Title: Development of Bioactive 3D-Printed Scaffolds Functionalized with Okara-Derived Peptides for Tissue Regeneration

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Abstract

3D-printed scaffolds represent an innovative strategy to promote tissue regeneration [1,2]. The present study aims to produce a scaffold functionalized with bioactive peptides obtained by soybean okara, a sustainable raw material obtained from residues of soy and oat-based beverage production. Firstly, we investigated the biological properties of soybean okara-derived hydrolysate (OH) previously obtained through enzymatic hydrolysis [3], evaluating its anti-inflammatory and antioxidant properties on human dermal fibroblasts (BJ-5TA cells). The OH sample demonstrated significant antioxidant activity, modulated inflammation markers and promoted cellular regeneration, indicating a positive role in wound healing processes. Then, OH was employed to functionalize a the polycaprolactone (PCL) thermoplastic matrix through the creation of a printable bio-based filament suitable for 3D printing. This filament functionalized with OH was employed to fabricate a scaffold that was tested on human fibroblasts, confirming its biocompatibility, antioxidant, anti-inflammatory and wound healing properties. Cellular studies revealed a reduction in pro-inflammatory cytokines and beneficial modulation of reactive oxygen species (ROS) and a positive modulation of antioxidant Nuclear Factor Erythroid 2-related factor 2 (Nrf2) and catalase (CAT) key molecular target. This combined approach validated the therapeutic potential of okara-derived peptides both as free agents and embedded within a 3D-printed polymeric device in regenerative medicine.

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2. Im, H.; Kim, S.H.; Kim, S.H.; Jung, Y. Skin Regeneration with a Scaffold of Predefined Shape and Bioactive Peptide Hydrogels. *Tissue Eng Part A* **2018**, *24*, 1518–1530, doi:10.1089/TEN.TEA.2017.0489/ASSET/IMAGES/LARGE/FIGURE10.JPEG.
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