A Novel Point-of-Care Theranostic for Gram-Negative Sepsis: Synthesis and Application of Polymer Nanoparticles for Rapid Endotoxin Capture

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Lipopolysaccharides (LPS) are harmful biomolecules found on the surface of gram-negative bacteria and are responsible for over 50% of cases of sepsis, the leading cause of death in US hospitals. Our previous research dealt with the computational design of selective fluorophore-conjugated nanoparticles capable of binding LPS molecules. In this study, these results were translated into experimental synthesis and application of molecularly imprinted polymers by precipitation polymerization. Control polymers were synthesized without LPS present, as well as 6 batches of nanoparticles with varying cross-linker to monomer to initiator ratios. FT-IR results showed itaconic acid polymers forming more pronounced alkenyl and H-bond interactions when compared to HPMA polymers, indicating higher LPS-specificity. SPR confirmed sensitivity on the order of 2.2 pM under blood plasma-like conditions, and fluorescence spectroscopy established a correlation between LPS concentration and fluorophore intensity ($p<0.05$). SEM imaging was done to confirm the morphology of nanoparticles. Size distribution was confirmed by an Izon Q-nano instrument, revealing an average diameter of 94 nm, optimizing at a 3:2 cross-linker to monomer ratio. Based on comparisons to the standard LAL assay, all characterization confirms tremendous viability of NPs as low-cost solution for point-of-care diagnostic testing within ICUs for gram-negative sepsis in the form of a fluorescence-based assay, as well as pharmaceutical solution decontamination. In vitro biocompatibility testing is underway to confirm potential use as an intravenous or dialysis treatment for infected patients.

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