

## Fabrication and characterization of antibacterial herbal drug-loaded poly-lactic acid/cellulose acetate composite nanofibers for wound dressing applications

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Interactive polymeric electrospun nanofibers is considered a very promising matrix for treatment of chronic wounds. The 3 dimensional structure of nanofibers allow it to mimic the extracellular matrix of the tissues. Also the ability to deliver bioactive ingredients allow it to further promote wound healing and preventing infections. Polylactic acid (PLA) is a versatile biopolymer that is widely used as a biomaterial. However, one of the major issues which limits its further application in tissue engineering purposes is its hydrophobic nature and poor cellular interaction. In this study, an antibacterial electrospun nanofibrous scaffolds, with diameters around 400–1000 nm, were prepared by physical blending PLA with a hydrophylic biopolymer, cellulose acetate (CA), to achieve desirable properties such as better hydrophilicity, excellent cell attachment and proliferation. For preventing common clinical infections, an antimicrobial agent, Thymoquinone, TQ was incorporated into the electrospun fibers. TQ is the active ingredient of *Nigella sativa* and it is well known for its antibacterial properties and ability to promote wound healing. The potentiality of the prepared scaffolds, regarding being used as an interactive wound dressing, has been investigated including, swelling behavior, WVP and porosity. The release profile of TQ from the prepared scaffolds was also examined at the physiological pH (7.4) and temperature (37 °C). The antimicrobial efficiency of the prepared scaffolds against gram negative and gram positive bacteria were determined by the agar diffusion assay. The interaction between fibroblasts and the TQ-loaded PLA: CA scaffolds such as viability, proliferation, and attachment were characterized. TQ-loaded PLA: CA scaffolds showed burst TQ release after 24 h, compared with medicated PLA scaffolds, followed by a sustained release rate for 9 successive days. The presence of CA in the nanofiberous scaffolds improved its hydrophilicity, and water uptake capacity. Furthermore, it created a moist environment for the wound, which can accelerate wound recovery. The results also indicated that medicated PLA: CA nanocomposite scaffolds showed a significant antibacterial activity against both gram positive and gram negative bacteria. TQ-loaded PLA: CA composite scaffolds enhanced cell viability, attachment and proliferation, as compared to TQ-loaded PLA nanofibers. A preliminary in vivo study performed on normal full thickness mice skin wound models demonstrated that TQ-loaded PLA: CA (7:3) scaffolds significantly accelerated the wound healing process by promoting angiogenesis, increasing re-epithelialization and controlling granulation tissue formation. Our results suggest that TQ-loaded PLA: CA nanocomposite mat could be an ideal biomaterial for wound dressing applications.

**Keywords:** Poly-lactic acid, cellulose acetate, wound dressing, chronic wounds

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