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Review Article

POLYMERIC NANOFIBERS – A FUTURISTIC DELIVERY SYSTEM: A REVIEW

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Abstract:

Nanofibers are an interesting versatile material used in a very wide range of biomedical applications such as burn and wound care, organ repair, and treatment for osteoporosis and various diseases. The nanofibers are usually fabricated by using electrospinning method. There are various polymers that are employed in preparation of nanofibers by electrospinning method. A detailed discussion has been made on Chitosan, starch, chitin and use of biodegradable polymers like PVA, PEO for fabrication of nanofibers in this article.

Keywords: Drug delivery, Nanofibers, Electrospinning, Chitosan, Starch, Polyvinyl alcohol.

Introduction:

Nanofibers are the fibers having dimensions of 100nm (Nanometer) or less as defined by the National science foundation (NSF) (1).

The fibers are typically round-shaped and their diameter can be easily set by adjusting the process parameters. (2)

There are numerous research carried out around the world in past decades on nanofibers which has brought out different properties such as superior mechanical strength which comes from the complexly arranged molecular chains in the structure and less possibility of surface damages thus reducing cracks (3). The other property which makes them so special is that the superb pore interconnectivity of the fibers which are highly porous and increased surface area (4).

The above mentioned properties of nanofibers make them unique and have more applications in various fields such as drug delivery, tissue engineering, protective clothing for military, filtration of media, wound dressing and certain food products such as DHA (docosahexaenoic acid), folic acid, betacarotene, and epigallocatechin gallate using various polymers for enhancing their chemical stability. (5)

There are various approaches or techniques for the producing nanofibers but majorly they are synthesized by electrospinning technique.

The other different technique by which nanofibers would be produced are the methods such as drawing, template synthesis, phase separation, self assembly and as mentioned previously by electrospinning (5). These can be shown in fig (1).

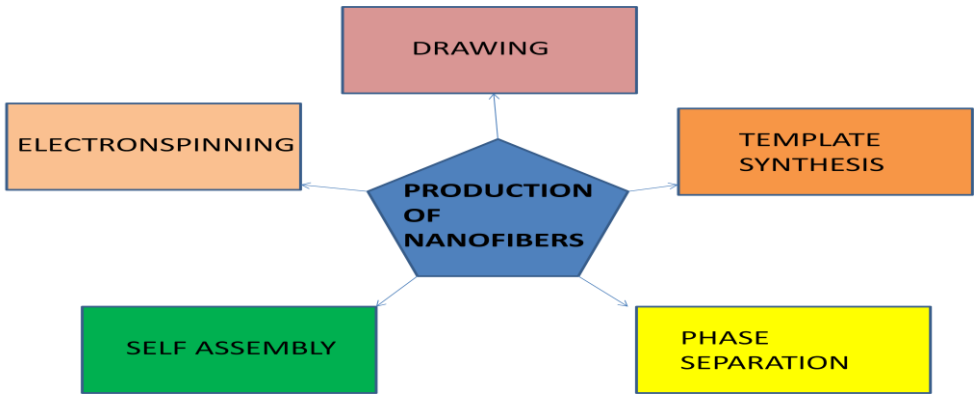

Fig 1: **Shows a schematic representation of production of nanofibers by the various approaches.**

Drawing technique:

The fibers produced by drawing technique are extruded through a spinneret and drawn mechanically as the polymer solidifies. This technique is the simplest of all other approaches. This technique involves the use of strong materials which have good tensile strength, cohesiveness to aid the stress experienced by the fibers during pulling or stretching process and the nature of the material shall be viscoelastic. This process produces long single nanofibers and one at a time (5).

Template synthesis:

Another formulation method is template synthesis, during which a nanoporous membrane forms a template for creating nanofibers. during this methodology the polymeric compound solution is separated by the template membrane from the solidifiying solution. The solution is forced fed through a membrane by a cylindrical column. Then the polymeric solution passes through the membrane and nanofibers kind once it comes into contact with the solidification solution. This methodology cannot turn out one-by-one continuous nanofibers Poly(ε-caprolactone) (PCL) has been with success made by extruding PCL solution through a porous alumina template and solidifying in wood alcohol (5).

Phase separation:

An alternate method to manufacture nanofibers is by phase separation which involves the various processes like dissolution of polymer, gel formation, extraction of solvent, freezing and freeze drying. The commonly used

polymers in this methodology are PLLA (poly L-lactic acid) and PLLA-CL (poly L-lactic-co-caprolactone). To manufacture nanofibers, a polymeric solution is formed with utilizing tetrahydrofuran, a gel is prepared by addition of a non-solvent to the polymeric solution. Then the solvent is extracted from the gel and then kept in freezer at around -18˚C for a couple of hours. This frozen gel is freeze dried for a week to manufacture PLLA nanofibers. The main drawback of this method is that its time consuming and fewer polymers can be used. (5)

Self assembly:

In this approach the nanofibers are constructed with the help of single previously existing component as a building block. In this method the molecules would be arranged into orderly fashion by non covalent interaction and resulting structural characteristics of the nanofibers are oriented by factors like pH, co-assembling of molecules, temperature. As said in phase separation this method is also time consuming. (5)

Electrospinning:

This method is the most employed for production of nanofibers. By this technology solid thin-fibers of diameter 10 to 1000 nm are produced. This technique yields high production rate when compared to other approaches. This technique was patented in 1934 by formhals. The setup of electrospinning is very simple and has low cost. Its unique setup includes a syringe which holds the polymeric solution in it, which is attached to a pump for constant pumping of polymeric solution from the syringe. The positive electrode is connected to the spinneret which is inturn attached to the syringe. The negative electrode is connected to collector plate but (grounded usually). At certain voltage, the polymeric solution from the spinneret is charged enough to bypass the surface tension of the solution and causes the polymeric solution to eject from the spinneret tip to the collector. As the polymer jet travels in the air towards the collector plate the solvent evaporates and the jet solidifies yielding a fibrous mat on the collector plate (5, 6) as depicted in fig 2. As mentioned earlier this method is the most widely used method. The nanofibrous structure of electrospun scaffold can mimic the ECM and varying the conditions permits control over fiber diameter and fiber orientation within a lattice or mesh (7, 8)

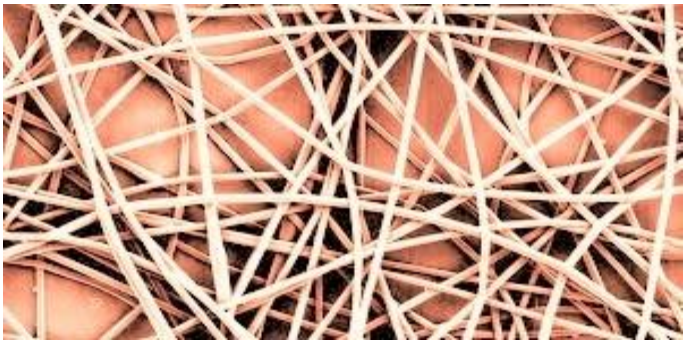

Fig 2 : Shows a SEM image of electronspun nanofiber.

Concentration of the polymeric solution is important for the electron spinning method, if the concentration of the polymeric solution is more then, the yield of the fibers will be discontinuous. Even the viscosity of the polymeric solution plays a major role in this method since insufficient viscosity produces electronspray of the solution instead of electrospinning (6). The viscosity of polymeric solution also helps in determination of morphological characteristics as well as size of the fibres (5).various other parameters have been listed in **Table 1.**

Table 1: **Effect of Electrospinning parameters on fiber morphology.(9,13).**

Slno	Parameters	Morphology of the Nanofibers
1	Conductivity	In general, higher the conductivity smaller the nanofibers Higher conductivity yields smooth bead-less nanofibers.
2	Molecular weight of the polymers	As the molecular weight of polymer increases there will be decreased number of beads or droplets in the nanofibers.
3	Concentration and viscosity	In general, lower the concentrations and viscosity of the solution leads to production of beads and high concentration and viscosity will reduce the above condition
4	Feed rate or flow rate	It should be optimum so as reduce the formation of beads. Generally low feed rate often yields smaller diameter of the nanofibers.
5	Voltage applied	Increase in the voltage applied reduces the fiber diameter
6	Temperature	Temperature should be ambient so as to dry the fibers, but its been noticed that increasing the temperature will decrease the fibers diameter.
7	Distance between the syringe tip and collector or reciver	Formation of beads in the fibers, with too small and too large distance, hence optimum distance is required for uniform fibers.

Many synthetic and natural biopolymers have been electrospun. Poly(glycolide) (PGA), poly(lactic acid) (PLA), and their copolymers poly(glycolide-co-lactide) (PLGA) and poly(caprolactone) (PCL) are synthetic polymers that have been electrospun into fibrous membranes for tissue engineering applications. These synthetic polymers have been used successfully as delivery systems but many of them are not permitted for use in food applications. (5) Certain polymers have been listed in the **Table 2**.

Table 2: **Electrospun Polymers and Corresponding Literature.**

Slno	Polymers	Solvents used	Reference articles
1	Polyurethane and PEO	Tetrahydrofuran and Dimethylformamide	the structure and morphology of polyurethane nanofibers was studied. Fiber diameter as low as 30nm was prepared.(28)
2	Polyethylene terephthalate (PET)		The thermal properties of electrospun PET and PEN fibers made from melts

	and Polyethylene naphthalate (PEN)		was investigated.(28)
3	Poly (p-phenylene terephthalamide) (PPTA)	95–98 wt % Sulphuric acid	The crystal structure and morphology of electrospun Kevlar fibers was studied.(29) from Dupont) Fibers from 40 nm to a few hundreds of nm were produced.(28)
4	Polyethylene-co-vinyl acetate (PEVA), Poly lactic acid (PLA) and blend of PEVA and PLA.	Chloroform	The potential of electrospun fiber mats as a drug delivery system for the release of tetracycline hydrochloride was studied.(30) Electrospun PEVA _ PLA blended fibers were 1–3 μm in diameter, while the PLA fibers were around 3–6 μm.(28)
5	Poly (methyl methacrylaterandom) PMMA-r-TAN	Mixed solvent of Toluene and DMF	Dietzel et al. produced electrospun fiber mats with specific surface chemistry from random copolymers of PMMA-r-TAN. They have demonstrated that the atomic concentration of fluorine at the surface of electrospun fibers was twice the amount seen in bulk materials.(31) The fiber diameter was in the range of 2 μm to 300 nm.(28)
6	Poly-L-Lactide	Dichloromethane	Zeng Jun et al. electrospun PLA fibers and observed the cylindrical morphology of fibers with diameters ranging from 800 nm–2400 nm.(28, 32)
7	Styrene-Butadiene-Styrene (SBS) triblock copolymer	75% THF and 25% DMF	Examination of the morphology of fibers with respect to micro phase separation and experimented with annealing for accelerating the ordering process and stress relaxation.(33) The electrospun fibers were around 100 nm in diameter.(28)

8	Polycaprolactone	Acetone	Reneker et al. studied the onset of the bending instability during spinning and observed the formation of a closed single and double loop fiber structure called "Garland".(34) This garland structure has been observed in other copolymers like vinylidene fluoride, tetra fluoroethylene, and polyethyloazoline.(34) The fiber diameter varied from 1 micro m to 1.5 μm.(28)
9	Polyvinyl chloride	THF, DMF	Lee et al. studied the effect of volume ratio of mixed solvents on the structure and morphology of electrospun fibers.(28, 35)
10	Polyaniline/PEO blends	Chloroform	Fine fibers with desired conductivity by using Polyaniline /PEO polymeric blends was produced. (36) The fiber diameters were in the range of 950 nm to 2.1 μm (28)
11	a) Polyethylene oxide b) Polyvinyl alcohol c) Cellulose acetate	a) Water/chloroform b) Water c) Acetone	The morphological characteristics of electrospun polymeric fibers in the diameter range of 200–800 nm was studied.(28, 37)
12	Polyethylene oxide (PEO)	Water	Doshi and Reneker have experimented with the spinning of PEO fibers from aqueous solutions and studied the relationship between process and solution parameters on fiber characteristics.(38) Electrospun fibers were about 0.05 to 5 microns in diameter.(28)

Gelatin, alginate, Collagen, Zein, and Cellulose derivatives are different kinds of food biopolymers which have been electrospun before. Non-toxicity, biodegradability and strong mechanical performance are some of the advantages of these biopolymers. Many of these polymers cannot be electrospun in an aqueous solution, but they can be spun readily by mixing the aqueous solution with Polyethylene oxide. The difficulty of spinning these aqueous biopolymer

solutions can be attributed to their properties such as low viscosity and high electrical conductivity. This problem can be overcome by blending the biopolymer solution with Polyethylene oxide. (5)

The nature of polymer, that is whether it is polyanionic or polycationic, plays a vital role in the development of control-release drug delivery system. Various natural and synthetic polymers, e.g. natural polymers, like alginic acid, guar gum, xyloglucan, pectin, chitosan, and so on. And synthetic polymers, like poly(lactic acid), poly(DL-lactideco-glycolide) and poly-caprolactone, HPMC, and so on, have been employed in the electrospinning process alone or in blend with other polymers to develop suitable nanofiber system for drug delivery.(9)

Polyvinyl alcohol (PVA)

Polyvinyl alcohol (PVA) has been widely studied due to its amazing film forming ability, high hydrophilicity, greater chemical resistance and excellent mechanical properties. These various properties have led to its skillful utilization in different fields including biotechnology and biomedical areas. Hence, electrospun PVA fibers are excellent candidates for filtration, drug delivery, tissue engineering scaffolds, nanosensors or biocatalysts immobilization. (10)

PVA nanofibers have supported enzyme immobilization such as cellulase, acetylcholine estersase, laccase, glucose oxidase. Even though PVA has many advantages, but it also has certain disadvantages such as the high water dissolution and poor mechanical strength have limited them from further applications. One of the applications is listed below that PVA has been used in immobilization of naringase which hydrolyses narigin to naringenin and there are no interamolecular interactions with PVA. Thus, it showed that the nanofibers, so obtained were stable and also adequate for enzyme entrapment, retaining high catalytic activity. Yet another application is that PVA in combination of glutaraldehyde in entrapment of cellulase enzyme as nanofibers. (10)

Almond gum as Nanofibers: Almond gum is obtained as a exudates which is natural, biodegradable and non-toxic polysaccharide. The almond gum is exudated from sweet almond trees (*Prunus dulcis* L., *Prunus communis* L) belonging to family Rosaseae. It is structurally composed of arabinogalactan and has two major fractions namely water insoluble fraction and the other is water soluble fraction.

Almond gum has made itself a potential candidate for preparation of nanofibers due to following advantages such as the high molecular weight, high thermal stability, as mentioned earlier the non-toxicity, and most importantly the cost and availability. Almond gum can be electronspun due to its high molecular weight. (11, 12)

Atefe Rezaei et al., found that almond gum/PVA can be electronspun into nanofibers with diameter size less than 100nm. Their research work has been briefed in this paper for better understanding of the almond gum/PVA

nanofibers. The FTIR analysis of the nanofibers gives vital information of almond gum and PVA have crosslinked by etheric bonds. Chemically the C-OH group of almond gum and OH groups of PVA had been linked. (11)

PVA as mentioned above that it is non-toxic polymer and is soluble in water and also can be easily electrospun at room temperature. PVA plays a important role in reducing the charge repulsion among the polyanions of almond gum chains and thus increases the corresponding molecular entanglement. (11)

As discussed earlier in electrospinning concentration is critical parameter and in this case concentrations higher than 10% resulted in much higher viscosity resulted in difficulty of polymeric solution that had to be ejected from the needle. As well as the concentrations of polymeric solution did not produce uniform fibers. The prepared almond gum/PVA nanofibers were able to protect vanillin from heat by chemical interaction between the polymers. (11)

Chitin-Chitosan Nanofibers:

Chitin is chemically β-(1-4)-poly-N-acetyl-D-Glucosamine. A polysaccharide is most widely distributed in the nature. It is majorly present as a structural component of exoskeleton of crab, shrimp shells, insects and also present in cellwall of fungi and yeast. Chitin's strength and flexibility makes it a very suitable for surgical thread and also has an added advantage that its biodegradability i.e, as the wound heals it gets degraded. Also there has been reports that it fastens wound healing in humans.

These Chitin and Chitosan can be processed without difficulty into different products like Nanofibers, micro/nanoparticles, sponges, hydrogels, scaffolds.

Both chitin and chitosan are biodegradable, biocompatible, non-toxic, hydrating agents as well as antimicrobial agents. The derivatives of chitin and chitosan including glucosamine and chitosan oligosaccharides are used as functional foods.

Numerous works have reported that chitin and chitosan are employed in various applications such as wound healing **(**13**)**, tissue engineering, stem cell technology, drug and gene delivery. (14).

The nanofibers formed by using dry powder of chitin developed strong hydrogen bonds after separating from the matrix thus fibrillation into nanofibers kept wet after removal of the matrix. It was observed in the work of Kazuo Azuma et.,al that the slurry prepared from dry chitin powder was first made to pass through a grinder in presence of acetic acid to fibrillate the chitin nanofibers bundles which resulted in a viscous chitin slurry that on disintegration formed uniform network of nanofibers with high aspect ratio. On the other hand when the slurry was made to pass through a grinder in absence of acetic acid to fibrillate the chitin nanofibers bundles resulted in dry, unable to disintegrate and were also thicker nanofibers bundles. The reason for disintegration was the drying process of chitin

caused stronger hydrogen bonds between hydroxyl groups, acetamide and amino groups. Therefore, this new process can be successfully implemented because of the electrostatic repulsive forces between the nanofibers. The electrostatic repulsion force arising from the cationic surface charges was sufficient to break the strong hydrogen bonds. This method could provide a prominent advantage for the industrial utilization of chitin in terms of continuous supply, storage stability, transportation costs, storage space, and so on, because chitin nanofibers can be prepared by a simple process from light, less quantity, and non-perishable dried chitin. Because other acidic chemicals are also available to facilitate fibrillation, including ascorbic acid, lactic acid, citric acid, and so on, we can select acidic additives as per their applications. This method is also applicable to commercially available dry chitin powder from crab shells composed of nanofibers of different thicknesses, and having range from 10 to 100 nm. (14)

Chitosan fiber is the most popular form arising from its adequate drainage of exudates and adherence to wound bed to avoid dead space. Chitosan is a lineal polysaccharide comprising of randomly arranged β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D-glucosamine (acetylated unit). It is formed by treating the chitin shells of shrimp and other crustaceans with an alkaline substance, like sodium hydroxide. Chitosan is useful in bandages to decrease bleeding and also has antibacterial property. It is useful in various formulations and also be used to help deliver drugs through the skin. (13)

Chitosan is an attractive material for electrospinning. However, chitosan is difficult to electrospun into a nanofibrous structure because it has a polycationic character in acidic aqueous solutions due to the many amino groups in its backbone. The polycationic nature of chitosan increases the surface tension of the solution considerable. A strong electrical force is needed to produce electrospun chitosan nanofibers, and particles are often formed during the electro spinning process, which is likely due to the repulsive forces between the ionic

group in the chitosan backbone in an acidic solution.(13)

The work of anjali has showed us that Natural polymers are used as lead compounds for design of therapeutic drug delivery systems for treatment of different ailments. Chitosan and Neomycin sulphate have proven wound healing properties individually.

The combination of these two, polymers and incorporation of drugs into the composite nanofibers show improvement in wound healing property. The drug loaded nanofibers shown significant difference in antibacterial activity when compared to neomycin cream. Percentage of wound contraction was more for wounds treated with neomycin sulphate loaded chitosan nanofibers than when compared to the blank nanofibers and neomycin cream. With this above

results, neomycin sulphate loaded chitosan combination has shown better results when compared to chitosan nanofibers and neomycin cream alone in wound healing activity. (13)

Through electrospinning, biocompatible polymers can be spun into a nano-sized mesh. This nano-mesh is composed of fibers with a high surface area, and a nano-sized diameter that can be used to mimic a natural extra-cellular matrix (ECM), which acts as scaffolding that allows cells to attach, proliferate, differentiate, and develop essential functions within tissue. Providing cells with an artificial ECM encourages tissue growth and therefore promotes healing. Using chitosan as a component in the extracellular matrix would also promote healing due to chitosan's unique biological properties.(13)

Chitosan is biodegradable, biocompatible, nontoxic, a haemostatic, and a natural Antibacterial agent. The nanomesh is similar to an ECM and would promote cellular Attachment and growth and would thus promote tissue healing; while chitosan would promote healing and reduce the chance of infection due to its bioactive and antibacterial properties. Decreasing healing time reduces the chance for scar tissue forming and resulting adhesions (15) Because this additional layer of chitosan is also a biodegradable polysaccharide, the entire product would still dissolve away within the body after a designated time.(13)

Fibers directly electrospun onto the injured skin could form a fibrous dressing, supporting healthy tissue to regenerate without going through tradition formation of scar. Nano-pore sizes also avert bacteria whose width mostly at micro scale from invasion that otherwise may infect the vulnerable wound. Nanofibers used to fabricate both dry as well as moist wound. These polymeric nano-fibers are hemostatic, having good absorbent properties and are suitable for full thickness wound. The frequency for changing dressing is less and provide gelation and moist healing which is suitable for any type of wound whether it is resulting acute or chronic conditions.(13)

These biopolymeric fibers generate insitu moist healing environment and the consequent high absorbency and de-bridgement of wound site (16) Due to its low adherent property on to the skin surface for any type of tissue, it provides better gaseous exchange which is preventing from bacterial infections. The advantage of nanofibers used in wound healing, as it absorbs excess of exudate and blood at wound site. Moreover, they behave as thermal insulator.

The nanofibers were prepared by using the following process, chitosan was dissolved in tricholoroacetic acid to form a solution and stored at room temperature for 24 hours for protonation. Then blend was loaded with 2 % NS solution and was stirred at 80° C for another 5 hrs in the magnetic stirrer. Electrospinning was performed as follow under room temperature. The syringe was located in a syringe pump and dispensed at a rate of 0.8 mL/h. A voltage of 15

kV using a high voltage power supply was applied across the needle and ground collector, which was placed at a distance of 12–15cm. The collector plate is covered by aluminium foil and nanofibers are obtained. (13)

Chitosan nanofibers are slightly soluble in water. Recently, Chitosan has been found to have potential in the area of biomedical science and engineering due to its distinctive biological properties, including biocompatibility and oxygen and water vapour permeability, biodegradability and minimally induced inflammatory responses *in vivo*. It was reported that chitosan loaded Neomycin Sulphate nanofibers could be useful for the culture of fibroblasts and keratinocytes, because it could enhance adhesion, growth and differentiation of cells with benefits similar to those extra cellular matrices. In addition, nanofibrous scaffolds of biocompatible Chitosan have great potential as dressing for wounds when combined with NS because they have a high specific surface area and nanoporous structure, and show good adhesion to damaged skin.

The Chitosan-Neomycin Sulphate nanofibers mats were in the nanometer range, were nontoxic and biocompatible, and displayed controlled-release characteristics, demonstrating excellent antimicrobial activity against Gram-positive S. aureus and Gram-negative E.coli and show increase in percent of wound contraction and decrease in wound healing time. It can be concluded that by the work of anjali that the prepared Chitosan-Neomycin Sulphate nanofibers can be used as a prospective delivery carrier for Neomycin Sulphate. (13)

Starch as nanofibers:

Starch is a kind of inexpensive and biocompatibility biopolymer which widely exists in plant tissues, such as stems, seeds, roots, rubbers, and leaves (17, 18). It can be cross-linked and linked with some materials susceptible to pH, redox agents, and enzyme due to its multiple hydroxyl groups. Thus, increasing efforts have been devoted to the study of the ST-based drug delivery system. Starch-based carriers can achieve targeted drug delivery and controlled drug release, and can minimize the stimulating effects of drugs on the gastrointestinal and other digestive organs (19, 20). However, there are some limits to the fabrication of Starch-based drug-loaded fibers by electrospinning. Most Starch's are composed of two structurally distinct moles: amylase and amylopectin. The amylase / amylopectin ratio varies with botanical origin. Most common Starch's have less amylase components, and thus their solutions show poor electrospinnability. Starch-based drug-loaded nanofibers by electrospinning, using inexpensive starch as the carrier and water as the solvent. (17)

Ampicillin is a class of penicillin antibiotic with beta-lactamic structure. Ampicillin has been extensively used because of its inhibitory effect on gram-negative bacteria and gram-positive bacteria, especially for E coli, influenza

bacillus, salmonella, shigella, and proteus (21, 22). So far, there are only limited reports on the fabrication of Ampicillin -loaded composite nanofibers by electrospinning (23–26).

Tang, Shanshan, et al. have prepared Ampicillin-loaded Starch-based nanofibers by electrospinning. The inexpensive maize ST was used as the biopolymers, and water was used as the sole solvent. Two nontoxic and biocompatible and biodegradable polymers, polyvinyl alcohol (PVA) and polyethylene oxide (PEO), were added for enhancing the electrospinnability of Starch aqueous solutions. (17)

The Ampicillin-Starch-Polyethylene oxide solutions (5.0 wt%, the total concentration) were prepared, respectively, by dissolving corresponding reagents in distilled water. The Starch and Ampicillin solutions were slowly added drop by drop in the PEO solution in succession under stirring condition. The mixed solution was sealed in an Erlenmeyer flask and further stirred for 24 h under room temperature, before it was used for fabricating the Ampicillin-Starch-Polyethylene oxide composite fibers applying an electrospinning setup. The Ampicillin-Starch-Polyvinyl alcohol solutions (8.0 wt%, the total concentration) were prepared, respectively, by dissolving corresponding reagents in distilled water. After the Starch solution and Ampicillin solution were added drop by drop in the PVA solution, the mixed solution was further stirred for 24 h under room temperature. Electronspinning was carried out at room temperature. The operating voltage was 15 kV, and the spinning rate was controlled by adjusting the flow of the Starch-based solution. After 2 days the nanofibers were collected. (17)

Tang, Shanshan, et al. Initially, tried to fabricate nanofibers with pure starch by electrospinning, using inexpensive maize Starch as the biopolymer and water as the solvent. However, all attempts failed, which might be due to the low amylose/amylopectin ratio. The amylose component of Starch is largely linear and assumed to readily associate side-by-side, which enables the solutions of high-amylose Starch to exhibit good electrospinnability. (27) Most common Starch's have low amylase/ amylopectin ratios, and thus their solutions always exhibit poor electrospinnability, especially when water is used as the solvent. As a result, in their experiments, PVA and PEO were introduced for improving the electrospinnability of Starch aqueous solutions. (17)

After PEO was added into the starch aqueous solution, the Starch-Polyethylene oxide composite fibers were successfully fabricated. This implies that the addition of Polyethylene oxide can significantly improve the electrospinnability of Starch aqueous solutions. The morphology of Starch-Polyethylene oxide composite fibers was similar to that of PEO fibers. The fibers were randomly oriented, and their surfaces were smooth and imporous. The diameters of Starch-Polyethylene oxide composite fibers were in a range of 100–500 nm. Moreover, when the Starch-Polyethylene oxide ratio increased from 1:4 to 2:3 the average diameter of fibers slightly decreased. These results

might imply that more ST content should result in thinner fibers. However, we failed to fabricate thinner ST/PEO composite fibers, when we tried to further reduce the content of PEO. Thus, the ultimate Starch-Polyethylene oxide ratios were determined as 1:4 and 2:3. Then, Ampicillin was added into the aqueous solutions having starch and Polyethylene oxide, and the Ampicillin-Starch-polyethylene oxide composite fibers were successfully formed by electrospinning. (17)

The formed fibers exhibited that it was almost cylindrical in shape, and the diameter of about 170 nm. No crystalline materials were observed on the surface of the fiber. This might show that Ampicillin molecules were highly dispersed in the fiber rather than accumulated on the surface of fibers. (17)

PVA could be electrospun into nanofibers using water as the solvent, and the Starch-based membranes could be successfully fabricated after PVA was added in the Starch aqueous solutions. the Starch-Polyvinyl alcohol composite fibers were randomly oriented, and the diameters of the fibers were in a range of 100–200 nm. Comparing the above data it can be found that the average diameter of pure PVA fibers about 200 nm was smaller than that of pure Polyethylene oxide fibers about 500 nm, which might mean that the PVA aqueous solution exhibited better electrospinnability than the Polyethylene oxide aqueous solution. As a result, in the processes of fabricating the starch-based nanofibers, the polymer content might be reduced, through replacing Polyethylene oxide by PVA. The highest Starch-polymer ratio could be increased from 2:3 to 1:1. Comparing with the Starch-Polyethylene oxide system, similar regularities could be found in the Starch-Polyvinyl alcohol system. Firstly, the average diameter of Starch-Polyvinyl alcohol composite fibers about 150 nm, was smaller than that of pure PVA fibers about 200 nm. Secondly, the surfaces of the Ampicillin-Starch-Polyvinyl alcohol fibers were smooth, and no crystalline materials were observed, which indicated that Ampicillin molecules were highly dispersed in the fibers. Finally, when Ampicillin was introduced into the Starch-based composite nanofibers, a large number of beads occurred. (17)

Ampicillin-loaded Starch based composite nanofibers via electrospinning by using water as the only solvent. The addition of PVA and Polyethylene oxide can effectively enhances the electrospinnability of Starch aqueous solutions. Ampicillin molecules were highly dispersed in the nanofibers, and the results of DFT (density functional theory) calculation shows that Ampicillin can form hydrogen bond interactions with Starch molecules. The Starch-based composite nanofibers showed effective and controlled drug release properties. The release of Ampicillin from the Starch-based composite nanofibers can be efficiently controlled through adjusting the ratio of Starch to polymers, drug loading, species of the polymers, and weight of the tablets. Lower ratio of Starch to polymer, higher drug loading, higher weight of the tablet, and the polymer with lower dissolvability must be applied, in order to

successfully release the drug for long time. Due to this result, the release time of drug can be controlled from tens of minutes to tens of hours. There work suggests that production of nanofibers by electrospinning can serve as an iconic technique in the field of Pharmaceutical for drug delivery system, and the Starch-based composite nanofibers might emerge as appropriate materials for controlled release of drugs. (17)

Nanofibers are fabricated by various polymers by electrospinning process as listed in **Table 3**. (13) The nanofibrous materials containing activated carbon particles can filter many chemical substances even at submicron particles. Nanofibers are into drug delivery of anti cancer, anti diabetic, vital vitamins as food as well as nutraceutical formulations. The medical feild of nanofibers has gained lot of advantages in recent years with wonderful application on transplant surgery, dental application, cosmetic and skin care, wound dressing, wound healing, in the treatment of burns and so on. (13, 14)

Table 3: **Polymers used in electrospinning with their application(13).**

Slno	**Polymers**	**Application by electrospinning**
1	Poly(ε-caprolactone) (PCL)	Bone tissue engineering
2	Poly(l-lactide) (PLLA)	3D cell substrate
3	Gelatin/polyaniline	Tissue engineering scaffolds
4	Collagen/chitosan	Biomaterials
5	Gelatin	Scaffold for wound healing
6	Chitosan/PEO	scaffold, drug delivery, wound healing
7	Poly(vinyl alcohol)	Wound dressings
8	Polyurethane (PU)	Nonwoven tissue template wound Healing
9	Poly(lactide-co glycolide) (PLGA)	Biomedical applications, wound Healing

Conclusions:

Nanofibers are fabricated in various techniques, but most common technique employed for fabrication is Electrospin method. Polysaccharides like starch, almond gum have to be combined with polymers like PVA and PEO for electrospinning to form nanofibers. Chitin, Chitosan have also shown good electrospinnability. Hence we can conclude that there are various polymer used in fabrication of the nanofibers by electrospinning method as discussed in this manuscript for drug delivery, drug encapsulation, drug carrier for controlled release and other purposes.

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