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Electrospinning fibres for the controlled delivery of antibiotics

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Statement of the Problem: We are studying the controlled release of antibiotics from multi-layered electrospun matrices.

Purpose: The purpose of this study is to investigate the design and application of multilayered electrospun micro-nanofibres as controllable drug-delivery devices, an important avenue in modern medicines design.

Methodology: Many formulations of electrospun poly- ϵ -caprolactone (PCL) and poly(ethylene-co-vinyl acetate (PEVA) have been designed, prepared as micro-nanofibre layers, and assayed for the controlled release of the clinically useful antibiotic tetracycline (Tet) HCl with potential applications in wound healing and especially in complicated skin and skin-structure infections. Tet HCl was also chosen as a model drug possessing a good UV chromophore and capable of fluorescence together with limited stability.

Findings: Tet HCl was successfully incorporated (essentially quantitatively at 3% w/w) and provided controlled release from multi-layered electrospun matrices. The Tet HCl release test was carried out by a total immersion method on 2x2 cm square electrospun fibrous mats in Tris or PBS heated to 37°C. The formulation PCL/PEVA/PCL with Tet HCl in each layer gave a large initial (burst) release followed by a sustained release. Adding a third layer to the two layered formulations led to release being sustained from 6 days to more than 15 days. There was no detectable loss of Tet chemical stability (as shown by UV and NMR) or bioactivity (as shown by a modified Kirby-Bauer disc assay). Using Tet HCl-sensitive bacteria, *Staphylococcus aureus* (ATCC 25,923), the Tet HCl loaded three layer matrix formulations still showed significant antibacterial effects on days 4 and 5.

Conclusions & Significance: Electrospinning provides good encapsulation efficiency of Tet HCl in PCL/PEVA/PCL polymers in micro-nanofibre layers which display sustained antibiotic release and may find applications in drug releasing wound dressings

Recent Publications

1. N Alhusein, I S Blagbrough, and P A De Bank (2012) Electrospun matrices for localized controlled drug delivery: release of tetracycline hydrochloride from layers of polycaprolactone and poly(ethylene-co-vinyl acetate). *Drug Delivery Translational Research*. 2(6):477-488. Doi 10.1007/s13346-012-0106-y.
2. N Alhusein, P A De Bank, I S Blagbrough, and A Bolhuis (2013) Killing bacteria within biofilms by sustained release of tetracycline from triple-layered electrospun micro/nanofibre matrices of polycaprolactone and poly(ethylene-co-vinyl acetate). *Drug Delivery Translational Research*. 3(6):531-541. Doi: 10.1007/s13346-013-0164-9.
3. N Alhusein, I S Blagbrough, and P A De Bank (2013) Zein/polycaprolactone electrospun matrices for localized controlled delivery of tetracycline. *Drug Delivery Translational Research*. 3(6):542-550. Doi 10.1007/s13346-013-0179-2.
4. N Alhusein, P A De Bank, and I S Blagbrough (2015) Nanofibers, Electrospun Polycaprolactone: Controlled Drug Delivery. in: *The Encyclopedia of Biomedical Polymers and Polymer Biomaterials*. 1st edn. Taylor and Francis Group. ISBN 19781439898796. 7:5239-5249.
5. N Alhusein, I S Blagbrough, M L Beeton, A Bolhuis, and P A De Bank (2016) Electrospun Zein/PCL fibrous matrices release tetracycline in a controlled manner, killing *Staphylococcus aureus* both in biofilms and ex vivo on pig skin, and are compatible with human skin cells. *Pharmaceutical Research*. 33(1):237-246. Doi:10.1007/s11095-015-1782-3

Biography

Ian S Blagbrough is a Chemist teaching Pharmacists And Pharmacologists, Chemists and Natural Science students at the University of Bath where he has carried out natural products and molecular pharmaceuticals research for 27 years. He has expertise in pharmaceutical analysis and the evaluation of modern medicines, especially those based upon the applications of natural products. His passion is for molecular pharmaceuticals leading to molecular medicine improving health and wellbeing. He has supervised 27 PhD students to successful graduation and together they have co-authored 133 papers and book chapters. In 2016, he won the Excellence in Doctoral Supervision Prize as the best PhD supervisor at the University of Bath. He is also a holder of the BPC Conference Science Medal for his international contributions to the Pharmaceutical Sciences. He has been an adjunct Full Professor in the School of Pharmacy at USC, CA, USA, for 7 years.

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