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## Composite electrospun aligned PLGA/curcumin/heparin nanofibrous membranes for wound dressing application

Wound healing is a complex process involving many interdependent and overlapping sequences of physiological actions. Ideal wound dressings can replace native skin functions in full thickness skin wounds through faster healing rate and also by reducing scar formation. The application of exogenous lactate released from poly(lactic-co-glycolic acid) (PLGA) polymer accelerates angiogenesis and the wound healing processes. 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 is 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 479nm 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.

### Biography

Jyh-Ping Chen has been a Professor in Chemical and Materials Engineering at Chang Gung University since 1997. He is currently a Researcher at the Department of Plastic and Reconstructive Surgery, Chang Gung Memorial Hospital and holds joint appointments as Professor in the Department of Materials Engineering, Ming Chi University of Technology, and Research Center for Food and Cosmetic Safety and Research Center for Chinese Herbal Medicine, Chang Gung University of Science and Technology, Taiwan, ROC. He has received his BS degree in Chemical Engineering from National Taiwan University in 1981 and PhD in Chemical Engineering from Pennsylvania State University in 1988. He has published over 150 papers in SCI journals with more than 3500 citations. He is a Guest Editor or Editorial Board Member for 12 international journals and a peer reviewer for more than 50 reputed SCI journals. His current research interests include biomaterials, tissue engineering and drug delivery.

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