Synthesis and Development of Polymer Microparticles for Nutrient and Vaccine Delivery

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Polymer-based microparticle (MP) platforms have emerged as powerful tools for addressing critical global health challenges by affording precise control over therapeutic protection and release kinetics. Tailored MP systems can be created through two complementary pathways: the development of novel polymer compositions that provide tunable properties for cargo stabilization and controlled release, and innovative particle-design strategies that optimize encapsulation, degradation, and release kinetics. This thesis presents the design, synthesis, and application of three advanced polymer-based MP platforms that leverage these approaches to enhance nutrient stability and enable single-injection, self-boosting vaccine delivery.

In the first study, poly(β-amino ester) (PAE) MPs were developed as a solution for the stabilization and oral delivery of micronutrients. These degradable MPs effectively encapsulated thermally and chemically sensitive nutrients, such as vitamin A, ensuring protection under harsh cooking and storage conditions. By optimizing the tunable properties of PAE and gaining mechanistic insights through molecular dynamic simulations, this platform achieved improved nutrient stability and rapid gastrointestinal release, offering a scalable and environmentally friendly approach to combat micronutrient deficiencies.

In a separate effort, a polyanhydride-based core-shell MP platform was designed for single-injection, self-boosting vaccines. To mimic traditional multi-dose vaccination schedules, controlled degradation of the polyanhydride material enabled pulsatile antigen release while maintaining stability for acid-sensitive antigens, such as diphtheria toxoid. Fabricated using the StampEd Assembly of polymer Layers technique and optimized through machine learning models, this system demonstrated robust immune responses *in vivo*, presenting a promising strategy for addressing under-immunization in regions with limited healthcare access.

Building on the need for improved vaccine technologies, a controlled release injectable system (CRIS) was developed for the stabilization and delivery of mRNA therapeutics. This platform integrated antioxidant-stabilized mRNA-lipid nanoparticles within a PLGA core-shell structure, enabling both long-term stabilization and controlled release. Immunization studies confirmed the CRIS system's capacity to deliver single-injection, self-boosting mRNA vaccines, while reducing dependence on cold-chain storage and multi-dose administration.

Collectively, this thesis advances polymer-based MP delivery systems by addressing challenges in stabilization and controlled release of nutrients and vaccines. The findings establish a strong foundation for next-generation nutrient and vaccine delivery platforms, offering innovative solutions with the potential to improve health equity and outcomes worldwide.

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