PLGA/Chitosan based Composite Microspheres for Drug Delivery

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Statement of Purpose: Design and synthesis of new biomaterials for drug delivery is a promising, but challenging research area. A number of polymeric biomaterials have been extensively studied in the past few years based upon the properties of biodegradability and biocompatibility. PLGA is a biocompatible, biodegradable and FDA approved polymer. When PLGA is developed for systemic application, its surface is typically protected by other hydrophilic polymers such as poly(ethylene glycol) (PEG), poly(vinyl alcohol) (PVA) to help prolonged circulation and evasion of immune clearance. But PEG and PVA can interfere with the interactions between drug carriers and target cells, and negatively influence the therapeutic outcomes. To overcome this challenge, we proposed a design to use chitosan as an alternative surface coating of PLGA. We hypothesized that our design provides a sustained and controlled drug delivery system, improves delivery efficiency, and reduces toxic side effects. Magnesium gluconate (MgG) was encapsulated with PLGA as a therapeutic drug. The core objective of this project was to test the microspheres with respect to the physical and chemical properties, cell-microsphere interactions, drug loading, and drug delivery.

Methods: MgG encapsulated PLGA/chitosan microspheres were synthesized using modified emulsion solvent evaporation technique. In briefly, 0.5g PLGA was dissolved in 2 ml DCM. 100 mg MgG dissolved in 2 ml water was added to PLGA solution and sonicated 1 minute on ice bath for proper dispersion. 200 mg chitosan was dissolved in 20 ml water (pH 5), which also contained 2 ml 2% PVA. The PLGA solution with MgG was added dropwise to the chitosan solution and stirred 12 hours for chitosan adsorption, DCM evaporation and particle hardening. 2% PVA solution prevented aggression of emulsion droplets. The resultant solution was centrifuged at 3,000 rpm for 30 minutes to separate the particles. The separated particles were washed three times with DI water to purify and remove excessive surfactant. Finally, the particles were lyophilized and preserved in freeze at 4°C for evaluation and analysis. Also, PLGA, PLGA/chitosan and PLGA/MgG microspheres were synthesized using the same solvent evaporation technique for comparison.

Results: The composite microspheres showed smooth surface, spherical shape, and the average size of microspheres is less than 1 µm. This smooth surface, size and spherical shape of microspheres are promising for sustained drug delivery release profile. Quantification of chitosan were analyzed using ninhydrin assay and the amount of chitosan adsorbed on PLGA was found significant for prolonged circulation and enhancing cellular uptake. The magnesium ion release curve provided sustained release profile.

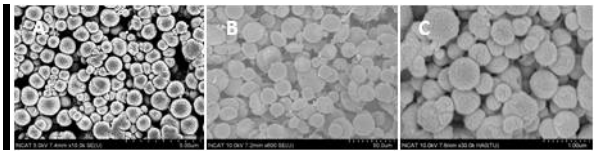

Figure1. SEM images of microspheres. (A) PLGA, (B) PLGA/chitosan, (C) PLGA/chitosan/MgG

Conclusions: Both natural and synthetic biodegradable polymers are ideal for drug delivery systems as compared to non-degradable polymers. PLGA as a hydrophobic polymer is an ideal drug carrier, but its incompatible surface property and high degradation rate sometimes make it unacceptable. The combination of hydrophobic and hydrophilic systems is a promising strategy to overcome this unacceptability. Similar to this concept in this study we proposed a design to synthesize composite microspheres consisting of two biodegradable polymers (PLGA and chitosan) and one biodegradable therapeutic (MgG). This study suggests that MgG encapsulated PLGA/LMWC microspheres possess good potential for efficient and safer drug delivery. Drug loading efficiency, in vitro drug release study, and cell viability test will be performed in future.

References:

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