# New Fluorinated Polyphosphazene Biomaterials for Controlling Microbial Infections

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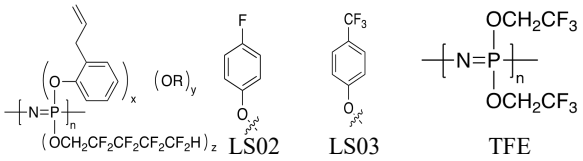
**Statement of Purpose:** Development of new biocompatible biomaterials with improved resistance to microbial infections is important for successfully implementing blood contacting medical devices. Polyphosphazenes (PPs) are hybrid inorganic – organic high polymers and have great potential uses in medical devices, and have different properties by changing side groups on the P-N backbones. Previously we developed fluorinated crosslinkable poly[bis(octafluoropentoxy) phosphazenes] (X-OFPs) that reduced bacterial adhesion/biofilm formation and blood coagulation responses.[1,2] In this study we incorporated fluorophenoxy and trifluoroethoxy side groups to X-OFP based polymers to further improve the properties of X-OFPs on resistance to bacterial adhesion and biofilm formations for the purpose of application in medical device coatings.




Scheme 1. Chemical structures of general fluorinated PPs and substituents of LS02 and LS03, and TFE.

**Methods:** New PPs were synthesized with incorporation of side groups (R= 4-fluorophenoxy, termed LS02, and R= 4-(trifluoromethyl) phenoxy, LS03) based on the X-OFP platform (Scheme 1). OFP and X-OFPs with different crosslinking densities (X-OFP$_{3.3}$, X-OFP$_{8.1}$, and X-OFP$_{13.6}$) and poly[bis(trifluoroethoxy) phosphazene] (TFE) were also synthesized for comparison. All polymers were dissolved in Methyl Ethyl Ketone for casting on 316 stainless steel (316SS) surfaces to fabricate coatings, and crosslinked under UV for 2h. Bacterial adhesion experiments were carried out in petri dishes with the bacteria *S. epidermidis* and *S. aureus* for 1h at 37°C under shaking. Biofilm formation experiments with the same strains were carried out in a CDC biofilm reactor at 37°C over the course of 10 or 14 days, respectively. All samples were fixed in 2.5% glutaraldehyde, stained with appropriate fluorescence labels and examined using fluorescent microscopy. 316SS and polyurethane (PU 2080A) were taken as controls.

**Results:**

Characterization of fluorinated PP materials. Fluorinated PP material surfaces are normally hydrophobic due to the fluorocarbon chemistry, with water contact angles in the range of 94-111°. The incorporation of crosslinking allylphenoxy groups and fluorophenoxy side groups had a minimal effect on surface wettability after UV crosslinking. After crosslinking, there is no significant change in surface chemistry detected from XPS and FTIR data. The surface stiffness of fluorinated PP coatings on 316SS disc surfaces were measured using AFM nano-indentation technique and presented as surface modulus. The results show that modulus of TFE is only about half of OFP surface, and much smaller than other X-OFPs and new polymers LS02 and LS03. Further, we found the incorporation of fluorophenoxy groups increased the surface mechanical strength compared to X- OFP$_{8.1}$ and X-OFP$_{13.6}$.

Bacterial adhesion and biofilm formations. Bacterial adhesion was found significantly reduced on all polyphosphazene polymers compared to 316SS and PU2080A controls. LS02 and LS03 polymers containing fluorophenoxy side groups exhibited significantly lower bacterial adhesion compared to other X-OFP and TFE polymers for both *S. epidermidis* and *S. aureus* strains (Fig. 1). All polyphosphazene coatings also showed significant inhibition of biofilm formation compared to 316SS and polyurethane (Fig. 2). LS02 and LS03 had lower percentages of biofilm coverages compared to other PP polymers, suggesting fluorophenoxy side groups are effective in reducing bacterial adhesion and biofilm formations.

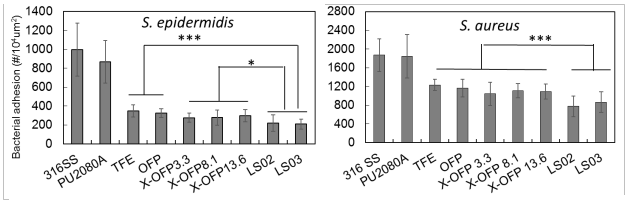



Figure 1. Bacterial adhesion on biomaterials surfaces.

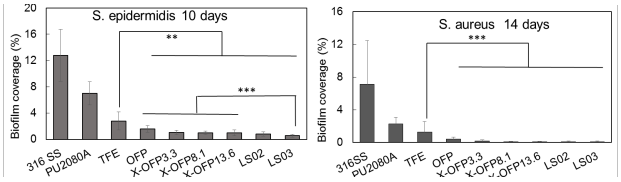



Figure 2. Biofilm coverages on biomaterial surfaces with *S. epidermidis* for 10 days and *S. aureus* for 14 days.

**Conclusions:** Fluorinated polyphosphazenes with fluorophenoxy side groups decrease bacterial adhesion and biofilm formation. Fluorophenoxy side groups appear good candidates for incorporation into X-OFP structures for generating improved resistance to microbial infection.

**References:**

1. Xu, et al. J Biomed Mater Res. 2020;108B:3250–3260.
2. Xu, et al. Acta Biomater. 2018; 67:87-98

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