DEVELOPMENT OF A HIGH-THROUGHPUT FLOW BIOFILM REACTOR SYSTEM FOR THE STUDY OF BACTERIAL INTERFERENCE AGAINST UROPATHOGENIC COLONIZATION ON SILICONE URINARY CATHETERS

UNIVERSITY of HOUSTON

Christopher Thang, Mengfan Wang, Thomas Cashin, Chengzhi Cai

Department of Chemistry, University of Houston, Houston, TX, United States

1. INTRODUCTION

The prevention of pathogenic colonization on medical devices remains a significant challenge, especially in high-nutrient environments that accelerate the production of biomass leading to biofouling of these devices. Catheter-associated urinary tract infections (CAUTIs), contracted from indwelling catheters, are the most common type of nosocomial infection. Our prior research has shown that benign *fim+ E. coli* 83972 biofilms on silicone substrates coated with a monolayer of PAMAM-mannoside derivatives greatly reduced uropathogenic colonization under static conditions. In this project, a 34-channel catheter array system was designed to investigate our bacterial interference strategy under *in vivo* flow conditions.

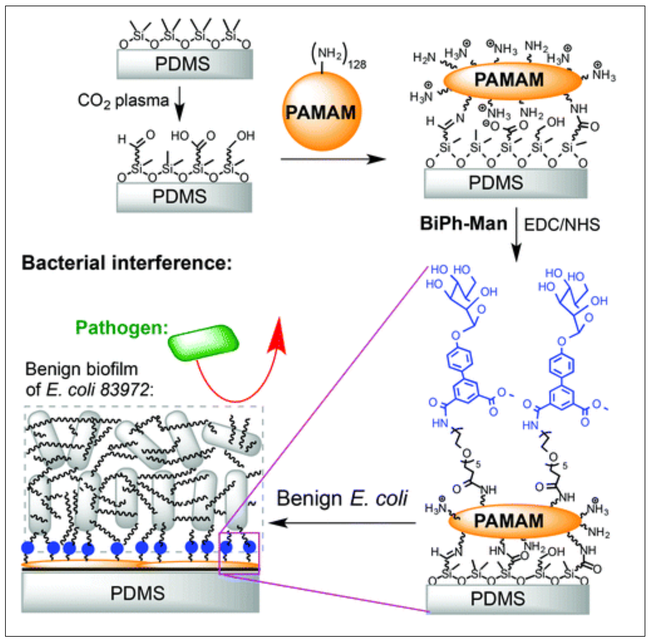


Fig. 1.

Benign *fim+ E. coli 83972* biofilms formed on surfaces with biphenylmannoside ligands (BiPh-Man) connected to a PAMAM dendrimer platform on a PDMS silicone interface significantly reduce uropathogenic colonization in static conditions.

- Zhu ZJ, Wang J, Lopez AI, Yu F, Huang YK, Kumar A, Li S, Zhang LJ, Cai CZ. Surface presenting alpha-phenyl mannoside derivatives enable formation of stable, high coverage, non-pathogenic *Escherichia coli* biofilms against pathogen colonization. Biomat Sci, 2015, 3, 842-851.
- Zhu ZL, Chen YX, Li SH, Lin H, Qin GT, Cai CZ. Ortho-substituted phenyl mannoside derivatives promoted early-stage adhesion and biofilm formation of E. coli 83972. ACS Appl Mater Interfaces, 2020, in press.

2. MODEL DEVELOPMENT

The catheter model system consists of three main parts: an ultraviolet (UV) disinfection subsystem; a 100L artificial urine preparation, storage, and flow guiding subsystem; and a 34-channel catheter array. The catheter array also consists of three parts: an inlet chamber with a germicidal UV lamp; a channel array consisting of 34 modified (see Introduction) silicone Foley catheter tubes, and an exhaust chamber accommodating 2 UV lamps. All three UV Lamps are held within quartz sleeves. A constant flow of artificial urine (AU) mixed from four concentrated solutions and DI water enters the inlet chamber, allowing AU to flow through silicone catheters coated with non-pathogenic *fim+ E. coli* 83972 biofilms. Channels will be inoculated with different uropathogens and mixed concentrations of uropathogens. AU samples from the end of each catheter channel will be collected for analysis. A webcam is used to monitor the droplet rate of each silicone catheter to ensure no catheters become clogged. In addition to UV exposure, liquid waste is treated with bleach disinfectant before being pumped into a sink outlet for disposal.

Figure 3 Legend

- **(a)** DI H_2O Outlet
- **(b)** Water Sediment Filter
- **(c)** UV Sterilizing Devices
- **(d)** 100 L Tank: Artificial Urine
- **(e)** Biosafety Hood
- **(f)** Catheter Model
- **(g)** 76 L Waste Storage, Treatment, and Disposal

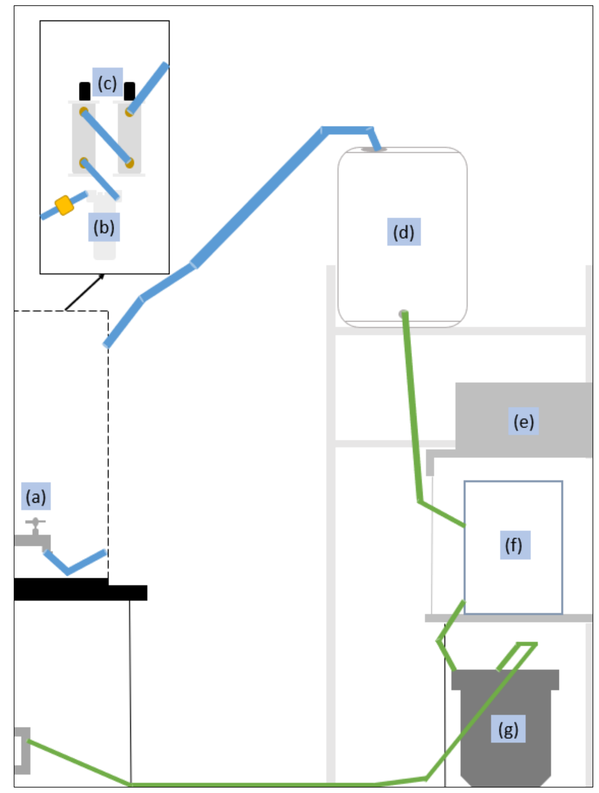


Fig. 3. Overview of Experimental Setup

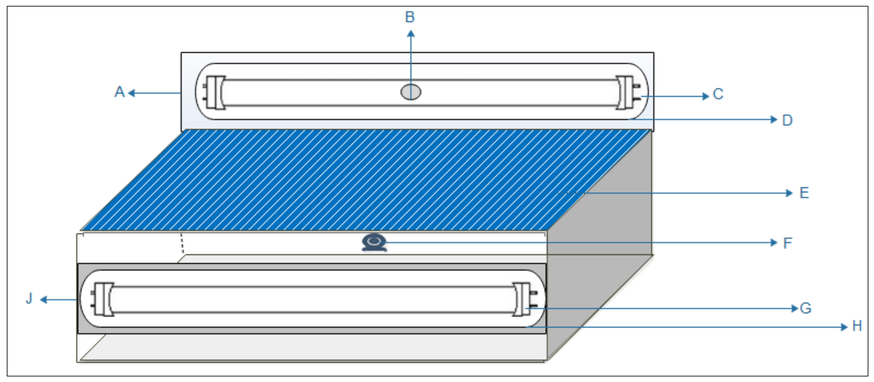


Fig. 4 Design of the catheter model (by Nhien Nguyen)

Figure 4 Legend

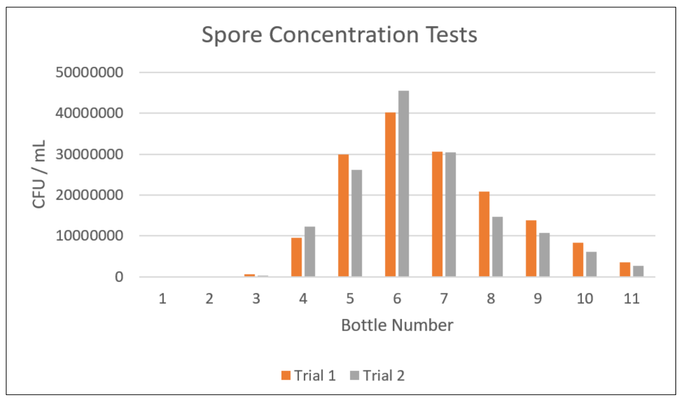
- **(A)** Inlet chamber
- **(B)** Inlet
- **(C/G)** Ultraviolet (UV) lamps
- **(D/H)** Quartz sleeves
- **(E)** 34 Foley silicon catheter array
- **(F)** Webcam for droplet monitoring*
- **(G)** Exhaust chamber

* Uses LabView software written by Dr. Hope Queener at the UH College of Optometry for *in situ* measurements of individual catheter flow rate

3. SPORE TESTS

To test the efficiency of UV lamp exposure within the model on bacterial spores (a potential contaminant significantly resistant to UV), 0.3 mL of Bacillus subtilis 5609 spores (from Prof. M. Fujita, UH) were injected into initial DI H2O inlet tubing leading into the UV lamp sterilization system. The runoff of water through the UV treatment system was then collected across 11 bottles (400 mL fractions). 150 µL samples from each bottle were plated to test bacterial spore concentration after UV exposure. The experiment was then duplicated The results of both trials are represented below in Figure 2. The results indicate that the highest spore number was recorded in bottle 6 of the runoff. Bottle 6 had the highest concentration of spores and will be used to test UV lamp sterilization efficiency.

Fig. 2. Estimated CFU from each of the 11 test tube samples after LB agar plating. Greatest bacterial colony formation observed from the Bottle 6 samples which was 4.0 * 10^7 to 4.5 * 10^7 CFU/mL. Bottles 1, 2, 3, 11 had dilution factors of 10. Bottles 4-10 had dilution factors of 100.



4. CONCLUSION

The system is developed as a CAUTI model under stimulated, *in vivo* conditions. The catheters are coated by (mixtures) of at least eight nonpathogenic species under a defined flow rate up to four weeks. These isolates were provided by Dr. Jennifer Walker at UTHealth. AU samples from each catheter outlet will be collected and bacterial plate counting used to confirm the presence of live bacteria. Samples will also be analyzed with 16S rRNA sequencing (with Dr. Gunaratne, UH) and mass spectrometry-based proteomic analysis to identify bacterial species present. This catheter-model project opens vast possibilities toward studying the interactions among nonpathogenic and pathogenic bacteria involved in CAUTI and its prevention based on the bacterial interference strategy.