Fabrication and Evaluation of 3D Printing Scaffolds Using Biodegradable Aliphatic Polycarbonate

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Statement of purpose: In tissue engineering, 3D printing is an excellent technique for the precise fabrication of 3D scaffolds, and through this, it can be made into a layer-by-layer structure that is almost similar to a human organ. Fused deposition modeling (FDM), one of the 3D printing technologies, has the advantage of inexpensively producing a liquid biodegradable polymer into a solid 3D scaffold with appropriate porosity and precise structure. The ink material used for FDM printing should have good thermal stability, should have biocompatibility and biodegradability for application in the body, and tissue should be formed in the scaffold when transplanted in vivo. Therefore, biodegradable polymers such as polyesters are widely used as ink materials for 3D printing. Recently, aliphatic polycarbonate has attracted attention as a biodegradable polymer with excellent biocompatibility and thermal stability. Because aliphatic polycarbonates form diols and carbon dioxide when biodegraded, they are generally considered safe and non-cytotoxic substances. Therefore, aliphatic polycarbonate is widely used in the field of tissue engineering as a support for drug and cell delivery. In this study, we prepared poly(1,4-butylene carbonate) (PBC), an aliphatic polycarbonate, by condensation polymerization, and evaluated its potential as a biomaterial ink for FDM 3D printing. Therefore, the purpose of this study was (1) to evaluate the printability of PBC, to determine whether a biodegradable 3D printed scaffold can be precisely fabricated as a porous structure, and (2) to ensure that the printed PBC scaffold is sufficiently tissue-generating after implantation in the body. The purpose of this study is to evaluate whether the structure can be maintained until it is ready, and whether the physicochemical properties (biodegradation and compressive modulus) can be appropriately adjusted, and (3) whether the printed PBC scaffold has low immunogenicity and good biocompatibility. Finally, we would like to show the results of the potential application of PBC as a candidate for biomaterial ink for 3D printing application.

Methods: PBC, an aliphatic polycarbonate, was prepared by bulk polycondensation using 1,4-butanediol and dimethyl carbonate. For the characterization of PBC, NMR, GPC, DSC, and TGA were used. The temperature, pressure and speed were controlled using the FDM 3D plotter system, the printability of PBC was evaluated, and a 3D printing PBC scaffold was manufactured. To evaluate cell compatibility, mesenchymal stem cells (hMSCs) were loaded onto a sterile PBC scaffold and then cultured in 24-well plates for 7 days, and the same amount of hMSCs were cultured in a well plate as a control. Thereafter, the adhesion and proliferation of hMSCs were evaluated using WST-1 assay and SEM. For in vivo evaluation, sterile PBC scaffolds were transplanted onto SD rats. After 4, 8, and 16 weeks of transplantation, the PBC scaffolds were removed. NMR, GPC, SEM, and compressive strength were measured to evaluate the biodegradability and strength change of the PBC scaffold according to the implantation time. The tissue and blood vessels created inside the scaffold were observed using a camscope. The biocompatibility and immunogenicity of the 3D printing PBC scaffold were evaluated through histological staining analysis (H&E, ED1).

Results: When the PBC prepared using bulk polycondensation was characterized, the structure of the aliphatic polycarbonate and the appropriate molecular weight and dispersity were confirmed. Through thermal characteristic evaluation, excellent thermal stability of PBC as a biomaterial ink for FDM printing was confirmed. The printability of the PBC was evaluated by controlling the temperature, extrusion pressure, and printing speed, and it was confirmed that it was printed in the same way as the designed scaffold under the conditions of 180 ˚C, 300 kPa, and 15 mm/s. When the in vitro cell viability of the PBC scaffold was evaluated, the viability of hMSC was slightly lower than that of the control (culture plates), but it was confirmed that the cells could adhere to the PBC scaffold and gradually proliferate. Similar to the previous results, the proliferation of hMSCs attached to the PBC scaffold was visually observed in SEM, and it was confirmed that they had appropriate cell compatibility. The in vivo implanted PBC scaffold gradually collapsed as the implantation time increased, and the line thickness decreased, the amount of by-products due to biodegradation increased, and the compressive strength decreased. Through these results, it was possible to confirm the biodegradability of the PBC scaffold. Through histological staining, it was confirmed that blood vessels and tissues were formed inside the scaffold, and when calculated as a rate constant, the scaffold degradation rate and tissue growth rate were similar, confirming that it was excellent as a biodegradable scaffold. In addition, it was confirmed that the inflammatory response in vivo was small, and this result is because the biodegradation by-product of the PBC scaffold is based on carbon dioxide. Therefore, it was proved that it is a scaffold with low autoimmune reaction and excellent biocompatibility.

Conclusions: Using FDM 3D printing, a sophisticated PBC scaffold could be fabricated, and excellent biocompatibility and biodegradability in vivo, along with proper cell adhesion and proliferation of the PBC scaffold, were confirmed, and showed very little immune response. In addition, the applicability of the scaffold as a biodegradable scaffold was confirmed through similar results to the degradation rate and tissue growth rate. As a result, PBC can be applied as a new biomaterial ink for 3D printing as well as has high potential as a customized artificial organ and tissue regeneration material.