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Core-Shell Nanofibers for Prevention of Postsurgical Adhesion

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Abstract : In this study, we propose to use electrospinning to fabricate porous nanofibrous membranes as postsurgical anti-adhesion barriers and to improve the properties of current post-surgical anti-adhesion products. We propose to combine FDA-approved biomaterials with anti-adhesion properties, polycaprolactone (PCL), polyethylene glycol (PEG), hyaluronic acid (HA) with silver nanoparticles (Ag) and ibuprofen (IBU), to produce anti-adhesion barrier nanofibrous membranes. For this purpose, PEG/PCL/Ag/HA/IBU core-shell nanofibers were prepared. The shell layer contains PEG + PCL to provide mechanical supports and Ag was added to the outer PEG-PCL shell layer during electrospinning to endow the nanofibrous membrane with anti-bacterial properties. The core contains HA to exert anti-adhesion and IBU to exert anti-inflammation effects, respectively. The nanofibrous structure of the membranes can reduce cell penetration while allowing nutrient and waste transports to prevent postsurgical adhesion. Nanofibers with different core/shell thickness ratio were prepared. The nanofibrous membranes were first characterized for their physico-chemical properties in detail, followed by in vitro cell culture studies for cell attachment and proliferation. The HA released from the core region showed extended release up to 21 days for prolonged anti-adhesion effects. The attachment of adhesion-forming fibroblasts is reduced using the nanofibrous membrane from DNA assays and confocal microscopic observation of adhesion protein vinculin expression. The Ag released from the shell showed burst release to prevent E Coli and S. aureus infection immediately and prevent bacterial resistance to Ag. Minimum cytotoxicity was observed from Ag and IBU when fibroblasts were culture with the extraction medium of the nanofibrous membranes. The peritendinous anti-adhesion model in rabbits and the peritoneal anti-adhesion model in rats were used to test the efficacy of the anti-adhesion barriers as determined by gross observation, histology, and biomechanical tests. Within all membranes, the PEG/PCL/Ag/HA/IBU core-shell nanofibers showed the best reduction in cell attachment and proliferation when tested with fibroblasts in vitro. The PEG/PCL/Ag/HA/IBU nanofibrous membranes also showed significant improvement in preventing both peritendinous and peritoneal adhesions when compared with other groups and a commercial adhesion barrier film.

Keywords : anti-adhesion, electrospinning, hyaluronic acid, ibuprofen, nanofibers
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