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Background: Chronic wounds represent a major problem for the quality of life of patients and healthcare systems. Infection can be one of the major reasons that wounds fail to heal or turn chronic. Given the rise in multidrug resistant bacteria, there is an urgent need to treat these infections without the use of antibiotics. Nitric oxide (NO) is a promising alternative to antibiotics with no known resistance mechanism.[1] Electrospinning is a cost effective and easily scaleable manufacturing method of which can fabricated nanofibrous mats of high porosity and surface-to-volume, ideal for wound dressing materials.[2] In this study we report on the fabrication and characterisation of NO-doped cellulose acetate (CA) electrospun nanofiber mats and their antimicrobial efficacy against both gram negative and gram positive bacteria.

Methods: CA nanofibers containing a NO donor were produced by electrospinning. CA 15wt% was dissolved in a DMAC:acetone solvent system. The resultant solution of CA was electrospun at varying voltages to optimise the morphology of the nanofibers. The chemistry and the morphology of the of the nanofibers were assessed by Fourier-Transform infrared spectroscopy (FT-IR) and scanning electron microscopy (SEM). Chemiluminescence was used to study the payload and release of NO. The antimicrobial efficacy of the fibres tested over 24 hours against Staphylococcus aureus and Pseudomonas aeruginosa. Cytotoxicity and cell migration assays of the fibres was tested over 72 hours using HACAT keratinocytes and WS1 Fibroblasts.

Results: The morphology of CA nanofibers were analysed by SEM and were between 378±300nm and 400±200nm. Tethering of the NO donor onto the CA nanofibers did not affect the morphology or the diameter. The chemical composition of the CA nanofibers were investigated before and after NO donor loading. The CA nanofibers were analysed by FTIR and the characteristic peaks observed were C=O, C-CH3 and C-O-C of cellulose acetate at 1775, 1370 and 1100cm^{-1}. Inclusion of the NO donor was confirmed by the presence of peaks in the FTIR representative of N-O stretching at 1550cm^{-1}. Chemiluminescence was used to analyse the release of NO from the fibres. An initial burst was seen, followed by sustained release over 24 hours. Antimicrobial testing demonstrated that NO-releasing nanofibers were able to effectively reduce bacterial adhesion of S aureus and P aeruginosa at 4 hours and 24 hour time points. Cytotoxicity assays demonstrated that NO-releasing nanofibers were not cytotoxic to keratinocytes or fibroblasts. Cell migration assays showed that there was no negative impact on wound close with the introduction of NO-releasing nanofibers.

Conclusions: The NO releasing CA nanofibres displayed sustained release of NO and efficacy against gram-positive and gram negative bacteria in vitro. Whilst having no negative effect against cells found in the wound healing environment. Further investigation is required to determine the sustain the release of NO to increase dressing wear time.