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Multifunctional conducting polymer fibres for drug delivery applications

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Abstract

Advances in the fabrication of neuroprosthetic electrodes have attracted considerable interest from biomedical researchers. These electrodes are incorporated into a neuroprosthetic device capable of, electrically stimulating and recording of neuron activity. Critical to the successful application of these electrodes is their biocompatibility, stable conductivity, lower impedance and flexibility whilst maintaining appropriate mechanical properties [1] .

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Multifunctional Conducting Polymer Fibres for Drug Delivery Applications

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INTRODUCTION

Advances in the fabrication of neuroprosthetic electrodes have attracted considerable interest from biomedical researchers. These electrodes are incorporated into a neuroprosthetic device capable of, electrically stimulating and recording of neuron activity. Critical to the successful application of these electrodes is their biocompatibility, stable conductivity, lower impedance and flexibility whilst maintaining appropriate mechanical properties [1] . A relatively new conducting material, namely organic conducting polymers (OCPs), is being utilized in the fabrication of electrode structures capable of electrically stimulating cells as well as recording cellular activity The unique characteristics of OCPs such as biocompatibility with higher surface area, compare to traditional conductors such as metals, make them an appropriate choice to apply in biomedical research [2]. Two types of OCPs namely poly(3,4-ethylenedioxythiophene) (PEDOT) and polypyrrole (Ppy) have been shown to be biocompatible conductors with lower impedance and have been employed to coat metal electrode surfaces, resulting in an enhancement of electrode/cellular communication [3]. Moreover, these structures have widely been used for controlled release of a range of biomolecules such as anti-inflammatory and antibiotic drugs. Fabrication of conducting fibers has previously been achieved by us and applied to a biomedical application [4]. In the work presented here, we discuss the fabrication of OCP wetspun fibers (PEDOT:PSS-CHI/Ppy) incorporating the antibiotic drug ciprofloxacin hydrochloride (cipro). These conducting fibers were tested for their mechanical, electrical and drug deliver properties using a range of techniques and were shown to possess good electrical and mechanical properties. We also show that it is possible to control the release of cipro from the conducting fiber and that the incorporated and released cipro is still active against gram positive and gram negative bacteria.

APPROACH

Poly(3,4-ethylenedioxythiophene) poly(styrenesulfonate) (PEDOT: PSS) pellets were obtained from Agfa (Orgacon dryTM, Lot A6 0000 AC) with water content of 9.8m/m% H_2O and used as supplied. High molecular weight Chitosan (CHI) was purchased from Sigma (>75% deacetylation) and Ciprofloxacin Hydrochloride was obtained from MP Biomedical Inc. (Lot No. of 8460H) with M_W = 367.84. Pyrrole monomer was purchased from Merck and distilled prior to use and stored at -20^{o}C when not in use. Deionised Milli-Q water (18 MΩ cm^{-1}) was used to prepare all aqueous solutions. The release of Ciprofloxacin hydrochloride was measured in Phosphate Buffer Saline (PBS) solution with pH≈ 7.4 prepared by dissolving standard PBS tablet (Merck, Germany) in 1 L Milli-Q water (18MΩcm^{-1}). Concentrated acetic acid was purchased from Sigma and diluted using Milli-Q water. The wetspinning method was used to fabricate PEDOT:PSS-CHI fibres by injecting PEDOT:PSS with concentration of 25 mg/ml into the 1.0 wt% chitosan solution. The feeding rate of wetspinning pump was 15 mL/hr using a 5.0 mL syringe with a detachable needle (20 gauge) used as a spinneret. The PEDOT:PSS-CHI fibers were washed and dried under tension after wetspinning. The second layer (Ppy) was polymerised electrochemically onto the PEDOT:PSS-CHI fibre, from a 0.2 M pyrrole monomer containing 5.0 mM Ciprofloxacin hydrochloride in MilliQ water. The electrochemical polymerisation was performed under galvanostatic mode utilizing a platinum mesh (counter electrode), Ag/AgCl (reference electrode) and the PEDOT:PSS-CHI fiber as the working electrode. The release of ciprofloxacin was measured by UV.vis spectroscopy at a wavelength of 270nm. For electrically stimulated release, the cell contained a platinum mesh auxiliary, Ag/AgCl reference and the PEDOT:PSS-CHI/Ppy.Cipro fiber. Samples of release mediums were collected over three days with each aliquot being collected and replaced with fresh PBS. The aliquots were kept at 2 ^{o}C until drug measurements were performed.

RESULTS AND DISCUSSION

The PEDOT:PSS-CHI fibres were wetspun by the injection of a PEDOT:PSS solution into a solution of chitosan (1 wt%) and the fiber formation occurring by the reaction between negatively charge of PSS and positively charge of amine group in chitosan. The morphology of fibers was analyzed using scanning electron microscopy (SEM) and show a compact and dense structure with average diameter of 56 ± 7 μm (Fig. 1A – white arrow).

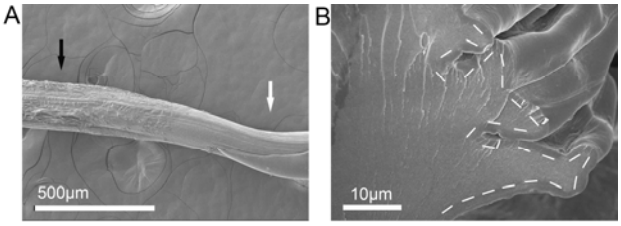
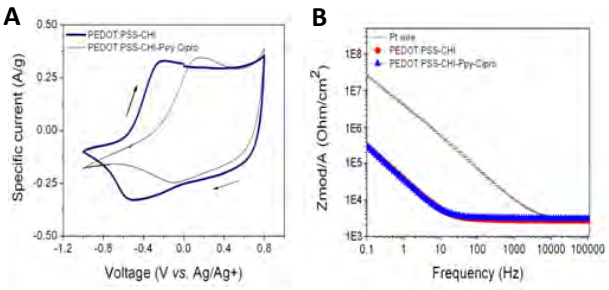


Fig 1. (A) Scanning electron microscopy (SEM) image of PEDOT:PSS-CHI fibre without (white arrow) and with (black arrow) the Ppy.Cipro layer. (B) SEM image of cross-section of fibre. (The white lines show the Ppy.Cipro layer) [5].

The electrochemistry and conductivity of these fibres was analyzed (Fig 2A and B) and was shown to be suitable to allow a second conducting polymer layer to be electrochemically deposited onto. The second layer was composed of polypyrrole doped with the antibiotic ciprofloxacin (Ppy.Cipro). The SEM in Fig 1A and 1B shows a change in morphology of fibres before and after polymerisation of second layer.



The release of ciprofloxacin hydrochloride from Ppy.Cipro under passive and electrically stimulated conditions was measured by UV.vis over 3 days (Fig. 3). The non-stimulated (passive) release showed most of ciprofloxacin was released during first 9 hours followed by a plateau. While, the release of ciprofloxacin increased in higher concentration and longer time points by electrical stimulation.

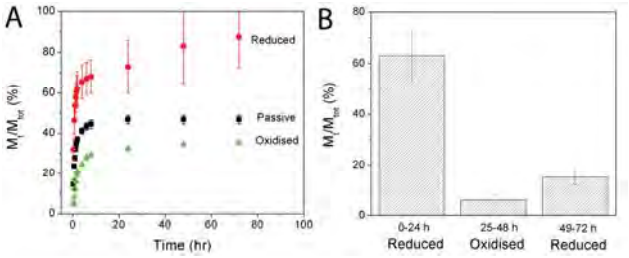


Fig 3. (A) release profile of Cipro release during oxidized, reduced and passive state of conducting polymer within 72h. B) Release profile of Cipro with switching between oxidized and reduced state of Ppy layer.

CONCLUSION

Conducting polymer fibres have been fabricated via wet-spinning method and represents solid and promising structures to incorporate antibiotic drug. The release of ciprofloxacin has been investigated under passive and stimulated conditions. The results showed the capability of these novel fibres to control drug release in specific timeframe required and demonstrated promises in drug delivery applications.

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