



Silk Based Nanofibrous Biomaterials for Tissue Engineering and Regenerative Medicine (Term): Transcending New Frontiers

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Article History

Published on 5 April 2019

As a plausible solution to the issues of ever increasing global cases of degenerative maladies, dearth of apposite organ-donors, sky-rocketing medical expenditures and incessantly clambering morbidity rates, research in the realm of tissue engineering and regenerative medicine (TERM) has paced up appreciably in the last few years.¹ In this regard, a handful of laboratories across the world is dedicated toward engineering appropriate biomaterials for TERM. Amongst others, nanostructured silk based scaffolds have carved a unique niche in the quest of suitable biomaterials with desirable biochemical, topographical, mechanical features and tailorable degradation profile for 3D tissue-specific temporal and spatial tuning. Silk is a proteinaceous biopolymer, produced by a number of insects of the Lepidopteran order. The literature databases like SCOPUS, PubMed are constantly being enriched with various reports, patents and reviews on silk based biomaterials at the nanoscale for TERM and allied applications. The prospects include delivering bio-cargoes (genes, drugs, etc.), chemo/bio sensing and bioimaging etc. Silk based micro/nano-fluidics applications also demand special mention. This wonder material with hierarchical nanoscale organizational attributes can be engineered into numerous formats like nanofibrous mats, films, hydrogels etc. Pertinently, the biomedical prospects of various silk worm (both mulberry and non-mulberry types) silk (comprising of fibroin and the sticky sericin) as well as spider silk, the synthesis of which represents nature's elaborate microfluidic manoeuvres have been probed into.² It is highly encouraging to witness fruitful results (with possibilities of commercial translatability) emanating out of recent endeavours, including some of the *avant garde* research works that have been executed in various Indian laboratories, to harness silk based nanobiomaterials for TERM. Of pertinence is to note that the prospects of electrospun nanofibrous silk based mats for engineering various soft and hard tissues have been successfully delved into. A few exemplary evidences that stand in testimony to this fact are cited underneath.

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Doi: <http://dx.doi.org/10.13005/msri/160102>

Osteochondral degeneration, bone-joint injuries and arthritis irk millions globally. To address these issues, 70S bioactive glass sol and silkworm silk were formatted using layer-by-layer electrospinning into an inexpensive, implantable bilayered nanofibrous composite (Fig. 1) in a collaborative research work between IIT Guwahati, India and UCL, England.³

We had shown that the biphasic composite endowed a spatially confined biomimetic microenvironment, imitating the osteochondral interface and thereby, supporting the proliferation and maturation of osteogenic and chondrogenic cells.³

On the other hand, non-mulberry silk fibroin protein (endowed with cell-binding motifs: arginine, glycine, and aspartate, i.e., the RGD sequence) based electrospun bioactive nanofibrous dressings, loaded with growth factors and LL-37 antimicrobial peptide, have been reported to assist tissue-remodelling and accelerate wound healing in alloxan-induced diabetic rabbit model. Revelation of speedy granulation tissue development, angiogenesis, re-epithelialization of wounds, gene expression studies and demonstration of corresponding extracellular matrix deposition vouched for the prospects of the nanofibrous dressings for chronic diabetic cutaneous wounds.

A study on nerve tissue regeneration using silk at the nanoscale also grabbed commendable interest. Researchers had successfully documented structural and functional regeneration of severed sciatic nerves in Sprague Dawley rats using gold nanoparticle-doped electrospun silk protein based nerve conduit, pre-seeded with Schwann cells.⁵ The display of stretching and jumping ability of the test animals (with excellent sciatic function index), corroborated by muscular regeneration (tracked via needle electromyogram-based documentation of motor unit potentials) post implantation of the conduits, merit special mention.

These success stories have garnered immense international attention, both in the media and amidst the scientific fraternity. Although, a number of *in vitro* or preclinical studies have attested the prospects of electrospun silk based nanofibrous biomaterials for TERM, however, reports on *in vivo* studies and clinical trials are still scanty. This necessitates inter-institutional collaborative research, involving the participation of material scientists as well as biomedical professionals, apart from conceptualization and fruition of an innovation-ecosystem.

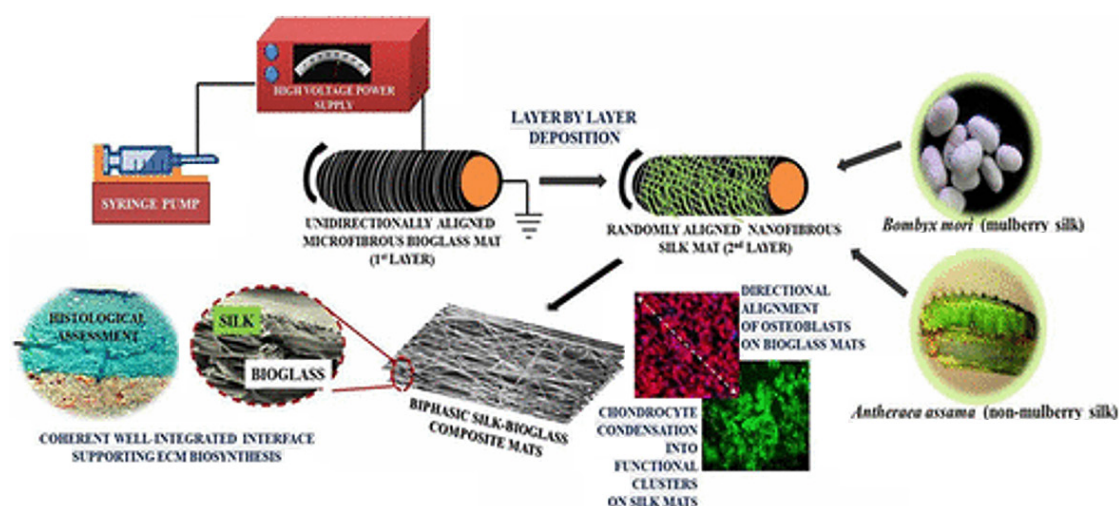


Fig. 1: Schematic representation of the mimicking of the hierarchical complexity at the osteochondral interface using mulberry and non-mulberry silk-bioactive glass composites. Reproduced from Reference [3] under Creative Commons Attribution (CC-BY) License.

Acknowledgement and Funding source

I acknowledge the receipt of funding as a co-investigator for the work reported in reference 3 under DST-UKIERI PROJECT (DST/INT/UK/P-110/2014), '*Electrospun silk bioglass scaffold for interfacial tissue engineering*' (Indian PI: Dr. B.B. Mandal, IIT Guwahati, India and UK PI: Prof. J.C. Knowles, University College London, UK)

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