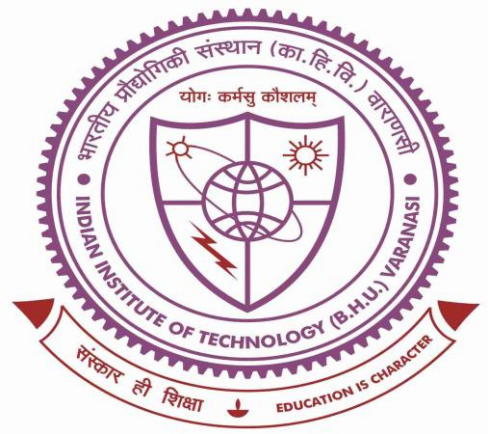
Development of Gelatin grafted Poly(D,L-Lactide) based Scaffolds for Biomedical Applications



ABSTRACT

Submitted in partial fulfillment

for the Award of Degree

By

Balavigneswaran C.K

School of Biomedical Engineering

Indian Institute pf Technology

(Banaras Hindu University)

Varanasi

Roll No. 13021002 **2018**

7. SUMMARY AND FUTURE DIRECTION

This chapter describes brief summary of my research presented in the thesis and emphasizes the implications could be done in the future.

7.1. Summary

This thesis presents synthesis and characterization of linear and star shaped gelatin grafted poly(D,L-Lactide) for biomedical applications. Specifically it involved to tailor the chemical property of poly(D,L-Lactide) (PDLLA) to make it useful for a variety of biomedical applications. The modification of PDLLA by gelatin presented in this study is different from conventional modification that usually involve immobilization of Gelatin onto PDLLA film or scaffolds.

We initially synthesized ss-pLG which is an efficient biocompatible and hydrophilic polymer with cell adhesive surface. The modified polymer improved thermal behaviour compared to its unmodified polymer ss-PDLLA. 3D scaffolds prepared gelatin grafted ss-pLG polymers was compatible to 3T3-L1 cells and blood RBCs. Further, ss-pLG scaffolds facilitated improved cell proliferation with interconnected cellular morphology within the 3D matrix. Degradation kinetics revealed that half of the ss-pLG scaffold was degraded after 7 days in lysozyme medium owing to their hydrophilicity nature.

In another study, we synthesized l-pLG with cell adhesive properties. The mechanical strength of l-pLG scaffolds was higher than ss-pLG scaffolds because of the variable levels of gelatin grafting. The cell proliferation of C2C12 and L929 cells was found significantly more in l-pLG and ss-pLG scaffolds, respectively; which may be attributed to the strength compliance of scaffolds. On the other hand, variable levels of gelatin grafting also controlled the degradation behaviour, where degradation of ss-pLG notably higher compared to l-pLG scaffolds after 7 days of incubation in proteinase k and proteinase k+ lysozyme mixture containing PBS medium.

Further, we evaluated the anti-amyloidogenic property of ss-pLG using BSA as a model protein. It was observed that ss-pLG possesses significantly higher potential than Gel to inhibit the formation of amyloids that may be attributed to the branched ss-pLG, which could reduce thickness of lamella. The inhibition of amyloid fibrillation was due to the strong interaction of ss-pLG with BSA. ss-pLG also rescued the neurotoxicity, which was observed in Aβ cell line model, MC65 cells. Further, ss-pLG was shown to be an efficient capping agent for AuNPs.

In addition, we also fabricated the hybrid scaffolds from ss-pLG and Gel which are cross-linked with GPTMS. The cross-linking of silane significantly increased the hydrophobicity of the hybrid polymer. The rate cell proliferation within the hybrid scaffolds was decreased after day 3, which could be attributed to the release of silica from the matrix. The *in vivo* subcutaneous implantation study showed that Gel, ss-PDLLA and ss-pLG scaffolds degraded completely after week 4, wheras the hybrid scaffolds h-ss-pLG and h-Gel were not degraded as they were cross-linked with silane. The histology analysis showed higher infiltration of cells and the healthy morphology of cells and nucleus was observed in all scaffolds after week 1. On the other hand, the infiltration of cells was lower in hybrid scaffolds after week 4.

7.2. Future Direction

The work presented in this thesis involved fabrication of scaffolds from the synthesized gelatin grafted poly(D,L-Lactide) for Biomedical applications. However, there are some areas have not been explored in this present investigation. Therefore, the unexplored parts can be studied in the future, which are given below.

- Studying the l-pLG and ss-pLG coated nanoparticles for their anti-amyloidogenic property and other possible medical applications
- Studying the mechanical property of h-Gel and h-ss-pLG
- Investigation of cancerous drug delivery kinetics from the hybrid scaffolds.
- Synthesis of l-pLG and ss-pLG terminated with $–NH_2$ functionality. Wide range of cross-linkers is commercially available in the market to covalently cross-link $–NH_2$ terminated polymers. This could be further used to improve the stability and mechanical strength of the scaffolds.