

核-壳结构壳聚糖/聚乙烯醇-聚碳酸亚丙酯超细纤维的制备*

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摘 要 利用同轴电纺丝技术制备出具有核-壳结构的壳聚糖/聚乙烯醇-聚碳酸亚丙酯电纺丝纤维,考察了溶剂复配对成纤的影响,采用扫描电镜和透射电镜对纤维的形貌、结构、直径分布等进行了探索,并在优化的工艺条件下,将羟基磷灰石负载在内层结构中.研究表明,采用氯仿/*N,N*-二甲基甲酰胺(1/1)复配溶剂可有效避免聚合物溶液在喷丝口处的凝结现象.同单纺纤维相比,核壳结构的纤维直径分布较宽,纤维壳层和核层界限清晰.红外谱图分析证明羟基磷灰石可负载在纤维的核结构中.

关键词 静电纺丝, 核-壳结构, 壳聚糖, 聚碳酸亚丙酯

近年来,对静电纺丝装置的改进使静电纺丝技术得到了迅速发展,同轴静电纺丝就是其中一种.2003年,Sun^[1]等最早通过同轴静电纺丝技术制备出核壳结构的纳米纤维,对内外层纺丝液同时施加高压,使得喷出的两层液体为同心分层流,由于纺丝过程中两种液体在喷口处汇合的时间很短,加上聚合物液体的扩散系数较低,芯层和表层液体在固化前不会混合在一起,从而固化形成核-壳结构纳米纤维.核-壳结构的电纺丝的优势在于:首先,解决了某些不能单纺的聚合物的纳米纤维的制备难题,如聚乙烯醇/聚苯胺(PVA/PAni)同轴共纺,解决了 PAni 不能单纺的难题^[2];其次,可以获得中空结构的纳米纤维,如 Ignacio 等^[3]将一种四乙基正硅酸盐(TEOS)溶胶作为外层溶液,以橄榄油或甘油作为内层模板,利用同轴纺丝技术制备出直径为 500 nm 纤维管;另外,核-壳结构电纺丝可以在内层负载某些药物和生物活性因子,作为药物缓释载体及组织工程支架,如将牛血清白蛋白 FITC-BSA 负载在内层纺丝液体中,以疏水性聚己内酯 PCL 为外层,核壳结构微纳米纤维 PCL-r-FITC-BSA/PEG 可以明显的缓解 FITC-BSA 在释放初期的突释现象^[4].目前,国内已有很多关于利用普通电纺丝技术制备组织工程支架等生物医用材料的报道^[5,6],但鲜见有关利用同轴电纺技术制备出芯层含有生物活性物质的微纳米纤维材料方面的研究报道.

壳聚糖(CS)是世界上产量仅次于纤维素的第二大天然高分子,具有良好的生物相容性、降解性,特别是其分子链具有聚阳离子电解质特性,使其在作为负载药物等生物活性分子等方面具有独特的优势,因此我们将 CS 作为内层基质的主体,但由于纯壳聚糖电纺成纤性极差,而且脆性很高,因此,我们采用成纤性好、与 CS 相容性好、已经在生物材料领域广泛应用的聚乙烯醇(PVA)作为其添加物,改善内层溶液的成纤性以及力学性能,对 CS/PVA 的共纺我们曾经作了系统研究^[7,8],本文选用 CS/PVA 作为内层基质;外层基质选用疏水性聚酯-聚碳酸亚丙酯(PPC),PPC 是一种以二氧化碳和环氧丙烷为原料制备的一种新型可降解脂肪族聚酯^[9],本文利用同轴电纺技术制备出了 CS/PVA(core)-PPC(shell)纤维,并进一步在内层负载生物活性物质羟基磷灰石(HAp),为同轴静电纺丝技术在药物缓释和组织工程支架领域的应用提供了一种新的思路.

1 实验部分

1.1 原材料

CS, $M_w = 1 \times 10^5$, DA 85%,浙江金壳生物化学有限公司生产;PVA,聚合度 3500,醇解度 88%,日本可乐丽公司生产;PPC,分子量为 7×10^5 ,内蒙古蒙西集团提供.纳米级 HAp,国药集团上海化学试剂有限公司生产.氯仿(CHCl_3)和 *N,N*-二甲

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基甲酰胺(DMF)均为分析纯,北京化工厂生产.

1.2 实验装置

自制的同轴电纺丝装置.如图 1 所示,高压静电发生器(BGG4-21,北京机电院高压技术研究所)提供正电高压,流量泵(WZS-50FZ,浙江大学医学仪器有限公司)可以分别控制内外层溶液的流速,16 # 和 8 # 的不锈钢制注射器针头分别作为外层和内层的喷丝口,产物用接地的铝箔接收.

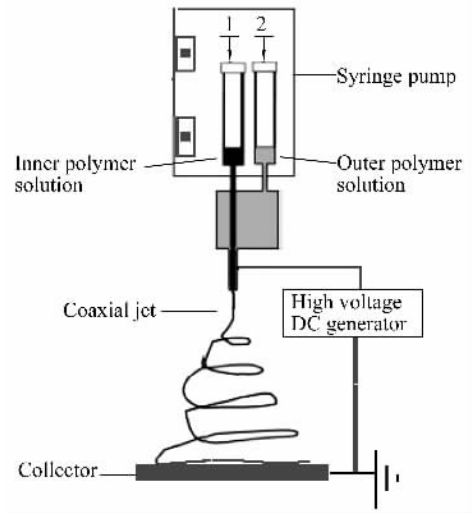


Fig. 1 Experimental set-up of co-electrospinning for core-shell structure nanofibers preparation

1.3 纤维的制备

内层纺丝液的制备如文献[7]所述,将 7 wt% 的 CS 浓醋酸水溶液与 10 wt% PVA 水溶液按(CS/PVA 质量比 70/30)比例混合均匀;将 PPC 按 20 wt% 分别溶解在体积比依次为 10/0,7/3,1/1,3/7 以及 0/10 的 CHCl_3 /DMF 混合溶剂中,单独纺丝进行研究,最终采用 CHCl_3 /DMF (1/1)的混合溶剂作为外层 PPC 溶液的溶剂.

在同轴共纺过程中,内外喷丝口同时与高压发生器正极相连,流量泵控制流速,当电压达到临界值时,在铝箔上得到产物膜.

在优化的成纤条件下,将 HAp 共混入内层纺丝液中,超声分散,制备内层负载有 HAp 的核-壳结构纤维.

1.4 纤维的形貌表征

样品经喷金后,在扫描电子显微镜(S-450,日本日立公司)下观察表面形貌,并采用图像分析软件测量 30 根纤维的直径并计算出纤维的平均直径.

为观察纤维的核-壳结构,将镀上碳膜的铜网放置在接屏上收集少量纤维,在透射电子显微镜(H-7650,日本日立公司)下观察纤维的双层结构.

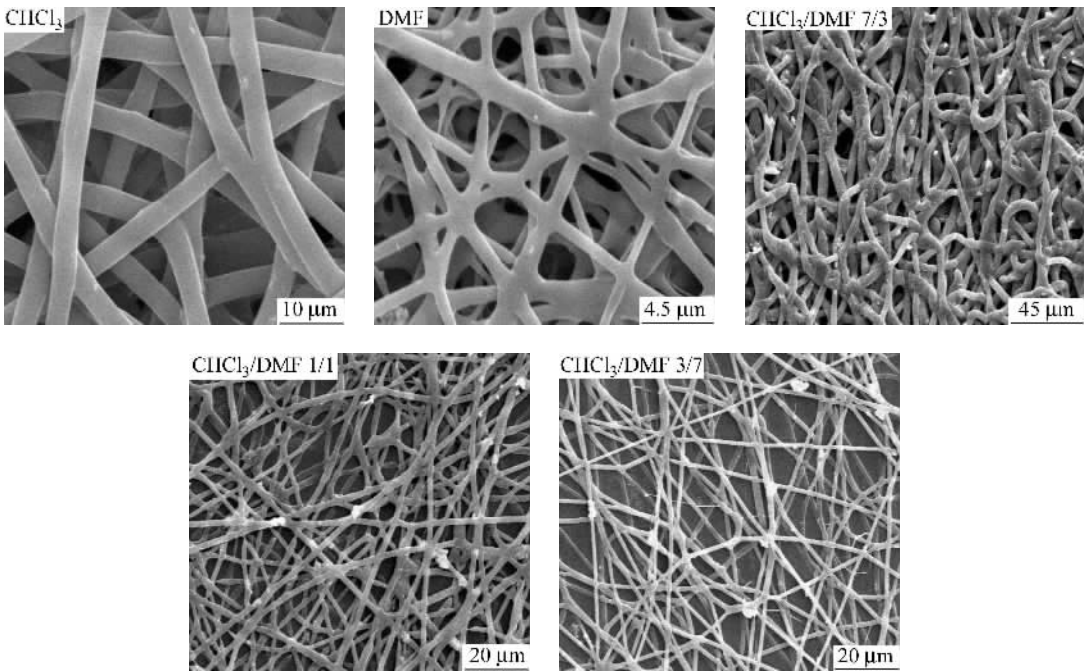


Fig. 2 SEM images of electrospun fibers prepared from PPC solutions in different volume ratios of chloroform/DMF 200 g/L PPC solution, Voltage = 25 kV, Distance = 12 cm, 8 # needle

2 结果与讨论

2.1 CHCl₃/DMF 溶剂复配对 PPC 成纤的影响

在同轴共纺实验中发现,单独采用 CHCl₃ 作为外层 PPC 的电纺溶剂时,液滴凝结在喷丝口,无法得到连续的纤维膜.可能是由于内层的 CS/PVA 为水溶性体系,而外层为油性体系,内外溶液完全不混溶导致了聚合物溶液在喷丝口凝结,类似的现象也有报道^[10],如果内外层溶液采用相同或可相混溶的溶剂有助于减小两流体之间界面张力^[2],可有效改善这一现象.因此本实验外层采

用 CHCl₃/DMF 混合溶剂,利用 DMF 与水及 CHCl₃ 均能混溶的特点,改善核壳结构纤维的成纤性.

首先考察了 CHCl₃/DMF 溶剂复配对 PPC 单纺的影响.所制备的 PPC 溶液参数、电纺纤维形貌以及直径分布分别如表 1 和图 2、3 所示.从图中可以看出,以单一氯仿为溶剂,则纤维的平均直径最大,达到 3.6 μm.随着 DMF 的加入,纤维的平均直径减小,当 CHCl₃/DMF 1/1 时,纤维的平均直径最小,仅为 380 nm.当溶剂中 DMF 的含量逐渐增大时,溶液的电导率逐渐增大,而粘度下降(表 1 所示).一般来讲,对单一聚合物体系,溶液粘度

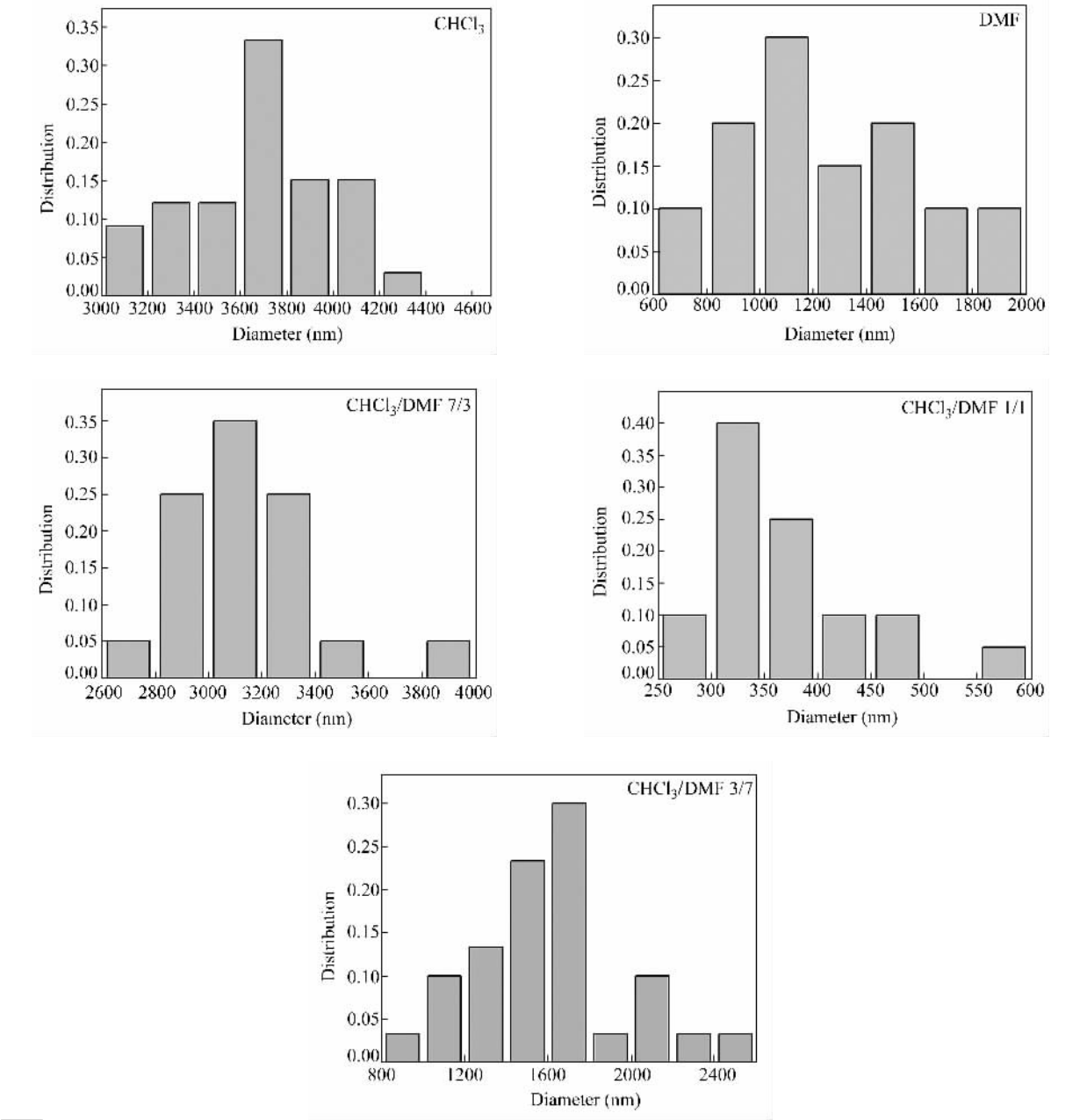


Fig. 3 Diameter distributions of fibers prepared from PPC solutions in different volume ratios of chloroform/DMF

Table 1 Processing parameters of PPC solutions in different volume ratios of chloroform/DMF

CHCl ₃ :DMF	CHCl ₃	7:3	1:1	3:7	DMF
Electrical conductivity ($\mu\text{s}\cdot\text{cm}^{-1}$)	0.02	3.24	7.12	11.05	13.43
Viscosity ($\text{mPa}\cdot\text{s}$, 25 $^{\circ}\text{C}$)	2210	2020	1980	1620	1450

增大,电纺纤维的平均直径也增大,而溶液电导率增大,纤维直径减小,由于加入 DMF 后溶液电导率和黏度均发生改变,对纤维形貌产生综合作用,使得 PPC 纤维直径的改变无明显规律性.考虑到兼顾内外层溶液的相容性和纤维的直径均一性,溶剂为 CHCl₃/DMF (1/1) 的溶剂体系的纤维直径分布范围最窄(300 ~ 600 nm),纤维形貌较好,以它作为同轴纺丝的外层溶液,既可以改善纺丝过程中液滴的凝结现象,也有利于形成界限分明的

双层结构纤维.

2.2 同轴电纺丝纤维的形貌及微观结构

图 4 显示了单层 CS/PVA (70/30) 电纺丝纤维, CS/PVA (core)-PPC (shell) 的同轴纺丝纤维以及在此基础上内层负载 2 wt% HAp 的同轴纺丝纤维的形貌.图 5 列出了上述几种纤维直径分布图,从图中可以看出,与传统的单一溶液电纺丝相比,同轴纤维的直径分布较宽,这是因为同轴纺丝的过程中液滴在喷丝口形成复合的泰勒锥,在电场力的作用下复合的泰勒锥被牵伸形成复合的纺丝纤维落在接受铝箔上,除此之外部分外层纺丝液或内层纺丝液在电场力的作用下劈裂成细小的纤维,这就造成了同轴纺丝的纤维直径分布较宽.

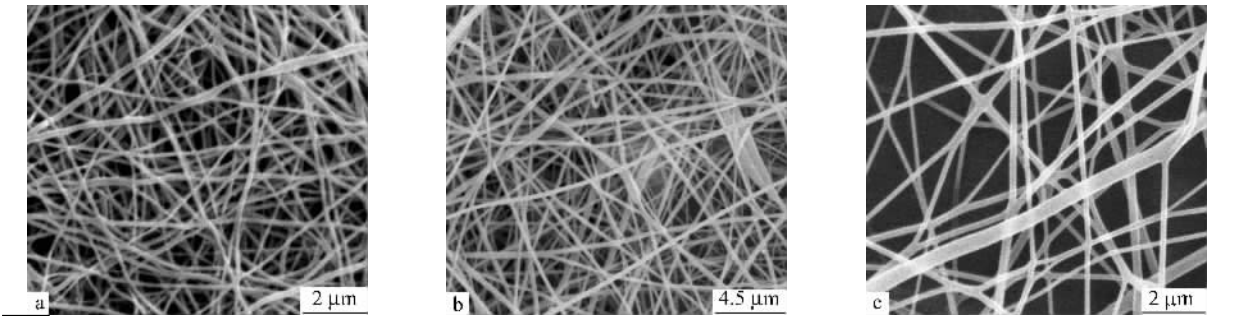


图 4 SEM images of electrospun fibers of CS/PVA (70/30) (a), CS/PVA (core)-PPC (shell) (b) and CS/PVA/HAp (core)-PPC (shell), HAp 2wt% (c)

PPC was dissolved in chloroform/DMF (1/1); Voltage = 25 kV, Distance = 12 cm; a) 8 # needle, (b) and (c) $Q_{\text{inner}}, Q_{\text{outer}} = 1 \text{ mL/h}$

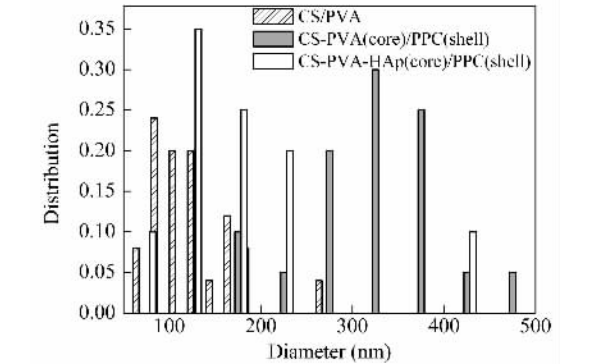


Fig. 5 Diameter distributions of the electrospun fibers

图 6 为得到的 CS/PVA (core)-PPC (shell) 纺丝纤维的内部结构照片,图 6(a) 中核层与壳层之间界面清晰,内外层纤维直径均匀,在同轴电纺过程中,在从泰勒锥顶部喷射出来后,带电的流体会经历一个“鞭动”的不稳定过程再落在接受装置上,喷射流在空气中经历的时间很短,大约是毫秒数量级,远小于内外两流体发生显著扩散所需的时间,

因此会形成复合纤维核层与壳层之间清晰的界限^[1,11],而图 6(b) 中内层纤维出现直径不均一现象,这与纺丝过程中出现了内层带电流体的不稳定流动及不稳定弯曲有关^[12].另外,通过透射电镜发现,有些纤维并没有清晰的核壳结构,这主要是因为首先同轴纺丝和单独的内外层溶液纺丝共存,这就造成收集到的纤维可能是单层的纤维,其次同轴电纺过程是一个动力学过程,许多因素包括内外层溶液的流速,界面之间张力以及两聚合物溶液的粘弹性都会影响核壳结构纤维的形成^[1,11].由于加入的羟基磷灰石的含量较少,并且容易出现团聚现象,仅从截取的纤维局部 TEM 上有时不易观察到 HAp,所以用红外谱图进一步表征 HAp 的存在.图 7 为加入羟基磷灰石前后同轴纺丝红外谱图,加入羟基磷灰石后红外谱图上 1080 cm^{-1} 处的主峰出现一个肩峰(1038 cm^{-1}),这是 PO_4^{3-} 的 ν_3 振动吸收峰,说明羟基磷灰石被载入同轴纺丝中.在关于溶液的浓度、流速以及粘度

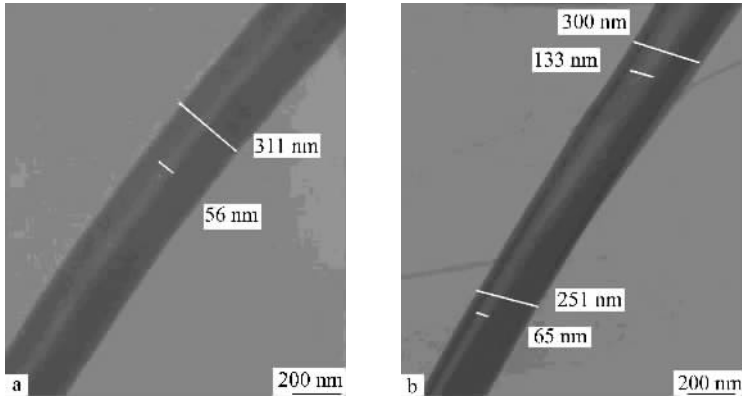


Fig. 6 TEM images of coaxially electrospun CS/PVA(core)-PPC(shell) fibers
a) Segments of the fibers with a sharp boundary ; b) Segment of the fibers with skewed inner component

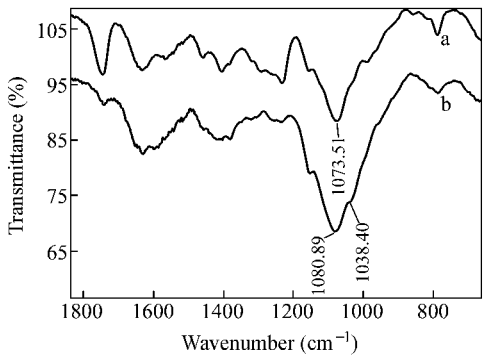


Fig. 7 FTIR spectra of coaxially electrospun nanofibers
a) CS/PVA (core)-PPC(shell) ; b) CS/PVA/HAp(core)-PPC(shell)

这些参数对同轴电纺丝的影响以及加入羟基磷灰石后的复合纤维在药物缓释及组织工程领域的应用将在后续工作中详细研究.

本文应用同轴纺丝技术制备出 CS/PVA (core)-PPC(shell)超细纤维,采用 CHCl₃/DMF 复配溶剂有效避免了聚合物溶液在喷丝口处的凝结现象.通过 SEM 和 TEM 观察到同轴纺丝纤维的直径分布较宽,可获得界限清晰的核壳结构,将羟基磷灰石共混入内层纺丝液中,可制备出负载生物活性陶瓷的复合纤维,为后续将核壳纤维应用在药物缓释、组织工程方面提供了研究基础.

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PREPARATION OF CORE-SHELL STRUCTURED CS/PVA-PPC FIBERS BY COAXIAL ELECTROSPINNING

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Abstract The preparation of core-shell fibers was of particular interest for those core materials that would not form fibers via electrospinning by themselves, and co-electrospinning could also facilitate manufacturing of polymer nanotubes. Furthermore, coaxial electrospinning would provide an alternative and simple means to encapsulate drugs to deliver a biomolecular drug in a sustained fashion. In this study, core-shell structured chitosan (CS)/poly(vinyl alcohol) (PVA)-poly(propylene carbonate) (PPC) fibers were prepared by coaxial electrospinning. The coaxial electrospinning setup in this study was a compound spinneret, consisting of two concentrically arranged capillaries that were flatted stainless steel needles. A certain amount of the two polymer solutions were contained separately in two plastic syringes connected to the coaxial spinneret, and the flow rate in each capillary was adjusted in a double-way medical syringe pump. The liquid flowing on the outside was PPC solution, and the inner liquid was CS/PVA solution. First, the effects of mixed solvents on electro-spinnability of PPC solutions were investigated to choose an appropriate solution system using a conventional electrospinning setup. The properties of PPC solutions in chloroform/dimethylformamide (DMF) mixed solvents with different volume ratios were tested, and the solution conductivity had a tendency to increase ranged from 0.02 to $13.43 \mu\text{s} \cdot \text{cm}^{-1}$ when DMF proportion had increased. The morphology and diameter of fibers were determined with scanning electron microscopy (SEM). The results indicated that the use of chloroform/DMF (1/1) mixed solvents could avoid agglomeration of polymer at the capillary tip during coaxial electrospinning process, and contributed to good morphology and most narrow fiber distribution of the fibers ($300 \sim 600 \text{ nm}$). Secondly, the morphology and structure of the core-shell fibers were characterized by SEM and transmission electron microscopy (TEM). In addition, hydroxyapatite (HAp) was successfully encapsulated into the core of composite fibers, which was characterized by fourier transform infrared spectroscopy (FTIR). The SEM and TEM observation indicated that the total diameter of the CS/PVA(core)-PPC(shell) fibers amounted to about 300 nm , whereas the diameter of the core region was about 60 nm . The core-shell structure could clearly been seen with a sharp interface between the core and shell fiber. In some cases, however, the interface was perturbed, due to an onset of instability. The diameter range of core-shell structured fibers was broader than general single-fluid electrospun fibers, which attributed to the flow instability of the inner dope and the bending instability during the electrospinning process. FTIR results showed the appearance of a peak at 1038 cm^{-1} due to the PO_4^{3-} wagging, which confirmed the presence of HAp in the final fibers. The present study would provide a basis for further design and optimization of processing conditions to control the structure of core-shell composite fibers, and ultimately obtain novel functional biomimetic fibers applied in drug release and tissue engineering.

Keywords Electrospinning, Core-shell structure, Chitosan, Poly(propylene carbonate)