller units, or molecules; the arrangement of these smaller molecular units determines the general form of a macromolecular nanofiber. The primary disadvantage of this technique is that it is labor-intensive, time-consuming, generates little, and has inadequate control over fibre diameters. Furthermore, this method's ability to create nanofibers is limited to smaller bioactive components that could self-assemble independently or in reaction to external cues [25, 28].

1.1.5 Freeze Drying

This fibre synthesis process is also known as ice segregation-induced self assembly or solid-liquid phase separation. It consists of three primary steps: At very low temperatures (-70 to -80 0C), the mixture is first frozen in order to encourage the growth and nucleation of ice crystals. Water can be sublimated immediately without going through any chemical processes or creating any undesirable byproducts when the frozen sample is put in an assembly and its pressure is reduced to a few mm-hg using partly vacuum. This procedure is called primary drying, and the bulk of the unfrozen water in the material is eventually removed by desorption in a secondary drying step. Freeze drying (FD) offers a number of noteworthy benefits over other techniques. Consequently, there has been an increasing amount of interest in producing nanofibers. Unlike other techniques like electrospinning and self-assembly, it can create nanocomposites with tunable dimensions straight out of polymeric materials like chitin without the need for pretreatments or chemicals that direct the structure. In addition, a high temperature or further leaching are not necessary for the freeze-drying process phase, and the scaffold-building process is better suited for biomedical applications because it uses water and ice crystals instead of an organic solvent. Although there are many advantages to the freezedrying process, it is still challenging to employ it to make composites with hierarchical structures, including perfused systems. The resultant nanofiber mats can be utilised as templates for the production of synthetic fibres, drug delivery systems, or macroporous carbon nanocomposite. The freeze-drying method has been extensively studied in the context of reconstruction [29]. The use of freeze-drying has garnered a lot of focus on developing three-dimensional nanofibrous scaffolds [30, 31] for tissue regeneration.

1.2 Electrospinning Methods

Electrospinning is a process that creates fibres by applying a high voltage to a polymer solution that is flowing across a tip of the needle. Several electrospinning methods can be categorised by looking at the solvent source and the kind of needle tip [32].

1.2.1 Monoaxial Electrospinning

The polymeric solution is used during the entire electrospinning process. applying a high voltage to the needle tip while pumping the polymeric solution across it. When a voltage is applied, the polymer liquid can expand to take on the shape of the hanging drop, whereas surface tension usually creates a sphere. When the electrostatic repulsion of a charged polymer liquid is greater than the interfacial tension, a cone-shaped structure called a Taylor's cone is produced. The jet starts at the needle's tip, and fibres spread out across a metallic collector that is grounded. It is helpful in the production of nanofibers with a single medication [33].

1.2.2 Side-by-side Electrospinning

Typically, two or more capillaries, one beneath the other and one parallel to it, indicate side-by-side spinnerets. To produce the the Janus beads-on-a-string product line was developed using a side-by-side electrospinning method that was distinguished by a homemade eccentric spinneret. Janus beads-on-a-string were manufactured via a side-by-side electrospinning method using a homemade eccentric spinneret. One side of the Janus beads on a string used the hydrophilic polymer polyvinylpyrrolidone K90 (PVP K90) to form nanofibers and carry a first model drug, while the other side used the hydrophobic polymer ethylcellulose (EC) to form particles and carry a second model drug. Due to the fact that the different polymer matrices and topologies of Janus nanocomposite have different impacts on two features of drug release [34].

1.2.3 Coaxial Electrospinning

Coaxial or triaxial electrospinning is believed to become the most effective method for producing electrospun core-sheath nanofibers. The most effective way to provide a prolonged release of the medication. A core solution and a sheath solution must flow simultaneously via separate capillaries in order to form a fibre [36]. To produce a fibre having different interior and outside components, such hollow and functional fibres.Coaxial electrospinning can be used to create coresheath structural fibres with a range of core and sheath solutions, which may include coatings [37]. During coaxial electrospinning, a smaller capillary that concentrically fits inside the larger capillary is added to the spinneret, changing its form to one that is coaxial. Whereas the outer needle has a sheath solution, the inner needle has a core solution. When the inner and outer nozzles pump two different spinning solutions simultaneously, a core-shell droplet is produced at the nozzle's output. Recent work by Hai et al. demonstrated the Taylor cone formation mechanism in typical one-fluid electrospinning and techniques for coaxial electrospinning [39]. Peiwen et al. (2020) used this method to generate electrospun nanofibers with the antibiotic emodin inside a hydrophilic PVP core and encasing it in a sheath of hygroscopic cellulose acetate in order to provide a long-lasting activity against the S. aureus resistant bacterial strains [40].

1.2.4 TRIAXIAL ELECTROSPINNING

It is frequently possible for molecules held in coaxial fibre cores to be released under control when the fibre sheath material is not hygroscopic. When the sheath layer is hygroscopic either because hygroscopic polymers are used or water-soluble compounds are added water molecules create pathways between the fibre core and the surrounding air. Because of this, release from the core occurs quite quickly and is more akin to burst release than to controlled release.

Owing to their frequent hygroscopicity and strong biocompatibility, a variety of materials (such as One challenge is that many in vivo applications choose gelatine, collagen, peptides, etc.) for the sheath layer. To solve this issue, three-layer (core, intermediate, and sheath) structured fibres are made via triaxial electrospinning. The intermediate layer acts as a buffer zone between the outermost core and the exterior sheath. The triaxial fibre technique is essential for achieving high biocompatibility when using hygroscopic material for the sheath. In this case, rather of being swiftly released through dissolving, the bioactive ingredients from the hydrophobic intermediary layer forces the core to permeate through it [41]. Triaxial fibres were made by Nagiah et al. (2020) with a PCL core layer, a 50:50 PLGA sheath layer, and an intermediate gelatinous layer [42]. The drug's mechanism of release widely acknowledged processes for drug release from biodegradable polymers are erosion and diffusion. The drug employed and its concentration will have an impact on the release mechanism and polymer breakdown [43]. Drugs are released from biodegradable polymers in vivo by both of these processes, and a crucial element in this process is the ratio of erosion to diffusion rate. The breakdown of biodegradable polymers used in medication administration is primarily caused by enzymatic and hydrolytic reactions. An interaction between the connections inside the

polymer network and the molecules of water.Hydrolysis is the process by which ester linkages continually reduce the polymer chain until it reaches the monomers. Drugs can be released from biodegradable polymers when water molecules break chemical connections with polymer chains during enzymatic breakdown, weakening the structural consistency of polymeric materials [44].

2. PHARMACOLOGICAL APPLICATIONS OF NANOFIBERS

This section's core subjects are the primary and most widely used application of nanofibers for drug delivery that has been reported in the literature, as well as the process used to produce them.

2.1 Antibiotics

New, highly adaptable, and diverse antibiotic administration methods could lower the dangers of overdosage and the growth of bacterial resistance through targeted action at the infection site. Electrospun nanofibers have unique properties that make them a potentially attractive starting point for the creation of an innovative antibiotic drug delivery system [45, 46]. Pisani et al. (2019) developed electrospun nanofibers that are loaded with gentamicin sulphate and composed of polylactic acid and polycaprolactone (PLA-PCL). They could be applied after surgery to prevent the formation of bacterial biofilms. An aminoglycoside antibiotic with a high prevalence of side effects and a limited oral absorption is gentamicin sulphate. When administered intravenously or intramuscularly, such as renal and ototoxicity. One potential solution to reduce side effects and increase antibacterial efficacy is to develop a targeted medication delivery system [47]. Behbood et al. (2017) built the bio mucoadhesive oral delivery mechanism by loading the glycopeptide antibiotic vancomycin into blended fibres of chitosan and gelatin [48].The enhanced absorption and bioavailability of such types of implants, their steady release, and Their three main advantages are the elimination of first-pass metabolism.

2.2 Anticancer medications

Cytotoxic drugs like doxorubicin, which can cause apoptosis and interrupt the cell cycle, are used in cancer chemotherapy to reduce the growth of the tumour [49]. since of the tumor's fast growth, there is a high degree of vascularization since the healthy tissue needs to get more nutrients. This means that the major site of biodistribution for the medicine is the tumour, where it needs to act [50]. On the other hand, there is ample evidence of the grave side effects of cancer chemotherapy. Consequently, the creation of localised delivery systems for chemotherapy drugs may preserve the drug's cytotoxic effects while reducing the patient's systemic toxicity. The reason why electrospun scaffolds are a good choice for chemotherapeutic delivery systems is very potent drug release tunability and good biocompatibility [51]. Kuang et al. (2018) developed a scaffold with a controlled release of doxorubicin [52]. The scientists employed two hydrophilic and hydrophobic polymers, polyethylene oxide (PEO) and PLLA, in the mix electrospinning process. To enhance the therapeutic effect, the release underwent two revisions. In the early stages, part of the medication can be rapidly released to suppress the tumour phases. Conversely, the subsequent phase has a profile of extended release in order to prolong the course of treatment.

2.3 Ocular diseases

Typically, eye drops—saline solutions with active pharmaceutical ingredients—are used to treat ocular illnesses. The system has a low bioavailability because of its small volume, the quick turnover of the tear film, and the numerous physiological barriers that drugs must cross. Since solid delivery systems may have less clearance than liquid ones, they may have a better bioavailability for ocular illnesses [53, 54]. This has led to an increased focus on these delivery methods. Tawfik et al. produced coaxial electrospun nanofibers in 2020 using two different drugs in two different areas to treat ocular irritation and halt the microbiological infection's spread [55]. The anti-fibrotic drug pirfenidone, which is prescribed in clinics to treat eye disorders, was placed into a PLGA shell. On the other hand, the antibiotic moxifloxacin was present in the hydrophilic PVP core. Gottelet al. (2020) used a solid in situ gelling method based on Phytagel/pullulan electrospun nanocomposites to treat topical eye diseases [56]. The reason the authors developed a method to bend the scaffold into a particular shape is because the structure of the eye, applying solid medication is more challenging than applying eye drops. The authors created a technique to bend the scaffold into a specific shape because the Applying solid medication is more difficult than applying eye drops due to the shape of the eye.

2.4 Anti-fungal drugs

Polymeric electrospun is also being researched for the transdermal delivery of several antifungal medicines tiny filaments. Harini et al. [57] investigated the antifungal potential of polycaprolactone (PCL)/egg lecithin-based nanofibers to treat cutaneous fungal infections.
The produced nanofibers, measuring 127.7±43.7 nm in diameter, were found to be non-toxic to human dermal fibroblasts using confocal microscopy. Additionally, they showed remarkable antifungal efficacy in vitro against a range of fungi, such as topical fungal infections-causing Trichophyton mentagrophytes and Epidermophyton.

2.5 Anti-inflammatory drugs

Additionally, pharmaceutical researchers have investigated the use of electrospun nanofibers for the transdermal delivery of several anti-inflammatory drugs. Ibuprofen-impregnated cellulose-based nanofibers .Shi et al. investigated the acetate/poly (vinyl pyrrolidone) basis for transdermal delivery. With a diameter of 167±88 nm, ibuprofen was dispersed consistently and in an amorphous form across the optimised nanofibers' nanofibrous network. In comparison to a conventional transdermal patch containing the same medication, the created nanofibers showed better in-vitro skin penetration, which was followed by higher permeability to water vapour, indicating them high thermal stability [58].

2.6 Wound care management

As the largest organ and the outermost covering of the body, the skin serves three main purposes: defence, equilibrium in addition to sensibility. Because skin acts as a barrier between the body's internal and exterior environments, protecting it from pathogens and injuries, skin is particularly vulnerable to harm [59, 60]. Research is increasingly focused on creating nanofiber-based dressings with high porosity, a high surface area to volume ratio, and the ability to replicate the skin extracellular matrix. Unlike their conventional processes, these nanofibrous dressings were intended to promote wound healing through the creation of a comfortable environment [61]. The capacity to include active components, such as drugs, may improve healing or provide antibacterial medications that reduce inflammation from wounds [62]. Guo et al. (2020) developed a pH-responsive nanofibrous scaffold for the sequential administration of two medications in the treatment of wounds. The fibres were created by combining a chitosan/polyethylene oxide mixture with PCL and a shell of lidocaine hydrochloride, which is used to reduce inflammation. curcumin, a medication with anti-inflammatory properties, into the centre. Both sodium bicarbonate and chitosan were included in the object's centre, leading to the pH-responsive activity [63]. Chitosan (CS) is a great option for wound care treatment because of its superior haemostasis [64] and wound healing properties [65, 66]. Since CS has limited spinnability due to the stiffness of the polymeric chains, spinning agents like polyethylene oxide are commonly added to increase spinnability [67].

3. CONCLUSION:

The exploration of nanofibers as a cutting-edge carrier system for drug delivery presents a compelling narrative of innovation and potential in the medical field. This comprehensive review underscores the transformative impact of nanofibers, delineating their unique attributes and diverse applications, while also recognizing the challenges and future directions in this burgeoning field.Nanofibers, owing to their high surface area, tunable properties, and customizable architectures, emerge as a pivotal platform for revolutionizing drug delivery strategies. The ability to precisely engineer these structures, utilizing various fabrication techniques and a plethora of materials, offers unparalleled opportunities for tailored drug encapsulation, controlled release, and targeted therapeutic interventions.Throughout this review, the versatility of nanofibers across different medical domains has been showcased. From cancer therapeutics to regenerative medicine, wound healing, and infectious disease treatment, nanofibers exhibit immense potential. Their capability to encapsulate a wide range of drugs, protect them from degradation, and release them in a controlled manner presents a promising avenue for enhancing therapeutic efficacy while minimizing side effects.However, challenges such as scalability, standardization of fabrication techniques, and long-term safety evaluations remain pertinent. Addressing these challenges will be instrumental in realizing the full potential of nanofibers in clinical applications.In conclusion, this review highlights the transformative role of nanofibers as a novel and versatile carrier system in drug delivery. As research continues to unravel their capabilities and address existing limitations, nanofibers stand poised to significantly impact medical treatments, offering personalized and efficient therapeutic solutions across a spectrum of ailments.

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