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Non-concentric multi-compartment fibers fabricated using a modified nozzle in single-step electrospinning

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ABSTRACT

Multi-compartment fibers with well-defined regions and functional media hosting potential provide co-encapsulation opportunities for a variety of bio-molecules, drugs and even nutrients. In this research, fibers possessing multiple compartments were prepared using the single-step electrospinning method and a modified non-concentric multi-needle. Polyvinyl pyrrolidone (PVP) was used as the fiber shell material, while ketoconazole (KCZ, model drug) and Sudan Red (model probe) were encapsulated as two separate segments running along the fiber length. Multi-compartment fiber morphology and structure were examined using optical and electron microscopy. The effect of flow rate on fiber morphology was also investigated and the release of encapsulated KCZ and Sudan Red was examined using UV spectroscopy. The results present an efficient and promising method to engineer multi-compartment fibers in a single step for several biomedical applications *in lieu*.

1. Introduction

Ongoing developments in advanced drug delivery systems have been the cornerstone of several pharmaceutical and bio-engineering remits for the last three decades and have focused on a host of novel engineering methods for polymeric excipient materials. Key properties of polymeric structures such as porosity, high surface-to-volume ratio, flexibility on several scales, morphology and structure size tailoring are a few drivers for their emergence as suitable drug encapsulating forms [1]. Although several methods (e.g. bubble electrospinning, bubbfil spinning and centrifugal electrospinning) [2–5] exist to engineer continuous or medicated (bio-active) polymeric fiber systems on a larger scale; the electrospinning (ES) method is probably the most facile and is operational at ambient conditions making it ideal for sensitive biomolecules or other biologics (e.g. cells and proteins)[6]. Furthermore, such single matrix-based drug delivery systems offer controlled and site-specific delivery of molecules of interest [7]. Several other challenges, currently being investigated using well established dosage forms, such as multiple drug loading and compartmentalization need to be explored further for these emerging fiber systems.

Complex fibers exhibiting multiple-compartment, therefore, provide a real opportunity to incorporate several actives and desired properties into one polymeric drug dosage system [8]. This is also increasingly important since the use of two or more drugs (e.g. targeting both symptom and underlying cause) is becoming more common and is also a major feature of polypharmacy [9]. To this end, several multi-compartment fibers have been explored on the reduced drug toxicity and improved biocompatibility *via* controlled drug release [10]. However, the co-encapsulation of two drugs, or two model materials, into a fiber core which run throughout the fiber length in adjacent non-concentric fashion is rare and needs to be explored.

In this study a modified ES nozzle head was developed to enable multi-compartment fiber production in a single polymer engineering step *via* the ES technique. PVP is a synthetic, biocompatible and non-toxic polymer which has been widely applied as a pharmaceutical excipient [11]. KCZ is an active drug agent and has been utilized to treat superficial and internal fungal indications [12]. Multi-compartment fibers were prepared using PVP as the shell matrix material, with KCZ and Sudan Red formulations as two

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separate inner compartmentalized thread-like chambers. The effect of process parameters on fiber morphology and stability were explored. Drug and model probe release profiles were assessed.

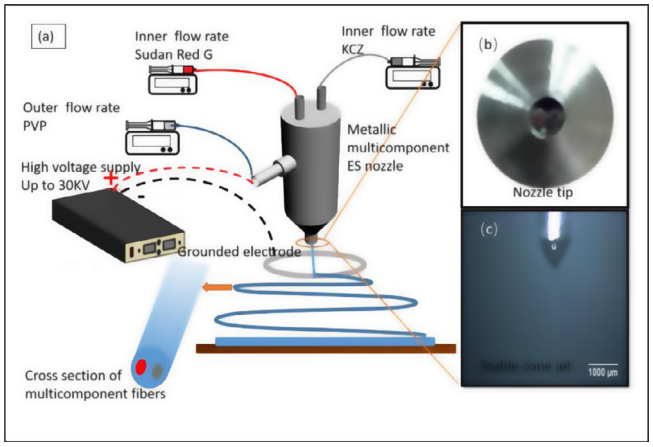

Fig. 1. (a) A schematic diagram of the electrospinning set-up. (b) The modified nozzle head. (c) A digital image of a stable cone-jet captured during the electrospinning process.

2. Material and methods

2.1. Solution preparation

Polyvinyl pyrrolidone (PVP,$M_w = 1.3 \times 10^6$ g/mol), Sudan Red and Tween80 were purchased from Sigma-Aldrich, USA. Ketoconazole (KCZ, 99.7%) was provided by Zhongtian Instrument, China. Phosphate buffer saline (PBS, pH7.4) and ethanol were supplied by Sinopharm Chemical, China. Dimethyl-silicone oil (viscosity ~ 100 mPaS) was purchased from Aladdin chemistry, China. Deionized water was produced with a Milipore Milli-Q ultra-pure purifier (USA). PVP solutions were prepared by dissolving known quantities of PVP in ethanol through magnetic stirring(VELP-ARE magnetic stirrer, Italy) for 2hrs to form a concentration of 20%w/v. Sudan Red and KCZ was dissolved in silicone oil separately at a concentration of 0.5%w/v.

2.2. Electrospinning process

Multi-compartment fibers were generated using a dual-core shell ES set-up shown in Fig. 1a. The set-up comprised a high voltage power supply (Glassman Inc, USA), three syringe pumps (KD Scientific KDS100, USA). Two non-concentric metallic capillaries were located inside an outer enveloping metal needle to assemble

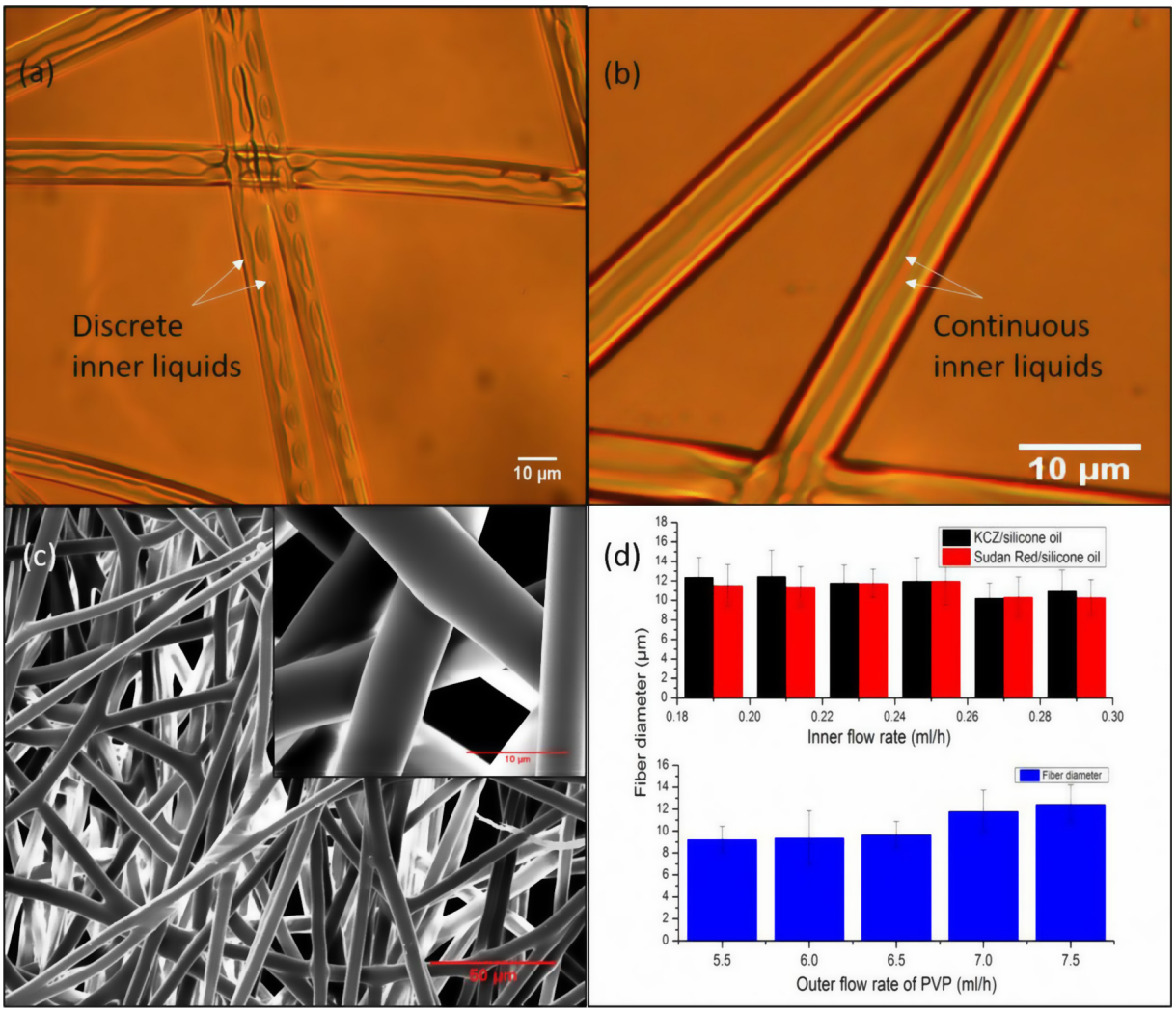

Fig. 2. (a) An OM of a multi-compartment fiber showing discrete silicone oil distributions. (b) An OM of a multi-compartment fiber exhibiting continuous oil encapsulation streams. (c) SEM of multi-compartment fibers. (d) Mean fiber diameter distribution in relation to inner and outer flow rates of selected media.