Colloids and Surfaces B: Biointerfaces 132 (2015) 216–224

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

# Tunable, antibacterial activity of silicone polyether surfactants

Madiha F. Khan[a], Laura Zepeda-Velazquez[b], Michael A. Brook[a,b,*]

[a] School of Biomedical Engineering, McMaster University, 1280 Main St. West, Hamilton, ON, Canada L8S 4M1
[b] Department of Chemistry and Chemical Biology, McMaster University, 1280 Main St. West, Hamilton, ON, Canada L8S 4M1

ARTICLE INFO

*Article history:*
Received 22 December 2014
Received in revised form 18 April 2015
Accepted 10 May 2015
Available online 18 May 2015

*Keywords:*
Antibacterial activity
Nonionic surfactants
Silicone polyethers
Live-dead stain
Turbidometric screen

ABSTRACT

Silicone surfactants are used in a variety of applications, however, limited data is available on the relationship between surfactant structure and biological activity. A series of seven nonionic, silicone polyether surfactants with known structures was tested for in vitro antibacterial activity against *Escherichia coli* BL21. The compounds varied in their hydrophobic head, comprised of branched silicone structures with 3–10 siloxane linkages and, in two cases, phenyl substitution, and hydrophilic tail of 8–44 poly(ethylene glycol) units. The surfactants were tested at three concentrations: below, at, and above their Critical Micelle Concentrations (CMC) against 5 concentrations of *E. coli* BL21 in a three-step assay comprised of a 14–24 h turbidometric screen, a live-dead stain and viable colony counts. The bacterial concentration had little effect on antibacterial activity. For most of the surfactants, antibacterial activity was higher at concentrations above the CMC. Surfactants with smaller silicone head groups had as much as 4 times the bioactivity of surfactants with larger groups, with the smallest hydrophobe exhibiting potency equivalent to sodium dodecyl sulfate (SDS). Smaller PEG chains were similarly associated with higher potency. These data link lower micelle stability and enhanced permeability of smaller silicone head groups to antibacterial activity. The results demonstrate that simple manipulation of nonionic silicone polyether structure leads to significant changes in antibacterial activity.



## 1. Introduction

Silicone surfactants find applications in areas ranging from polyurethane foam stabilization [1] to facilitating delivery of agricultural active ingredients [2], including herbicides [3]. Agricultural adjuvants, **1**, known colloquially as superwetters, are low molecular weight compounds comprised of a trisiloxane head group and low molecular weight oligomeric poly(ethylene glycols) (PEG) of low polydispersity index: different manufacturers place different chemical groups at the PEG terminus. By contrast, higher molecular weight silicone surfactants, such as dimethicone copolyol (DC3225C) **2** and related rake, AB, or ABA block copolymers are complex oligomeric or polymeric materials with broad molecular weight distributions (Fig. 1). The combination of low surface energy and high mobility of the silicone constituents gives these surfactants unusual properties not possessed by organic derivatives.

It is known that some silicones, including superwetters, exhibit biological activity. Several studies have reported the toxicity of superwetters to fruit fly larvae [4], some aphids [5–7], citrus leafminers [8], and armyworm larvae [4,9], among others. An interesting comparison of three related silicone surfactants showed that spider mites responded quite differently to different surfactant chemical structures. The superwetter with the smallest hydrophobic head group of the three siloxane polyalkylenoxide copolymers, Silwet L-77, **3** was highly toxic, while L-7607 was less so, and L-7200 was nontoxic (the structures of the latter two compounds are not publicly available, but the authors rely on the description in the paper confirming they have larger, hydrophobic head groups) [10]. Enhanced biological activity was related to the surface activity: lower surface activity surfactants with larger head groups were less toxic to the mites.

This structure–function relationship for silicone surfactants has not been examined in detail, but is important to study, both because the materials are so widely used in commerce and because the little available information suggests the biological activity is tunable. One application that could benefit from surfactants with species-specific potency is the development of antibacterial materials (substances that kill bacteria or inhibit their growth) [11] for

* Corresponding author at: Department of Chemistry and Chemical Biology, McMaster University, 1280 Main St. West, Hamilton, ON, Canada L8S 4M1. Tel.: +1 905 525 9140x23483; fax: +1 905 522 2509.
*E-mail address:* mabrook@mcmaster.ca (M.A. Brook).

http://dx.doi.org/10.1016/j.colsurfb.2015.05.016
0927-7765/

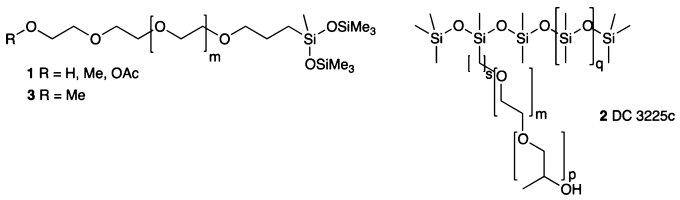


**Fig. 1.** Structures of superwetters and a rake silicone surfactant.

hospitals. Death caused by the increasing prevalence of *Clostridium difficile* and Methicillin-resistant *Staphylococcus aureus* (MRSA) in hospitals [12], for example, is an important challenge of the 21st century. The issue is caused, in part, by the overuse of broad-spectrum antimicrobials in surface disinfection protocols [13], which can lead to transferrable resistance from non-target bacteria to problematic analogs [14,15]. Hence, compounds like Silwet L-77 that have shown selective toxicity to biological organisms may be promising lead candidates for antibacterials, particularly on surfaces.

Recently, we reported the synthesis of a series of closely related silicone surfactants [16]. The hydrophilic tails were methyl-terminated, low polydispersity $(PEG)_{44}$ or $(PEG)_{15}$ polyethers. However, the silicone head groups varied in size, number of silicone groups and number of phenyl groups. We were interested in exploring the changes in biological activity that accompanied the structural and surface activity differences between the surfactants against *Escherichia coli* (*E. coli*). This bacterium serves as a convenient material for a preliminary assessment of bioactivity. Once aspects of the biological activity of these surfactants are determined, then applications can be considered. Surfactants that do not significantly affect organisms can be considered for use as formulation aids. By contrast, those that are toxic to bacteria might have utility in cleaning/disinfecting protocols, but only after their toxicity to mammalian cells is determined. A commercial superwetting material ACR-008 UP (Fig. 2) was used as a positive control.

## 2. Experimental

### 2.1. Materials

Compounds Si10-PEG44, Si4Ph6-PEG44, Si7-PEG15, Si7-PEG44, Si4Ph3-PEG15, Si4Ph3-PEG44 and Si4-PEG44 (nomenclature: Si*X*, where *X* is the number of siloxane units; if Si-phenyl groups are present their number is indicated with Ph*Y*, *Y* = 3.6; PEG*ZZ*, where *ZZ* is the number of $OCH_2CH_2$ units in the surfactant) were prepared following the procedure of Grande et al. [16] Siltech Corp provided ACR-008 UP. These surfactants were used as received. Poly(ethylene glycol) methyl ether (PEG) of $\sim M_n$ 2000, and SDS were purchased from Sigma Aldrich and Bioshop Inc., respectively. Sodium phosphate dibasic heptahydrate ($Na_2HPO_4{\cdot}7H_2O$), sodium phosphate monobasic ($NaH_2PO_4{\cdot}H_2O$) and sodium chloride (NaCl) were purchased from Fisher Scientific, EMD Chemicals Inc. and Caledon Laboratories Ltd. respectively. *E. coli* BL21(DE3)pLyS was obtained from the Promega Corporation. Bacto™ yeast extract, Difco™ granulated agar, and Bacto™ tryptone were purchased from Becton, Dickinson and Company (BD). A live-dead *Bac*light™ Bacterial Viability kit (L-7012) was acquired from Invitrogen's Life Technologies.

### 2.2. Stock reagents

Luria–Bertani (LB) agar plates were created using 10 g of tryptone, 5 g of yeast extract, 10 g of NaCl, 15 g of agar and 1 L of deionized water ($dH_2O$), in accordance with accepted protocols [17]. Note, no antibiotics were added to the mixture since the general antibacterial activity of surfactants was being tested. Fresh plates were made periodically – typically one day before the start of antibacterial testing – and sealed and stored in their original packing at 4 °C until needed. One liter stock solutions each of LB media (same recipe as for agar plates minus the agar) and 0.9% PBS (2.21 g of $NaH_2PO_4{\cdot}H_2O$, 11.26 g of $Na_2HPO_4{\cdot}7H_2O$, 9 g of NaCl, 1 L $dH_2O$ [pH 7.4]) were made, sealed, autoclaved and stored at room temperature. The sterility of all materials, including pipette tips and

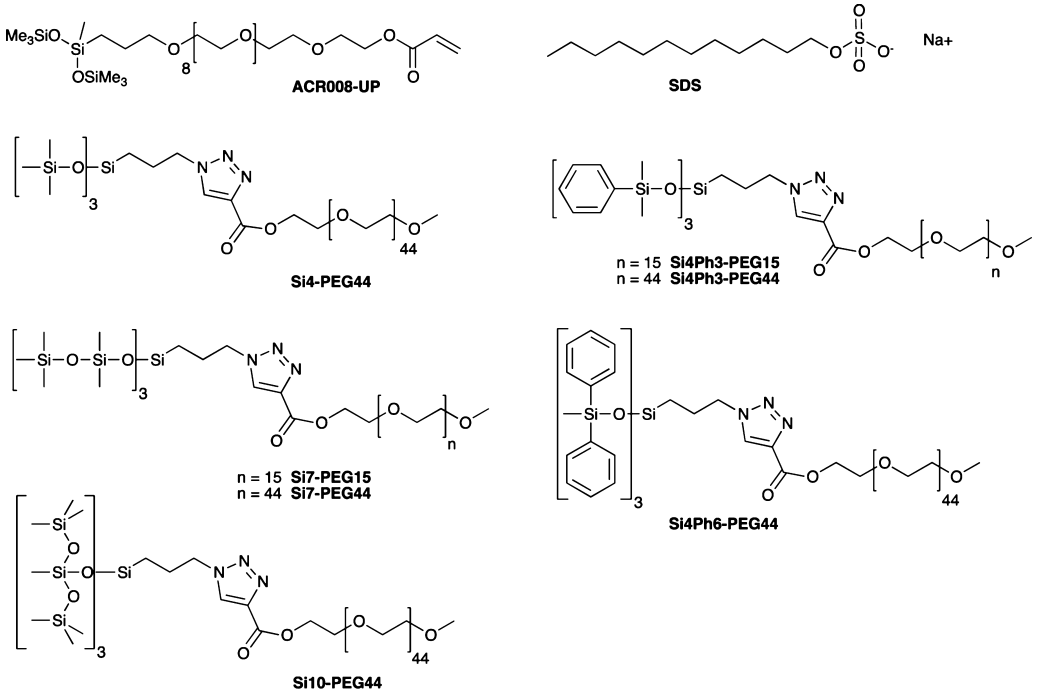


**Fig. 2.** Nonionic silicone polyether surfactants screened for biocidal behavior.