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Development of 45S5 Bioactive Glass–Alginate Composite Granules for Bone Grafting

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Introduction

- **Clinical challenge:** critical-sized bone defects caused by trauma, tumours or infection cannot heal spontaneously and require effective bone graft substitutes.
- **Loose granules:** 45S5 bioactive glass (BG) is osteoconductive and forms hydroxyapatite (HAP), but particulate grafts migrate from the defect site, impairing bone repair.
- **Hydrogel strategy:** ionically crosslinked sodium alginate immobilizes BG particles in a 3D biomimetic network and prevents premature washout.

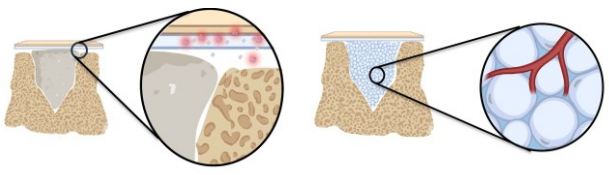


Figure 1. Loose BG particles migrate (left); hydrogel granules stay in the defect (right).

Objective

Develop and characterize 45S5 BG–alginate composite hydrogel granules (0, 10 and 20 wt.% BG) produced by simple extrusion dripping for bone tissue regeneration.

Methodology

- **45S5 BG** (46.1 SiO_2–24.4 Na_2O–26.9 CaO–2.6 P_2O_5, mol%): melt-quenched, ball-milled (12 h) and sieved (< 44 µm, 325 mesh).
- **Suspensions:** 2 wt.% sodium alginate with 0, 10 and 20 wt.% BG.
- **Extrusion dripping:** nozzles of 200–1060 µm, 50 mm drop height, 1 M $CaCl_2$ bath (24 h crosslinking), then 12 h washing in distilled water.
- **Characterization:** XRD, FTIR, particle size, cytotoxicity (L929), rheology, SEM, micro-CT, stability and bioactivity in SBF (21 days), MTS and ALP (MC3T3).

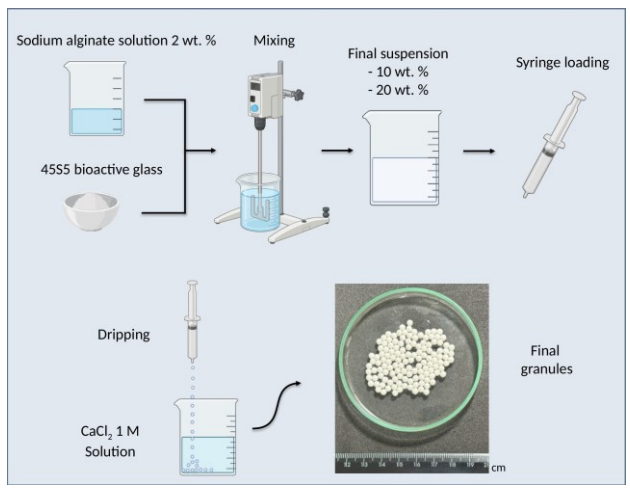


Figure 2. Granule fabrication by extrusion dripping.

Results and Discussion

Precursor BG and suspensions

- Amorphous glass with minor soluble carbonates; D_{50} = 24.3 µm (D_{90} = 747 µm, agglomerates); non-cytotoxic up to 250 µg/mL (L929).
- Suspensions: shear-thinning (n ≈ 0.35, p > 0.05), negligible thixotropy.

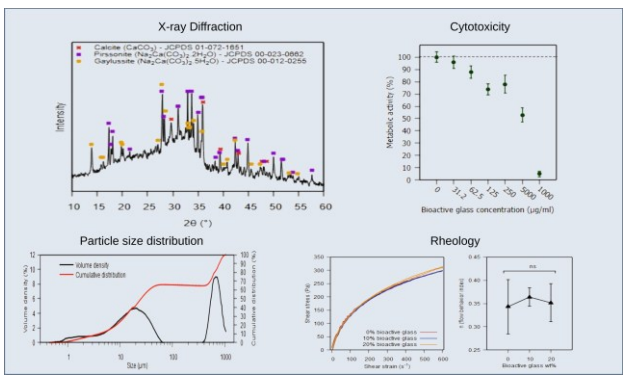


Figure 3. XRD, cytotoxicity, particle size and rheology of the precursors.

Granule size

- Reproducible dripping for nozzles ≥ 410 µm (Ø ≈ 2500–3450 µm); 200–250 µm nozzles clogged by ~200 µm BG agglomerates.

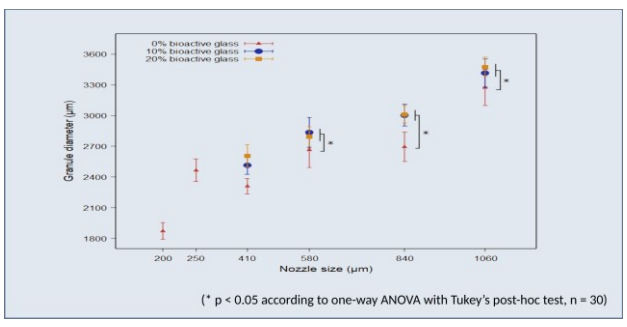


Figure 4. Granule diameter vs. nozzle size.

Internal structure

- 0% BG collapsed on freeze-drying; 10% and 20% BG kept their spherical shape, with homogeneous BG dispersion and open interparticle pores.

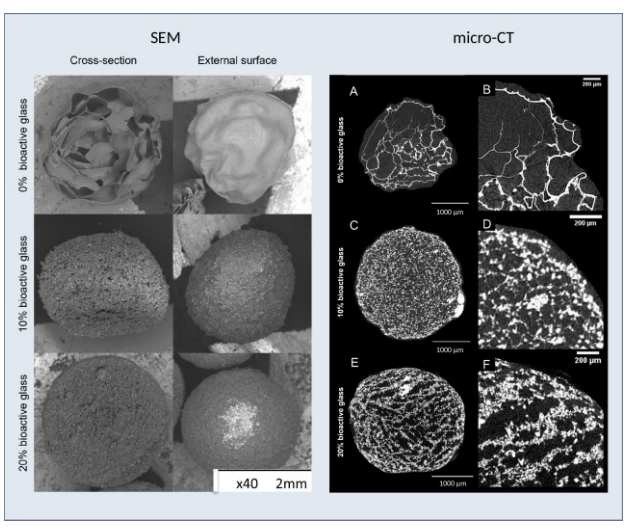


Figure 5. SEM and micro-CT of the granules.

Stability in SBF

- All granules stayed intact for 21 days; 20% BG showed the lowest mass variation and highest dimensional stability (p < 0.05).

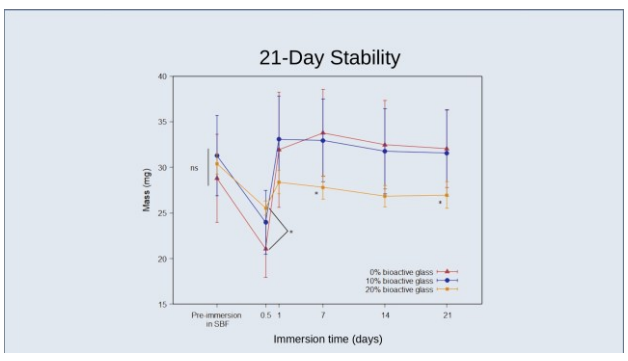


Figure 6. Granule mass during SBF immersion.

Bioactivity (HAP formation)

- XRD (2θ ≈ 26° and 31.8°) and FTIR (PO_4^{3-} bands at 560 and 600 cm^{-1}) confirmed HAP in 20% BG granules after 2–3 weeks in SBF.

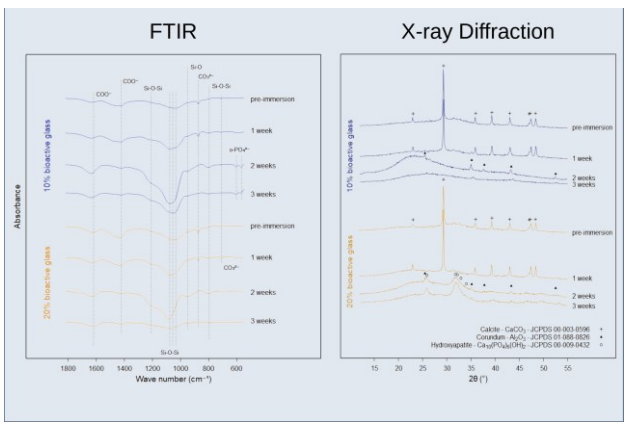


Figure 7. FTIR and XRD of granules after SBF immersion.

Osteogenic potential (MC3T3)

- MTS: higher activity with BG at days 14–28 (20% > 10% > 0%, p < 0.05). ALP: enhanced by BG (p < 0.01), highest at 20%; ALP/MTS peaked at day 14, confirming osteoblastic differentiation.

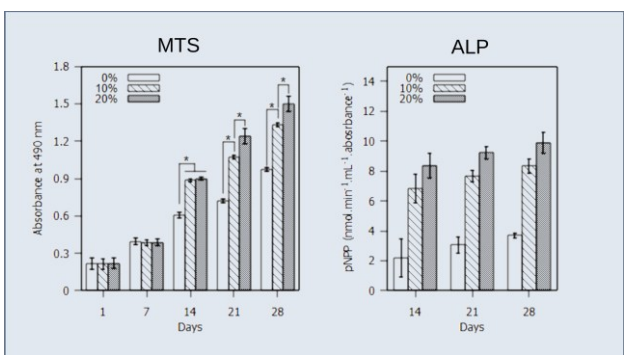


Figure 8. MTS and ALP of MC3T3 cells.

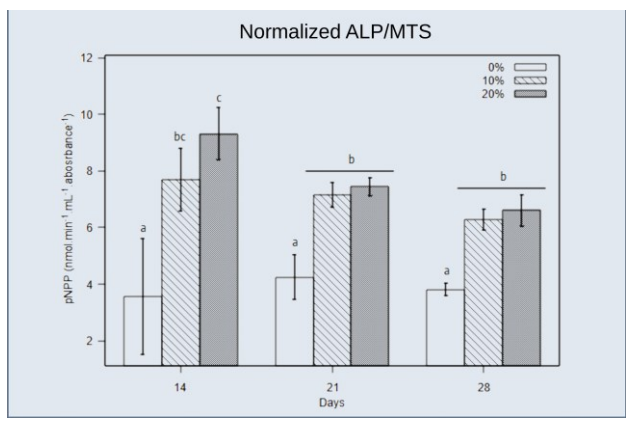


Figure 9. ALP normalized by MTS.

Conclusions

- Simple, low-cost extrusion dripping produces reproducible spherical BG–alginate granules (nozzles ≥ 410 µm).
- BG particles are uniformly dispersed in an open porous structure and stay immobilized in SBF for at least 21 days.
- 20 wt.% BG granules promote HAP precipitation and enhance MC3T3 proliferation and differentiation.
- A promising ready-to-use synthetic bone graft that prevents particle migration.

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