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Composite Electrospun Aligned PLGA/Curcumin/Heparin Nanofibrous Membranes for Wound Dressing Application

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Abstract : Wound healing is a complicated process involving overlapping hemostasis, inflammation, proliferation, and maturation phases. Ideal wound dressings can replace native skin functions in full thickness skin wounds through faster healing rate and also by reducing scar formation. Poly(lactic-co-glycolic acid) (PLGA) is an U.S. FDA approved biodegradable polymer to be used as ideal wound dressing material. Several in vitro and in vivo studies have demonstrated the effectiveness of curcumin in decreasing the release of inflammatory cytokines, inhibiting enzymes associated with inflammations, and scavenging free radicals that are the major cause of inflammation during wound healing. Heparin has binding affinities to various growth factors. With the unique and beneficial features offered by those molecules toward the complex process of wound healing, we postulate a composite wound dressing constructed from PLGA, curcumin and heparin would be a good candidate to accelerate scarless wound healing. In this work, we use electrospinning to prepare curcumin-loaded aligned PLGA nanofibrous membranes (PC NFMs). PC NFMs were further subject to oxygen plasma modification and surfaced-grafted with heparin through carbodiimide-mediated covalent bond formation to prepare curcumin-loaded PLGA-g-heparin (PCH) NFMs. The nanofibrous membranes could act as three-dimensional scaffolds to attract fibroblast migration, reduce inflammation, and increase wound-healing related growth factors concentrations at wound sites. From scanning electron microscopy analysis, the nanofibers in each NFM are with diameters ranging from 456 to 479 nm and with alignment angles within □ 0.5°. The NFMs show high tensile strength and good water absorptivity and provide suitable pore size for nutrients/wastes transport. Exposure of human dermal fibroblasts to the extraction medium of PC or PCH NFM showed significant protective effects against hydrogen peroxide than PLGA NFM. In vitro wound healing assays also showed that the extraction medium of PCH NFM showed significantly better migration ability toward fibroblasts than PC NFM, which is further better than PLGA NFM. The in vivo healing efficiency of the NFMs was further evaluated by a full thickness excisional wound healing diabetic rat model. After 14 days, PCH NFMs exhibits 86% wound closure rate, which is significantly different from other groups (79% for PC and 73% for PLGA NFM). Real-time PCR analysis indicated PC and PCH NFMs down regulated anti-oxidative enzymes like glutathione peroxidase (GPx) and superoxide dismutase (SOD), which are well-known transcription factors involved in cellular inflammatory responses to stimuli. From histology, the wound area treated with PCH NFMs showed more vascular lumen formation from immunohistochemistry of α-smooth muscle actin. The wound site also had more collagen type III (65.8%) expression and less collagen type I (3.5%) expression, indicating scar-less wound healing. From Western blot analysis, the PCH NFM showed good affinity toward growth factors from increased concentration of transforming growth factor-β (TGF-β) and fibroblast growth factor-2 (FGF-2) at the wound site to accelerate wound healing. From the results, we suggest PCH NFM as a promising candidate for wound dressing applications.

Keywords : Curcumin, heparin, nanofibrous membrane, poly(lactic-co-glycolic acid) (PLGA), wound dressing
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