Computational and Experimental Design of MIP Nanoparticles: A Novel Theranostic Solution to Detect and Neutralize Endotoxins

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Endotoxins, or lipopolysaccharides (LPS), are harmful biomolecules found on the surface of gram-negative bacteria. They are characterized by Lipid A, a toxic component that interacts with LBP (LPS-binding protein) to initiate septic cascade, causing possibly fatal fevers or disease. Past efforts to detect and extract LPS have been hampered by the presence of certain proteins, high synthesis costs, or incompatibility with body fluids. In this research, the lock-and-key mechanism of molecularly imprinted polymers was utilized to design selective fluorophore-conjugated nanoparticles that are capable of simultaneous LPS detection (quenching) and neutralization (competitive inhibition). A novel polymer matrix was created by utilizing GROMACS (molecular dynamics) and Autodock (molecular docking) software to optimize LPS affinity and simulate several template-monomer interactions. Analysis of system stability, binding energy, and non-bonding interactions indicated that itaconic acid copolymerizes with EGDMA to form the most effective molecular imprints for LPS. These computational results were tested experimentally through the synthesis of MIP nanoparticles by precipitation polymerization, Soxhlet template extraction, and morphological, elemental, and fluorescence characterization. FTIR results showed the formation of LPS-specific bonds between the template and functional monomers, and spectroscopy indicated a correlation between LPS concentration and fluorophore intensity. Based on procedural comparisons to the standard LAL assay, these polymers able to detect and bind to endotoxins for a fraction of the cost and can potentially be applied both in vivo and in pharmaceutical solutions to decrease the effects of gram-negative sepsis and LPS contamination worldwide.

Awards Won:

Third Award of $1,000