博　士　論　文　の　内　容　の　要　旨

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論文題目	Preparation of bio-based polymeric nanocomposite scaffolds for advanced biomedical applications バイオメディカル応用を目的としたバイオベースの高分子ナノコンポジット足場の作製

（博士論文の内容の要旨）

Nanofibers are very porous materials with a high surface area. Therefore, they are the most suitable textile materials for scaffolding application as their morphological structure is similar to that of the human extra cellular matrix.

Medical textiles are emerging and quickly developing in the biomedical sector starting from basic wound dressing materials to scaffolds intended for use in typical surgical operations. Current studies reveal that the bio-based polymeric electrospun nanofiber mats (ENMs) have gained great attention for the fabrication of biomaterials. However, the improvement in mechanical properties of such materials has remained a big research gap.

Conventionally, polyesters are not considered eco-friendly materials due to their petroleum origin and their slow degradation in the land-fill. However, they are abundantly present in our daily life and researchers found that they can benefit human health when applied as biomaterials for regenerative medicine. Polycyclohexylenedimethylene (PCT) is a type of polyesters with very good mechanical properties but it has been challenged by the constraint of the very high temperature required for its processing.

Isosorbide has attracted a great deal of attention due to its biocompatibility,

biodegradability, non-toxicity and its wide abundance on earth. The introduction of this monomer by a synthesis method has contributed in overcoming the aforementioned problem and lowering the processability temperature of PCT.

This thesis covers two main studies related to biomedical applications starting with our first project that states the possibility to apply polyester materials incorporated with Isosorbide derived from corn glucose in the biomedical field. We prepared Poly (Ethylene-glycol-co-1,4-Cyclohexane di-methylene-co-isosorbide terephthalate) (PEICT) and Poly (1, 4 cyclohexane di-methylene-co-isosorbide terephthalate) (PICT) nanofibers as well as their blended composition (BLEND) for the first time and we could successfully manufacture these three types of nanofibers in the form of artificial blood vessels (ABV) with different diameters using electrospinning technique, we also underwent a detailed characterization of the resultant scaffolds. Interestingly, a compacted morphology and enhanced wettability were imparted onto the surface of BLEND ABVs. In addition, BLEND has showed a comparatively higher biodegradation rate in parallel to tunable tensile strength. Thus, the fabricated BLEND composite scaffolds tend to be promising for application in the biomedical field.

In our second project, we focused on the preparation of PEICT ENMs to further investigate the reason of the low cell infiltration, thus we produced PEICT ENMs at a higher polymer concentration to obtain nanofibers with a bigger average diameter for the infiltration of fibroblast cells. PEICT ENMs showed very good cell adhesion and viability revealing its potential to be used as biomaterials.

From the first main study of this thesis, it was observed that the surface properties of polymeric materials can be modified by a simple blend electrospinning. Therefore, we tried to explore the surface properties of two bio-based polymers, namely Polyglycolic acid (PGA) and Collagen for an intended application in surgical procedures with an improvement in handling properties. It was concluded that PGA/collagen (60:40) was the optimal blend ratio which resulted in nanofibers with improved surface wettability, which is ultimately good for cell adhesion.

The highlighted outcomes of the research chapter-wise are given below.

CHAPTER 1

In chapter 1, an introduction to the electrospinning technique has been discussed along with the current issues related to biomaterials used in the biomedical field, and how the polymer-based materials have the potential to address these problems at some extent. An overview of the materials used in this research is also detailed.

CHAPTER 2

This work suggested new biomass polymeric nanofibers which can be used for industrial applications such as tissue engineering and scaffolding. Isosorbide is an eco-friendly natural biomaterial abundantly available on earth and best fitted for the functional textile substrates. Bio-based polyester copolymers PICT and PEICT nanofibers were prepared in tubular shapes to mimic small diameter (<2mm) blood vessels, they were characterized and investigated for biodegradation. we reported successful human breast cell culture and adhesion on the surface of blended composition of PICT and PECIT with the ratio 50:50.

CHAPTER 3

In this chapter, PEICT is further explored for the cell culture of fibroblast cells in parallel to cell viability. The average nanofiber diameter was increased as a results of increased polymer concentration for electrospinning of PEICT ENMs. This research clarified that the surface properties and average diameter of nanofibers play an important role for cell culture applications depending on the cell type and size.

CHAPTER 4

In chapter 1 and 2, the reason of good cell infiltration was revealed as a relationship with the surface of nanofibers, thus, in chapter 4 we tried to check the effect of surface treatments on the wettability and morphology of nanofibers surface, as these properties are considered key for cell culture applications. In this study, in lieu of conducting a simple in-vitro cell culture assay, we attempted to optimize the surface affecting parameter on biocompatible polymers, therefore, we chose two bio-based polymers, namely PGA and Collagen were blended at different ratios and 60:40 PGA/Collagen was observed as optimal blend in the context of handling properties which were further improved by using a cage-type collector for electrospinning to impart respective texture on the surface. Basically, optimized blend surface was treated using two techniques, Plasma treatment (Nitrogen) and Ozonation to improve the wettability and the treatment parameters were optimized with respect to morphological stability. The proposed method of cage-type manufacturing opens a new door to continuous electrospinning with tunable morphology, having the potential to be used for biomedical applications in the future.