Official Journal of TESMA
Regenerative Research
www.regres.tesma.org.my
E-ISSN 2232-0822
Tissue Engineering and Regenerative Medicine Society of Malaysia

Regenerative Research 2(2) 2013 39-42

ELECTROSPUN GELATIN COMPOSITE NANOFIBRES: A REVIEW ON STRUCTURAL AND MECHANICAL CHARACTERIZATIONS

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ARTICLE INFO

Published online: 24th Dec, 2013
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KEYWORDS

Electrospinning
Gelatin
Nanofibre
Biomedical
Scaffold
Biodegradability

ABSTRACT

Research in gelatin has undergone significant progress in the last decade because of its many merits such as, excellent biocompatibility, biodegradability and commercial availability at low cost. To further improve the properties, gelatin was blended with other polymers and electrospun to produce a new composite material for various biomedical applications. This article presents a concise review on the latest research advancement in the gelatin-blend electrospun nanofibres focusing more on the structural and mechanical properties of the nanofibres fabricated via various electrospinning techniques.

1.0 Introduction

Gelatin (GE) has been studied intensively over the past decade because of its biocompatibility, biodegradability and commercial availability at low cost as it can be easily obtained from animal tissues rich in collagen. Gelatin can be fabricated in many forms such as, dense and porous hydrogels, films, and micro or nanoparticles depending on its applications. Electrospinning technique has been recognized as an efficient method for fabricating gelatin nanofibres for various applications including tissue engineering scaffolds.

The hybridization of gelatin with other synthetic polymers is widely practiced as the hybrids/blends always provide improved bio-mechanical properties. The large number of functional side groups present make gelatin readily undergoing chemical cross-linking with other biopolymers, natural polymers and minerals. This characteristic widens the possibility of gelatin blends to be tailored for biomedical applications as presented in Table 1. In this paper, the structural and mechanical properties of the recently developed electrospun nanofibres fabricated from gelatin blended with other biopolymers, natural polymers and minerals are highlighted. At the end of this review, readers will be able to apprehend the potential of electrospinning technique to produce gelatin composite/hybrid nanofibres with superior performance at low cost.

Table 1: Gelatin blends and their prospective applications

Gelatin Blends	Prospective Applications	References
GE-PHB	Skin regeneration	[1]
GE- Silk Fibroin	Drug delivery	[2]
GE-Heparin	Vascular tissue application	[3]
GE-alginate	Corneal tissue	[4]
GE-minerals	Artificial bone	[5]
GE-PCL	Ear shaped cartilage	[6]
GE-PVA	Drug delivery	[7]
GE-PEO	Wound dressing	[8]
GE-PLGA	Intestinal stent	[9]
GE-PLA	Peripheral nerve repair	[10]
GE-PLGA-EL	Soft tissue engineering	[11]
GE-nylon6	Hard tissue engineering	[12]

2.0 Structural Characterization

Gelatin is a polyelectrolyte with rigid chain conformation resulted from high number of hydrogen bonds and ionizing groups. This makes fabrication of gelatin nanofibre through electrospinning more difficult than a synthetic polymer. To improve electrospin ability, the gelatin is often blended with other polymers such as, polycaprolactone (PCL), polyhydroxybutyrate (PHB) and polyvinyl alcohol (PVA). The gelatin has also been reported to be blended with minerals primarily aiming to mimic the natural bone extracellular matrix (ECM). Choi and Kim (2012) [5] have successfully electrospun gelatin blended with calcium (Ca) and phosphate (P). The GE-minerals electrospun nanofibres exhibited a fully interconnected pore structure with narrow pore size distribution of around 377 nm for GE-P and slightly larger pores of 682 nm for GE-Ca. No recrystallization of the gelatin observed as the crystallographic analysis displayed broad diffraction peaks indicating amorphous characteristic of GE-Ca and GE-P. Similarly, no crystallization was also observed in the GE-PHB electrospun nanofibres. However, fibre diameter was observed to be decreased to 230nm with increased gelatin composition in the GE-PHB to 50:50 compositions [1]. The flow rate, applied electrostatic potential and gelatin concentration were found to influence nanofibre diameter significantly. The smallest diameter down to 146 nm of GE-PEO electrospun nanofibre was successfully fabricated at 25 kV of voltage and 0.25 ml/h of flow rate [8].

The structure of gelatin-blend nanofibre was found to facilitate accommodation of higher cell densities than tissue culture treated polystyrene (TCTP). The cell proliferation rate was higher in the electrospun nanofibre with rich gelatin content because e of high hydrophilicity exhibited by gelatin fibres [9]. It is known that the hydrophilic surface induces high cell adhesion. Li *et al*. found that the inclusion of gelatin and elastin (EL) in the GE-PLGA-EL blend electrospun nanofibres enhanced the interaction between the scaffolds by engaging integrin mediated adhesion [11]. Likewise, higher gelatin content in the GE-nylon 6 (70:30) nanofibres was proven to accelerate the proliferation and differentiation of osteoblast cells with the highest cell viability [12]. The biocompatibility of gelatin blends was also tested on the GE-PCL electrospun nanofibres. The blends displayed the HaCaT cells adhered and spread on the scaffolds after 24 hours of seeding and the cells continuously proliferated and reached 85% confluency after 7 days of culture [13]. All these cell culture studies corroborated that the inclusion of gelatin in the polymers improved the biocompatibility of the ultimate composites.

3.0 Mechanical Characterization

The electrospun nanofibres for tissue scaffolds must be able to withstand and resist the mechanical forces exerted by the cells. The ability to support the mechanical forces resulted from actin-myosin filament binding and sliding within cytoskeleton, is crucial in determining cells' shapes and cellular functions, such as proliferation, differentiation, motility, cell migration etc. [14]. Themechanical properties of gelatin-blend electrospun nanofibres are influenced by the fiber diameter. The mechanical strength increases as the fiber diameter decreases. Linh *et al*. observed that the fiber diameter of gelatin-blend nanofibres dictated by the blend composition [7]. In their work, they depicted that the average diameters of GE/PVA nanofibres reduced as the concentration of gelatin increased and consequently, the strength of the fibre increased. Later in another study Linh *et al* also found that the incorporation of biphasic calcium phosphate (BCP) into the GE/PVA blend increased the stiffness of the composite nanofibres as a response from the interfacial adhesion of the BCP to the blends [15]. The addition of 50% BCP to the GE/PVA blend increased the strength of the composite nanofibre to 8.4 MPa from 4.2 MPa at 0% BCP concentration, while the strain value reduced as the concentration increased. In contrast, the GE/PCL blend nanofibre displayed better deformability and flexibility but poor strength performance. Zhang *et al*. reported that the GE/PCL composite nanofibre had higher elongation and energy tension break, which was double of pure GE nanofibre but showed poor strength in compared to the pure GE nanofibre [16]. The poor strength of GE/PCL nanofibre might be due to less entanglement and weak physical interaction among the chains of mixed polymers. The mechanical strength of the GE/PCL composite nanofibre could be improved by optimizing the electrospinning technique. Chen *et al*. reported that the mechanical strength of GE/PCL composite nanofibre improved by applying mixed electrospinning technique at GE/PCL ratio of 7:3 [17]. They achieved ultimate strength of up to 3.0 MPa, and more than 250% strain value with this technique. Similarly, Kolbuk *et al*. observed better mechanical performance of GE/PCL blend nanofibre electrospun onto drum collector over plate collector [18]. This

might be due to preferred molecular orientation of the blend nanofibre fabricated onto drum collector. The nanofibre composite strength could be improved further by increasing the rotational speed of the drum collector [19]. Nevertheless, the elasticity of the GE/PCL composite nanofibre appeared to be compromised after immersion in the culture media over extended time period. The strain value of almost 400% was recorded after 8 hours immersion of GE/PCL electrospun nanofibre in the culture media, and inversely the elongation to fracture value dropped almost 50% after two weeks of immersion, which is most likely because of rapid degradation of GE [13].

The ultimate strength of GE/PHB composite nanofibre was found to be increased with the increase of the gelatin concentration. The strength increased up to 14.6 MPa up on cross-linking of the GE/PHB nanofibre in glutaraldehyde [20]. The elasticity of the cross-linked gelatin nanofibre was also improved after cross-linking with the glutaraldehyde. In another study, glyceraldehyde was used as a cross-linker for the gelatin blend nanofibre [10]. The GE/PLA composite nanofibre exhibited improved mechanical strength and stiffness after treated with 0.7% glyceraldehyde. However, the elasticity of the GE/PLA nanofibre reduced after treated with glyceraldehyde of more than 0.5%. The mechanical properties of the electrospun nanofibre could be further improved by fabricating core-sheath nanofibre through co-axial electrospinning. This technique was first reported by Loscertales *et al*. in 2002 by designing multi-channel spinneret consisting of core and sheath channels [21]. The co-axial electrospinning set is schematically illustrated in Figure 1. The co-axially electrospun GE/PVA nanofibre with GE as a sheath and PVA as a core demonstrated increase in stiffness and tensile strength, and decrease in plastic deformation. This could be due to the phenomenon that the PVA electrospun core had preferred molecular alignment that caused transformation of semi-crystalline plastic PVA into more crystallized, stronger and elastic PVA [22]. Poor mechanical properties of the GE/PVA composite nanofibre were observed by Merkle *et al*. [22] after reversing the core-sheath orientation (GE as a core and PVA as a sheath). The stiffness dropped drastically from 235 MPa in GE/PVA (sheath/core) to 91 MPa in GE/PVA (core/sheath) and ultimate strength dropped from 13 MPa to 3 MPa accordingly. Likewise, the incorporation of gelatin more than 7.5% as a core in GE/PCL composite nanofibre fabricated by coaxial electrospinning resulted in poor mechanical properties [23]. In coaxial electrospinning, the selection of materials is vital to reduce the mixing of the materials that are coaxially electrospun. The fabrication of GE/PHB composite nanofibre by coaxial electrospinning technique with 2% PHB as a core and 20% gelatin as a sheath exhibited slightly lower mechanical strength in compared to GE/PHB composite nanofibre produced by typical electrospinning system [20].

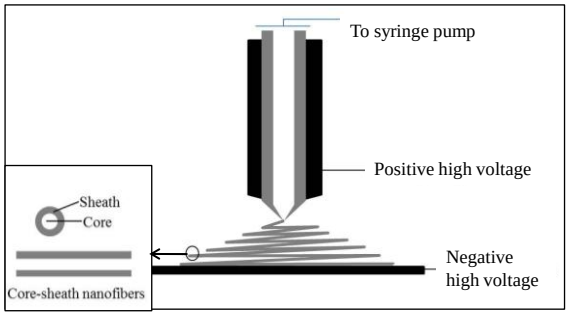

Fig.1 Co-axial electrospinning set-up [21]

4.0 Conclusion

Gelatin being a naturally occurring material is biocompatible, biodegradable and commercially availability at low cost. By now, with much progress in polymer processing technology, the electrospun gelatin and its blend nanofibres hold very high potential to cater for various tissue engineering applications.

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