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In-situ synthesis of magnetic iron-oxide nanoparticle-nanofibre composites using electrospinning

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ABSTRACT

We demonstrate a facile, one-step process to form polymer scaffolds composed of magnetic iron oxide nanoparticles (MNPs) contained within electrospun nano- and micro-fibres of two biocompatible polymers, Poly(ethylene oxide) (PEO) and Poly(vinyl pyrrolidone) (PVP). This was achieved with both needle and free-surface electrospinning systems demonstrating the scalability of the composite fibre manufacture; a 228 fold increase in fibre fabrication was observed for the free-surface system. In all cases the nanoparticle-nanofibre composite scaffolds displayed morphological properties as good as or better than those previously described and fabricated using complex multi-stage techniques. Fibres produced had an average diameter (Needle-spun: 125 ± 18 nm (PEO) and 1.58 ± 0.28 μm (PVP); Free-surface electrospun: 155 ± 31 nm (PEO)) similar to that reported previously, were smooth with no bead defects. Nanoparticle-nanofibre composites were characterised using scanning electron microscopy (SEM), energy dispersive X-ray spectroscopy (EDX), dynamic light scattering (DLS) (Nanoparticle average diameter ranging from 8 ± 3 nm to 27 ± 5 nm), XRD (Phase of iron oxide nanoparticles identified as magnetite) and nuclear magnetic resonance relaxation measurements (NMR) (T1/T2: 32.44 for PEO fibres containing MNPs) were used to verify the magnetic behaviour of MNPs. This study represents a significant step forward for production rates of magnetic nanoparticle-nanofibre composite scaffolds by the electrospinning technique.

1. Introduction

Nanoparticle-nanofibre composites have been subject to a vast amount of research due to their functionality and unique chemical and physical properties [1,2]. Nanofibres (NF) are widely used for a number of different industrial and medical applications and their use has been extended by functionalizing NFs with metal nanoparticles (NP) in areas such as regenerative medicine, sensing, catalysis and microelectronics [3–7]. In any application of NPs, the primary concern is the formation of the desired NPs in the correct size and material composition. There are a number of different fabrication techniques currently used for NP-NF composites, with most involving multiple step procedures. The most commonly used method involves using a suitable method to synthesize nanoparticles, including precipitation and co-precipitation, chemical vapour condensation, reverse micelle mechanism, thermal decomposition, reduction and liquid phase reduction [8], and subsequently extracting the nanoparticles and then combining them with a polymer solution to be electrospun [9,10]. Another technique involves adding a metal salt (precursor) to a polymer solution and electrospinning [11]. The fibres can then be treated post fabrication by subjection to thermal, chemical or radiolytic treatment (or combinations thereof) to reduce the metal ions to NPs. More recently, research has focused on developing techniques involving a reduced number of steps. Saquing et al. presented a one-step synthesis technique to incorporate silver NPs into Poly(ethylene oxide) (PEO) NFs where silver nitrate ($AgNO_3$) was reduced using PEO as the reducing agent [12].

Magnetic scaffolds have gained attention in a range of fields, however; the relatively slow production rate of such nanostructures has often limited their successful widespread application. The inherent superparamagnetic properties of magnetic NPs (MNPs) are of particular interest, and have been studied for a range of applications including; contrast improvement for magnetic resonance imaging [13], targeted drug delivery [14], gene therapy [15], hyperthermia treatment [16], filtration [17,18], glucose sensing [19], peroxidase mimetic activity [20] and cell separation [21]. Ismail et al. have recently shown iron oxide nanoparticles to show antimicrobial properties, inhibiting the growth of both gram-negative and gram-positive bacteria [22]. Cai et al.

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included iron oxide NPs in NFs composed of chitosan and gelatin to improve both mechanical and antibacterial properties [7]. In another recent important publication for the application of MNPs to regenerative medicine, Meng et al. reported that the presence of a nanofibrous material containing MNPs inserted within a bone fracture site in a rabbit model increased osteocalcin expression by osteoblasts and improved healing rates over 100 days [23]. In their work, iron particles were pre-synthesised using a modified emulsion technique and then added to a Poly(DL-lactide)/Dimethylacetamide solution along with hydroxyapatite nanoparticles before electrospinning. The authors did not fully discuss the specific electrospinning apparatus or the fabrication methodology other than that the implant was prepared by addition of pre-synthesised MNPs to an electrospinning system and the resulting nanofibrous mat was folded to produce a 0.5 cm^2 construct for bone repair. If it is assumed that the common single-needle electrospinning system was employed this would be an extremely time consuming, multi-stage process. In order for advances in the application of MNPs and functional polymer scaffolds to be translated into commercial viability and widespread testing the fabrication process must be simplified and scaled.

For many biological and medical applications, it is advantageous to include MNPs within a biocompatible scaffold for delivery and retention at a targeted site. Fabrication of these materials is generally two-stage process, with the NPs synthesised separately and then added to a scaffold material. This process presents familiar challenges such as particle agglomeration and uneven distribution throughout the eventual scaffold. In this study, in-situ synthesised MNPs within nanofibrous scaffolds were prepared by the co-precipitation technique [24] coupled with electrospinning. This allows for a homogenous distribution of nanoparticles throughout the fibres. Poly (ethylene oxide) (PEO) was chosen as the electrospinning polymer due to its excellent fibre-forming properties, biocompatibility, chemical stability and water solubility, removing the necessity for harsh solvents. In addition, Poly (vinyl pyrrolidone) (PVP) was also used to illustrate the effect of the choice of electrospun polymer on average particle diameter.

Electrospinning has previously been used to immobilise NPs [5,23], however the production rate of conventional electrospinning systems is limited, preventing the technique from being practically applied on a large scale [25]. Examples of free-surface electrospinning processes that directly fabricate fibres containing MNPs are not found in the current literature. The requirement for production of MNP-containing fibres at an industrial scale for in vivo or clinical testing makes this research particularly relevant and important for future direction within regenerative medicine and other applications.

To address the issue of low throughput in the presented research, scaffolds were prepared using a one-step technique combining in-situ particle synthesis with electrospinning. One where the particle synthesis and polymer solution preparation are carried out in one step, allowing electrospinning to be carried out immediately having only prepared one solution. The in-situ synthesis of magnetic nanoparticles within an electrospinning system allowed for homogenous particle dispersion through sub-micron fibres as well as production scale-up using a commercially available “free-surface” electrospinning system.

2. Experimental section

2.1. Materials

Poly(ethylene oxide) (PEO) (M_w = 900 kDa), Poly(ethylene oxide) (PEO) (Mw = 400 kDa), poly(vinyl pyrrolidone) (PVP) (Mw = 55 kDa), sodium borohydrate ($NaBH_4$) (≥97% pure), sodium chloride (NaCl) (BioXtra, ≥99.5% pure), ferrous chloride ($FeCl_2$) (96% pure), ferric chloride ($FeCl_3$) (97% pure) and pentaerythritol triacrylate (PETA) (technical grade) were purchased from Sigma-Aldrich UK. All water used was millipore-filtered. All reagents were used as received without further purification.

2.2. Solution preparation

PEO (M_w = 900 kDa)/water stock solution was prepared at a concentration of 5%(w/w). PEO (M_w = 400 kDa)/water stock solution was prepared at a concentration of 5.5%(w/w). Both PEO stock solutions were supplemented with 10% PETA with respect to polymer weight. PVP/water stock solution was prepared at a concentration of 47%(w/w). Two solutions of ferrous/ferric chloride were mixed at a 2:1 M ratio to a total iron concentration of 1.3 mM and 1.3 M. A solution of sodium borohydride (2 M) was prepared in deionized water. Both the ferric/ferrous chloride and sodium borohydride solutions were prepared fresh before each experiment.

2.3. Electrospinning via needle-aperture

For electrospinning via a needle-aperture system, each polymer stock solution (25 ml, PEO M_w = 900 kDa and PVP Mw = 55 kDa) was supplemented with sodium borohydride solution (500 μl, 2 M) and mixed vigorously for 5 min to ensure homogenous distribution. Subsequently, the $FeCl_3/FeCl_2$ solution (500 μl) was added to the polymer solution. An immediate colour change was observed on addition of the iron solution due to particle formation. The reaction was allowed to proceed for 20 min at room temperature under continuous agitation before being loaded into a 5 ml syringe. Electrospinning was performed using the PROFECTOR LIFE SCIENCES SPRAYBASE® system with a 16-gauge (I.D. 1.19 mm) blunt end stainless steel needle with an aluminium foil collector substrate. Electrospinning parameters were as follows; voltage 15 kV (PEO) and 18 kV (PVP), feed rate 0.5 ml/h and a tip to collector distance of 17 cm. The electrospinning process was allowed to proceed for 1 h before fibres were collected for imaging, at which time a 3 × 3 cm square of the foil collector substrate was removed and imaged directly without sputter coating or other treatments.

2.4. Electrospinning via free-surface technique

To investigate scale-up of the NF production free-surface electrospinning was employed using the EL MARCO NANOSPIDER Lab 200 system. This technique is a relatively recent adaptation to the standard electrospinning approach [26] and is designed to permit the formation of several polymer jets simultaneously in order to scale up fibre production. A schematic diagram showing the free-surface electrospinning set-up employed is presented in Fig. 1. A five 228-fold increase in fibre production (g/hour) was observed between the needle and free-surface techniques. PEO (40 ml, M_w = 400 kDa) was added to a 50 ml universal container. A different molecular weight PEO was used compared to the needle based process (M_w = 900 kDa) this allowed the formation of fibres with similar diameters, while maintaining concentrations within the electrospinning solutions; the solutions were supplemented with the same amount of precursor for nanoparticle

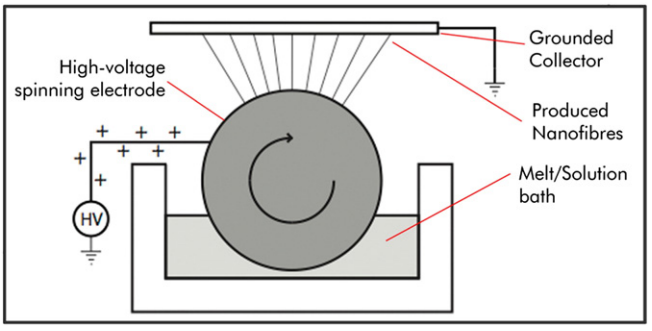

Fig. 1. A schematic diagram showing a free-surface electrospinning set-up. A polymer solution/melt is held in a bath and a spinning electrode connected to a high voltage power supply is utilized to form multiple jets. Nanofibres are electrospun upwards and collected on a grounded collector plate.