A Novel Scaffold Platform Technology for Guided Tissue Regeneration and Cell Delivery

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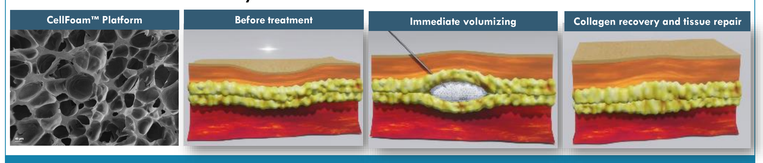
Abstract

Degeneration and loss of tissue function represent significant medical challenges. These issues are gaining more attention today, with a growing number of studies dedicated to regenerative therapies [1-3], such as skin regeneration and wound healing [4-6] .

This research introduces an innovative scaffold technology for guided tissue regeneration and cell delivery. This technology is based on the **CellFoam™** platform, which utilizes enzymatically crosslinked gelatin foam. The platform supports cell growth and survival for tissue repair, stimulates the regeneration of autologous tissue cells, and serves as a vehicle for cell delivery.



Methods and Materials

CellFoam™, an enzymatically crosslinked gelatin foam, was synthesized into foam particles (**FPs**). CellFoam™ was characterized for its mechanical properties using rheological measurements by AG-R2 Rheometer in a frequency sweep test.
The size of the FPs was evaluated using MasterSizer 3000 by the laser diffraction method, and the morphology of the FPs was assessed by Scanning electron microscopy (SEM).

In an in vivo rodent cell delivery study Luciferase Adipose Derived Mesenchymal Stem Cells (luc-ADMSC) were delivered using CellFoam™ by intradermal administration and compared to injection of the Luc-ADMSC without CellFoam™. Following the injection, the cells viability was assessed by the total florescence flux detected using IVIS up to 10 days.
In another preclinical study, CellFoam™ FPs were injected into the subcutaneous rat skin tissue. 30d post-injection, the tissue response was evaluated using histology by H&E and Mason trichome staining.

CellFoam™ FPs Size Distribution

Sample	DX10 (µm)	DX50 (µm)	DX90 (µm)
FPs-1 (99% ethanol)	51.9±0.4	82±1	123±2
FPs-2 (99% ethanol)	50±5	79±1	117±2
FPs-1 (Hydrated)	65±1	137±3	230±5
FPs-2 (Hydrated)	53±1	129±2	225±3

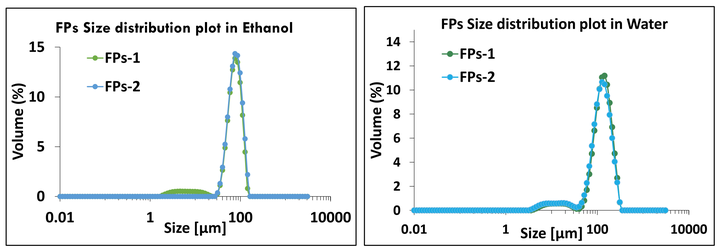


Figure 2. Hydrated and dehydrated FPs diameter values and size distribution plots of 2 formulations of FPs measured using Mastersizer 3000 (n=5) .

CellFoam™ FPs Morphology

Scanning Electron Microscopy (SEM)

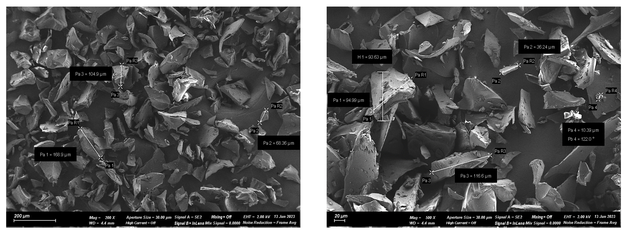


Figure 3. SEM images of CellFoam™ FPs at 200X and 500X magnifications.

The morphology of the FPs was assessed using SEM, showing non-spherical micro-scaled particles with refined edges.

Size distribution of 2 formulations of FPs showed that FPs in 99% ethanol (de-hydrated) resulted in median diameter values of approximately 80 µm for both formulations.
The hydrated FPs resulted in a bigger diameter of FPs for both formulations due to the swelling process of the FPs.

FPs-1 had a higher median diameter after swelling. This outcome may be a result of a lower crosslinking density of the formulation.

CellFoam™ Mechanical Properties

CellFoam™ Dynamic and Static Rheology test

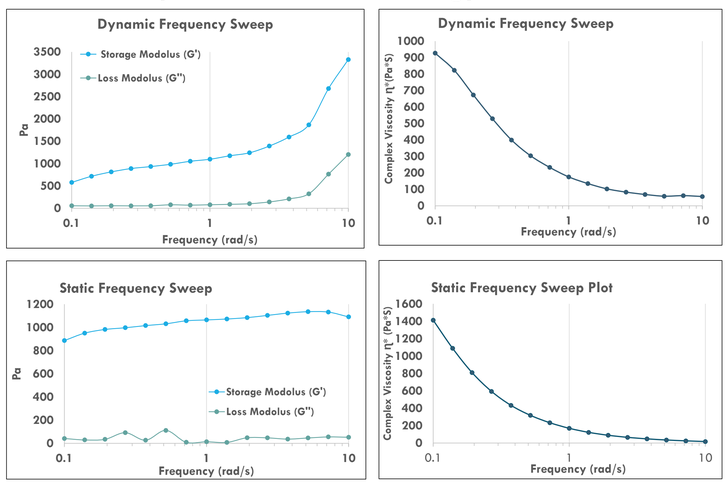


Figure 4. Dynamic (top) and static (bottom) frequency sweep test of CellFoam™. The storage and loss modulus (left) were measured and the complexed viscosity was assessed (right) at frequency of 0.1-10 Hz.

A frequency sweep test of CellFoam™ was conducted in both dynamic and static modes. The dynamic mode illustrates the mechanical properties of CellFoam™ during the crosslinking process over time, whereas the static mode reflects the mechanical properties of CellFoam™ after it has fully crosslinked into a stable structure.

The dynamic crosslinking of CellFoam™ exhibited an increase in both the storage and loss modulus throughout the test. In contrast, the static test demonstrated relatively stable values for the storage and loss modulus.
During the test, the complex viscosity was also recorded. As anticipated, higher viscosity values were obtained in the static mode, which can be attributed to the complete crosslinking of CellFoam.

CellFoam™ FPs For Tissue Regeneration

Optimal scaffold for fibroblast stimulation and skin regrowth

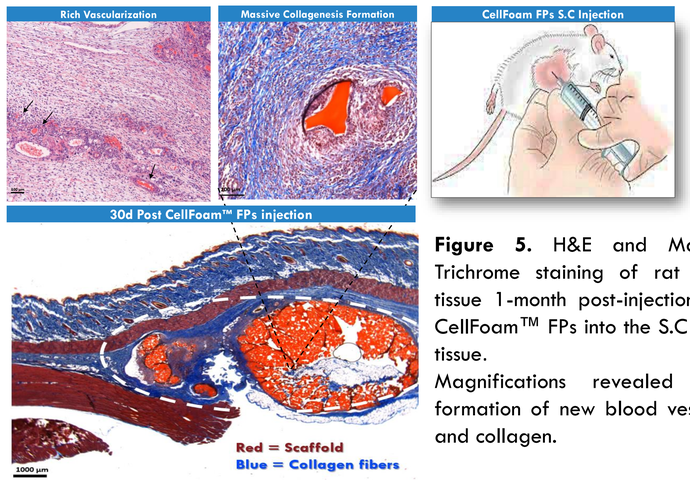


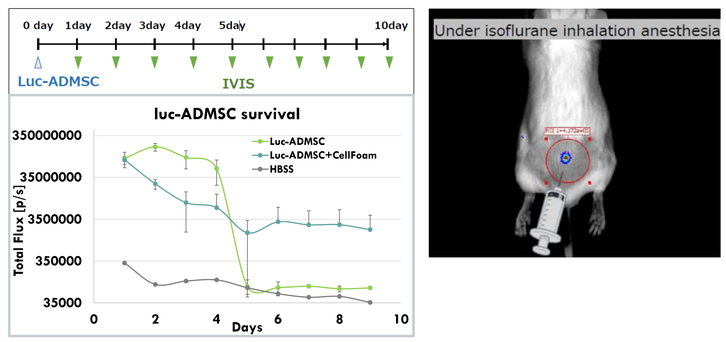
Figure 5. H&E and Mason Trichrome staining of rat skin tissue 1-month post-injection of CellFoam™ FPs into the S.C skin tissue.
Magnifications revealed the formation of new blood vessels and collagen.

FPs were injected into the subcutaneous skin tissue, Histology of 1 month post-injection, resulted in a new self-collagen generation, with supporting vascularization, indicating the ongoing regeneration process of the skin tissue.
Synchronized with the tissue repair process, the absorption process is ongoing with no adversity and with massive collagenesis formation.

CellFoam™ as cell delivery platform

Mouse model IVIS- Intradermal administration of Stem Cells

An in vivo rodent cell delivery study of Luciferase Adipose-Derived Mesenchymal Stem Cells (luc-ADMSC) with CellFoam™.



The measured fluorescence total flux of cells using the IVIS was higher when the Lucefirase Adipose-Derived Mesenchymal Stem Cells (luc-ADMSC) were delivered using Cellfoam™.

Higher viability and prolonged survival of cells delivered with CellFoam™, compared to cells injected with HBSS medium into the dermal tissue, ™ up to 9 days post-injection.

Conclusions

CellFoam™, a crosslinked gelatin foam, has been introduced as an optimal scaffold platform technology with unique mechanical properties.
This all demonstrates superiority in stimulating and supporting skin tissue regeneration and holds potential as a delivery system for cells to enhance cell-based therapies.

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