Comparative studies of the performance of silk fibroin microparticle scaffolds with bioceramics for bone regeneration

Anuya Nisal[1], Rucha Deshpande[1], Swati Shukla[1], Premnath Venugopalan[1, 2], Raeesa Sayyad[1], Shalmali Salunkhe[1], Amod Kale[3], Narendra Deshmukh[3]

[1]Serigen Mediproducts Pvt. Ltd, Plot no. 39, Electronic Co-op estate, Parvati Paytha, Pune 411009, India.
[2] Polymer Science and Engg. Dept. CSIR-National Chemical Laboratory, Homi Bhabha Road, Pashan, Pune 411008, India.
[3]Intox Private Limited, 375, Urawade, Tal. Mulshi, Pune 412115, India.

Email of Presenting Author: anuya@serigenmed.com

DISCLOSURES: **A. Nisal**: 3A; Dr. Anuya Nisal is Founder and CEO of Serigen Mediproducts and receives salary from the company. 4; Dr. Anuya Nisal owns stock in Serigen Mediproducts as a founding Director of the company. **R. Deshpande**: 3A; Dr. Rucha Deshpande is an employee of Serigen Mediproducts and receives salary from the company.. 4; Dr. Rucha Deshpande has been offered stock options for Serigen mediproducts. **S. Shukla**: 3A; Dr. Swati Shukla is a Cofounder and paid employee of Serigen Mediproducts and receives salary from the company. 4; Dr. Swati Shukla owns stocks in Serigen Mediproducts. **P. Venugoapalan**: 4; Dr. Premnath Venugopalan owns stock in Serigen Mediproducts as Founder of company. **R. Sayyad**: None. **S. Salunke**: None. **A. Kale**: None. **N. Deshmukh**: None.

INTRODUCTION:
Synthetic bone void fillers based on calcium ceramics are used to fill cavities in the bone and promote bone regeneration. In this work, we have compared the safety and efficacy of silk fibroin (SF) bone void fillers with currently used and commercially available bioceramic bone void fillers. Further, we have also evaluated two types of SF scaffolds, which have strikingly different structural attributes. The SF scaffolds are prepared using simple lyophilization technique and their performance is compared with microparticle SF scaffolds.
METHODS:
The biocompatibility of scaffolds was assessed by cytotoxicity, cell adhesion and immunogenicity assays along with acute, and subacute toxicity studies in animal models as defined by ISO10993 standards. A reverse transcriptase polymerase chain reaction supported the comparative analysis of various biomarkers expressed during differentiation of human mesenchymal stem cells (hMSCs) seeded on these scaffolds. Further, the performance of the microparticle SF scaffold to support bone formation was evaluated in *in vivo* bone implantation studies (IAEC 17644) in a rabbit model using calcium sulphate ($CaSO_4$) bioceramic as a reference material.
RESULTS:
The studies confirmed that hMSCs cultured on SF scaffolds exhibit higher expression of early to late markers such as Runx2, BMPs, collagen, osterix, osteopontin, and osteocalcin as compared with ceramic-based scaffolds. This observation was further validated by studying the expression of alkaline phosphatase and calcium deposition. We also show that scaffolds made from the same material - SF, but characterized by very different structural attributes, have diverse outcomes in stem cell differentiation. Further, animal studies in the rabbit femur model, showed >2X number of osteoblast and osteoclast cells as compared to $CaSO_4$ implantation sites indicating active bone remodeling. Moreover, the SF microparticle scaffold implantation sites had a reduced incidence of secondary fractures as compared to the $CaSO_4$ implantation sites.
DISCUSSION:
Enhanced expression of markers at various stages of stem cell differentiation and reduced incidence of secondary fractures, suggests that SF microparticle scaffolds could be used as bone void fillers with reduced post-surgical complications.
SIGNIFICANCE
SF microparticle scaffolds are a promising alternative that facilitate superior healing of fracture defects as compared to commercial calcium-based bone void fillers.

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