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Fabrication of patterned polymer-antibiotic composite fibers *via* electrohydrodynamic (EHD) printing

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ABSTRACT

The electrohydrodynamic atomization (EHDA) fabrication route for the preparation of polymeric biomaterials and drug delivery systems has gained extensive popularity over the last decade particularly for drug loaded particle (electrospraying) and fiber (electrospinning) morphologies. In this study, patterned micron scaled structures of polyvinyl pyrrolidone (PVP), polyethylene oxide (PEO) and tetracycline hydrochloride (TE-HCL, an antibiotic) composites were demonstrated *via* EHDA printing. A selection of patterns (parallel lines, grids and arcs) were generated indicating structure complexity potential. Printing parameters (such as collector speed, working distance and applied voltage) were assessed for their impact on fiber diameter. Linear polymer-drug composite fibers (~700nm-5 μm) were deposited using the EHDA printing technique providing precision deposition control – not demonstrated with conventional EHDA engineering platforms. Fourier-transform infrared spectroscopy (FTIR) analyses revealed PVP-PEO blend behavior and also the incorporation of the active into the polymeric matrix. The release of antibiotic from patterned structures was demonstrated over 5 h which is comparable to existing polymer based matrix systems. The printing of active-polymeric fibers provides an innovative approach to develop tailored pharmaceutical dosage forms (shape, size and formulation) with minimal excipients. It also provides patient driven dosage engineering which is beneficial for personalized medicines. Printed medications (*via* single step) have potential to reduce costs, improve patient compliance and lead to the development of personalized medicines.

1. Introduction

The last decade has witnessed an emergence in fiber (micro and nanometer) utilization and concept development for engineering, science and technology. These developments have demonstrated advances in electronics [1,2], sensors [3], energy, tissue healing and drug delivery [4,5]. This drive is partly attributed to several advantages arising from structural properties displayed by micron – nanometer scaled fibrous systems. Firstly, the reduced diameter, when compared to existing coarse filaments, gives rise to larger surface-to-volume area ratios, enabling quicker reactions or interactions. Secondly, improved flexibility and other crucial mechanical (e.g. tensile strength) properties meet specific desired attributes in several emerging fields (e.g. skin and cartilage tissue repair) [6,7]. Nanometer and micron-scaled fibers have shown promising potential as matrix carriers and miniaturized dosage forms for drug delivery [8]. The electrohydrodynamic (EHDA) method (e.g. electrospinning (ES)) for preparing active encapsulated fibers, while permitting drug amorphisation in a single step, has become a very popular formulation processing technique [9–11]. The one-step nature of drug-fiber generation also negates the use of further excipients (reduced number of formulation steps) which often leads to increased material and manufacturing costs [12].

ES is an efficient technique for fabricating polymeric nanometer scaled fibers both in terms of process parameters and ambient condition operation [13], which has led to the development of ultrafine micro and nanometer structures for a host of applications [14]. However, the physics underpinning the process is complicated. When a sufficient voltage is applied to an electrically conducting solution or liquid drug formulation (which is flowing

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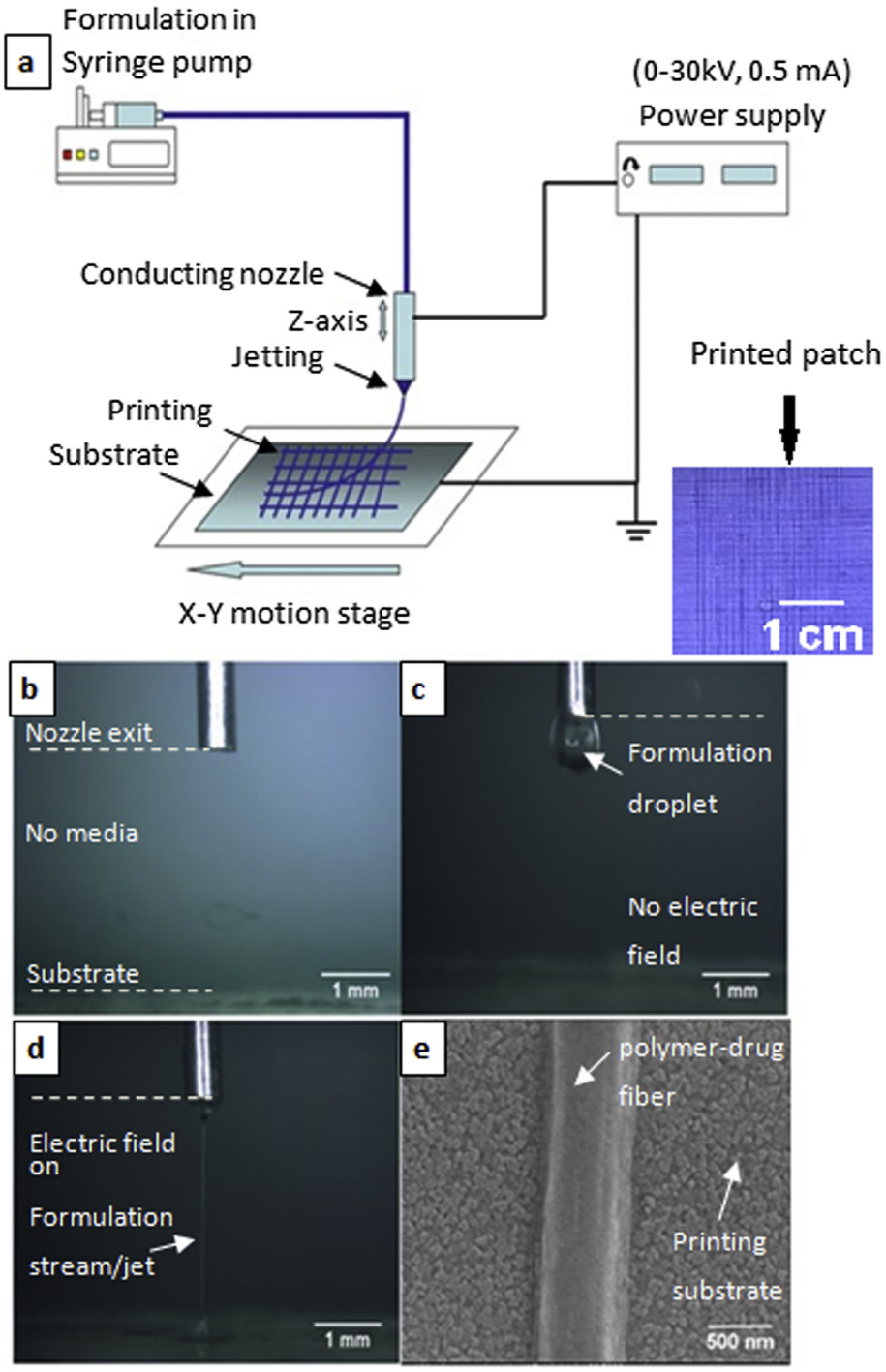

Fig. 1. (a) Schematic of EHDP set-up, (b) EHDP nozzle, (c) the dripping mode and (d) formation of the Taylor cone and the printing jet. (e) Printed nanofiber with a diameter of ~700 nm.

through a metallic nozzle), the conventional hemispherical liquid drop (at the nozzle exit) distorts into a Taylor cone and forms a liquid jet. Subsequently the electrified jet undergoes rapid stretching and solidification [15–18]. The jet is stable near the edge of the nozzle exit but as this moves away from the capillary, it becomes unstable and elongates due to 'whipping' motions arising from bending instabilities. The 'whipping' process encountered during the ES technique leads to the formation of uniform fibers [19]. The formation of nanometer scaled fibers is optimized by several operating and material parameters (which mainly revolves around the polymer solution) [20,21]. Material properties include polymer molecular weight, polymer concentration, solution viscosity, electrical conductivity, permittivity and surface tension [22,23]. Process attributes include the collecting substrate surface; nozzle-to-collector distance, nozzle geometry & alignment, auxiliary electrodes, applied voltage, flow rate and velocity of collector [24]. For open air systems circumstantial factors also exist which include: relative humidity and the ambient temperature [25]. Due to bending instabilities encountered during the ES process, fibers are typically collected in random and chaotic webs or mats. This