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Pentablock copolymer nano formulation for controlled ocular delivery of protein therapeutics

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Purpose: Recurrent intravitreal injections are obligatory to maintain therapeutic levels at choroid and retina for wet-MAD treatment. Several drug administrations to retina may result in possible impediments such as retinal hemorrhage, retinal detachment, endophthalmitis, and patient nonconformity. The objective of this research is to synthesize and assess pentablock (PB) copolymers for the precise and non-aggressive delivery of macromolecules in the treatment of posterior segment diseases of the eye.

Method: Unique biodegradable pentablock copolymers were synthesized using sequential ring opening polymerization process. Different ratio and molecular weight of each block (polylactide, polyglycolide, polyethylene glycol and polycaprolactone) were utilized for synthesis in order toimprove the release profile of Human Immunoglobulin (IgG) from nanoparticles formulation. Nanoparticles were characterized by particle size, entrapment efficiency, and drug loading. Circular Dichroism spectroscopy and ELISA techniques were applied to assess configuration and binding affinity of the released IgG. After 48 hour exposure of PB copolymers to human conjunctivae epithelial cells (HCEC) and macrophage (RAW 264.7) cell lines,*In vitrocell* viability studies were performed with LDH and MTS assays. *In Vitro* release studies were executed in PBS (0.1M, pH 7.4) at 37°C. Furthermore, biocompatibility of pentablock copolymers was evaluated by exposing polymers to RAW 264.7 for 24 hours and release of inflammatory mediators; IL 1β, IL 6, and TNF α were examined by ELISA method.

Results: Characterization of nanoparticles demonstrated discrete effects as a result of different molecular weights as well as type of end blocks of pentablock copolymers on several pre-formulation parameters including burst release effect, drug entrapment efficiency, and drug loading capacity. Pentablock copolymers demonstrated more than 90% viability in HCEC and RAW 264.7 cell lines. Circular Dichroism spectroscopy and ELISA showed retention of conformation and binding affinity of released IgG. Pentablock copolymers showed negligible release amount of inflammatory mediators from RAW 264.7 cell line.

Conclusion: Pentablock polymer technology can be applied for ocular delivery of therapeutic macromolecules particularly proteins. This mode of intravitreal delivery can reduce side effects related to recurrent intravitreal injections.

Biography

Mary Joseph grew up in Tanzania, Africa. After completing high school, Mary moved to USA to continue with her education, where she graduated from Bowling Green State University on May 2010 with Bachelor of Science in Chemistry. Mary worked with Ben Venue Laboratories Inc. a branch of German pharmaceutical company as pharmaceutical technician. After 1.5 years, Mary was promoted to production specialist position where she watched over technical transfers (TT) and process validation (PV) of chemotherapy injectable drugs from one facility to another among other projects. After working with Ben Venue Laboratories for 2.5 years, Mary decided to join UMKC on August 2013 to pursue Ph.D. in Pharmaceutical Sciences under the supervision of Dr. Ashim K. Mitra.

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