Sustained Release Anti-VEGF by Microparticles for Treating Wet Age-Related Macular Degeneration

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Statement of Propose：

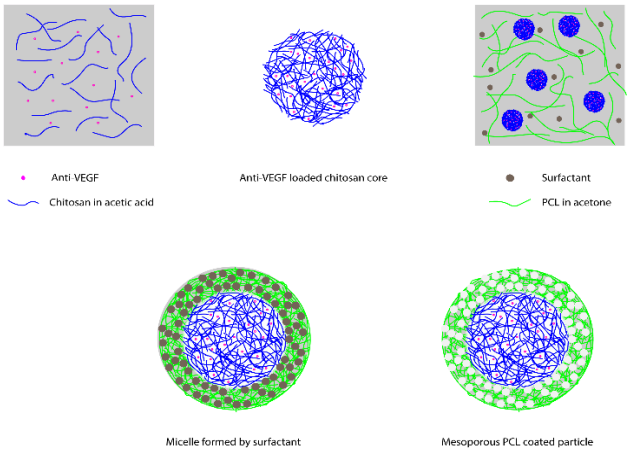
Age-related macular degeneration (AMD) is the fourth most common causes of blindness[1]. Overexpression of vascular endothelium growth factor (VEGF) that stimulates neovascularization in the choroid. These abnormal blood vessels break through the Bruch's membrane towards macular and lead to irreversible damage to the photoreceptors and retina[2,3]. The current treatment requires monthly intravitreal injection of anti-VEGF such as bevacizumab or ranibizumab blocking VEGF from initiating the angiogenesis. However, frequent injection often leads to infection, elevated intraocular pressure and rhegmatogenous retinal detachment[4]. Furthermore, patient compliance is low. To this end, we have developed a biodegradable drug delivery system which can control the drug release several months to potentially alleviate the patient's incompliance and reduce the side effects associated with monthly injection.

Methods:

Core-shell structured microparticles were prepared via direct emulsion. Chitosan core was synthesized following the reported method[5] with minor changes. The Shirasu porous glass (SPG) membrane was used to obtain a uniform particle size via water-in-oil emulsion. Polycaprolactone (PCL) dissolved in acetone was deposited on the chitosan cores to form a nanoporous PCL shell with the assistance of non-ionic surfactant CO-520. Then the microparticles were collected by centrifugation and lyophilization. Scanning electronic microscopy (SEM) and dynamic light scattering (DLS) were used to characterize the size and surface energy of the chitosan core and PCL coated particles. Drug releasing profiles chitosan microparticles and PCL coated microparticles incubated in phosphate buffered saline were determined by UV-Vis spectrophotometry at 270 nm. To assess *in vitro* cytotoxicity of chitosan microparticles with and without the PCL coatings, human retinal pigmented epithelial (ARPE-19) cells were incubated with the particles.

Results:

The positively charged chitosan core can ionically interact with the negatively charged anti-VEGF[6] to reduce the drug diffusion. The shell was designed to resist erosion to prevent the burst release of drug. Moreover, the nanoporous structure of the shell had crucial effects on the achievement of slow drug release, which provided more stable drug concentration and the therapeutic efficacy in a longer period. Both chitosan and PCL are FDA approved materials. The particle size of 15 μm could be injected into porcine vitreous humor through the sclera via a 30-gauge needle.



Scheme 1. Synthesis approach of core-shell structured microparticle

Conclusion:

Addressing critical challenges for treating wet AMD, we developed a novel core-shell microparticle to control the anti-VEGF release several months and preliminarily investigated its biocompatibility and release *in vitro*.

References:

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