Design and validation of cellulose acetate scaffolds by phase inversion for bone fracture healing

Álvaro González-Garcinuño[1,2,*], Antonio Tabernero[1,2], Eva Martín del Valle[1,2], Deepak Rania[3], Hanna Isaksson[4].

1) *Department of Chemical Engineering, University of Salamanca, Plaza Los Caídos s/n, 37008 Salamanca, Spain*
2) *Institute for Biomedical Research in Salamanca (IBSAL), Paseo de San Vicente 87, 37007, Salamanca, Spain*
3) *Department of Orthopedics, Lund University, Lund, Sweden*
4) *Lund Biomechanics group, Department of Biomedical Engineering, Lund University, Lund, Sweden*

The development of biomimetic scaffolds capable of supporting and accelerating bone regeneration is a topic that has been reaching importance during the last decades for regenerative medicine.

This work focuses on the engineering of cellulose acetate (CA) scaffolds, reinforced with hydroxyapatite (HA) and functionalized with rutin, to address the mechanical and biological requirements of bone tissue engineering. Using a chemical engineering approach, the scaffolds were fabricated via the phase inversion technique, where the influence of varying solvent systems (including DMSO, acetone, and acetic acid), polymer concentrations, and HA loadings were systematically investigated to control the final morphology. The optimized formulation, consisting of 0.22 g/mL CA in a 50:50 DMSO–acetone mixture with 2.5% HA, resulted in a hierarchical porous architecture. Characterization through SEM and micro-CT revealed a complex internal structure characterized by macrovoids, finger-like longitudinal channels, and a network of interconnecting micropores (3–4 μm), essential for effective nutrient transport, waste removal, and deep cellular infiltration.

The mechanical integrity of the scaffolds was also tested to evaluate the viability to be used for bone healing. The results showed compressive (3.39 ± 1.70 MPa) and flexural (4.20 ± 0.92 MPa) moduli within the lower range of human trabecular bone, providing sufficient structural support during the initial stages of healing.

Long-term stability was assessed through in vitro degradation studies over 70 days, showing controlled mass loss and maintaining structural viability. From a biological perspective, the scaffolds demonstrated excellent biocompatibility; assays with MC3T3 pre-osteoblastic cells showed a significant increase in cell viability over time (first week), with SEM imaging confirming robust attachment and migration through the porous matrix.

Furthermore, the integration of rutin as a bioactive agent provided a controlled release profile—governed by the Peppas–Sahlin model—suggesting a synergistic mechanism of diffusion and polymer relaxation. These results indicate that the combination of CA and HA through phase inversion produces membranes that can be considered as an interesting platform for bone repair. These membranes successfully integrated structural biomimicry with controlled drug delivery to enhance therapeutic outcomes (microbial infection) in orthopedic applications.