Fabrication of Hydrogel Microparticles for Acute Treatment of Penetrating Brain Injuries

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Traumatic brain injuries (TBIs) are the resulting damage from an external force to the head. The advancement of the secondary injury increases the risk of reduced cognitive recovery. Glucocorticoids have been investigated for potential treatment of TBIs and other neuroinflammatory processes as anti-inflammatory therapeutics. Their application has been restricted due a variety of complex side effects, including adrenal suppression, edema, and reduced plasticity of the hippocampus[1]. By utilizing a localized drug delivery system, these systemic concerns could be minimized. In previous studies, semi-interpenetrating networks (semi-IPNs) incorporating dexamethasone-conjugated hyaluronic acid (HA-DXM) as a macromolecular prodrug were developed, and showed a reduction of neuroinflammation and improvement of motor function when applied to the cortical surface following a TBI[2,3]. A subtype of TBIs are penetrating brain injuries (PBIs), which occur when a foreign object strikes the cranial cavity, creating an opened wound with irregular geometry. Therefore, there is a need for an injectable form of hydrogels. The previous studies utilized a photoinitiated crosslinking method that was confirmed to be unscalable in an emulsion setting, therefore this work focused on finding a new hydrogel crosslinking method compatible with microgel fabrication. Utilizing a Michael-type reaction, thiolated gelatin (gelatin-SH) and poly(ethylene glycol) diacrylate (PEGdA) were successfully crosslinked to form hydrogels. Native hyaluronic acid (HA) was incorporated to model HA-based macromolecular prodrugs. The effects of gelatin-SH concentration and HA (700 kDA and 1.5 MDa) on crosslinking time, storage modulus, swelling, and degradation were studied. Utilizing a water-in-oil emulsion, hydrogel microparticles were successfully fabricated. These studies demonstrate that gelatin-SH/PEGdA can create microparticles capable of conforming to the irregular geometry of PBIs.

References:

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