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Thermo-Responsive Injectable Hydrogels for the Delivery of Drugs to Treat Osteoarthritis

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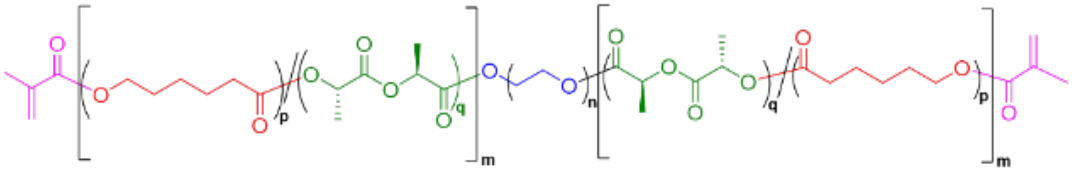
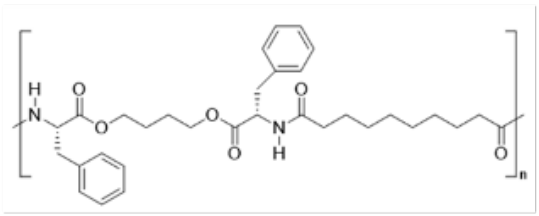
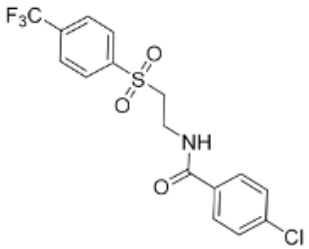
Osteoarthritis (OA) is a chronic condition, whose prevalence is increasing due to the aging population as well as other factors such as increasing rates of obesity. Peroxisome proliferator-activated receptor δ (PPARδ) antagonists such as GSK3787 have shown potential for halting progression of OA in preliminary research. However, they should be delivered locally to avoid systemic side effects and released slowly in the joint to achieve a sustained therapeutic effect over a period of months. In this study, we developed hydrogels based on methacrylate-capped



Hydrogel formulation base: methyl acrylate capped triblock copolymer



PBSe



GSK 3787

Figure 1: Chemical structure of PCLA-PEG-PCLA, PBSe polymer used and the model drug GSK3787.

poly(caprolactone-co-lactide)-poly(ethylene glycol)-poly(caprolactone-co-lactide) (PCLA-PEG-PCLA) triblock copolymers. These polymers undergo thermo-responsive physical gelation, as well as covalent cross-linking by free radical polymerization, upon injection in the joint. We compared the direct loading of GSK3787 into the hydrogel with the loading of GSK3787 into poly(ester amide) particles, followed by loading of these particles into the hydrogel. It can be seen from SEM images that incorporating particles decreased the porosity of the hydrogel structure.

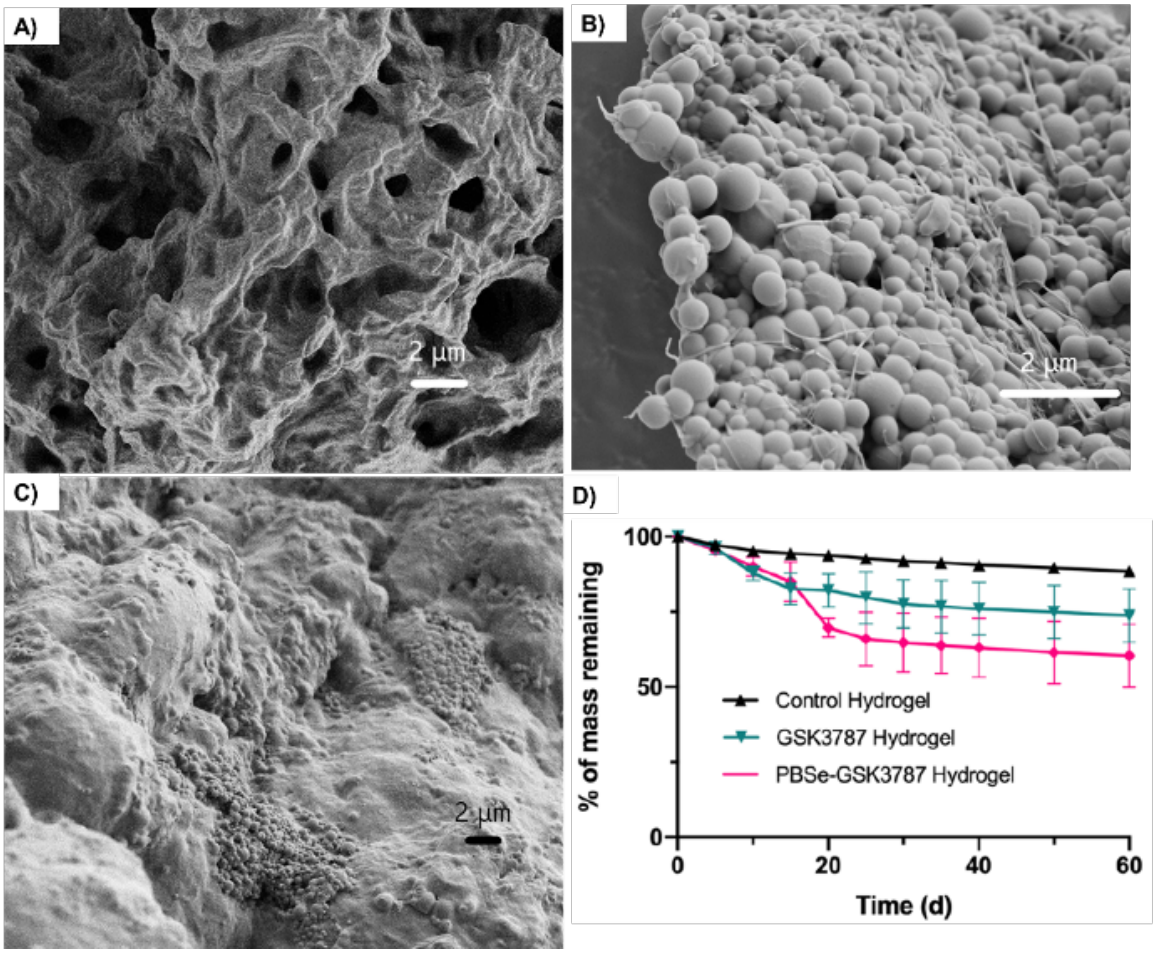


Figure 2: A) Blank hydrogel, B) GSK3787 loaded particles (PBSe-GSK3787), C) particle loaded hydrogel and D) degradation study of hydrogels.

Drug or particle-loading into the hydrogel led to modest decreases of the compressive moduli of the hydrogels, which were on the order of 50 – 100 kPa. About 40% mass loss over 60 days was observed for the hydrogels. In vitro release studies showed that incorporation of the drug into the particles led to slower release than when the drug was incorporated directly into the hydrogels. Overall, these results illustrate the potential of these hydrogels for intra-articular drug delivery for OA treatment.

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