3D-printed hydrogel scaffolds with bioactive glass and antibacterial *propolis*-loaded ZIF-8 for tissue regeneration

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Hydrogels containing bioactive glasses (BGs) are promising composites for tissue regeneration applications, however, bacterial infection remains a problematic challenge that can compromise the healing process. Thus, there is a growing demand for a bioactive and antibacterial hydrogel scaffolds. In this study, alginate dialdehyde-gelatin (ADA-GEL), a hydrogel composite with suitable printability and biocompatibility was selected for 3D printing of BG-containing hydrogels. Spherical SiO_2–CaO BG nanoparticles (~300 nm in diameter) were synthesized to endow bioactivity, and their apatite-forming ability after 7 days of immersion in the simulated body fluid (SBF) was confirmed by Raman spectroscopy and X-ray diffraction.

To introduce antibacterial functionality, *propolis*-loaded ZIF-8 (ZP) was synthesized. ZIF-8, Zn-based metal organic framework, exhibits slight solubility in the aqueous solutions and thus provides sustained release of antibacterial Zn^{2+} ions and *propolis* extract, a natural antibacterial agent. Antibacterial assays demonstrated a significant inhibition of bacterial growth at 250 $\mu g.mL^{-1}$ concentration of ZP particles, reducing the viability of *E. coli* and *S. aureus* bacteria to 32% and 2%, respectively. At this concentration ZP particles maintained biocompatibility as confirmed by indirect cellular viability assays using MG-63 cells.

For scaffolds fabrication, BG and ZP particles (at 0.2 % w/v each) were dispersed in ADA solution (5% w/v), followed by the addition of GEL solution (7.5% w/v) to initiate Schiff's base reaction (in DPBS at 37 °C). The hydrogel scaffolds was obtained through 3D printing and then stabilized by post-crosslinking using $CaCl_2$ solution. Incorporation of both particles reduced hydrogel degradation in HBSS medium after 7 days from 27% to 9%. While BG and ZP particles are expected to provide bioactivity and antibacterial properties, further studies will evaluate. scaffold features in terms of cell viability and antibacterial effect.

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