Biomaterials 114 (2017) 121–143

Contents lists available at ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Review

Electrospinning versus microfluidic spinning of functional fibers for biomedical applications

Jie Cheng [a, 1], Yesl Jun [b, 1], Jianhua Qin [c, **], Sang-Hoon Lee [a, b, d, *]

[a] School of Biomedical Engineering, College of Health Science, Korea University, Seoul, 02841, Republic of Korea
[b] KU-KIST Graduate School of Converging Science and Technology, Korea University, Seoul, 02841, Republic of Korea
[c] Division of Biotechnology, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, 116023, China
[d] Department of Bio-convergence Engineering, College of Health Science, Korea University, Seoul, 02841, Republic of Korea

ARTICLE INFO

Article history:
Received 8 July 2016
Received in revised form
29 September 2016
Accepted 27 October 2016
Available online 5 November 2016

Keywords:
Electrospinning
Microfluidic spinning
Tissue engineering
Drug delivery
Polymer
Micro & nano fiber

ABSTRACT

Micro- or nanofiber-based materials have extensive applications in biomedical fields due to their capability to mimic many aspects of physiological microenvironment *in vivo*. Fabricating micro- or nanofibers using biocompatible and biodegradable materials is becoming of great interest in the area of biomaterials and tissue engineering. Among the various technologies, electrospinning and microfluidic spinning are the two promising approaches to produce fibers at micro- and nano-scale. Choosing an appropriate spinning method is critical important for a specific application. Although some review papers on each spinning method have been published, a review comparing these two methods has not been reported yet. In this review, we present an overview of the two spinning methods including the spinning principle, their unique features and materials selections. Several applications of fibers spun by both methods, especially in tissue engineering, organ function regeneration and drug delivery are introduced. The current challenges, future directions and potential applications of these approaches are discussed as well.

1. Introduction

Nature has provided inspiration for a variety of engineering projects. The connective tissues in our bodies, for example, have inspired investigators to develop new methods for producing micro- or nanofibers. Generally, connective tissues consisting of amorphous gel-like non-fiber ground substances, fibers, and cells are essential for living organisms. Diverse fibers, such as collagen and elastin, play a key role in forming and maintaining the shape of these tissues. Inspired by such tissues in living creatures, many scientists have started to engineer tissues in the laboratory using a variety of highly porous scaffolds to promote cell adhesion and proliferation, e.g., sponge-like sheets, foams, highly complex structures, and fibers [1–4]. Among these porous scaffolds, the scaffold consisting of micro- or nanofibers offers the advantages of being able to control the pore sizes precisely and the orientation of the porous structure and can provide cells with microenvironments that mimic the physiological milieu. To date, various spinning methods have been developed to produce micro- or nanoscale fibers and the most commonly used methods among them are electrospinning and microfluidic spinning. These methods can also control the shape, surface features, and chemical composition of a single fiber. The 2D and 3D scaffolds consisting of these fibers can provide chemical and physical cues to regulate cellular behaviors including cell adhesion, proliferation, extracellular matrix (ECM) production, morphogenesis, and differentiation.

Electrospinning is one of the two main electrohydrodynamic atomization techniques, the other main electrohydrodynamic atomization technique is electrospraying, a powerful technique for monodisperse particles preparation [5]. Electrospinning is a typically used dry spinning process, which was first developed over seventy years ago [6]. It produces fine polymer fibrous mats composed of fibers whose diameters range from several microns down to 100 nm or less. The basic difference between electrospinning and electrospraying lies in the concentration and viscosity of the polymer solution. Polymer solution with low viscosity is the prerequisite for electrospaying, in contrast, the high viscosity is the

* Corresponding author. School of Biomedical Engineering, College of Health Science, Korea University, Seoul, 02841, Republic of Korea.
** Corresponding author. Division of Biotechnology, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, 116023, China.
E-mail addresses: jhqin@dicp.ac.cn (J. Qin), dbiomed@korea.ac.kr (S.-H. Lee).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.biomaterials.2016.10.040
0142-9612/

Abbreviations

Solvent

HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
THF	tetrahydrofuran
DCM	dichloromethane
DMF	N, N-dimethylformamide
TFE	2,2,2-trifluoroethanol
TFA	Trifluoroacetic acid
DMA	Dimethylacetamide
DMSO	Dimethyl sulfoxide
DMAC	Dimethyl acetamide
LiCl	Lithium chloride
CPSA	Camphorsulfonic acid
IPA	isopropyl alcohol

Polymer

PVA	Poly(vinyl alcohol)
PCL	Polycaprolactone
PEUU	Poly(ester urethane)urea elastomer
PLA	poly(lactic acid)
PLGA	Poly(lactic-*co*-glycolic acid)
PAN-MA	Poly(acrylonitrile-*co*-methylacrylate)
PCE	Poly(ε-caprolactone)-poly(ethylene glycol)
PGS	Poly(glycerol sebacate)
MET	Metronidazole benzoate
PCU	Polycarbonate-urethane
NIPAm	N-Isopropylacrylamide
pNIPAm	Poly(N-isopropylacrylamide)
PDMS	Polydimethylsiloxane
PVP	Polyvinyl pyrrolidone
PU	Polyurethane
PHBV	Poly(3-hydroxybutyrateco-3-hydroxyvalerate
PMMA	Poly(methyl methacrylate)
PEGdma	Poly(ethylene glycol) dimethacrylate
PLLACL	Poly(L-lactic acid)-co-poly-(ε-caprolactone)
PEO	Polyethylene oxide
PES	Polyethersulfone
PS	Polystyrene
PGA	Poly(glycolic acid)
PDS	Polydioxanone
PANi	Polyaniline
PPC	Poly(propyl carbonate
PCHC	Poly(cyclohexyl carbonate
PCL-PEG-PCL, PCEC	Poly(ε-caprolactone)-poly(ethylene glycol)-poly(ε-caprolactone)
PCE	Poly(ε-caprolactone)-poly(ethylene glycol)
PPHOS	Poly[(glycine ethyl glycinato)$_1$(phenylphenoxy)$_1$ phosphazene]
PNmPh	polyphosphazene
PEGDA	poly(ethylene glycol) diacrylate
PEGDMA	poly(ethylene glycol) dimethacrylates
4-HBA	4-hydroxybutyl acrylate
PBI	Polybenzimidazole
PMMA	Poly(methylmethacrylate)
PPDO-*co*-PCL-*b*-PEG-*b*- PPDO-*co*-PCL	Poly(*p*-dioxanone-*co*-caprolactone)-*block*-poly(ethylene oxide)-*block*-poly(*p*-dioxanone-*co*-caprolactone)
PGA	Propylene glycol alginate
PLL	Polylysine
DA	Diacetylene
PDA	Polydiacetylene
GelMA	gelatin methacrylamide
Gtn–HPA	gelatin–hydroxyphenylpropionic acid
Alg-Ph	alginate-phenolic hydroxyl
Gel-Ph	gelatin-phenolic hydroxyl
PBI	poly(2,2′-(m-phenylene)-5,5′-bibenzimidazole)
PAN	polyacrylonitrile
PSF	polysulfone
PS	polystyrene
PUA	polyurethane acrylate
PETMP	Pentaerythritol tetrakis (3-mercaptopropionate)
DA.	diacetylene

prerequisite for electrospinning. In electrospraying, the electrified polymer jet is broken into small droplets due to the low viscosity, and these droplets further solidify into particles through rapid evaporation [5]. In electrospinning, the viscous polymer solution forms a hemisphere at the tip of the needle due to surface tension, and a charged polymer jet is further formed. This jet solution gradually concentrates and solidifies into fibers after a series of physical process including “bending instability” and “whipping motion” [5]. Electrospining requires the high DC voltage in the range of several tens of kVs for the spinning. A variety of natural and synthetic polymers were used as materials for the tissue engineering application. By the recent progress of electrospinning technology, fibers with diverse shapes, such as tubular shapes, and multiple-fiber structures have been fabricated.

Microfluidics is a technology to enable the precise manipulation of fluid within microscale channels, which has shown considerable promise for application in biomedicine [7]. After PDMS was firstly introduced into the microfluidics field in 1998, more complex microfluidic devices were able to be fabricated through soft lithography method, which greatly accelerates the development of the microfluidics technology [7]. Recently, microfluidics technologies have shown the potential to solve problems that have not yet been solved by traditional macroscale methods, particularly in the diagnostic field [7]. Microfluidics-based diagnostics devices could be attractive candidates to replace traditional diagnostics approaches because they are simpler, faster and more sensitive than traditional methods [7]. Besides applications in diagnostics, microfluidics is also a powerful tool to fabricate structural materials like fibers. Microfluidic spinning, as a typically used wet spinning process, was developed about 10 years ago [8,9]. Progress in microfluidic technology has enhanced the ability to control a very small quantity of liquid, resulting in the development of new chemical assays and the production of large quantities of microstructures, such as particles, fibers and tubes, without use of complicated devices and facilities. It is especially notable that microfluidic spinning can continuously produce microfibers with a uniform diameter and spatiotemporal control. Although fibers spun by both methods have attracted extensive attention and used widely in tissue engineering and drug delivery, each method has its unique features. To date, many review papers for each spinning method have been published; however, a review comparing these methods has not been reported to the best of our knowledge [10–25].

In this review, we present an overview of both spinning