Evaluation of crosslinked gelatin-polyvinylpyrrolidone scaffold for application in drug delivery and tissue engineering

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INTRODUCTION: The objective of this study was to process and evaluate a suitable scaffold matrix system for drug delivery and tissue regeneration. A bioinspired approach was applied. The scaffold based on natural polymer gelatin, blended with polyvinylpyrrolidone, and crosslinked by genipin, was 3D printed by semi-solid extrusion (SSE). This 3D printing technique does not require high temperature or UV curing, so it allows the use of thermo- and UV-sensitive drugs, cells, or other biological components. The influence of genipin, a natural crosslinking agent, and its content on the mechanical properties and the cytotoxicity of obtained scaffolds were investigated.

EXPERIMENTAL: Type A gelatin from porcine skin (~300 g Bloom) (GA), polyvinylpyrrolidone (K30) (PVP), and genipin (G) were purchased from Sigma-Aldrich (Sigma-Aldrich Co., St. Louis, MO, USA); glycerol 85%, used for good printability, was purchased from Zorka Pharma (Zorka Pharma HEMIJA d.o.o., Sabac, Serbia). 3D printing was performed on the Ultimaker 2+ printer (Ultimaker B.V., Utrecht, Netherlands) adapted with Discov3ry paste extruder (Structur3d Printing, Kitchener-Waterloo, ON, Canada). The solutions of gelatin/PVP (1:1) and glycerol were prepared for 3D printing as in previous research [1]. For the crosslinking, G was added to polymer solutions 30 min before printing. Three series of samples were processed: pure polymer blend, with 0.5% w/w G and with 1.0 % w/w G. Characterization of obtained scaffolds was performed by FTIR analysis, SEM analysis, and mechanical testing (tensile test and micro-indentation) using the same equipment as in previous research [1]. Cytotoxicity analysis was performed according to ISO 10993-5 standard.

RESULTS AND DISCUSSION: The FTIR analysis revealed the reaction between ester groups of G and primary amine groups of gelatin. As a consequence of this reaction, the characteristic dark blue colour was achieved [2]. The improvement in mechanical properties (tensile strength, modulus of elasticity, hardness, and reduced modulus of elasticity) of crosslinked scaffolds was observed with the increase in G content. FESEM images have shown good morphology of scaffolds. Qualitative and quantitative cytotoxicity assessment in a direct test indicated the absence of cytotoxicity in tested preparations. The cytotoxicity index based on the metabolic activity of cells in an indirect test showed up to 20% reduction of viability compared to the control, indicating the absence of cytotoxicity.

CONCLUSIONS: The obtained scaffold has appropriate mechanical strength; it is biodegradable and without cytotoxicity. Due to these properties, and by applying SSE 3D printing of this material loaded with drugs or other components, it is possible to obtain a scaffold for delivering drugs, cells, or genetic materials into the surrounding tissue and promote regeneration.

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