Design and Development of an Injectable Hydrogel for Cartilage Repair

Arjan Atwal[1,2], Ali Mahnavi[1,2], Nicholas Forsyth[1,3], Martyn Snow[4], Pooya Davoodi* [1,2]

* Corresponding author: p.davoodi@keele.ac.uk

[1]Guy Hilton Research Centre, Keele University, Staffordshire, ST4 7QB, UK
[2]School of Allied Health Professions and Pharmacy, Keele University, Staffordshire, ST5 5BG, UK
[3]Vice Principals' Office, University of Aberdeen, Kings College, Aberdeen, AB24 3FX, UK
[4]Department of Arthroscopy, Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, B31 2AP, UK

Articular cartilage injuries present a significant clinical challenge due to the tissue's limited intrinsic capacity for self-repair. Without effective treatment, such defects frequently progress to osteoarthritis, a debilitating disease that compromises patient mobility, diminishes quality of life, and places a substantial burden on healthcare systems. Existing clinical strategies, including microfracture and autologous chondrocyte implantation (ACI), are often associated with complications such as fibrocartilage formation and donor site morbidity. Injectable hydrogels have emerged as a promising minimally invasive approach for cartilage repair, owing to their ability to conform to irregular defect geometries, ease of administration, and capacity to incorporate bioactive agents. However, traditional bulk hydrogels are limited by tightly crosslinked polymer networks with nanoporosity, which can restrict nutrient transport and hinder cell migration.

To overcome these limitations, we developed a granular injectable hydrogel system composed of microparticles assembled from fragmented bulk hydrogels, thereby introducing interstitial microporosity to enhance cellular interactions and tissue integration. The hydrogel formulation was composed of gelatin methacryloyl, hyaluronic acid methacryloyl, and chemically modified platelet lysate. Bulk formulations were first optimized through live/dead viability assays, DNA and glycosaminoglycan quantification, and immunofluorescent staining for hyaline cartilage-specific markers. Granular hydrogels were fabricated by extruding and fragmenting the optimized bulk gels into microparticles, followed by centrifugation. These constructs were evaluated using the same in vitro assays and further tested in an ex vivo osteochondral defect model.

Our results demonstrated that while the optimized bulk hydrogel supported chondrocyte viability and promoted hyaline-like matrix production, the granular hydrogel substantially improved repair outcomes. The enhanced microporosity facilitated cell infiltration, more extracellular matrix deposition, and better integration with host cartilage. Immunostaining confirmed that the regenerated tissue was rich in type II collagen and aggrecan, resembling native hyaline cartilage.

These findings underscore the potential of granular injectable hydrogels as a robust platform for articular cartilage regeneration.