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# Recent Trends in the Fabrication of Starch Nanofibers: Electrospinning and Non-electrospinning Routes and Their Applications in Biotechnology

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**Abstract** Electrospinning a versatile and the most preferred technique for the fabrication of nanofibers has revolutionized by opening unlimited avenues in biomedical fields. Presently, the simultaneous functionalization and/or post-modification of as-spun nanofibers with biomolecules has been explored, to serve the distinct goals in the aforementioned field. Starch is one of the most abundant biopolymers on the earth. Besides, being biocompatible and biodegradable in nature, it has unprecedented properties of gelatinization and retrogradation. Therefore, starch has been used in numerous ways for wide range of applications. Keeping these properties in consideration, the present article summarizes the recent expansion in the fabrication of the pristine/modified starch-based composite scaffolds by electrospinning along with their possible applications. Apart from electrospinning technique, this review will also provide the comprehensive information on various other techniques employed in the fabrication of the starch-based nanofibers. Furthermore, we conclude with the challenges to be overcome in the fabrication of nanofibers by the electrospinning technique and future prospects of starch-based fabricated scaffolds for exploration of its applications.

**Keywords** Electrospinning · Starch nanofibers · Tissue-engineering · Wound dressing · Drug delivery

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## Introduction

Electrospinning is an electrostatically driven process for the fabrication of nanofibers [1, 2]. Over the recent decades, this technique has explored novel avenues while fabricating scaffolds out of wide range of polymers from both natural and synthetic sources [3, 4]. Among the various nanostructures that have been accustomed in various biomedical applications, the nanofiber morphologies are preferred due to their versatile properties such as high surface area, better porosity, and effective mechanical properties besides their simple and cost-effective fabrication process [5]. The realistic applications of both natural and synthetic polymers have been examined so far but the later possess an advantage over former ones. The rationale is because of their intrinsic properties such as biodegradability, biocompatibility, non-toxicity, minimal immunogenicity and efficient bioactivity responses shown towards various animal models [6, 7]. Furthermore, these natural polymers are mainly exploited for various applications (e.g., in tissue-engineering [8] biomedical field [9] and in filtration [10] etc.). These natural polymers explored so far in the aforementioned applications are mostly derived from plant and animal sources [11]. Polysaccharides like starch, cellulose, and xylan are the polymers derived from plants. On the other hand, the collagen, chitin/chitosan, heparin sulfate, chondroitin sulfate, and hyaluronan are derived from animals [12]. The natural polymers owing efficient biocompatibility and biodegradability which are essential for any materials to be used in tissue-engineering and in various biomedical applications. However, they possess some drawbacks such as poor solubility, low tensile strength, and large surface tension [13, 14]. Thus, the fabrication of nano-composites incorporating the natural polymers along with synthetic polymers is usually explored to overcome these shortcomings, using electrospinning technique [15].

Starch is one of the important renewable resources and is considered as the second largest source of biomass on earth after cellulose [12, 16]. This homo-polysaccharide is composed of glucose units linked by glycosidic bonds [17]. The major constituents of starch are amylose and amylopectin. On one hand, amylose is a linear polymer of D-glucose units linked with α(1–4) glycosidic bond and possesses polymerization in the range of 300–10,000 units corresponding to its origin [18]. On the other hand, amylopectin being a highly branched polymer, besides having α(1–4) glycosidic bonds, there are α(1–6) glycosidic bonds present at branch points [19]. The properties of thermal decomposition and resistance towards heat, low shear/stress resistance, and high retrogradation have limited the applicability of starch [20]. Therefore, various chemical and physical modifications of a native starch have been intended to overcome these limitations [21]. Playing click chemistry reactions like cross-linking and substitutions with reporter molecules and biomolecules, resulting in pre-gelatinization have potentiated the use of starch in biomedical and tissue-engineering fields [8, 22, 23]. Starch gelatinization by the desired amount of water and subsequent heat treatment translates the use of starch as a thermoplastic polymer resulting in various structures such as foams, films, and sheets, thus being the important feature of the starch [23, 24]. Basically, gelatinization is the process of structural disruption that results in swelling of starch granules followed by subsequent hydration and solubilization under the influence of water and/or other solvents and further, the heat can enhance the process [25]. Retrogradation another important characteristic of the starch provides the unique separation attribute to starch from water upon cooling [26]. Owing to several pitfalls like high hydrophilicity, weak mechanical strength, and structural integrity in the hydrated state, it has been explored in various fields by eliminating these limitations using several modifications [27]. For instance, the modification of starch to

form oxidized, hydroxyethylated, and acetylated starch had been used for various applications besides the native starch [28, 29]. Moreover, the starch-based nanocomposites have also been developed with the intention to improve the various properties of the native starch. This includes efficient spinnability and hence in this way exploring the various avenues and dimensions of the starch-based scaffolds in different fields [30, 31].

This review, besides the detailed introduction of the electrospinning technique, also summarizes the ways of spinning of the starch nanofibers using various solvents. It also describes how changes in different parameters of electrospinning process can affect the morphology and nano-topography of nanofibers. Furthermore, the summary of the techniques other than electrospinning employed so far in the fabrication of the starch-based nanocomposites is also reviewed. This is followed by the section about the versatility of the starch-based nanofibers in context of its applications in fields like tissue-engineering, wound dressing, drug delivery, and filtration. Briefly, this review summarizes all the major possible fabrication techniques with regard to fabrication of the starch-based nanostructures along with their applications. Future researches, towards the exploration of the starch, surely will open new avenues and dimensions in terms of clinical translations of starch-based scaffolds.

## Electrospinning Technique

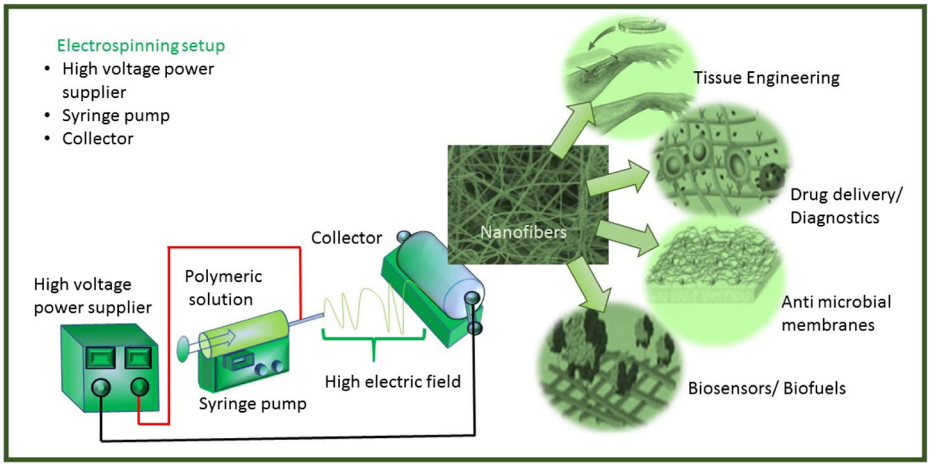
The fabrication of the wide-range of fibers from distinct polymeric solutions can be achieved by various methods. However, the electrospinning is the most common and versatile technique among others with the various numbers of controllable parameters for better and efficient morphology of fabricated fibers.

### Principle of Electrospinning

Electrospinning is a novel and versatile process for the fabrication of the fibers having diameters at the nanoscale [32]. Under the influence of the high electric field, it involves the formation of the Taylor cone resulting in subsequent formation and acceleration of the thin jet out of a polymeric solution into nanofibers. The electric field (in kilovolts) is supplied by the high voltage instrument installed within the electrospinning apparatus. Besides, it includes the syringe pump that can hold the syringe filled with the polymeric solution, the hypodermic needle of which is connected with the cathode originating from the power supply. Furthermore, a rotating and/or plate collector can be connected to the anode of the voltage supplier, allowing deposition of fibers emancipating out of needle tip. The nanofibers can be harvested from the collector after the event of electrospinning process. Thereafter, the deposited nanofibers can be subjected to various characterizations and evaluated for different applications [33, 34] (Scheme 1). The micro-architecture and nanotopographies of the fibers can be easily controlled and governed by various processing parameters. These properties positively influence the versatility of this technique [35].

### Governable Parameters in Electrospinning

The various parameters that can be regulated and managed according to experimental requirements are solution properties, processing, and ambient parameters [32, 36] (Scheme 2). These



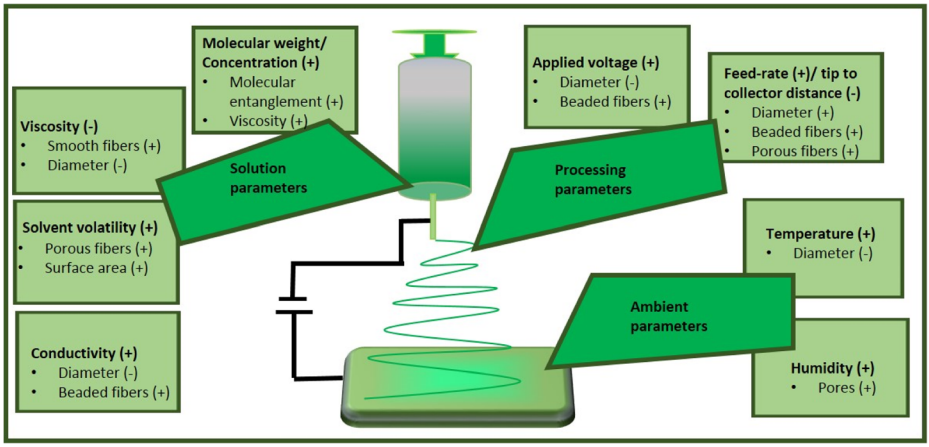

**Scheme 1** Representation of the electrospinning setup for the fabrication of nanofibers and their possible applications

parameters can be controlled in order to achieve the fabrication of fibers with desired and excellent morphology.

*Solution Properties*

It includes the properties of concentration, molecular weight, viscosity, volatility, electrical conductivity, and surface tension of the solution. These properties have the considerable effect on the architecture in terms of compactness and conglomeration between the nanofibers [35, 37].

**Solution Concentration** The appropriate solution concentration is the important parameter to be considered for the fiber formation. The increased solution concentration impacts the viscosity of the solution and hence results in the larger diameter of the nanofibers. Moreover,




**Scheme 2** Schematic illustration of the various parameters that regulate the process of electrospinning and their effect on the nanofiber morphology

as the concentration of the solution increases from low to high, the shape fluctuates from the spherical to spindle morphologies [38]. Figure 1 shows the effect of changes in solution concentration on the morphology of the nanofibers. The low concentration solution tends to form beaded fibers (i.e., a defective morphology) and the optimum concentration of the solution results in fibers with uniform morphology [36].

**The Molecular Weight of the Solution** As the molecular weight of the solution increases, it results in the fabrication of fibers with the larger diameter, while as when low molecular weight polymer is used it leads to the formation of the beads in the nanofibers. So, for effective results, the molecular weight of the solution should be optimal [40]. Molecular weight significantly determines the solution properties such as solution concentration and viscosity. Therefore, this plays a major role in determining the fiber morphology and should be taken care of during the electrospinning process.

**Solution Viscosity** Solution viscosity is the key parameter that affects the morphology of the electrospun fibers. The increased viscosity of the solution produces the fibers with the larger diameter and minimum beads in the nanofiber. The less viscous solution results in the maximum beaded nanofibers with significantly small diameter [12]. The comparison between the fiber morphology of the two solutions with different viscosities can be visualized in (Fig. 1), which clearly represents the effect of the solution viscosities on fiber formation.

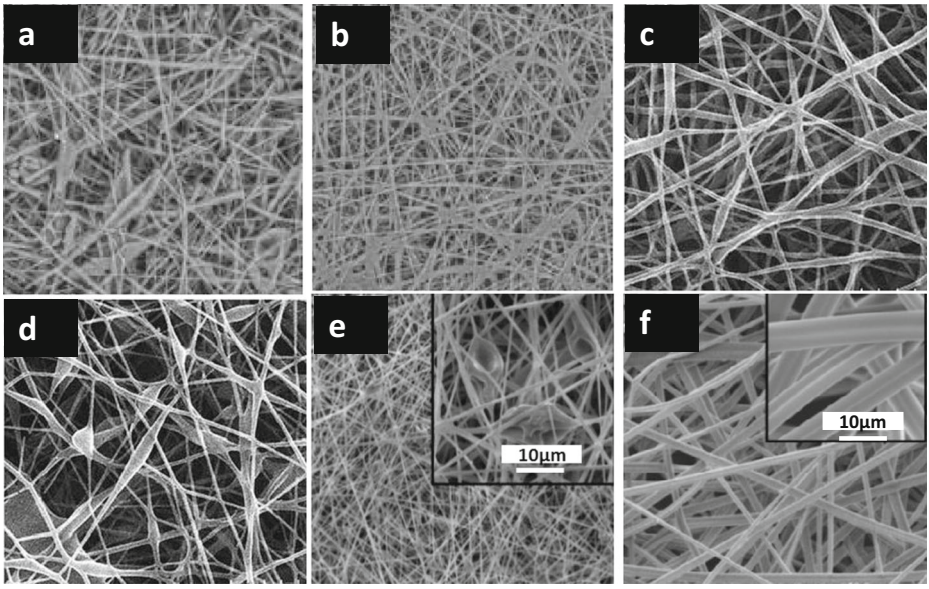



**Fig. 1** The figure represents the effect of various electrospinning parameters on fiber morphology. **a** (10 *w/v*) and **b** (15 *w/v*) show the effect of solution concentrations on the fiber morphology. **c** (345 ± 22.85) and **d** (341 ± 20.11) show the effect of the viscosity on fiber morphology. **e** (33.92 mN·m-1; 0.29 F·m-1) and **f** (30.71 mN·m-1; 0.14 F·m-1) show the effect of surface tension and conductivity on fiber morphology. Scale bar 500 μm in **a**, **b**, **c**, **d** and 50 μm in **e** and **f**. Reprinted with the permission from publishers of these works [10, 36, 39]

**Solvent volatility** The volatility of the solution is necessary when the resulting electrospun fibers find their applicability in targeted drug delivery. The high volatility contributes towards the formation of more porous and large surface area fibers [41]. On the other hand, the solvent with decreased volatility contributes the fibers with increased pore size and lower surface areas [42]. The solvent volatility is an important aspect of the fabrication process. When the solvents with decreased volatility are used to form the polymeric solution, the resultant residual solvent remains trapped in the nanofibers and thus can distort the morphology of the fibrous mats.

**Solution Conductivity** The efficient conductivity of the solution increases the electrostatic interaction on the jet and simultaneous effective jet elongation results in fibers with the smallest diameter. Moreover, the solution with poor conductivity results in the production of the fibers with the larger diameter (Fig. 1) [39]. The highly conductive solutions used for electrospinning can lead to the formation of excessive small fibers similar to that of spider-net like fibers [43, 44]. Conductivity is the parameter specific to the solvent and subsequently, the use of a particular solvent to form a polymeric dispersion thus attributes the conductivity to the whole spinning solution. Therefore, depending upon the required diameter and morphology of fibers can be controlled, thus the solvent nature and conductivity can prove useful in achieving the desired results.

**Surface Tension** Nature of solvent used to dissolve the polymer contributes towards the surface tension of the solution. The solution with reduced surface tension results to the fabrication of the fibers without beads and process of electrospinning to occur at the lower electric field [45]. Figure 1 represents the effect of the surface tension on the fiber morphology and these results clearly depict that the solution with higher surface tension produces fibers with distorted morphology (i.e., beaded fibers).

*Processing Parameters*

It includes the conditions like applied voltage to start the electrospinning process and the feed-rate at which polymeric solution is driven out from the syringe and collected on the collecting plate or drum.

**Applied Voltage** The increase in the electric current at which the process of electrospinning is going to proceed is directly proportional to the electrostatic forces acting on the solution jet. This high voltage contributes towards the fabrication of the fibers with small diameters. The decrease in applied voltage results in the fabrication of fibers with larger diameters [39]. However, increasing applied voltage beyond a particular limit does not affect the fiber diameter. The fiber diameter is dependent on the forces like viscoelastic, columbic forces including the surface tension. The applied voltage plays an important role in determining the columbic forces. Further, the balance between the three forces is seen at the moderate voltage, thus resulting in the fibers with narrow diameter distribution [39].

**Feed-Rate** Increased feed-rate of the polymeric solution while electrospinning results in the formation of the beaded fibers and with the larger diameter. On the other hand, the decreased feed-rate contributes towards the fibers with lesser diameters. The feed-rate should be optimum as that is necessary for the formation of the Taylor cone and thus proper driving of the ultra-fine threads towards the collector. When the flow-rate exceeds the optimum value, it affects the stability of the Taylor cone

and results either in beaded fibers or dripping of polymeric solution, instead of driving of the polymeric threads towards the collector. Moreover, the excessive dripping of solutions during an event of electrospinning from the needle tip can result in landing big chunk of polymer melts on the collector, thereby, causing the distortion of already deposited nanofibers, due to the presence of unevaporated solution. Therefore, optimization of this parameter is important in achieving the good results [38].

**Diameter of Needle** The increased diameter of the syringe needle does not affect the morphology of the resulting fibers especially the average diameter of the fibers. However, decrease in the diameter of needle results in the increased polydispersity of the fiber diameters, with the result the nanofibers with bigger and smaller diameter can be obtained during the fabrication process. It may be noted here that another study has investigated the electrospun poly(methyl methacrylate) nanofibers and has evaluated the effect of needle diameter using (18, 22 and 26) needle gauges. Their analysis revealed that there is no significant correlation between the average nanofiber diameter and needle diameter except that the wide-range of fiber diameter distribution was seen with the needle having the lesser diameter. Overall, the results were independent of needle diameter used for the fabrication process [46, 47].

*Ambient Conditions*

They cover the conditions like the temperature and humidity present in the environment where the electrospinning setup is installed and/or where the process of electrospinning is going to be performed.

**Temperature** Temperature plays a significant role in the fiber morphology as the higher temperature results in fabrication of nanofibers with lesser diameter [48]. The temperature significantly effects the viscosity of the polymeric solution. Higher temperatures can lead to early drying of the fibers before reaching the collector, which can be beneficial. However, the lower temperatures can cause clogging of the needle during the process of fabrication and fiber deposition on collector will be reduced. Therefore, temperature monitoring during the fabrication process can significantly contribute towards better results.

**Humidity** Increased humidity enhances the formation of the more porous nanofibers which plays a significant role in the cell adhesion and penetration. The study shows the direct proportionality between the humidity and pore size and pore diameter. However, there is no effect on the shape and/or diameter of the nanofibers with the increase in humidity [40]. It should be noted and kept in consideration that the effect of the humidity on different polymers shows variable effects. For example, in case of the cellulose acetate and poly(vinylpyrrolidone), the increased humidity results in the fibers with increased average fiber diameter. Therefore, this parameter needs optimization according to the nature and type of the polymer used for fabricating the nanofibers [49].

## Electrospinning of Starch/Modified Starch

Electrospinning has made the fabrication of the starch nanofibers possible and thereby contributed significantly towards the exploration of many distinct properties of this polymer.

Earlier the fabrication of amylose nanofibers was demonstrated in a US patent by dissolving the amylose in the NaOH solution. Followed by its extrusion into the concentrated aqueous ammonium sulfate which simultaneously resulted in the formation of the ultra-fine and tough fibers during coagulation [50]. It is noteworthy to mention that amylose being one of the constituents of the starch. However, being laborious, time-consuming, and expensive purification process associated with amylose limits its application [36]. On the other hand, amylopectin as the major constituent of the starch and being highly branched polymer affects the fiber formation during the electrospinning [51]. Thus, to make the production of the nanofibers out of starch polymer as an effective and economically feasible strategy, various approaches towards this goal have been explored [12]. In this context, Kong and Ziegler successfully achieved the electrospinning of starch fibers having a diameter in the range of microns out of 15 wt% corn starch (gelose 80). In this case, the starch was dissolved in 95% dimethyl sulfoxide solution and further spun by the process of wet electrospinning, in which the grounded collector was immersed in ethanol bath (Fig. 2). Further, to improve the crystallinity and crosslinking, the heat treatment with ethanol (50% *v*/*v*) and glutaraldehyde (25% *v*/*v*) was given to nanofibers in order to improve the water stability of the fibrous mat [52]. Adding more to this, another study utilized the starch derived from potato variety (i.e., Diacol Capiro R-12) and subsequently nanofibers were obtained using wet electrospinning in the same way as carried by Kong and Ziegler using dimethyl sulfoxide as a solvent [52]. Lancuski and coworkers successfully fabricated starch fibers by electrospinning of the maize starch using Hylon VII [53]. In this study, 17 wt% of starch was successfully electrospun using varying concentrations of formic acid as a solvent. The characterization of the fabricated fiber mats signify that dispersions with formic acid concentrations of 100, 90, and 80% resulted in fibers with diameters in the range of 80–300 nm (Fig. 3) [53]. Furthermore, another study investigated the glutinous rice starch and tapioca starch for electrospinning using only water as a solvent. In this study, the polymeric dispersions were stirred at 80 °C for 15 min before electrospinning. The results revealed that unlike tapioca starch in which the diameter was in the range of 1.3–14.5 μm, the glutinous rice starch failed to generate nanofibers during the electrospinning [54]. The problem in successful achievement of the nanofibers from starch is due to high amylopectin content which is a challenging aspect. This desires further exploration and investigation using out of box approaches. In this regard, researchers have attempted to explore other techniques. For example, the centrifugal or force spinning technique [55, 56] was used to fabricate the fibers using corn starch (amylopectin 68.89%) and potato starch (amylopectin 73.35%), which resulted in the fibers with the diameter in the range of sub-micron

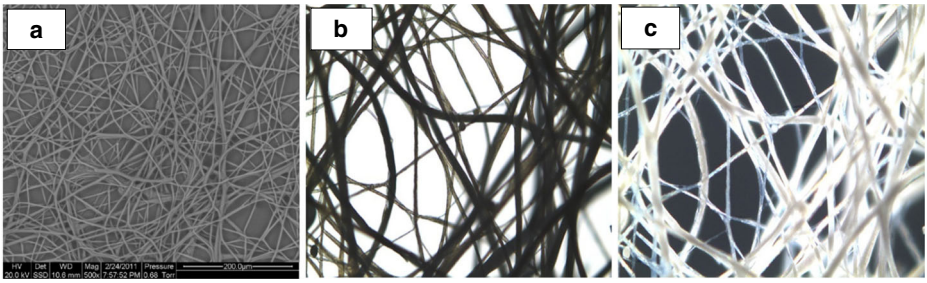



**Fig. 2** SEM images of electrospun corn starch fibers fabricated by the process of wet electrospinning (**a**); and optical micrographs of the same under normal light (**b**) and between crossed polarizers (**c**). Reprinted with the permission of Elsevier [52]

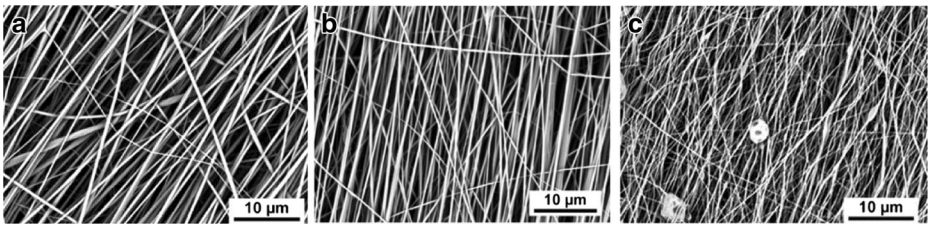



**Fig. 3** SEM images of the electrospun starch formate (Hylon VII) fibers using formic acid as a solvent, prepared from dispersion with 100 vol% formic acid concentration (**a**); 90 vol% (**b**); 80 vol% (**c**). Reproduced from Lancuski et al. with the permission of American Chemical Society [53]

size. This demonstrates the use of centrifugal or force spinning technique can be considered as an alternative to produce nanofibers out of starch with high amylopectin content [57].

Further, to achieve the successful electrospinning of the starch keeping in view the diverse and versatile applications of these nanofibers, various investigations are being conducted in this direction [21, 58]. As aforementioned, the high amylopectin content of the starch is the major barrier to be overcome in order to achieve the proper electrospinning of these nanofibers out of native starch. It also contributes to the poor water stability and mechanical properties of starch nanofibers [53]. Carrying forward this approach, various researchers attempted the electrospinning of the starch with certain modifications such as physical, chemical and enzymatic interventions [59, 60]. In this context, Xu et al. successfully achieved the fabrication of electrospun nanofibers from starch acetate. The nanofibers with varied degree of acetylation were achieved using formic acid/water as a solvent. This study further investigated the effects on the micro-architecture and nano-morphology of the fabricated nanofibers by changing various parameters like solvent, starch concentration, the degree of substitution etc. The outcome demonstrated that 90% (*v*/*v*) formic acid/water solvent system resulted in uniform and bead-free fibers. The maximum tensile strength was 17.9 MPa and the nanofibers with the degree of substitution 2.3 were able to keep 78% of tenacity [59]. Furthermore, the electrospinning of the HCl-treated oxidized starch was achieved by the Wang and colleagues. They used dimethyl sulfoxide as a single solvent in their study. It was observed that fibers were achieved successfully when the dispersion of modified starch/dimethyl sulfoxide was 19 wt% and the results were recapitulated while using 5 wt% of native starch/dimethyl sulfoxide solution. However, the viscosity of the solution decreased as a result of modification when compared with the native starch [60]. Similarly, another study used modified starch to produce the blend solutions of starch/poly(ethylene-alt-maleic anhydride). In this case, the fabrication of nanofibers was achieved using dimethyl sulfoxide as a solvent. Upon characterization of these nanofibrous meshes, it was revealed that this modification improvises the formation of the intermolecular bonds thus increasing the thermal stability of the electrospun nanofibers [61].

## Electrospinning of Starch Composites/Blends

Starch counters certain drawbacks in terms of its ability to be electrospun easily, hydrophilicity and lack of desired mechanical properties [15]. In order to circumvent these obstacles, the electrospinning of the starch with other polymers has been explored to utilize the use of starch

in nanofiber form [52]. This improvises the various properties of starch including mechanical properties, tenacity and electrospinning process. The blending with other polymers forming composites rules out these difficulties to a larger extent [12]. In this section, the electrospinning of the starch with other polymers (e.g., poly(caprolactone), poly(ethylene oxide), poly(lactic acid), poly(lactide-co-glycolide), and poly(vinyl alcohol) has been discussed (Table 1).

### Fabrication of Starch/ Poly(caprolactone) Composites

The poly(caprolactone) is a synthetic, semi-crystalline, and hydrophobic polymer with good solubility and efficient biocompatibility. Therefore, it is often blended with other polymers including that of natural polymers [74]. Tuzlakoglu and co-workers exploited this polymer along with the starch in the fabrication of the composite scaffold for bone tissue-engineering [62]. In this study, they integrated the micro-fibrous porous starch/poly(caprolactone) scaffold prepared by the fiber bonding technique mentioned elsewhere [75]. Upon our investigation, we found that the former paper also used the scaffold in their study from elsewhere reference at [75, 76]. However, in the references [75, 76] the fiber bonding method to produce the scaffold is lacking. Overall, their aim was to deposit the maximum number of nanofibers on porous starch/poly(caprolactone) scaffold which they somehow achieved without discussing the fiber bonding procedure. Furthermore, the electrospun starch/poly(caprolactone) nanofibers were fabricated by using chloroform and dimethylformamide solvents to prepare solutions for electrospinning. The nanofibers were collected on both sides of the preformed microfiber starch/poly(caprolactone) scaffold. This micro/nanocomposite scaffold was then successfully investigated for the toxicity tests using human osteoblast-like cell line (SaOs-2). The results demonstrated that the impregnation of the scaffold with the nanofibers potentiates the adhesion and viability of these cells (Fig. 4) [62]. In another study, by the same group, the starch/poly(caprolactone) nanofibers were fabricated by exploring the simple wet spinning process with the aim of obtaining the nanofibrous scaffold with enhanced porosity. In this study, chloroform was used as a solvent to dissolve 40 wt% starch/poly(caprolactone). The methanol used in this study acted as a coagulant during the wet electrospinning process. Following the plasma treatment, the biocompatibility of this composite scaffold was analyzed by using SaOs-2 cell line. The plasma treatment resulted in the excellent cell viability and advanced ALP activity. Thus, the prepared scaffolds can be considered as alternative candidates for advanced tissue-engineering application [63]. Further, Jukola and co-workers fabricated the starch/poly(caprolactone) nanofibers by the process of electrospinning and investigated the effect of various solvents on the fiber morphology. The solvents used for the solution in this study were acetic acid and chloroform. The morphological analysis revealed that the electrospinning solution with 15 wt% concentration or higher were appropriate to fabricate into fibers. In contrast, the solution with the concentration of 5 wt% failed to generate fibers [30, 77]. Another interesting study by Martins [77] and colleagues had attempted to develop the coalesce scaffold by incorporation of the poly(caprolactone) nanofibers fabricated by electrospinning with the starch/poly(caprolactone) scaffolds produced by the rapid prototyping [78]. The SaOs-2 cells were used in this study to investigate these scaffolds for cell adhesion, proliferation, and viability. The coalesce nanofibers fabricated by two-step process (i.e., by electrospinning and rapid prototyping) successfully improved the growth of the seeded cells [77].

**Table 1** Highlights of the fabrication of various starch-based composite nanofibers. The effects of applied voltage, solvent used and other electrospinning parameters on fiber morphology are summarized. (V) voltage, (D) distance between needle and collector, (F) flow rate, (T) temperature, (H) humidity, (ID) inner diameter

| Electrospinning solution | Solvent used | Electrospun fiber characteristics | Electrospinning Parameters | References |
|---|---|---|---|---|
| Starch/PCL (30/70 wt%) | Chloroform/DMF (7:3) | Resultant fibers were seen to have diameter around 400 nm and bead-less morphology. | V: 15 kV<br>D: 10 cm<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [62] |
| Starch/PCL (30/70 wt%) | Chloroform (40 *w/v*%) | Resulted in the fibers with diameter around 100 μm with 77% porosity. | V: ---<br>D: ---<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [63] |
| Starch/PCL (30/70 wt%) | Acetic acid and chloroform | The fiber diameter was 130 nm and 180 nm when solvent used was acetic acid and chloroform, respectively. | V: 30 kV<br>D: 25 cm<br>F: ---<br>T: ---<br>H: ---<br>ID: 0.86 mm | [30] |
| Starch/PCL (5 wt% and 10 wt%) | Starch in DMSO and PCL in DMF | Coaxial electrospun fibers with PCL in core and outer sheath as starch with mean diameter of 150 nm. | V: 25–30 kV<br>D: 20 cm<br>F:15–25 μL/min<br>T: ---<br>H: ---<br>ID: 2700 μm of one needle and 1560 μm of other | [64] |
| Hydroxypropyl starch/PEO (solutions with increased starch (30% to 90 wt%) content was prepared) | Water (10 wt%) | The resulted fibers possessed the diameters of 300 nm. However, the electrospun fibers with starch content 90% showed reduced diameter and beaded fibers. | V: 11–14 kV<br>D: 30 cm<br>F: 0.03 mL/h<br>T: ---<br>H: ---<br>ID: 1.27 mm | [15] |
| Ampicillin/Starch/PEO (5 wt%) | Water | The fiber diameter was seen in the range of 100-500 nm and the fiber diameter was reduced when compared with pure PEO fibers | V: 15 kV<br>D: ---<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [65] |
| Cassava starch/PLA (The starch concentration was kept constant at 0.5 and 2 wt% and varying concentrations of the PLA from 15, 20 and 25 wt% were analyzed) | Starch in DMSO and PLA in DCM | Resulted nanofibers upon analyzation revealed smooth morphology unlike fibers obtained from solutions with PLA/starch in 15/0.5 wt% and 25/0.5 wt% which show beaded morphology. | V: 20 kV<br>D: 20 cm<br>F: 10 μL/min<br>T: ---<br>H: ---<br>ID: 0.55 mm | [31] |
| Starch/PLGA | Starch in DMSO and PLGA in THF: DMF (3:1 *v*/v) | The fibers with non-uniform morphology were achieved with the diameters of 1.5 μm. Further, treatment with SBF | V: 12 kV<br>D: 16 cm<br>F: 25 μL/min<br>T: ---<br>H: --- | [66] |

**Table 1** (continued)

| Electrospinning solution | Solvent used | Electrospun fiber characteristics | Electrospinning Parameters | References |
|---|---|---|---|---|
| | | resulted in increased surface roughness. | ID: --- | |
| Potato starch/PVA (7 wt% and 8 wt%) | Ethanol (5 wt%) | Resulted fibers revealed the formation of the fibers with increased diameter. | V: 35 kV<br>D: 13 cm<br>F: ---<br>T: 20 ± 2 °C<br>H: 40 ± 2%<br>ID: --- | [67] |
| Cationic starch/PVA (1:3) (8 wt%, 10 wt% and 12 wt%) | Water | Fibers with 8 wt% concentration revealed good morphology and formation of nanofiber webs with increased fiber density. | V: 65 kV<br>D: 13 cm<br>F: ---<br>T: 20 ± 2 °C<br>H: 40 ± 2%<br>ID: --- | [68] |
| Starch/PVA (1:1 and 1:3) (10 wt%) | Water | The fibers with weight ratio of 1:1 and 1:3 demonstrated uniform fiber diameters and good morphology. | V: 20 kV<br>D: 25 cm<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [3] |
| Rice starch/ PVA (25 wt%) | PVA in water and rice flour starch in NaOH | The fibers obtained were observed to possess uniformity and the diameter was in the range of 36-151 nm. | V: 65 kV<br>D: 18 cm<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [69] |
| Rice husk ash /starch/PVA (9 wt%) | Water | The diameter of the fibers was in the range of 300 nm and the porosity of the nanofibrous mat was 70%. | V: 25 kV<br>D: 15 cm<br>F: 0.2 mL/h<br>T: ---<br>H: ---<br>ID: --- | [8] |
| Starch/PVA/Silver (50:50 wt% and silver 6 mg) | Ethanol (5 wt%) | Average diameter of the fibers was found 90–300 nm. | V: 35 kV<br>D: 15 cm<br>F: 0.5 mL/h<br>T: ---<br>H: ---<br>ID: 0.5 mm | [70] |
| Ampicillin/Starch/PVA (8 wt%) | Water | The average diameter of the fibers was seen smaller around 150 nm than pure PVA fibers with diameter 200 nm | V: 15 kV<br>D: ---<br>F: ---<br>T: ---<br>H: ---<br>ID: --- | [65] |
| Glutinous rice starch/PVA (2 w/v and 8 *w/v*) | Hot water | The diameter of the fibers was seen 191–263 nm with smooth morphology | V: 18–20 kV<br>D: 15 cm<br>F: 300 μL/h<br>T: ---<br>H: ---<br>ID: 0.9 mm | [71] |
| Starch/nanographene (25 wt%) | Formic acid | The fiber diameter was in the range of 30–50 nm and the fiber diameter distribution also narrowed compared to native starch fibers (20- 140 nm) | V: 23 kV<br>D: 20 cm<br>F:0.2 mL/h<br>T: ---<br>H: ---<br>ID: --- | [72] |

**Table 1** (continued)

| Electrospinning solution | Solvent used | Electrospun fiber characteristics | Electrospinning Parameters | References |
|---|---|---|---|---|
| Starch/gelatin/*Lawsonia inermis* extract (70/30 *v*/*v* with 30 v% extract) | Formic acid | The fiber diameter was found in the range of 50.82 ± 1.29 with beadles morphology of the fibers. | V: 15 kV<br>D: 13 cm<br>F:0.225 mL/h<br>T: 25 °C<br>H: ---<br>ID: 0.01625 mm | [9] |
| Starch formate/glycerol (17 wt%) | Formic acid | Coaxial electrospun fibers with glycerol as a core and starch as covering material posses with mean diameter 4.13 ± 1.05 μm. | V: 21 kV<br>D:10 cm<br>F: 5 and 2 mL/h<br>T: ---<br>H: ---<br>ID: 0.32 mm and 1.2 mm | [29] |
| Corn starch/guar gum (3 wt%) | Water | The beadles morphology of the fibers was seen with diameters 95 ± 27 nm (amylose content 28%) and 81 ± 14 nm in case of solution with amylose content 50%. | V: 18 kV<br>D:10 cm<br>F: 1 mL/h.<br>T: 50 °C<br>H: ---<br>ID: 0.390 mm | [73] |
| Starch acetate (20 wt%) | Formic acid/water (90:10 *v*/*v*) | Fibers with narrow diameter and good uniformity and tenacity were achieved. | V: 22 kV<br>D:10 cm<br>F:3 mL/h<br>T: 50 ± 5 °C<br>H: ---<br>ID: --- | [59] |

## Fabrication of Starch/Poly(ethylene Oxide) Composites

Poly(ethylene oxide) is a polymer comprising of monomeric units and has been widely used in biomedical and industrial applications [79, 80]. Hydroxypropyl starch/poly(ethylene oxide) blended nanofiber scaffolds were fabricated by the process of electrospinning by Silva and colleagues [15]. The dispersions with varied ratios of these polymers using water as a solvent were analyzed in this study. After fabrication, these scaffolds were treated with poly(methyl methacrylate) (PMMA) which unlike the polymers is hydrophobic in nature, hence, improving the water stability of these scaffolds. The morphological analysis indicated that the electrospinning solutions with 80% starch content were successfully fabricated into the fibers. However, the solutions with 90% starch failed to produce nanofibers during the electrospinning process. In addition, the composite scaffolds were able to retain their fibrous topography after post-PMMA treatment. The bioactivity analysis of these scaffolds by human fibroblast cell seeding revealed the improved cell adhesion and proliferation [15].

## Fabrication of Starch/Poly(lactic Acid) Composites

Recently, electrospinning process has been utilized in the fabrication of composite scaffold consisting of starch/poly(lactic acid) to enhance the various physical and chemical properties [81, 82]. Researchers have investigated the nanofibers fabricated from the single nozzle

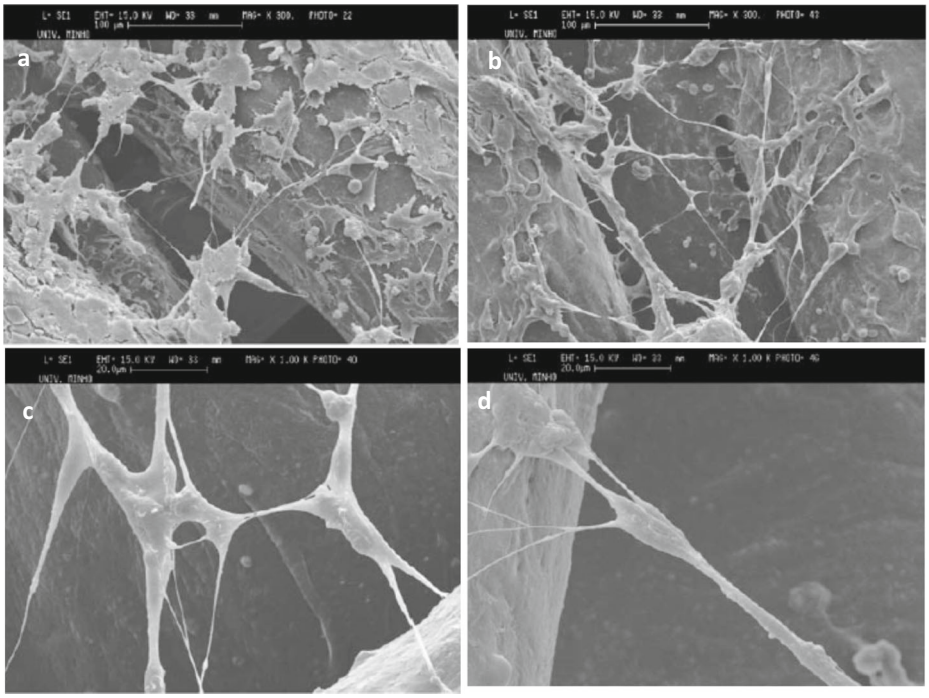



**Fig. 4** SEM images of the SaOs-2 seeded on the micro/nano composite scaffold after 7 days after 14 days. Scale bar in **a**, **b** is 100 μm and **c**, **d** is 20 μm. Reprinted with the permission of Springer Nature [62]

electrospinning process by blending the cassava starch/dimethyl sulfoxide along with the poly(lactic acid)/dichloromethane. Furthermore, the methanol was used as a conjugated solvent in order to improve the mixing of these two immiscible solutions and finally helping the fiber formation during the electrospinning. Moreover, solutions were prepared while increasing the poly(lactic acid) solution concentrations from 15 to 25 wt% while keeping the starch solution concentration constant at 0.5 and 2.0 wt%. The characterization of the nanofibers after fabrication indicated an increase in the poly(lactic acid) at solution level the fiber diameter increased by many folds. In addition, the cocktail solutions with increased viscosity and lower conductivity displayed beaded morphology of the fibers (Fig. 5) [31].

## Fabrication of Starch/Poly(lactide-co-Glycolide) Composites

Poly(lactide-co-glycolide) is a co-polyester formed from the polylactide and polyglycolide polyesters with efficient biodegradability and biocompatibility. However, due to its increased hydrophobicity, it is often blended with other polymers to give the composites hydrophilicity and other suitable attributes [83, 84]. In an attempt to achieve the successful fabrication of the starch/poly(lactide-co-glycolide) composite fibers, the co-axial electrospinning process was utilized by the Zhang et al. Following preparation, both the solutions were introduced for co-axial electrospinning. The morphology of the composite nanofibers revealed non-uniformity with the maximum diameter of 1.5 μm when compared to native poly(lactide-co-glycolide) nanofibers. Moreover, the composite

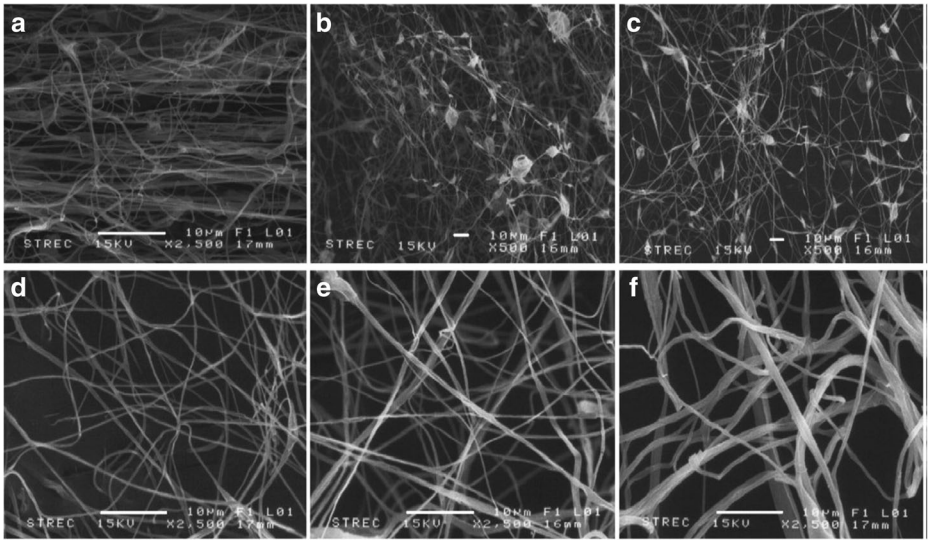



**Fig. 5** SEM images showing the fiber morphology of starch/PLA composite fibers fabricated from solutions 15 wt% (**a**), 20 wt% (**b**), 25 wt% (**c**) with starch content 0.5 wt% and (**d**, **e**, **f**) with starch content 2.0 wt%. Reprinted with the permission of Elsevier [31]

nanofibers when treated with the simulated body fluid for 7 days, at 37 °C resulted in rougher surfaces caused due to good hydroscopicity of starch as observed by SEM. Further, this extended the improved degradation rate and hydrophilicity of fibers [66].

## Fabrication of Starch/Poly(vinyl Alcohol) Composites

Poly(vinyl alcohol) is a synthetic polymer and is commonly used due to its hydrophilicity, biocompatibility, chemical and thermal stability [85]. Due to these attributes, it is widely used in the fabrication of composite fibers having applicability in biomedical applications [86, 87]. In this context, one study investigated the effect of the ethanol on the potato starch/poly(vinyl alcohol) composite fibers fabricated by the process of electrospinning. It was observed that the solution with 5 wt% starch content failed to generate the fibers, whereas 5 wt% addition of ethanol to this blend solution promoted the formation of the nanofibers. Therefore, it can be concluded that ethanol successfully improves the electrospinning of the starch [67]. In another example, cationic starch/poly(vinyl alcohol) in the mass ratio of 1:3 using water as a solvent was used to fabricate nanofibers. The solutions of 8, 10, and 12 wt% were investigated and only 8 wt% composition supported the nanofibers production with good morphology with increased nanofiber density. Moreover, the effect of the ethanol on nanofibers was also analyzed and the results revealed that addition of the ethanol affects the diameter of the resulting fibers. More specifically, when the ethanol concentration was increased from the 3 to 9 wt%, the nanofiber diameter also got increased [68]. Li et al. investigated the characteristics of the starch/poly(vinyl alcohol) composite nanofibers by introducing the bubble electrospinning process. In this novel study, the researchers were successfully able to produce nanofibers from 10 wt% aqueous solution of starch/poly(vinyl alcohol) using a bubble electrospinning process. The morphological results from the solutions with starch/poly(vinyl alcohol) in 1:1 and 1:3 weight ratio revealed uniform and smooth morphology of nanofibers

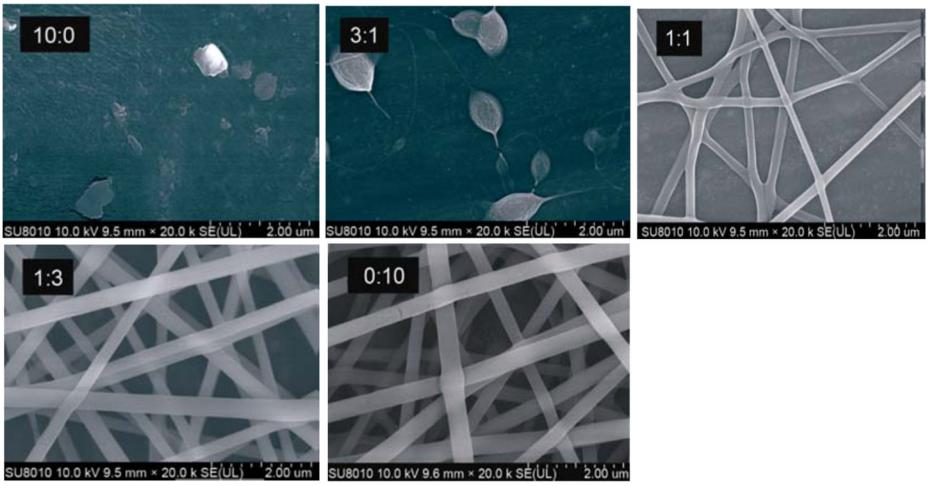



**Fig. 6** SEM micrographs of starch/PVA composite fibers fabricated by bubble electrospinning from solutions with varied starch/PVA concentrations 10:0; 3:1; 1:1; 1:3; 0:10 (*w*/*w*). Reproduced under the open access license (CC BY-NC-ND) [3].

(Fig. 6) [3]. Rice flour starch was also blended with the poly(vinyl alcohol) to form the nanofibers. Besides, the successful achievement of the nanofibers, it was also revealed that rice flour improves the tenacity and Young's modulus by promoting crystallization in the poly(vinyl alcohol) [69]. Further, exploration of the starch nanocomposites by Dicastillo and coworkers concluded starch/poly(vinyl alcohol) nanofiber composites as a new route to incorporate the nanocrystals of cellulose into poly(lactic acid) nanofibers. Following the preparation of the aqueous cellulose nanocrystal solution, the starch/poly(vinyl alcohol) were added to it under stirred conditions and the resulting dispersion was subjected to electrospinning process. Further, the resulting nanofibers were incorporated in poly(lactic acid) solution (using chloroform) with the addition of the poly(ethylene glycol) to enhance the casting process. Using this strategy, the starch/poly(vinyl alcohol) composite electrospun fibers blended with the cellulose nanocrystals significantly improvised the hydrophilicity of the poly(lactic acid) [88].

## Techniques Other than Electrospinning Employed for the Fabrication of the Starch-Based Nanofibers

Undoubtedly, the electrospinning is most commonly and preferred technique employed for the fabrication of the nanofibers. However, starch-based solutions are difficult to electrospun due to high amylopectin content [12]. Keeping this in consideration, various studies have explored to utilize other techniques in achieving the successful goal for fabrication of nanofibers from starch [76]. In this section, the techniques employed for the fabrication of the starch other than electrospinning are discussed. Recently, employed technique (i.e., extrusion) is a thermomechanical process that leads to the starch gelatinization by breaking the bonds of starch. This technique of fabrication of starch fibers by the process of extrusion affects various properties of the starch and therefore further explores the applications of the starch in various fields [89]. For example, the study has explored the starch (plasticized by the glycerol) and poly(ethylene oxide) composite dispersion by twin-screw extruder. The extrudates were air-cooled prior to

their palletization. Moreover, nanofibers were characterized by scanning electron microscope, polarized optical microscopy, infrared spectroscopy, differential scanning calorimetry, tensile testing and thermogravimetric analysis. However, this work did not reveal the application of the synthesized composite scaffold. Nevertheless, it provides another course of action to further explore the application of the starch-based composites in various fields [90]. The functionalization of the scaffolds after the synthesis is important to express their possible application in various fields. Keeping this in consideration, another recent study explored the application of the functionalized starch-based nanocomposite synthesized by the process of extrusion in tissue-engineering applications [91]. The extrusion and injection molding were the main processes employed in the construction and production of the composite scaffold of starch/ethylene vinyl alcohol/nanoforsterite. The nanoforsterite as an additive acted as a ceramic reinforcing phase, thus successfully improved various properties of the starch. Moreover, vitamin E was incorporated and as a result acts as a thermal stabilizer during this process [91]. This method can be considered as an alternative to electrospinning technique when the native starch-based nanofibers are needed. Further, the twin-screw extruder was employed in another study with the purpose of achieving the biodegradable composites of thermoplastic starch. In this case, the jute fiber reinforced starch-based composites have been prepared and investigated for effect of jute fiber on the starch. The jute fiber content of 15 wt% in the composite considerably improved the crystallinity, thermal stability and also proved helpful in providing the good tenacity and biodegradability to the native starch. However, the researchers have not mentioned the possible applications in their study except the speculation that the composite prepared have good potential to serve as an eco-friendly "green" materials owing its good biodegradability [92]. Salt-leaching is another technique that has been employed for the synthesis of the starch/cellulose composite nanofibers [93]. In this study, the combination of casting, salt-leaching, and freeze-drying were employed for achieving the desired composite scaffolds. The resulting nanostructure upon investigation revealed enhanced Young's modulus and tenacity, that was clearly contributed due to the nanofibers by blending with the cellulose. Moreover, the salt-leaching after the casting resulted in the more porous fibers with the diameter in the range of 40–90 nm. The scaffold after the morphological analysis and characterization was further investigated for application in tissue-engineering [93]. Studies have also explored the wet-spinning process (which is improvisation in conventional electrospinning technique) for fabricating starch-based nanofibers. For example, the starch-based composite scaffold was prepared by blending with the poly(ethylene-co-vinyl alcohol) using dimethyl sulfoxide as a solvent (Fig. 7). After fabrication, the scaffolds were characterized by the SEM for morphological analysis, micro-CT for overall topography of the scaffold followed by the cell culture studies. The results revealed that this scaffold holds good structural properties including the highly porous structure and efficient degradation properties, thus can act as a promising scaffold in tissue-engineering field [94]. In recent years, the starch-based composite hydrogels were fabricated by the process of in-situ polymerization [95]. The functionalization of the hydrogels by graphene oxide and hydroxyapatite was achieved as a result it contributed significantly towards the application in bone tissue regeneration. The resulted starch-graft-poly(acrylamide)/graphene oxide along with the hydroxyapatite incorporation as adsorbent was subjected to various characterizations like scanning electron microscopy, infrared spectroscopy, X-ray diffraction, and thermogravimetric analysis. Moreover, the biodegradability and biocompatibility analysis indicated a desired experimental results [95]. Another study explores the simple process of hand lay-up and hot pressing. The starch derived from

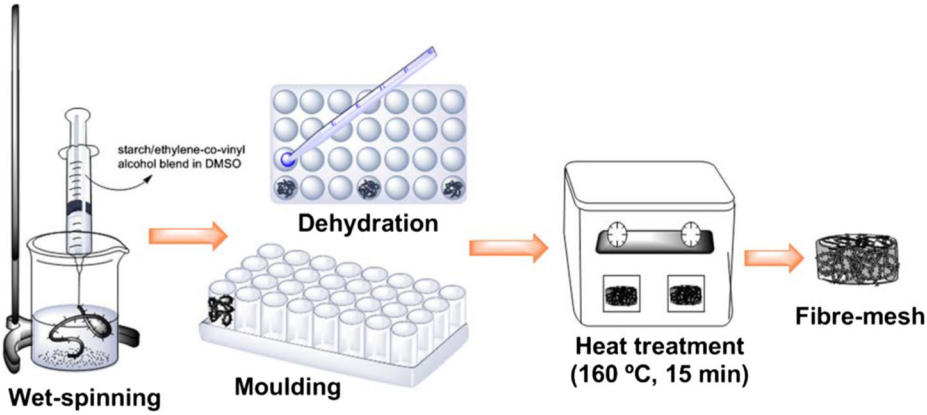



**Fig. 7** The representation of the fabrication of the fibers out of blend solution of starch/ethylene-co-vinyl alcohol using DMSO as a solvent by the process of wet-spinning. Reprinted from Susano et al. with the permission of Wiley Periodicals [94]

the defatted mango seed cake wastes was employed for the preparation of the resins along with modified sisal fibers. The as-spun sisal fibers were chemically treated with high temperature. Further, these nanofibers were immersed in gelatinized starch and subsequently squeezed several times. The resulting nanofibers were dried at 40 °C followed by the hydraulic press at 130 °C and 6 MPa pressure and finally subjected to characterization. These composite nanofibers were found to have better tenacity, better fiber characteristics and efficient resin-fiber interaction. Owing to their properties such as low cost, simple two-step processing, these composites can serve as green materials for various applications [96]. The fibers of the starch/starch-based composites are excellent scaffolds in terms of their tenacity and stability unlike starch films [97]. In this regard, the extensive studies are being carried in order to successfully overcome the barriers in the electrospinning of native starch into nanofibers owing high amylopectin content. One of the recent studies has employed the centrifugal spinning technique for the fabrication of the starch fibers [98]. The centrifugal force here is utilized to drive the polymeric jets out of spinnerets. The morphologies of the starch fibers (corn and potato starch) have been investigated using sodium hydroxide as a solvent. The effect of the amylopectin content on the morphology of the fibers was analyzed and hot blast temperature treatment during the process, proved as a good potentiator in appearance of fibers at the nanoscale. The researchers have only investigated the effect of amylopectin and high temperature on the fabrication of the starch fibers and have not highlighted the applications of the fibers [98].

## Versatility of the Starch-Based Scaffolds in Context of Applications

Starch, being second most abundant polymer on the earth, possesses superabundant availability with excellent biodegradability, biocompatibility, bioactivity, and hydrophilicity. Therefore, have been explored in various applications [70, 99]. Keeping in view the prospective use of the starch to serve as a versatile polymer in terms of its applications, this section will focus on the various applications of this polymer in the fields of tissue-engineering, biomedical fields, and others.

## Tissue-Engineering

Tissue-engineering is involved in the replacement, repair and/or to regenerate damaged tissue by fabricating different biocompatible scaffolds for in vitro and in vivo applications [100]. Tissue-engineering has opened new avenues in the field of regenerative medicine [101, 102]. The most important feature of any scaffold to be used in tissue-engineering is its ability to biomimic the physiological microenvironment (i.e., extracellular matrix) [103]. It may be noted here that the aligned nanofibers play a significant role in guiding the cell growth towards the fiber direction. The study revealed that unlike the random-morphology of the nanofibers, the scaffolds with aligned-morphology enhance the proliferation and differentiation of the cells including that of mesenchymal stem cells [104, 105]. Hence, to improve the functionality and the regeneration processes the fibers with aligned-morphology may efficiently serve the purpose of guided tissue regeneration. The various researches on starch-based polymers demonstrated the strong potential of these scaffolds to be used in the tissue-engineering application. In this context, the starch-based scaffolds such as starch/poly(caprolactone) scaffold have been prepared to investigate their potential in bone-regeneration [62]. Studies have explored the use of micro and nanofiber coalesced scaffolds fabricated from the starch and poly(caprolactone) polymers. The scaffolds have been prepared by fiber bonding process and rapid prototyping followed by the impregnation of the poly(caprolactone) nanofibers by the process of electrospinning. Further, these scaffolds have been investigated for potential use in bone-regeneration. It was demonstrated that upon seeding with the SaOs-2 cell line, these scaffolds revealed proper adhesion, proliferation and increased osteoblastic activity [77]. Rice husk ash derived from the processed rice husk and starch along with poly(vinyl alcohol) have been fabricated by the process of electrospinning to investigate its applications in bone tissue-regeneration. The rice husk ash/starch/poly(vinyl alcohol) composite upon seeding with the human osteoblastic cells (MG63) indicated that these scaffolds possess efficient biocompatibility with no negative effect on the viability and proliferation of cells [8]. The incorporation of the starch-based graphene oxide nanoparticles as a property enhancer into starch nanofibers have also been explored. This incorporation improvises the overall properties of the starch nanofibers including the osteo-bioactivity [72]. The process of electrospinning was carried to achieve this incorporation and the MTT assay using MG63 cells revealed good biocompatibility when graphene oxide nanoparticles concentration was equal or lower than 2.5 wt% [72]. Moreover, the starch-based nanofibers fabricated by the other techniques besides the electrospinning have also paved the new dimensions to explore the diverse applications of the starch. One of the recent studies has explored the nanocomposite starch/ethylene vinyl alcohol/forsterite prepared by the process of extrusion [91]. The nanoforsterite addition improvises the properties of the composite biomaterial. This blended scaffold gains its application in the bone tissue-engineering. This scaffold upon investigation after incubation in the SBF revealed decreased weight loss that was contributed due to incorporation of nanoforsterite. The MTT assay demonstrated improvisation in the cell adhesion and proliferation significantly, upon incubation with the mouse fibroblast cells (L929). As such, this scaffold can find its application in the bone-regeneration process [91]. In addition to this, Nasri and colleagues investigated the application of the starch/cellulose nanofiber scaffold after fabrication by the process of salt-leaching in bone tissue-engineering. After preparation, this scaffold was subjected to bioactivity analysis. The cells used in this study were chondrocytes isolated from the auricular cartilage of rabbits. Upon investigation at different time intervals after seeding with the scaffold, the MTT assay revealed excellent cell adhesion, viability and

proliferation. This scaffold can be further functionalized by various bioactive molecules to explore its application in regeneration of various tissues besides bone tissue-regeneration [93]. The researchers have also produced the fibrous starch-based scaffolds through a wet-spinning technique [94]. In this study, the properties of starch have been maneuvered using ethylene-co-vinyl alcohol to form composite scaffold. The in-vitro analysis of the scaffold upon seeding with the SaOs-2 cell line demonstrated good cell adhesion and viability. Additionally, enhanced cell proliferation was investigated by the quantification of DNA at different time intervals. These results demonstrate novel ways of fabrication, as well as new dimensions to the application of the starch-based scaffolds in bone tissue-engineering field [94]. Thus, starch-based scaffolds can serve as functional scaffolds in bone tissue-regeneration.

Besides, the exploration of the starch-based composite scaffolds in bone tissue-engineering, they have been explored in soft tissue-engineering also. For example, the composite of starch/poly(vinyl alcohol) scaffolds fabricated from the electrospinning technique have been investigated for potential use in soft tissue-engineering [70]. The silver nanoparticles are considered as natural antibiotics have been incorporated in the starch/poly(vinyl alcohol) composites. The fibroblasts isolated from the human skin have been used to investigate the bioactivity of these scaffolds by EZBlue cell assay. It was demonstrated that the fibroblasts show good viability and proliferation, and also the release of silver nanoparticles from these composites successfully prevented microbial growth. Thus, these scaffolds can be further used to study the dermal reconstruction post-injury, subject to the condition that higher amounts of silver nanoparticles should not implicate any toxicity [70].

## Biomedical Applications

Starch, besides its other applications, has also been frequently explored for various biomedical applications such as in wound dressing, drug delivery and biotherapeutics [11, 12, 106]. Electrospun starch acetate nanofibers have been studied for drug release properties. The diclofenac drug loading in this study has been achieved by dissolving the drug in the spinning solution and simultaneously the electrospinning was carried out. This resulted in the incorporation of diclofenac to starch acetate nanofibers. Additionally, the drug loading with sorption method was achieved after post-fabrication of nanofibers and the drug release was analyzed in both the cases. It has been revealed that the sorption method of drug loading was efficient than dissolution method. Further, the nanofibers with the degree of substitution 2.3 showed lower initial bursts and more sustained release subsequently [59]. Recently, in another study with the purpose of investigating the potential of the composite starch scaffolds for controlled release of various drugs. The nanofibers were successfully fabricated from the electrospinning process from ampicillin/starch/poly(ethylene oxide) solution. In this study, the dispersion in the ratio of 0.5:1:4 wt% and 0.5:2:3 wt% were prepared for electrospinning the solutions. Moreover, the solutions prepared from the ratio 1:1:4 wt% and 1:2:3 wt% were also explored for fabrication of nanofibers (Fig. 8). Following the fabrication, the investigations demonstrated that the ampicillin was dispersed efficiently in the nanofibers and this drug was able to form hydrogen bonds with starch. Further, the analysis revealed that these blended nanofibers possess controlled drug release potential [65]. The similar study explored the glutinous rice starch/poly(vinyl alcohol) composite polymer as a carrier for drug delivery. The release of chlorpheniramine maleate incorporated into the composite scaffold of starch has been investigated. The

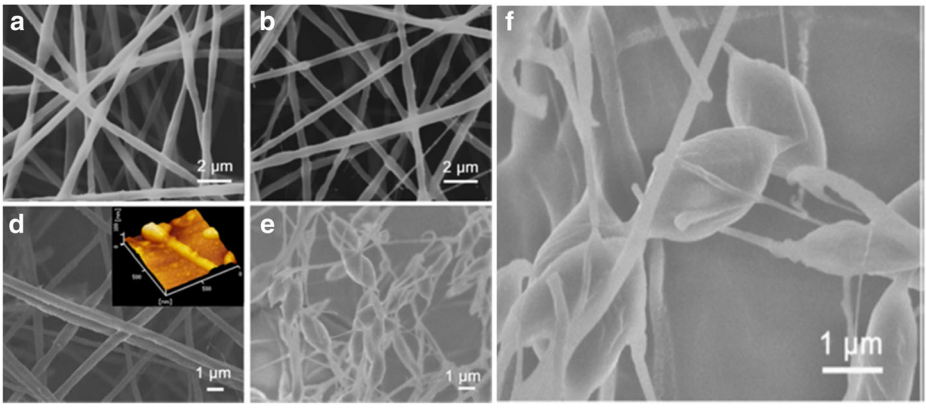



**Fig. 8** SEM and AFM images of the PEO nanofibers (**a**); starch/ PEO (1:4) nanofibers (**b**); and **d**, **e**, and **f** starch/ PEO (1:4) composite nanofibers with ampicillin content 0.5, 1.0, 2.0 wt% respectively. Reused with the permission of Springer Nature [65]

results revealed bi-phasic release of this drug from these scaffolds, releasing 60 and 90% of this drug in 10 and 120 min, respectively. Thus, this composite starch-based scaffold can prove as a potential drug delivery carrier [71]. Moreover, the starch-based composite scaffolds have also been explored in the wound dressing application in biomedical fields. Research studies have revealed that starch/poly(caprolactone) composite nanofibers synthesized by the process of co-axial electrospinning have been transformed into the template for wound dressing materials. The MTT assay on seeding with mouse fibroblast cell lines demonstrated good viability and proliferation of fibroblasts. Moreover, the increase in the starch concentration in the composite further enhances the cell viability [64]. Another study using the silver incorporated starch/ poly(vinyl alcohol) nanofibers as a scaffold investigated its potential antimicrobial activity for wound dressing applications. The cell seeding with human dermal fibroblasts revealed good cell viability and proliferation along with the antibacterial activity as a result of silver incorporation [70]. In another study, the researchers have analyzed the antibacterial effect of the composite scaffold of starch/gelatin with the *Lawsonia inermis* extract, incorporated during electrospinning process (in wounds induced by burn injury). After the fabrication of the composite, *Lawsonia inermis* starch/gelatin scaffold the bioactivity has been analyzed by the seeding with fibroblast cells L929. The MTT assay revealed cell proliferation and efficient antimicrobial activity against *S. aureus* and *E. coli.* The in vivo study examination using scaffold implantation in BALB/c mice demonstrated the re-epithelization and efficient angiogenesis. Thus, *Lawsonia inermis*/ starch/gelatin scaffold can serve as the promising wound dressing to cure burn injuries [9]. Besides, the promising applications of the starch in the aforementioned fields, it has an efficient encapsulation property for the protection of various bio-cargos [107]. For instance, the starch formate electrospun fibers along with glycerol as a fiber core were fabricated. Further on, this was used as an encapsulation material for *Lactobacillus paracasei* (Fig. 9). The characterization revealed that bacteria viability was retained up to 21 days. This proves that starch formate/glycerol nanofibers can serve as the potential template for encapsulation and thus can be used in encapsulating biotherapeutic materials and/or in preserving the bacteria (Fig. 10) [29].

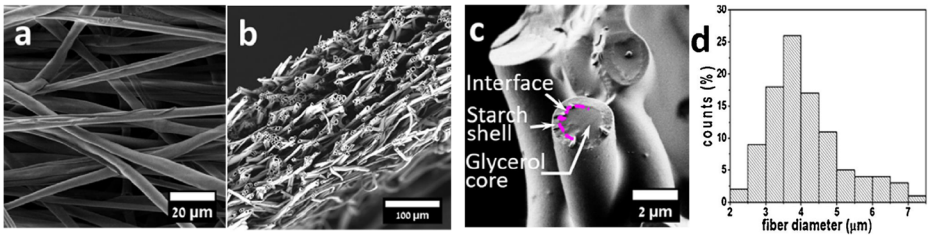



**Fig. 9** SEM images of electrospun starch-formate/ glycerol fibers (**a**); and cross-sectional view (**b**); cryogenic SEM (**c**); and diameter distribution of fibers fabricated by co-axial electrospinning (**d**). Reproduced with the permission of Elsevier [29]

## Other Promising Applications

The attempts to explore the fabrication of the food grade electrospun composite starch-based nanofibers as a packaging material and/or to encapsulate the food ingredients had been addressed. One such study exploits the starch and the guar-gum by the electrospinning process. The blended nanofibers of starch/guar-gum were successfully produced and thus this work can contribute further to achieving the goal for fabrication of food grade nanofibers for packaging food materials [73]. Moreover, the role of starch-based nanocomposites and/or biomaterials can also prove as excellent filtration membranes. Study has explored the electrospun starch/

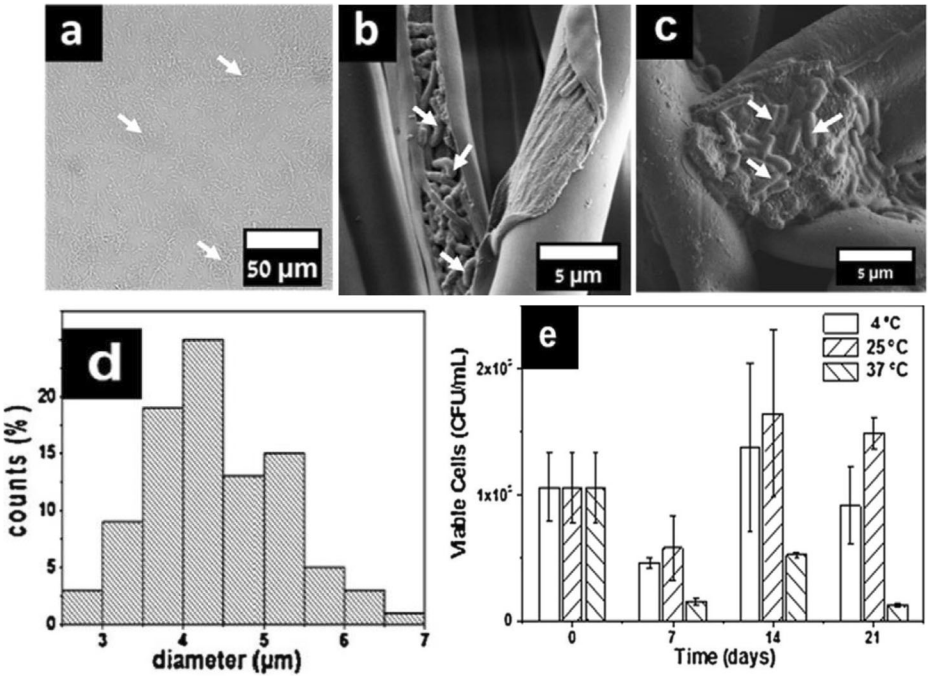



**Fig. 10** Optical microscope image of bacteria *L.paracasei* in glycerol (**a**); SEM images of the bacteria encapsulated in starch-formate/glycerol fibers (**b** and **c**) fiber; diameter distribution (**d**) and shelf life of the bacteria encapsulated inside fibers (**e**). Reprinted from Lancuski et al. with the permission of Elsevier [29]

poly(vinyl alcohol) nanocomposite scaffolds with the incorporation of silver nanoparticles. Exploring the properties of the rice flour starch membranes to restrict the particles greater than 0.1 μm and further to improvise the properties silver nanoparticles and β cyclodextrin has been incorporated into these composite membranes. Hence, serving as a promising multipurpose nano-filters [10]. In another study, the starch-based nanocomposite scaffold was synthesized by process of in-situ polymerization and the resulting scaffold of starch/poly(acrylamide)/graphene oxide/hydroxyapatite was successfully utilized for the removal of the malachite green dye out of an aqueous solution [95]. These applications further explore the various possibilities of the starch-based scaffolds in the fields other than biomedical, tissue-engineering and regenerative medicine.

## Conclusion and Future Prospects

The properties of the natural polymers such as desirable biocompatibility, biodegradability, chemical stability, non-toxicity, proper mechanical properties, and high porosity have provided unique advantages over synthetic polymers [108, 109]. However, the plant-based polymers such as cellulose and starch have been very less explored for applications in tissue-engineering and in other biomedical fields compared to animal-based polymers. Despite the fact that cellulose and the starch are the most abundant polymers on the earth [14, 110] and both share a common complex structure that limits their application in various fields [5, 110]. Moreover, the inefficient mechanical strength, hydrophilicity, decreased thermal stability, and difficulty in processability for electrospinning of the starch further limits its applications [12]. However, the fabrication of the starch-based blended nanostructures with the synthetic polymers has improved the spinnability of the starch and broadened the scope of functionalization with various components/molecules [12]. This also affects the original properties of the starch from expressing efficiently [57]. Thus, keeping in view the availability of starch/other plant-based polymers and their possible contribution, they can provide new avenues in different fields including regenerative medicine. Furthermore, there is a need to overcome the impediment and hurdles by more studies towards this objective.

There is a tremendous need to explore more about the fabrication of the native starch nanofibers, as this polymer can prove a promising candidate in the tissue-engineering, regenerative medicine and in the biomedical field. Moreover, the functionalization of the starch-based scaffolds by well-defined biomolecules such as the growth factors/differentiation factors can further open new avenues in regenerative medicine. Besides, various attempts have been made towards the exploration of the starch-based nanofibers, but until now, no FDA approval is available for application in the aforementioned fields. Therefore, the need to explore new fabrication strategies and clinical translations is mandatory to provide new heights to various emerging fields especially regenerative medicine.

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**Compliance with Ethical Standards**

**Conflict of Interest** The authors declare that they have no conflict of interest.

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