Healing Full-thickness Wounds in Rats using Decellularized Bovine Small Intestinal Submucosa with Enhanced with Cellulose Acetate/ Ag NPs Nanofibers

Akbari Asbagh, R. (Reza)[1], Tafti, SMA (Seyyed Mohsen Ahmadi)[2,3], Nazari, H (Hojjatollah)[2,4], Heirani-Tabasi, A. (Asieh)[2,4,5], Khorasani Zavareh, Z. (Zahra)[4,2], Hajikhani, K (Kiana)[4]

w[1] Tehran University of Medical Sciences, Colorectal surgery research center, Tehran, Iran

[2] Tehran University of Medical Sciences, Colorectal surgery research center, Tehran, Iran, Islamic Republic of

[3] Tehran University of Medical Sciences, Division of Colorectal Surgery, Tehran, Iran, Islamic Republic of

[4] Tehran University of Medical Sciences, Research Center for Advanced Technologies in Cardiovascular Medicine, Tehran, Iran, Islamic Republic of

[5] Tarbiat Modares University, Department of Cell Therapy and Hematology, Tehran, Iran, Islamic Republic of

Introduction

The formation of chronic wounds accounts for considerable costs in health care systems. Despite the several benefits of Decellularized small intestinal submucosa(SIS) as an appropriate scaffold for different tissue regeneration, it has shortcomings such as lack of antibacterial features and inappropriate mechanical properties for skin tissue regeneration. We aimed to examine the efficacy and safety of decellularized SIS scaffold enhanced with cellulose acetate(CA) and silver(Ag) nanoparticles for healing full-thickness wounds.

Materials & Methods

The scaffolds were prepared by decellularizing bovine SIS and electrospinning CA/Ag nanoparticles and characterized using a transmission electron microscope(TEM), scanning electron microscope(SEM), tensile testing, X-ray diffraction, and Raman spectroscopy. In vivo evaluations were performed using full-thickness excisions covered with sterile gauze as the control group, SIS, SIS/CA, and SIS/CA/Ag scaffolds on the dorsum of twenty male Wistar rats divided into four groups randomly with 14-days follow-up. All in vivo specimens underwent Masson's trichrome(MT), transforming growth factor-β (TGF-β) immunohistochemistry(IHC), and Hematoxylin and Eosin(H&E) stainings. The IHC and MT data were analyzed with the ImageJ by measuring the stained area. IBM® SPSS® Statistics 26 was used for statistical analysis, and the statistical significance was determined as P-value <0.05.

Results

The TEM results revealed that Ag nanoparticles are successfully incorporated into CA nanofibers with an average size of 20±2.67 nm and a diameter of 280±8 nm. Assessment of scaffolds hydrophilicity demonstrated that the contact angle of SIS, SIS/CA, and SIS/CA/Ag scaffolds were 103°±8°, 100°±2°, and 80°±4° respectively. The in vivo results indicated that the SIS/CA/Ag scaffold had the most significant wound closure (89.48%±2.04% on day 14, P=0.039). H&E staining of the in vivo specimens showed the formation of epidermal layers with the skin appendages only in the SIS/CA/Ag group on day 14. The percentage of the stained area of MT and TGF-β IHC stainings was the highest one in the SIS/CA/A group as evidence of greatest expression of collagen and TGF-β(37.17%±6.54% and P=0.002, 27.86%±4.37% and P=0.025 respectively).

Conclusion

The decellularized SIS/CA/Ag scaffolds provided the most significant wound closure compared to other groups and caused the formation of epidermal layers and skin appendages. Additionally, the collagen deposition and expression of TGF-β increased significantly in SIS/CA/Ag group.