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Abstract

Polyelectrolyte Complexed Nanoparticles Loaded with Eugenol-Containing Essential Oils against *Staphylococcus aureus* and *Pseudomonas aeruginosa* †

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Abstract: Infected diabetic foot ulcers (DFUs) are a frequent and costly complication of diabetes, with limb amputation being highly prevalent worldwide. Even if treated, recurrence is frequent, with pathogen clearance and degenerated tissue recovery being increasingly more difficult each time. Persistent pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the main microbial inhabitants of infected DFUs, often gaining antimicrobial-resistance to treatment [1]. Nanoparticle (NP)-mediated therapies may overcome this problem, as they are able to carry and protect loads from biodegradation, be internalized by the cell, and release the load(s) in a controlled manner [2, 3]. As payloads, plant-derived essential oils (EOs) exert quick and strong bactericidal action. Eugenol, in particular, is an amphipathic hydroxyphenyl propene, highly bactericidal towards *S. aureus* and *P. aeruginosa* [1]. This work proposes EO-encapsulation into polyelectrolyte complexed (PEC) NPs fabricated with natural, renewable, and bactericidal polymers [quaternized cellulose (QC) and carboxymethyl lignin (CML)] [4]. Glycidyltrimethylammonium chloride was added to microcrystalline cellulose to obtain QC. CML was obtained through reaction with monochloroacetic acid to softwood kraft lignin. The presence of a peak at 1482 cm^{-1} in Fourier-transform infrared spectroscopy (FTIR) spectra showcased vibrations of methyl groups of cationic quaternary amines grafted into the cellulose chain, while two absorption bands at 1645 cm^{-1} and 1417 cm^{-1} emphasized a successful introduction of negatively charged carboxyl groups into lignin's skeletal bonds. Minimum inhibitory concentrations (MIC) of cinnamon leaf oil (CLO) and clove oil (CO) EOs, rich in eugenol, were previously established using the broth microdilution method against reference strains of *S. aureus* and *P. aeruginosa*. The MIC values were 0.82 mg/mL and 0.83 mg/mL for CLO and 39.3 mg/mL and 52.8 mg/mL for CO, respectively [1]. At optimized pH, ionic strength and polyion concentration, EOs were added at MIC to the anionic polyion (CML) before complexation, then added to the polycation (QC) and ultrasonicated to form EO-loaded QC/CML PEC NPs. The loading efficiency of dialysis-purified NP dispersions was monitored by UV-Visible spectroscopy, being 83% for QC/CML/CLO NPs and 12% for QC/CML/CO NPs. Bright-field and fluorescence microscopy (using Nile Red) confirmed the formation of PEC NPs encapsulated with EOs. Antimicrobial activity of loaded PEC NPs was confirmed through the determination of agar diffusion and time-kill kinetics assays, similarly to Antunes et al. [1]. Preliminary data pointed to the potential of EO-loaded PECs to work as a therapeutic alternative to conventional strategies, or treatment adjuvant, to fight some of the pathogens colonizing DFUs.

Keywords: Nanoparticles; Polyelectrolyte complexes; Antibacterial; Plant extracts; Diabetic foot ulcers

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