Heparin functionalized core-shell type nanofabrics as a potent growth factor sequestering biomaterial for skin wound healing

アクシャット, ジョシー

（様式２）

氏　　名　：Akshat Joshi (アクシャット ジョシー)

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(創傷治癒のための増殖因子を捕捉可能なバイオマテリアルとしての
ヘパリン機能化コアシェル型ナノ繊維に関する研究)

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論　文　内　容　の　要　旨

Growth factors (GFs) are signaling molecules that are principle mediators in tissue regeneration. Biomaterial scaffolds employed as wound dressings are often hampered by their limitations to deliver GFs exogenously due to their instability and low half-life. Overdosing is often required, which raises further concerns as severe as carcinogenesis. Effective restoration of blood supply at the degenerative site while minimizing the use of exogenous GFs remains a pressing challenge for engineered regenerative medicine.

Considering such challenges, current research utilizes the exogenous and endogenous GFs sequestering ability of heparin functionalized PCL/gelatin co-spun nanofibrous dressings to facilitate synergistically driven tissue regeneration by utilizing combined therapeutic effect of exogenous and endogenous GFs, and thereby minimizing the sole dependency on exogenous GFs for tissue regeneration, that have severe concerns in terms of safety and efficacy.

This thesis consists of 6 chapters. The chapters are arranged in order to achieve the basic objective of this study. The following paragraphs will give a glimpse of the work content of each chapter:

Chapter 1: of the thesis discuss about the background and objective of this research. It also highlights the novelty of this study and how this study was advantageous over current available techniques for fabrication of wound dressings

Chapter 2: of this thesis provides a comprehensive review on delivery systems for wound healing.

It ushers in an introduction of wound healing and the mechanisms involved there forth outlining the physiology, mechanism of actions, wound types and wound management.

Chapter 3: in this chapter, co-electrospinning technique was optimized to fabricate core-shell type nanofabrics. By controlling various co-electrospinning parameters, uniform and bead-free core-shell type PCL/gelatin nanofabrics (PG) were produced that showed excellent balance between mechanical properties and biocompatibility. Also, the fabricated nanofabrics met all the criterion for its application as wound dressings. Results showed that PG nanofabrics were an ideal material for application as wound dressings owing to their excellent mechanical properties that mimic the skin elasticity, enhanced biocompatibility due to presence of gelatin as shell component as well as ideal Water Vapor Transmission Rate (WVTR) and surface wettability.

Chapter 4: in this chapter, the fabricated core-shell type nanofabrics were endowed with the ability for sequestering growth factors (GFs), both exogenous and endogenous ones. For this, we conjugated our fabricated nanofabrics to heparin via EDC/NHS mediated reaction. These heparin functionalized core-shell type nanofabrics, called as Hep-PG, showed excellent capability in sequestering GFs both exogenous and endogenous ones. Results showed tremendous application of heparin in sequestering GFs both exogenous and endogenous ones with high efficiency.

Chapter 5: in this chapter, the fabricated Hep-PG nanofabrics were employed as wound dressings to evaluate their potential in effective skin tissue regeneration. Endowed with properties of ideal wound dressings and capability in sequestering exogenous and endogenous GFs, Hep-PG nanofabrics promoted scarless and effective tissue regeneration within 14 days of treatment, by utilizing the synergistic effect between exogenously loaded bFGF and sequestered endogenous pro-regenerative GFs. Here we demonstrated a novel biomaterial-based approach with inclusion of heparin, to sequester GFs from exogenous and endogenous source, and how a synergistic effect of exogenous and endogenous GFs can lead to proper tissue regeneration. This was the first study till date which evaluated a combined role of exogenous and endogenous GFs based on heparin in achieving tissue regeneration,

Chapter 6: of this thesis gives a general conclusion and future study that can be incorporated to further advance the current study