Synthesis and Characterization of Diblock, pH-Responsive Drug Delivery mPEG-Poly(β-amino ester) Polymeric Micelles

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Introduction

Biocompatible micellar nanoparticles provide a platform to increase drug solubility, increasing cellular uptake, and leading to increased control of virus infection. We are interested in the utility of pH-responsive nanoparticles possessing the ability to deliver drug cargo intracellularly, in a pH-dependent manner, coupled with known and novel antiviral compounds. The presented research describes the assembly and characterization of mPEG-PAE (methoxy-polyethylene glycol PEG-Poly(β-amino ester) micelles. These micelles have been designed and synthesized to possess the ability to disassemble at pH 6.0, the pH of the trans-Golgi this will result in the release of encapsulated drug cargo, and presumably lead to failure of virus proteins to add complex sugars to high mannose chains and subsequent decrease in virus particle assembly and suppression of virus replication. Described in this poster is the synthesis of mPEG-PAE polymers and experiments leading to micellar formation of these polymers and biophysical characterization following encapsulation of with ribavirin, a broad-spectrum antiviral. Results show the proper formation and characterization of ribavirin encapsulated mPEG-PAE micellar nanoparticles and give promise to their use in suppression of virus infection.

Diblock Synthesis

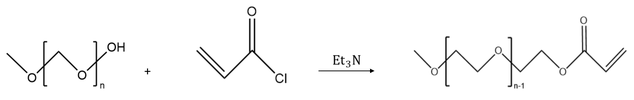

Figure 1. Synthesis of acrylated mPEG

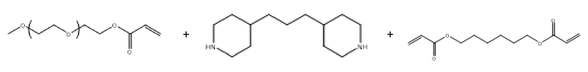

Figure 2. Synthesis of mPEG-PAE from mPEG-A, TDP, and HDD.

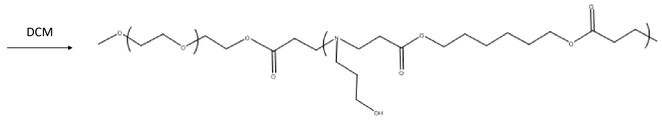

Figure 3. Complete structure of MPEG-Poly(β-amino ester).

Drug-Loaded Micelle Synthesis

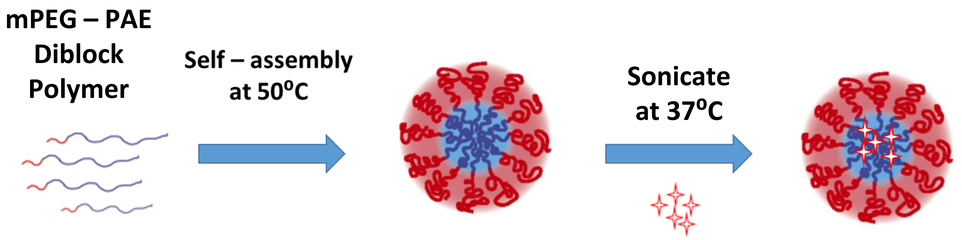

Figure 4. Reaction for the synthesis of ribavirin-loaded MPEG-PAE micelles.

Characterization

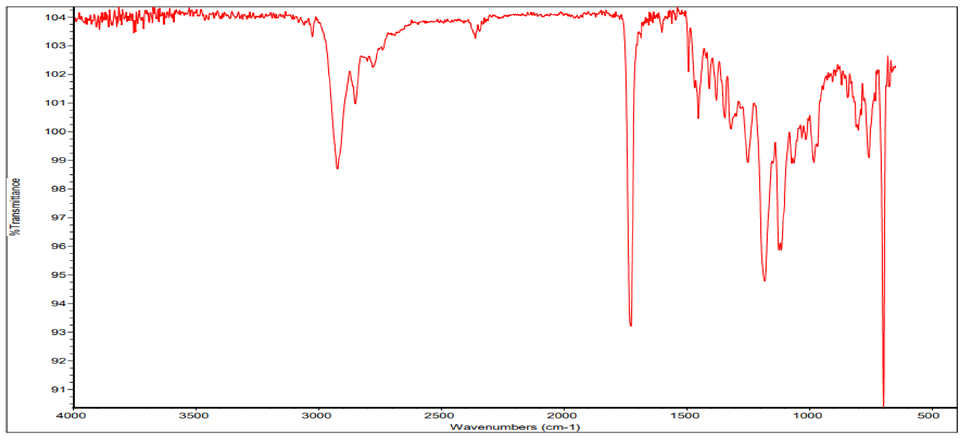

Figure 5. FT-IR analysis of experimental mPEG-PAE Diblock polymer. .

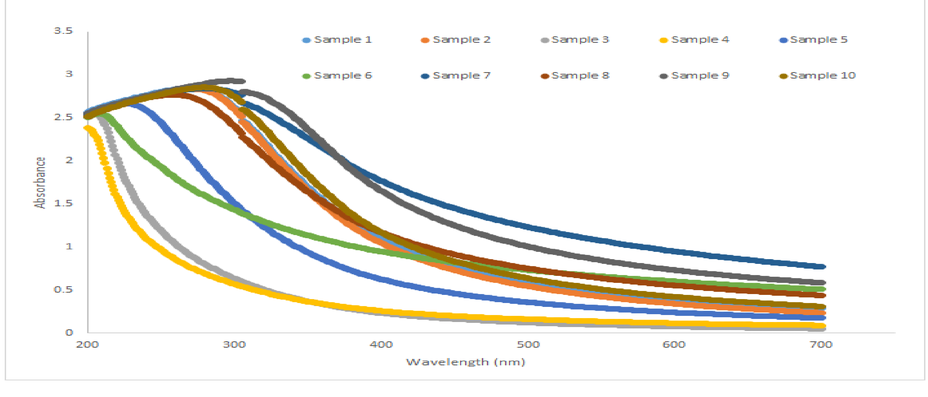

Figure 6. UV-Vis Spectroscopy analysis of ten runs for mPEG-PAE blank micelles

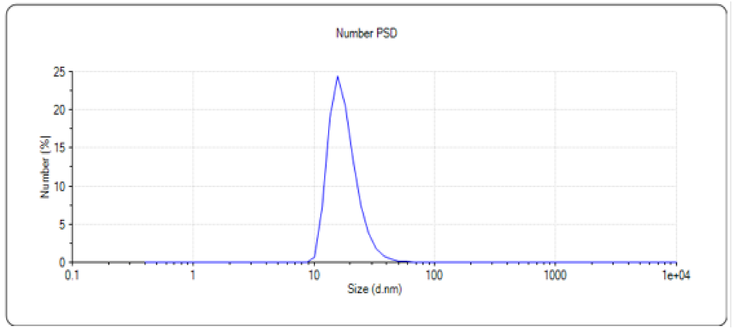

Figure 7. Number PSD of mPEG-PAE Blank Micelles (Average Diameter)

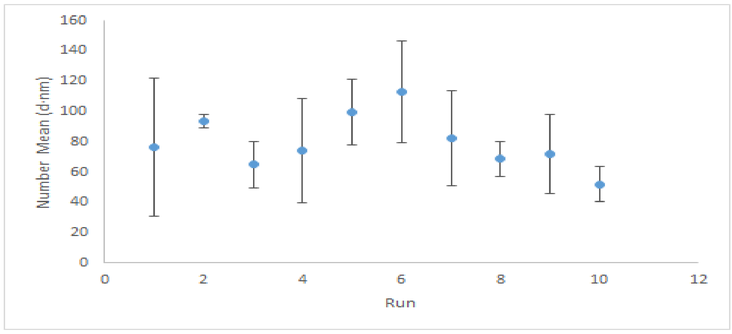

Figure 8. Number PSD (Average diameters) for 10 experiments of mPEG-PAE Micelles

Conclusion/Future Work

The research presented represents a new method to deliver antiviral compounds intracellularly: with micelles constructed with mPEG-PAE di-block polymers. Following additional characterization, mPEG-PAE micelles will be assessed for efficacy in intracellular drug delivery of antivirals and suppression of mosquito-borne viruses, such as dengue and Zika.

Acknowledgements

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