Hyperbranched Polyester Hydrogels with Controlled Drug Release and Cell Adhesion Properties

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Statement of Purpose: Designing advanced biomaterials with controlled release properties and cell adhesion characteristics can be beneficial to precisely control cellular behavior and facilitate the formation of specific functional tissues. Synthetic dendritic polymeric nanoparticles have received a great deal of attention in drug delivery applications due to their unique nanosized molecular structure and physicochemical properties. Dendritic polymeric nanoparticles (such as dendrimers and hyperbranched polymers (HPE)) have a highly branched, globe-like molecular shape with a multitude of functional groups at their periphery. However, the use of these highly branched polymeric systems for tissue engineering applications have not been broadly investigated. Here, we report synthesis and characterization of photocrosslinkable HPE hydrogels with sustained drug release characteristics for cellular therapies.

Methods: HPE (Generation 4) nanoparticles were synthesized according to conventional acid-catalyzed esterification reactions and HPE-A was prepared by the acrylation of HPE using acryloyl chloride. A prepolymer solution containing acrylated HPE was subjected to UV light to obtained covalently crosslinked hydrogel network. The hydrophobic osteogenic inducer dexamethasone acetate (DA) was uniformly distributed and encapsulated into HPE hydrogels to determine the release kinetic over the course of eight days.

Results: These HPE can encapsulate hydrophobic drug molecules within the HPE cavities, due to the presence of hydrophobic inner structure that is otherwise difficult to achieve in conventional hydrogels. The functionalization of HPE with photocrosslinkable acrylate moieties renders the formation of hydrogels with highly porous interconnected structure, and mechanically tough network. The compressive modulus of HPE hydrogels was tunable by changing the crosslinking density. The HPE hydrogels demonstrated the sustained release profile of the entrapped hydrophobic drug (dexamethasone). The feasibility of using these HPE networks for cellular therapies were investigated by evaluating cell adhesion, spreading and proliferation on hydrogel surface. Highly crosslinked and mechanically stiff HPE hydrogels have higher cell adhesion, spreading, proliferation compared to soft and complaint HPE hydrogels. We also investigated possibility of using HPE hydrogels for cell sheet engineering. Overall, we showed that hydrogels made from HPE could be used for biomedical applications that require control cell adhesion and control release of hydrophobic clues.

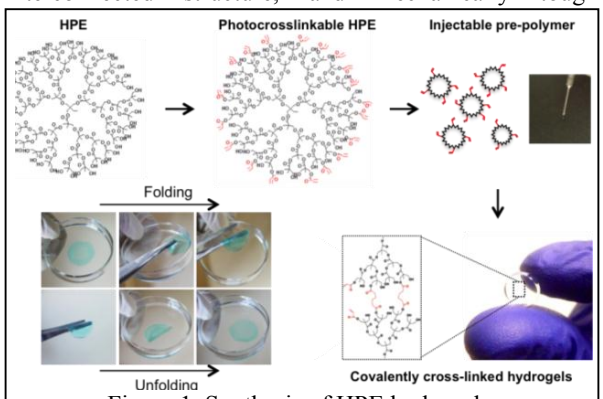

Figure 1. Synthesis of HPE hydrogels.

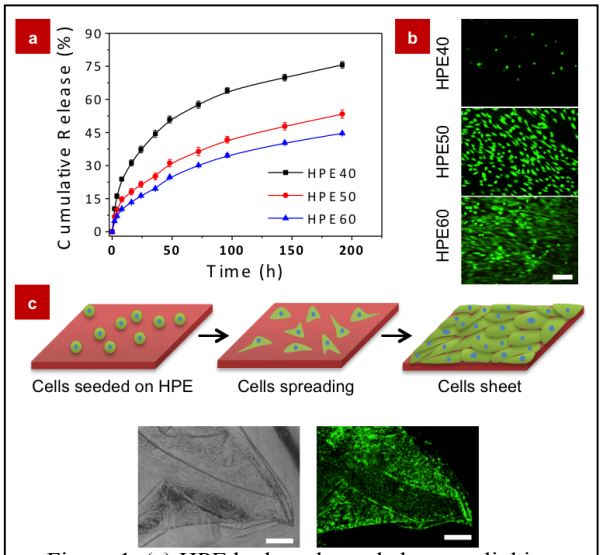

Figure 1. (a) HPE hydrogels made by crosslinking dendrimer nanoparticles show sustain release of entraped DA. (b) & (c) Increase in HPE nanoparticles concentration results in an increase in cells adhesion. (Scale bar 100 μm)

Conclusions: Hyperbranched polyester hydrogels made by crosslinking dendrimer nanoparticles with sustained drug release characteristic. Formation of covalently crosslinked nanoparticles network results in mechanically tough hydrogels with controlled cell adhesion properties. Controlled cell adhesion, spreading, and proliferation was also obtained by tuning HPE formulation thus enabling the development of cell-material platforms that can be applied and tailored to specific functionalities in tissue engineering applications.