Antibacterial Properties of Silicone Membranes after a Simple Two-Step Immersion Process in Iodine and Silver Nitrate Solutions

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Silicone is widely used in packing materials, medical equipment, and separation membranes. Since microbial cells easily adhere to the surface of silicone materials and form biofilms, techniques for incorporating antimicrobial activity into silicone materials are in high demand. This study describes the preparation of silver (Ag)/silicone composite membranes through a simple two-step immersion process, utilizing an iodine solution followed by a silver nitrate solution at room temperature. Scanning electron microscopy (SEM) observations revealed that particles with sizes of several nanometers to several tens of nanometers were present on the silicone membrane surface; these particles were identified as silver iodide using energy-dispersive X-ray spectroscopy (EDS). The Ag/silicone membrane possessed excellent antibacterial efficacy against Escherichia coli and Staphylococcus aureus, and the antibacterial efficacy (R) against both types of bacteria was R > 4, even after stomacher treatment or acidic treatment of pH 2-6 for 24 h. The mechanical strength of the silicone membrane was also maintained after antibacterial treatment, with Young’s modulus values of 7.9±1.2 MPa and 8.3±1.5 MPa for the untreated membrane and Ag/silicone membrane, respectively (p > 0.05). In addition, the reduction in permeation performance of the Ag/silicone membrane was only 20%, despite the antibacterial treatment on the membrane surface. This antibacterial treatment method of silicone membranes can be conducted at room temperature (25°C) without special equipment, and may be applied to other types of silicone materials.

Key words: Polydimethylsiloxane / Antibacterial activity / Biofilm / Silver / Iodine.

INTRODUCTION

Polydimethylsiloxane (PDMS)-based silicone materials are used widely in packing materials, cooking utensils, and medical equipment (Bae et al., 2015; Goveas et al., 2012; Hirahara et al., 2014; Shit and Shah, 2013). In addition, silicone membranes have industrial applications, such as in separation membranes for pervaporation (Han et al., 2001; Zhao et al., 2013). Silicone materials in food processing and medical institutions (e.g., tubes, packing materials, and membranes) are often in contact with water, which promotes the adhesion of microorganisms and biofilm formation, increasing the possibility of food poisoning and infections, degrading appearance, and increasing the likelihood of manufacturing defects. Therefore, prevention of microbial adhesion and biofilm formation on silicone materials is important.

Recent studies have reported methods for incorporating antimicrobial activity into silicone materials. For example, Schierholz et al. (1994) incorporated the antibiotic rifampicin into silicone materials to prevent microbial colonization. In their study, only high rifampicin doses were administered over several weeks to prevent bacterial colonization. McBride et al. (2009) incorporated triclosan and prepared cast silicone membranes. They reported that a prolonged antibacterial effect was
obtained by grafting polyethylene glycol (PEG) chains into the cast silicone membrane containing tricosan. In addition, many researchers have reported the production of antimicrobial-coated silicone materials by surface modification of silicone rubber, using methods such as immobilization of hydrogen peroxide-producing enzymes (e.g., cellulbiose dehydrogenase) via ultrasound-assisted coating (Lipovskt et al., 2015); immobilization of short peptides (tryptophan-rich, arginine-rich, and lysine-rich) through surface grafting polymerization induced by plasma ultraviolet exposure (Li et al., 2014); electrostatic layer-by-layer assembly of antifouling copolymers, bactericidal derivatives, and cellulbiose dehydrogenase (Vaterrodt et al., 2016); immobilization of polysulfobetaine polymers on crosslinked silicone layers through ozone treatment; covalent grafting of ultraviolet (UV) -induced polymerization and thiol-ene click reactions through surface grafting polymerization induced by plasma ultraviolet exposure (Li et al., 2014); electrostatic layer-by-layer assembly of antifouling copolymers, bactericidal derivatives, and cellulbiose dehydrogenase (Vaterrodt et al., 2016); immobilization of polysulfobetaine polymers on crosslinked silicone layers through ozone treatment; covalent grafting of ultraviolet (UV) -induced polymerization and thiol-ene click reactions (Li et al., 2012); and direct grafting of poly(N-vinylimidazole) on silicone by gamma-ray irradiation (Meléndez-Ortiz et al., 2015). Although several methods for incorporation of organic agents have been reported, they require complicated steps, special equipment, or high energy levels.

Silver is a particularly suitable antibacterial agent because of its oligodynamic effect at relatively low concentrations (Clement and Jarrett, 1994). Silver can bind to microbial DNA, generate reactive oxygen species, inhibit bacterial replication, and bind to the thiol groups of metabolic enzymes in the bacterial electron-transport chain, causing enzyme modification and inactivation (Russell and Hugo, 1994). Ciobanu et al., (2015) and Popa et al., (2015) used a thermal evaporation technique (0.01 Pa and >1100°C) to coat Ag-doped hydroxyapatite onto PDMS. Such an antibacterial composite was active against Candida albicans biofilms. In addition, composite samples containing Ag could be prepared using silver benzoate with PDMS (Bovero et al., 2013) or by mixing Ag-loaded zeolite with PDMS (Kaali et al., 2010). Oktay and Kayaman-Apohan (2013) prepared PDMS containing Ag by UV curing and sol-gel processes. Although these methods could produce effective antimicrobial-finished silicone materials, they required high energy, long reaction times, or complicated preparation steps.

Iodine molecules can accumulate at high concentrations in silicone membranes according to studies on the separation of iodine using these membranes (Sawai et al., 2012a). Nakamura et al. (2011) prepared iodine-releasing silicone membranes using an adsorption process, which produced membranes with high antibacterial activity. However, these membranes were not durable because the iodine was easily released from the membrane. Therefore, an Ag compound, such as silver iodine (AgI), was formulated with low solubility in the silicone used to construct the membrane. Fujimori et al. (2008) also doped AgI into nylon 6 by immersion in an iodide solution, followed by silver nitrate (AgNO₃) treatment to improve the fiber conductivity. In addition, the composite fiber exhibited antibacterial activity. Effective antimicrobial coating was thought to be possible by reacting Ag ion with the surface of the silicone membrane impregnated in advance with iodine. The present report describes the preparation of Ag/silicone composite membrane materials with high durability using a simple, two-step immersion process—first in an iodine solution and then in a AgNO₃ solution—at room temperature. In addition, the antibacterial and mechanical properties were investigated as well the durability of the prepared membranes.

MATERIALS AND METHODS

Preparation of Ag/silicone composite membranes

The Ag/silicone composite membranes were prepared using the following method, which is a modification of the procedure described by Fujimori et al. (2008). A 0.3-mm thick silicone membrane (ASONE, Osaka, Japan) was cut into 50 mm × 50 mm pieces. An iodine-potassium iodide solution was prepared by dissolving 0.03-0.15 M I₂ in 3.3 M KI solution. The silicone membrane was immersed in the I₂-KI for 1-24 h. The membrane was removed, rinsed twice with sterile pure water, and then immersed in 0.25-0.75 M AgNO₃ solution for 1-24 h. The membrane was removed, rinsed twice with sterile pure water, and disinfected with ethanol on a clean laboratory bench. All reagents were purchased from Wako Pure Chemicals (Osaka, Japan).

Antibacterial efficacy test

Escherichia coli NBRC 3301 and Staphylococcus aureus subsp. aureus NBRC13276 were obtained from the National Institute of Technology Evaluation Biological Resource Center (NBRC, Kazusa, Japan). They were incubated in nutrient broth (NB) with shaking (110 strokes/min) for 20 h at 37°C. Cultures were washed and resuspended in 1/500 NB at approximately 10⁶ CFU/ml. The bacterial suspension was stored in an ice water bath before use. Antibacterial efficacy (R) was evaluated according to JIS Z 2801 (2001). All growth media were purchased from Eiken Chemicals (Tokyo, Japan). A value of R > 2 was considered to indicate antibacterial efficacy.

Scanning electron microscopy (SEM) and elementary analysis

The surface of the Ag/silicone membrane was characterized using SEM and energy-dispersive X-ray spectroscopy (EDS; model SU9000, Hitachi High-Technologies
The SEM was conducted at an acceleration voltage of 0.5-30 kV and 1.7 mm working distance. The untreated silicone membrane was also characterized by SEM (JSF-7001F, Jeol Ltd., Tokyo, Japan).

**Tensile strength**

The tensile strength was measured according to Japanese industrial standard (JIS) K 6251-6 (2010). To do this, the Ag/silicone membrane was cut into a dumbbell shape with a parallel section width of 3.7 mm and a length of 25 mm using a dumbbell cutter. The Ag/silicone membrane piece was placed in a stretcher and uniaxially stretched at a tension rate of 10 mm/min, which was determined in a previous study (Wada et al., 2012). The Young’s modulus was estimated from the initial gradient of the stress-strain curves obtained, and the mechanical strength of the Ag/silicone membrane was evaluated. An untreated silicone membrane sample was also measured and served as the control.

**Evaluation of separation performance**

The separation performance of the Ag/silicone membranes was evaluated using the permeation and chemical desorption (PCD) method. Experiments were conducted according to the method of Sawai et al. (2012b). Briefly, two solutions with different chemical properties (a feed cell solution and a recovery cell solution) were separated by a silicone membrane fixed with a flange between two glass cells. A solution of pentachlorophenol (PCP: Wako Pure Chemicals) dissolved in an acidic solvent was placed in the feed cell, and the recovery cell was filled with an alkaline solution. The PCP molecules dissolved in the feed solution, being protonated at the hydroxyl group and thus uncharged, tended to penetrate into a hydrophobic silicone membrane.

The PCP (0.04 mM, pH 2) and NaOH (20 mM, pH 12.3) solutions were added to the feed cell and recovery cell, respectively. In a previous study (Sawai et al., 2012b), the permeation rate of PCP to the silicone membrane was optimized for the feed and recovery solutions. The solutions on both sides of the membrane were stirred constantly using magnetic stir bars. All work was conducted using glass cells and a magnetic stirrer contained in a thermostatic chamber at 25°C ± 1°C. High-performance liquid chromatography (HPLC) equipped with a UV detector was used to determine PCP concentration in the feed cell (C) and recovery cell under previously described conditions (Sawai et al., 2012b). When \( \ln(C/C_0) \) and time (t) were employed as the ordinate and abscissa, respectively, \( \ln(C/C_0) \) decreased linearly, indicating that a decrease in PCP concentration in the feed cell followed first-order kinetics [Eq. (1)] (Sawai et al., 2012b):

\[
\ln(C/C_0) = -(A/V)K_{CL} \ t
\]

where \( C_0, A, V, \) and \( K_{CL} \) are initial PCP concentration in the feed cell, effective membrane area and liquid volume in the feed cell, and overall mass transfer coefficient, respectively. The value of \( K_{CL} \) could be obtained from the slope of the line and was used as the permeation property of the PCP.

**Statistical analysis**

All experiments were performed in triplicate (\( n = 3 \)). Data points with bars represent mean ± standard error. Data were analyzed using one-way ANOVA (Tukey’s method) from BellCurve for Excel® (Social Survey Research Information Co., Ltd., Tokyo, Japan) to determine the significant difference of mean values. A value of \( p < 0.05 \) was considered statistically significant.

**RESULTS**

**Treatment condition and antibacterial efficacy**

Optimal preparation conditions for the Ag/silicone membranes were determined using *S. aureus*. Untreated silicone membranes did not possess antibacterial efficacy, and both *E. coli* and *S. aureus* were capable of growth of greater than two orders of magnitude on the surface within 24 h. Table 1 shows the influence of \( I_2 \) and AgNO\(_3\) concentrations in the immersion treatment.
TABLE 1. Effect of I₂ or AgNO₃ concentration on the antibacterial efficacy of AgI/silicone membrane against S. aureus.

| Concentration (M) | Antibacterial efficacy (R) *² ³ |
|-------------------|---------------------------------|
| I₂ *¹ | AgNO₃ *¹ | |
| 0.03 | 1.0 | 3.5 ± 3.2² |
| 0.08 | 1.0 | 4.9 ± 0.7² |
| 0.12 | 1.0 | 5.7 ± 0.8² |
| 0.15 | 1.0 | >6.0² |
| 0.15 | 0.25 | >6.0² |
| 0.15 | 0.55 | >6.0² |
| 0.15 | 0.75 | >6.0² |

*¹ Treatment time: 24 h
*² Antibacterial efficacy (R) was evaluated according to JIS Z 2801 (2001). When R > 2, the sample is considered to be effective.
*³ Different letters within columns indicate significant difference (p < 0.05).

TABLE 2. Effect of treatment time on the antibacterial efficacy of AgI/silicone membrane against S. aureus.

| Treatment time (h) | Antibacterial efficacy (R) *² ³ |
|-------------------|---------------------------------|
| I₂ *¹ | AgNO₃ *² | |
| 1 | 24 | 0.2 ± 0.0² |
| 2 | 24 | 1.3 ± 0.1² |
| 3 | 24 | 3.6 ± 2.1² |
| 6 | 24 | >6² |
| 12 | 24 | >6² |

*¹ I₂ concentration: 0.15 M (from Table 1)
*² AgNO₃ concentration: 0.25 M (from Table 1)
*³ When R > 2, the sample is considered to be effective.
*⁴ Different letters within columns indicate significant difference (p < 0.05).

(i) Immersion of 24 h on the antibacterial efficacy against S. aureus. Initially, I₂ concentration was varied while maintaining a constant concentration of 1.0 M AgNO₃. The antibacterial efficacy of the Ag/silicone membrane against S. aureus increased with I₂ concentration and reached R > 6 (detection limit: 100 CFU/sample) at 0.15 M I₂. Next, AgNO₃ concentration was varied while maintaining a constant concentration of 0.15 M I₂, which resulted in antibacterial efficacy of R > 6 at 0.25 to 0.75 M AgNO₃. The antibacterial activity of the AgI/silicone membrane was dependent on the uptake of iodine to the silicone membrane.

Under fixed I₂ and AgNO₃ concentrations of 0.15 and 0.25 M, respectively (Table 1), the influence of immersion time was investigated (Table 2). When I₂ and AgNO₃ immersion times were longer than 6 h and 12 h, respectively, a significant increase in antibacterial activity (R > 6) was obtained. Therefore, the AgI/silicone membrane could be prepared in a shorter amount of time while maintaining potent antibacterial efficacy. Subsequent studies were conducted using AgI/silicone membranes prepared under these conditions.

Survival ratio of E. coli on the AgI/silicone membrane declined significantly to 1/5 in 5 min, 1/5000 in 10 min, and was below the detection limit (<10⁵) within 20 min (Fig.1). In contrast, S. aureus was more resistant to the AgI/silicone membrane than was E. coli. The survival ratio did not change significantly within 8 h (p > 0.05), but sharply decreased at 9 h and dropped below the detection limit at 10 h.

**Observations of the prepared AgI/silicone membrane**

The silicone membrane changed color after I₂ and AgNO₃ immersion treatments (Fig.2). Initially, the silicone membrane was semitransparent, but turned brown after iodine treatment, indicating iodine accumulation in the membrane. Following AgNO₃ treatment, the membrane changed to white, indicating the formation of AgI.

The surface of untreated silicone membranes was flat and smooth, as shown in the SEM image [Fig.3(A)]. In contrast, SEM observations of AgI/silicone membranes revealed that particles with sizes of several nanometers to several tens of nanometers were present on the silicone membrane surface as dots after AgNO₃ treatment [Figs.3(B) and 3(C)]; typical particles are indicated by
The distance between particles with sizes of several tens of nanometers was relatively wide (approximately 100 nm). The bright-field and EDS images of the particles are shown in Fig.4(A) and 4(B), respectively (blue and red points correspond to Ag and I, respectively). The AgI particles were confirmed to be widely distributed on the silicone membrane. The positions of existing particles apparent in the bright-field image corresponded to those of concentrated AgI particles with sizes of several tens of nanometers.

**Mechanical strength of the Ag/silicone membrane**

The influence of the two-step immersion treatment on the mechanical strength of silicone membranes was investigated. Typical stress-strain curves of Ag/silicone membranes and untreated membranes are shown in Fig.5. No differences in the shapes of stress-strain curves were found in the untreated and Ag/silicone membranes. Young’s modulus values calculated from the initial gradient of the stress-strain curves were 7.9±1.2 MPa and 8.3±1.5 MPa for the untreated membrane and Ag/silicone membrane, respectively; no significant difference was observed ($p > 0.05$).

**Durability of the Ag/silicone membrane**

The Ag/silicone membrane was subjected to 10 times stomacher treatment and tested for antibacterial efficacy using JIS Z 2801. Even after 10 times stomacher treatment, antibacterial efficacy against *E. coli* and *S. aureus* remained $R > 6$ (data not shown).

Durability against acidic treatment was also investigated. Antibacterial efficacy of the Ag/silicone membrane was $R > 6$ after acidic treatment of pH 4-6 for 24 h. Although the efficacy significantly decreased to $R > 4.3$ upon pH 2 treatment, the remaining efficacy was sufficient (data not shown). The Ag/silicone membrane prepared for this study possessed both high antibacterial activity and durability against acidic treatment and physical stress such as stomacher treatment.
Separation performance

Typical transient behavior of PCP permeation through the Ag/silicone membrane using the PCD method is shown in Fig.7. The concentration of PCP in the recovery cell increased as PCP concentration decrease in the feed cell, indicating that PCP passed from the feed cell to the recovery cell. Tests using the PCD method confirmed that the Ag/silicone membrane retained permeation performance. The total PCP concentration from the feed side and recovery side is referred to as \( \text{Total} \). The total concentration did not reach the initial concentration in the feed cell, which indicates some PCP accumulated in the silicone membrane.

**DISCUSSION**

The method for preparing silicone membranes with antibacterial properties described here involved a simple two-step immersion process at room temperature without the need for special equipment. Although only membranes were investigated in this study, this method could be applied to a wide range of silicone-based materials as long as the treatment solutions (I\(_2\)-KI and...
AgNO₃ solution) can contact the surface. Thus, this is a very effective method to produce antimicrobial silicone materials and can be applied to silicone materials of varying shapes.

Other reports have showed simple immersion treatments. For example, Wu et al. (2014) described surface treatment of silicone membranes by immersion in chlorogenic acid solution, but the resulting antimicrobial activity was weak. Nakamura et al. (2012) prepared antibacterial silicone separation membranes by immersing the silicone membrane into an oleic acid silver-diethyl ether solution. Although this membrane possessed high antibacterial efficacy, the activity was decreased dramatically by stomacher treatment due to peeling of the silver oleic acid from the silicone membrane by the mechanical stress of the stomacher treatment. Silicone materials are often subjected to mechanical stress. The antibacterial activity of the Ag/silicone membrane in this study was very high, and did not decrease even after 10 times of the stomacher treatments. In addition, the Young’s modulus value of the Ag/silicone membrane was similar to that of an untreated membrane and consistent with the literature range of 2.5-12 MPa (Gray et al., 2003). Although no studies have been reported on the ability of Ag-incorporated silicone materials to tolerate acidic conditions, membranes are often exposed to acidic conditions, particularly in food processing. The retention of antibacterial efficacy after mechanical stress, such as stomacher, and acidic treatment, indicate the durability and usefulness of the Ag/silicone membrane.

The results from the PCD method indicated that once the PCP molecules permeated the membrane and emerged in the alkaline recovery solution, the hydroxyl group of the molecule was deprotonated to produce a charged phenolate anion (ROH → RO⁻). This charged phenolate species is poorly adsorbed by the silicone membrane, thus, it does not tend to migrate back to the feed cell. As a consequence, the PCD dissolved in the acidic solution in the feed cell eventually concentrates in the recovery cell. The Ag/silicone membrane also retained permeation capacity, likely because of the AgI particles with sizes of several tens of nanometers dotted on the silicone membrane surface, which did not block the permeability of the membrane. In a previous study (Sawai et al., 2012b), the overall mass transfer coefficient (Kₒₒ) of PCP to the untreated silicone membrane was (1.84±0.13) × 10⁻⁸ m/s. In contrast, when the Kₒₒ of PCP to the Ag/silicone membrane was calculated according to Eq. (1), the value obtained was (1.47±0.19) × 10⁻⁸ m/s, which is a reduction of approximately 20% compared to the untreated membrane, but was not significant (p > 0.05).

The efficacy of the Ag ion solution was demonstrated to be better against the Gram-negative E. coli than against the Gram-positive S. aureus. Minimum inhibitory concentrations of Ag ions against E. coli and S. aureus have been reported as 0.78 and 6.3 ppm, respectively (Matsumura and Tsuchido, 2001). Jung et al. (2008) reported that, in an aqueous solution containing Ag ions at 0.1 ppm, the E. coli concentration was below the detection limit within 1 h. However, the S. aureus concentration was reduced by approximately one order and two orders of magnitude at 2 h and 3 h, respectively. The present results do not contradict these data. On the Ag/silicone membrane described in the present study, the amount of E. coli decreased sharply within 1 h, while that of S. aureus remained high up to approximately 8 h. This difference between E. coli and S. aureus in sensitivity to Ag ions may be due to the thickness of the peptidoglycan layer, which may prevent the action of Ag ions through the bacterial cell wall (Jung et al., 2008). Feng et al. (2000) investigated the damage of the cell membrane induced by Ag and reported fewer morphological changes in S. aureus compared with those in E. coli.

The residual undissociated iodine from the first immersion step might also have provided an antibacterial effect. Nakamura et al. (2011) did not find a difference in the minimum bactericidal concentration of iodine against E. coli and S. aureus (both 10 mg/l). The survival ratios of E. coli in iodine solution were 4.5 × 10⁻³ and 2.8 × 10⁻² at 1 h and 2 h, respectively; whereas those of S. aureus were 1.3 × 10⁻³ and 6.9 × 10⁻⁴, respectively. In short, there was little difference between Gram-positive and Gram-negative bacteria in terms of susceptibility to iodine. This iodine antibacterial trend was quite different from that of the Ag ions described above and that of the Ag/silicone membrane shown in Fig.1. Although the antibacterial mechanism of the Ag/silicone membrane is unclear, the activity is believed to originate from the Ag ions.

These results suggest that the Ag/silicone composite membrane prepared by the two-step immersion treatment described here possessed superior properties. However, the ability of the Ag/silicone membrane to withstand other stresses, such as alkaline or heat treatment, was not investigated. In addition, long-term results were not evaluated. Studies on these aspects will be needed to confirm the findings and to further evaluate the material features.

CONCLUSIONS

An antibacterial silicone membrane was prepared through a simple two-step immersion treatment at room temperature. Silver iodide particles with sizes from several nanometers to several tens of nanometers were present on the silicone membrane surface. The antibacterial activity of the Ag/silicone membrane was very high,
and did not decrease, even after 10 times of stomacher treatments and acid treatment (pH 2). Furthermore, the mechanical and permeation properties of the silicone membrane were also maintained. The antibacterial treatment method of silicone materials described in this study can be applied not only to thin films, but also to products prepared through a molding process. This method was performed at room temperature and did not require any special equipment. This technique can be applied for diverse uses of silicone. Presently, the mechanism that mediates the antibacterial activity of the Ag/silicone composite membrane is not clear and requires further investigations. In addition, fungal growth on silicone materials is a concern, but was not investigated in the study described here. Therefore, additional studies are being planned to develop silicone materials that prevent fungal and bacterial colonization by improving the antibacterial treatment method.

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