

Core–Shell Hydrogel Based on Supercritical CO₂-Decellularized Pancreatic ECM for Functional β -Cell Encapsulation and Immune Protection

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Type 1 Diabetes Mellitus (T1DM) affects over 9 million people worldwide and is characterized by autoimmune destruction of insulin-producing pancreatic β -cells. While exogenous insulin remains the primary treatment, inaccurate dosing often leads to poor glycaemic control [1]. Pancreatic islet transplantation offers a potential curative approach; however, long-term success is hindered by immune rejection and poor graft vascularization [2].

To address these limitations, we developed a permeable, pro-angiogenic, immune-isolating core–shell hydrogel that replicates native pancreatic microenvironment [3]. The construct, a decellularized porcine pancreatic extracellular matrix (dECM) core, repopulated with insulin-producing β -cells, and an alginate shell. Supercritical carbon dioxide (scCO₂) was employed for tissue decellularization due to its capacity to efficiently penetrate the tissue and remove cellular components while preserving ECM biochemical integrity. Decellularization efficacy was confirmed by DNA quantification (Grisp GRS kit), endotoxin analysis (Pierce chromogenic kit), and assessment of dECM components (GAGs and collagen-Blyscan kits).

The resulting dECM was enzymatically digested with pepsin and photocrosslinked using ruthenium/sodium persulfate (Ru/SPS) under visible light to form a stable hydrogel. Rheological analysis was performed to assess mechanical properties. To enhance stability and immune protection, the dECM-Ru core was encapsulated within a CaCl₂-crosslinked alginate shell, generating the optimized dECM-Ru/Alg core–shell construct.

Encapsulated β -cells displayed high viability (Alamar Blue), proliferation (BrdU incorporation), and insulin secretion (immunostaining), confirming functional maintenance within the hydrogel. The construct demonstrated tuneable mechanical properties, nutrient permeability, and potential for vascular integration.

This dECM-Ru/Alg core–shell hydrogel provides a biomimetic, immune-isolating platform supporting β -cell survival and function, offering a promising strategy for cell-based therapies in T1DM.

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