ANTIMICROBIAL AGENTS AND ANTI-ADHESION MATERIALS FOR MEDICAL AND SURGICAL GLOVES

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RUBBER CHEMISTRY AND TECHNOLOGY, Vol. 94, No. 1, pp. 1–23 (2021)

ABSTRACT

Healthcare-associated infections (HAIs) can be common in healthcare settings, such as the intensive care unit and surgical sites, if proper precautions are not followed. Although traditional techniques are encouraged, such as educating the public and healthcare workers to practice proper handwashing or to double glove, they have not been fully effective in combating HAIs. The use of surface-modified antimicrobial gloves may be an alternative approach to prevent the transmission of pathogens between healthcare workers and patients. This paper gives a comprehensive review of strategies to produce antimicrobial gloves. The chemistry of some potential chemically synthesized antimicrobial agents and nature-inspired superhydrophobic surfaces are discussed. The principles of killing microbes must be understood to effectively select these materials and to design and fabricate surfaces for the reduction of bacterial adhesion. Also, current company trends and technologies are presented for gloves proven to effectively kill bacteria. Such glove use, when coupled with in-depth research on diverse surgical procedures and medical examinations, could ease the burden of HAIs. [doi:10.5254/rct.21.79901]

INTRODUCTION

It is not uncommon for patients and healthcare workers to suffer from the underlying consequences of healthcare-associated infections (HAIs) that may deteriorate their quality of life, or in some circumstances, lead to death.[1] HAIs are usually caused by the bidirectional migration of microorganisms between the hands of a healthcare worker and a patient's body during invasive surgical procedures, or via cross-contamination between the surfaces of inanimate objects in the patient's immediate surroundings (e.g., wardroom) or via medical implants or devices placed on or into the patients.[2,3] Some examples of HAIs are central line–associated bloodstream infections, catheter-associated urinary tract infections, surgical site infections, and ventilator-associated pneumonia.[4] *Acinetobacter* spp., *Clostridium difficile*, *Enterobacteriaceae*, *Klebsiella* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), *Mycobacterium abscessus*, hepatitis viruses, and human immunodeficiency virus (HIV) are some common examples of pathogens that cause HAIs.[4] To tackle this worrisome healthcare problem, there has been a spike in demand for rubber gloves, particularly antimicrobial gloves, into the medical and surgical markets.

Medical and surgical gloves act as an important barrier against the transmission of microorganisms and blood-borne pathogens in hospital settings.[2,3] Wearing gloves could potentially lower the risks of the patient–surgical team encountering blood and body fluids and lessen microbial dissemination and contamination in the clinical environment. However, the safety of patients and healthcare personnel is not 100% even with glove use because of unavoidable micro-

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perforations, punctures, or tears in the glove material via sharp needles, surgical knives, and prolonged use. Prolonged use of gloves produces a moist layer around the skin, thereby providing an ideal surface for the growth and proliferation of resident or transient microbial flora on the hands. The flora may include opportunistic pathogens, especially if the surgical antisepsis of the hands is not performed appropriately.[4–8] Consequently, this situation lead to blood-borne infections, such as postoperative infections in a patient's wound(s).

Significant developments have been implemented to improve the properties of medical gloves, such as powdered gloves that ease the donning process and powder-free chlorinated gloves that reduce skin sensitivity to polymer-coated surfaces and minimize the glove–skin contact.[9] One of the traditional approaches to achieving microbial reduction is double gloving, that is, wearing an additional pair of gloves to minimize the risks of pathogen transmission to healthcare personnel and to fortify the physical barrier protection.[10] Although double gloving provides significant physical barrier protection against the outer glove tear or puncture during a surgical operation, the downfall of double gloving is that it causes discomfort to the wearer and decreases dexterity during surgical procedures.[11]

Frequent handwashing is another approach to combat pathogen transmission in the hospital. Healthcare workers usually contaminate their hands when they come in contact with the skin of hospitalized patients, for example, during the cleaning procedures or a routine check-up. One of the most common skin preparation agents used for infections in clinical scenarios are alcohol-based disinfectants that have fast-acting and broad-spectrum antimicrobial properties.[12] However, frequent use of alcohol-based antiseptics may cause inflammation to the skin. In addition, there have been reported accidents in which operating rooms have caught on fire via the use alcohol-based solutions, resulting sustained injuries in the patients and staff.[13]

The traditional approaches mentioned above have not been proven to effectively reduce pathogen transmission; hence, the aim of this review is to highlight the recent advances in the development of antimicrobial coatings and materials for medical-use gloves and to outline future requirements and prospects for antimicrobial agent and material selection in antimicrobial glove design.

CURRENT RESEARCH ON ADVANCEMENT OF ANTIMICROBIAL AGENTS FOR SURGICAL GLOVE DEVELOPMENT

CHLORHEXIDINE GLUCONATE

Chlorhexidine gluconate (CHG) is a commercially available antiseptic and disinfectant aqueous (aq) solution that has been proven to be effective against most bacteria, provided that the bacteria are in their free form.[14] The mechanism of action of CHG involves the positively charged chlorhexidine molecule binding to negatively charged phospholipids in the microbial cell wall via electrostatic interactions. This electrostatic binding increases the permeability of the membrane and damages the surface structure. As a result, the cell wall ruptures, leading to an osmotic imbalance within the cell and loss of intracellular components. Eventually, the bacterial cells thus die.

Although chlorhexidine has been proven to kill bacteria, microorganisms in a biofilm are resistant to it. Biofilms are complex structures formed by a bacterial colony that aid as a protective medium.[15] Bonez et al. determined the susceptibility profiles of *Acinetobacter baumannii*, *Candida albicans*, *Escherichia coli*, MRSA, methicillin-susceptible *S. aureus* (MSSA), and *Pseudomonas aeruginosa* toward chlorhexidine through disk diffusion assays and minimal inhibitory concentrations (MICs).[14] The disk diffusion assay and MIC results showed that free forms of *P. aeruginosa*, *A. baumannii*, and MRSA were susceptible to chlorhexidine, but did not

sustain after biofilm formation. In other research, only a 40% decrease in viability was noted when a biofilm of *P. aeruginosa* was exposed to chlorhexidine.[16]

Bonez et al. also reported that chlorhexidine inhibited the biofilm of *C. albicans* at the same MIC as the planktonic form of the microorganism.[14] The results contradicted other findings that the biofilm of *C. albicans* was resistant to chlorhexidine by 8-fold.[17] Another study[16] found that chlorhexidine exerted an outstanding effect against the biofilm of *S. aureus*, whereby the viability of the microbe was reduced by 84%, in line with the findings of the Bonez et al. study.[14] Despite the lack of efficacy of chlorhexidine against biofilm formation, CHG gloves still have the potential to reduce the risk of exposure to infectious fluid-borne pathogens, should the latex barrier exhibit overt failure.

CHLORHEXIDINE AND QUATERNARY AMMONIUM SALTS

An innovative chlorhexidine antimicrobial glove has been developed by Ansell under the trade name GAMMEX® Powder-Free with AMT™. The glove demonstrated a significant antimicrobial effect on *S. aureus* and *Brevundimonas diminuta*.[18] Daeschlein et al. reported that the combination of chlorhexidine and water-soluble quaternary ammonium salts was sequestered within the droplet compartment and inserted between two thermoplastic elastomeric boundary layers.[18] This tri-layer antimicrobial surgical glove lowered the risk of bacterial entry after glove perforation compared with conventional single- or double-layer surgical gloves. If the glove was punctured, the antimicrobial agent would squeeze out from its layer and deposit at the local site of injury or puncture. Not only could it reduce microbial passage or blood-borne infection but also innovatively prevent multiple punctures that often occurred unbeknownst to a healthcare worker during a long medical procedure, thus overcoming bacterial re-growth.[19]

Besides killing bacteria, quaternary ammonium compounds (QACs) in a glove are reported to function as surfactants, decreasing the surface tension of abiotic surfaces and thereby preventing the adherence of microorganisms.[20] The antimicrobial mode of action takes place in a series of events starting with the attraction of cationic surfactant to the negatively charged bacterial cell surface, primarily Gram-positive bacteria, followed by hydrophobic interaction with the cell membrane, reaction between the components that make up the cytoplasmic membrane (proteins and lipids), and lastly cell disruption and interaction with the intracellular constituents. Therefore, QACs promote the leakage of essential intracellular constituents through the penetration of the membrane.[21] A study showed that synergy of mixtures of ethylenediaminetetraacetate with QACs was successfully modeled to inhibit Gram-negative bacteria, such as *P. aeruginosa*.[22]

Daeschlein et al. also confirmed the effectiveness of an antimicrobial glove by a significant reduction of microbial passage after exposure to contaminated broth containing *S. aureus* and *B. diminuta*.[18] The glove also showed efficacy toward transmitted enveloped viruses such as feline immunodeficiency virus, bovine viral diarrhea virus, and herpes simplex type 1 virus.[23]

GARDINE (BRILLIANT GREEN DYE AND CHLORHEXIDINE)

Reitzel et al. revealed the fabrication of novel antimicrobial gloves impregnated with antiseptic dyes in preventing the adherence of multidrug-resistant nosocomial pathogens.[24] A mixture of brilliant green dye and chlorhexidine (gardine) antiseptics was directly coated on a nitrile glove surface by using an organic solvent–based process. The gardine-coated glove is deemed as the prototype that demonstrated high antimicrobial efficacy toward nosocomial-resistant pathogens within 1 min.[24,25] This efficacy level greatly reduces the risk of horizontal transmission and cross-contamination of microbes in hospital settings.

TABLE I
PRESENCE OF BACTERIA OR YEAST ON GARDINE-COATED GLOVES AFTER A PERIOD OF EXPOSURE[24]

	Gardine-coated nitrile examination	Gardine-coated latex examination
Reduction of viable Gram-positive bacteria[a]		
MRSA[b]	30 s – >7 $\log_{10}$ CFU	30 s – >7 $\log_{10}$ CFU
	10 min – >7 $\log_{10}$ CFU	10 min – >7 $\log_{10}$ CFU
	30 min – >7 $\log_{10}$ CFU	30 min – >7 $\log_{10}$ CFU
	1 h – >7 $\log_{10}$ CFU	1 h – >7 $\log_{10}$ CFU
VRE[b]	30 s – 4.8 $\log_{10}$ CFU	30 s – 2.5 $\log_{10}$ CFU
	10 min – 6.8 $\log_{10}$ CFU	10 min – 4.8 $\log_{10}$ CFU
	30 min – >7 $\log_{10}$ CFU	30 min – 6.7 $\log_{10}$ CFU
	1 h – >7 $\log_{10}$ CFU	1 h – >7 $\log_{10}$ CFU
Reduction of viable Gram-negative bacteria[a]		
MDR-*E. coli*[b]	30 s – >7 $\log_{10}$ CFU	30 s – >7 $\log_{10}$ CFU/mL
	10 min – >7 $\log_{10}$ CFU	10 min – >7 $\log_{10}$ CFU/mL
	30 min – >7 $\log_{10}$ CFU	30 min – >7 $\log_{10}$ CFU/mL
	1 h – >7 $\log_{10}$ CFU	1 h – >7 $\log_{10}$ CFU/mL
MDR *A. baumannii*[b]	30 s – 6.4 $\log_{10}$ CFU	30 s – 6.2 $\log_{10}$ CFU
	10 min – >7 $\log_{10}$ CFU	10 min – >7 $\log_{10}$ CFU
	30 min – >7 $\log_{10}$ CFU	30 min – >7 $\log_{10}$ CFU
	1 h – >7 $\log_{10}$ CFU	1 h – >7 $\log_{10}$ CFU
Reduction of viable yeast[a]		
C. albicans[b]	30 s – 0.8 $\log_{10}$ CFU	30 s – 2.3 $\log_{10}$ CFU
	10 min – 6.8 $\log_{10}$ CFU	10 min – 6.8 $\log_{10}$ CFU
	30 min – >7 $\log_{10}$ CFU	30 min – >7 $\log_{10}$ CFU
	1 h – >7 $\log_{10}$ CFU	1 h – >7 $\log_{10}$ CFU

[a] Antimicrobial efficacy testing is conducted based on modified American Association of Textile Chemists and Colorists Method 100. The viable microbial cells after a certain period of exposure to tested glove segment is quantified on Mueller-Hilton agar (containing 5% sheep blood).
[b] Initial inoculum size of respective microbes applied on each glove segment is 10^8 CFU. The specific strains of each microbe were not provided by the author(s).

Glove efficacy was tested on some common hospital-acquired pathogens including Gram-positive bacteria such as VRE and MRSA, Gram-negative bacteria such as multidrug-resistant (MDR) *A. baumannii* and MDR-*E. coli*, and yeast-like fungi, particularly *C. albicans*, for a short period. The study was carried out using a protocol proposed by the American Association of Textile Chemists and Colorists (Table I).[24]

Gardine-coated latex and nitrile gloves showed their superior antimicrobial properties by killing all the microorganisms encountered within 1 h. The gardine-coated gloves completely killed MDR-*E. coli* and MRSA within 30 s and *A. baumannii* within 10 min. After 30 min, at least a 7-log reduction of viable cells (99.99999% reduction) was noted for *C. albicans*. For VRE, it took 30 min for the nitrile glove and 1 h for the latex glove to kill the bacteria. By contrast, the control showed no response to these pathogens. The results suggest that the coated nitrile and latex gloves had higher antimicrobial efficacy than the uncoated gloves (i.e., 0 $\log_{10}$ reduction for all the bacterial exposure time points).

GENDINE (GENTIAN VIOLET AND CHLORHEXIDINE)

The gendine antiseptic–coated glove was developed as a potential intervention to prevent the transmission of HAIs upon surface contact.[25] Similar to the gardine-coated glove, the gendine antimicrobial glove is made up of different antiseptics of which the brilliant green dye is substituted with gentian violet. Gentian violet is a triphenylmethane dye with antibacterial, antifungal, and anti-helminthic properties.[26] Although the exact mechanism of action of gentian violet is not known, it is hypothesized that the antimicrobial effects are due to alteration of the redox potential by the violet dye, formation of free radicals, inhibition of the formation of bacterial cell wall, and inhibition of protein synthesis.[26] Researchers investigated the antimicrobial formulations by using gentian violet dye and compared them with brilliant green dye formulations.[27] Their results showed that a low critical concentration of gentian violet was needed to be effective against *Candida*, *Streptococcus*, and *Staphylococcus* spp., whereas it was less effective against Gram-negative bacterial species, particularly *Proteus* and *P. aeruginosa*. The substitution of brilliant green for gentian violet dye also enhanced the chlorhexidine activity and assisted in the water-based fabrication process. In addition, it claimed to be more cost effective and environmentally safe compared with brilliant green.[28]

Studies have also been performed on the surfaces of multiple medical devices, such as central venous catheters, polyvinyl chloride endotracheal tubes, and silicone urinary catheters. The results showed the activity of gendine against biofilm over a few weeks.[29–31] However, assessment on the efficacy of gendine against viruses such as HIV and hepatitis are recommended. Further studies are required in patient care settings to confirm the anticipated antimicrobial efficacy in clinical use.

CHLORINE DIOXIDE

Chlorine dioxide (ClO_2) is a water-soluble gas that has broad-spectrum coverage against bacterial spores, bacteria, protozoa, and viruses.[32] The Southwest Research Institute had filed a patent on this technology for its slow and sustained release of ClO_2 incorporated into glove materials once activated by light or moisture, thereby producing a sustained anti-infective microenvironment close to surfaces.[32–35] A study conducted by Barza found that ClO_2-incorporated gloves seeded with the bacteria *S. aureus*, *E. coli*, *Salmonella* serotype Typhimurium, and *Listeria monocytogenes* showed a 1- to 3-log reduction within 20 min.[32] However, the efficacy test for ClO_2-incorporated gloves showed incomplete eradication of microorganisms that contacted the glove surface after 45 min of exposure.[33]

Furthermore, ClO_2 is equally effective against non-pathogenic variants that behave the same as pathogenic organisms of the same species, such as MSSA and MRSA.[32] The cellular mechanisms of cells exposed to ClO_2 are not known; however, it is suggested that the mechanism of bacterial disinfection of ClO_2 lies on its oxidative property that damages the inner cell membrane of bacterial endospores, with transmembrane ionic gradient loss eventually leading to potassium efflux.[35,36] By contrast, the virucidal activity of ClO_2 is attributed to its protein layer–denaturing effect, instead of nucleic acids.[37,38] A study found that ClO_2 was active against some fungal species, including *Chaetomium* spp., *Aspergillus* spp., and *Alternaria* spp.[39] It also removed the cysts of protozoa (*Giardia* spp.). The advantages of using ClO_2 are that it is easily produced and has broad-spectrum antimicrobial activity. Although it is reported to be effective at pHs 5–10, its disinfection capacity is not influenced by pH because it does not hydrolyze under normal circumstances. Hence, both the temperature and the alkalinity of water do not influence its disinfectant efficiency.[40]

POLY(HEXAMETHYLENE BIGUANIDE) HYDROCHLORIDE

Bador et al. examined the efficacy of synthetic antibacterial nitrile gloves coated with poly(hexamethylene biguanide) hydrochloride (PHMB), a polymeric disinfectant and antiseptic, externally and in non-antibacterial medical gloves worn by hospital staff after typical patient-care activities in the mixed surgical and medical intensive care unit (ICU) environment.[41]

In addition, an in vitro antibacterial efficacy study was conducted by Leitgeb et al. on PHMB-coated nitrile gloves by measuring the number of bacteria on gloves semi-quantitatively.[42] The results showed that 100% of the non-antibacterial gloves had positive cultures, whereas only 43% of the antibacterial gloves had positive cultures. The antimicrobial gloves successfully reduced the glove-mediated contamination in 57% of the investigated clinical activities. This effect was proven by the reduced number of bacteria recovered from the test surface. The study proved the success of cross-contamination prevention by using PHMB-coated gloves.

Koburger et al. found that a strong interaction of PHMB with negatively charged phospholipids leads to a broad antimicrobial spectrum covering Gram-positive and Gram-negative bacteria, intracellular bacteria such as *Mycoplasma* spp. and *Chlamydia* spp., and other fungi (especially *Aspergillus* spp. and *Candida* spp.).[43] By contrast, Gillbert and Moore found that *Pseudomonas* spp., *Acinetobacter* spp., or other Gram-negative, non-fermenting bacilli such as *Alcaligenes* spp. are unsusceptible to PHMB.[44]

MAGNESIUM FLUORIDE NANOPARTICLES

Investigations on using microwave chemistry to synthesize nanoparticles (NPs) with antimicrobial and anti-biofilm activities were reported previouly.[45–49] The continuous sonochemically generated cavitation bubbles in water increase the temperature, pressure, and cooling rates that would drive the production of NPs. Lellouche et al. reported the aq-based synthesis of nanosized magnesium fluoride (MgF_2) NPs in ionic liquid by using sonochemistry.[43] These MgF_2-NPs were tested against two common bacterial pathogens, *E. coli* and *S. aureus*. The results revealed that MgF_2-NPs not only inhibited bacterial colonization but also effectively restricted biofilm formation for more than 7 d. Lellouche et al. asserted that the NPs could have penetrated the cell and disrupted the cell membrane potential; therefore, they enhanced DNA binding and lipid peroxidation.[48] The results also suggested that the increase in concentration of NPs prevented the growth of bacteria progressively in a dose-dependent manner. For example, *S. aureus* was eliminated at an NP concentration as low as 0.01 mg/mL, whereas *E. coli* required the highest concentration of 1.0 mg/mL to be completely inhibited; hence, *S. aureus* was more sensitive to the NPs than *E. coli*. These differences could be attributed to the nature of the cell membranes of Gram-positive and Gram-negative bacteria toward MgF_2-NPs.[49] The major differences are the presence of an outer membrane in Gram-negative bacteria and the thickness of the cell wall between the two groups of bacteria. The bacterial cell wall ranges from 20 to 80 nm in thickness for Gram-positive bacteria and between 1.5 and 10 nm in thickness for Gram-negative bacteria.[50] The authors also conducted a confirmatory test by re-exposing the *E. coli* to the highest concentration NPs. The results once again revealed that the re-exposed *E. coli* showed the same growth yield and sensitivity as the bacteria that were not pre-exposed to the NPs, indicating that the *E. coli* was not resistant to the NPs.

Lellouche et al. also reported the NPs of MgF_2-NPs were the active species in inhibiting bacterial growth and biofilm formation. This was proven by several control experiments wherein the two separate aq magnesium acetate and fluoride nitrate precursor salts were dissolved in water, resulting Mg^{2+}(aq) or F^{-}(aq) that did not cause a similar growth or biofilm inhibitory effect as those of the NPs of MgF_2-NPs tested on both *E. coli* and *S. aureus* biofilm formation.[48] These results

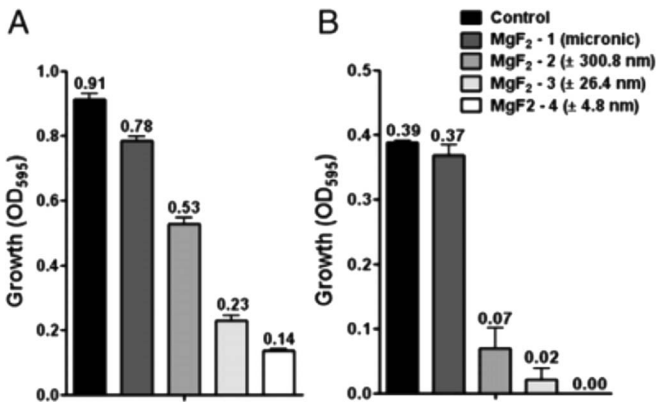

FIG. 1. — Bacterial growth yield against the concentration of MgF_2. Growth yield of (A) *E. coli* and (B) *S. aureus*.[45]

strongly suggest that the MgF_2-NPs and not the dissolved ions are responsible for the antimicrobial activity.

The size of NPs also played a role in bacterial aggregation at which the NPs size and the antimicrobial activity demonstrated a reverse correlation (Figure 1).[45] The results indicated that when the size of MgF_2 was 1 μm, 300.8 nm, 26.4 nm, and 4.8 nm, the respective growth yield of *E. coli* (Figure 1A) was 0.78, 0.53, 0.23, and 0.14, whereas the respective growth yield of *S. aureus* (Figure 1B) was 0.37, 0.07, 0.02, and 0.00. The authors asserted that small-sized NPs, particularly the nano-sized MgF_2, allowed the internalization of NPs via channels and pores, thus improving the penetration rate. The defined crystallographic structures and large surface-to-volume ratios in MgF_2-NPs increased the chemical surface-mediated reactivity and thus enhanced the antimicrobial activities of the NPs.[45]

*poly(methyl methacrylate)-N,N,N-trimethylated chitosan nps*Poly(methyl methacrylate)-*N*,*N*,*N*-trimethylated chitosan (PMMA-TMC) NPs are also reported to exhibit promising antimicrobial activities.[51–54] These NPs are prepared via mini-emulsion polymerization at neutral pH in which trimethylated chitosan, the simplest form of quaternized chitosan (QCh), is used as a polycationic stabilizer. It could increase the aq solubility as well as antimicrobial activity. Positively charged TMC was able to perform effective attachment to the negatively charged bacterial membrane permanently, resulting in the leakage of proteinaceous and intracellular components, and it eventually caused cell rupture and death.[54] Another study showed that TMC had better antibacterial activity than chitosan because it had a lower MIC and minimum bactericidal concentration.[55] The PMMA-TMC NPs showed antibacterial properties against *E. coli* and *S. aureus*. The bacteria showed no resistance to NPs, even after applying for seven successive cycles. At 3% PMMA-TMC latex solution, deposited NPs could not cover the entire film area. Hence, increasing TMC content in the PMMA-TMC solution might be able to improve the surface coverage of the film. The small-sizes PMMA-TMC NPs with high surface-to-volume ratio usually have a better reaction surface.[56,57]

Some studies have been conducted on the potential of replacing the inorganic lubricating powder with stabilized PMMA-TMC particles as a polymer coating layer by layer onto the sulfur-prevulcanized natural rubber (SPNR) film for glove applications.[58–61] These NPs were reported to form uniform coatings on the film via electrostatic force, increase the surface hardness and roughness, and reduce the surface friction. Interestingly, this coating technique was found to decrease the potential allergic or hypersensitivity reactions caused by the non-rubbers or

additives because there was no direct contact between the SPNR film and skin of a healthcare professional.[61–63]

ELECTROSPUN TRIMETHYLATED CHITOSAN-LOADED POLYVINYL ALCOHOL ULTRAFINE FIBERS

Trimethylated chitosan-loaded polyvinyl alcohol (TMC-PVAl) produced in the form of ultrafine fibers by using electrospinning techniques were also reported to be potential antimicrobial agents for glove applications.[64–69] The electrospinning techniques used high electrical voltages to charge the spinning solution in the syringe needle until the electrical force overcame the solution surface tension, forming the typical "Taylor cone."[64] This process promoted an interaction between TMC and the PVAl chains, which resulted in reduced intramolecular hydrogen bonds and formed ultrafine fibers.[63] The fibers were smoother and smaller in diameter when the voltage applied increased from 12 to 20 kV.[66] In addition, increased TMC concentration decreased the viscosity and increased the electrical conductivity of the spinning solution.

The antimicrobial properties of chemical-resistant nitrile gloves coated with the TMC-PVAl ultrafine fibers were investigated.[67] The coating improved antimicrobial properties of the gloves along with the surface coarseness and wettability. The efficacy of antimicrobial TMC-PVAl was tested against *P. aeruginosa*, *E. coli*, *A. baumannii*, and *C. albican*s. It was proven to be successful by the presence of zone inhibition, whereas no antimicrobial activity was found on the PVAl fiber–coated glove.[63] The antimicrobial properties of TMC-PVAl could be attributed to the linkage of polycationic TMC with the lipoteichoic acids of Gram-positive bacteria or with the lipopolysaccharide of Gram-negative bacteria. TMC competed with divalent metals such as magnesium and calcium ions on the cell wall, interfered the electrostatic interaction, broke the wall integrity, disturbed the membrane permeability, destabilized membrane, and eventually resulted in the loss of intracellular components.[68,69]

ANTIMICROBIAL MATERIALS WITH SUPERHYDROPHOBIC SURFACES FOR REDUCTION OF BACTERIAL ADHESION

Bacterial infections are largely attributed to the formation of biofilm, a protective film formed by a bacterial colony through the secretion of an extracellular matrix that contains water, polysaccharides, proteins, and DNA to protect the colony against antibiotic treatments, making it difficult to combat infections.[15,70] Wet surfaces often promote biofilm growth. As such, strategies on surface modification have become of interest to reduce bacterial adhesion and biofilm formation. One such approach is mimicking the natural superhydrophobic surfaces that have the property of low surface energy that can influence water repellency on the surface.[71] It has inspired academic and industrial fields to implement superhydrophobic surfaces as antibacterial surface coatings on medical gloves. The wetting behavior of liquid on a smooth and chemically homogenous surface is typically determined using Young's equation:

$$\cos\theta = \frac{\gamma_{sv} - \gamma_{sl}}{\gamma_{lv}}$$

where θ represents the contact angle, γ_{sv} is the surface tension between solid and vapor; γ_{sl} is the surface tension between solid and liquid, and γ_{lv} is the surface tension between liquid and vapor.[71,72] The diagram of a water drop on a smooth and chemically homogenous surface is illustrated in Figure 2.

Superhydrophobic surfaces favor water repulsion and possess droplet contact angles greater than 150°.[71–73] Heterogenous wetting is a phenomenon that commonly occurs on the superhydrophobic surface due to the entrapment of air between the liquid and solid surfaces,

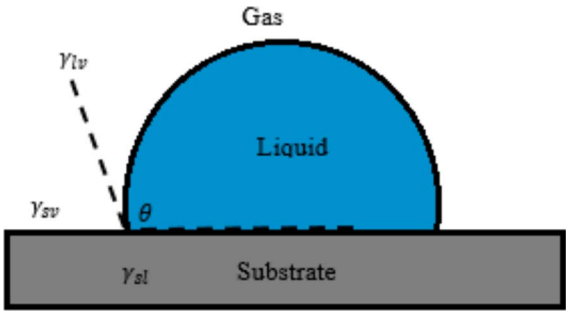

FIG. 2. — Young's equation diagram associated with the contact angle.

which could reduce the adhesion force of droplets to the solid surface. Similarly, this unique water repellency of the superhydrophobic surface also applies in the reduction of bacterial adhesion, hence enabling easy elimination of bacterial cells.

The type of superhydrophobic surfaces differs in terms of application and outcome. For example, the antibacterial fluorinated silica colloid superhydrophobic surface reduced the amount of *S. aureus* and *P. aeruginosa* by 99 and 98.2%.[74] Other examples include antibacterial silver-coated NPs superhydrophobic surface that killed 80% of bacteria (*Lactobacillus paracasei*, *Serratia marcescensi*, and *P. fluorescens*), and superhydrophobic surface cast by styrene-*b*-(ethylene-*co*-bytylene)-*b*-styrene (SEBS) had antibacterial properties against *E. coli*.[75,76] Moreover, the submicrometer- and micrometer-patterned polyurethane biomaterial inhibited the aggregation of *S. epidermis*; *S. aureus* and *E. coli* were successfully reduced by 99.9 and 99.4% on the nanoporous and nanopillared aluminum surface.[77,78] In addition, the fabricated zinc oxide fabrics caused the bacterium *K. pneumoniae* to develop a zone of inhibition; the superhydrophobic titania nanotube had minimal bacteria growth even after 24 h.[79,80] The types of superhydrophobic surfaces and their applications are summarized in Table II.

A study conducted on textiles hydrophobized with hexadecyltrimethoxysilane and films coated with silver NPs showed superhydrophobicity with a contact angle of 151.5 ± 1.4°.[81] Privett et al. conducted a similar study to compare the superhydrophobicity between silica colloid–modified xerogels and silica colloid or xerogel alone.[75] They found that silica colloids doped into xerogels resulted in the superhydrophobic interface of 167.7 ± 1.8° that was not attainable with either silica colloids or xerogels alone. Another characterization method was the determination of water droplets bouncing on the surface to characterize the magnitude of surface hydrophobicity. This technique uses water bouncing to determine the hydrophobicity of a surface, with a relationship established between water contact angle and number of bounces, and it is dependent on the surface's microstructure. In fact, a rounded microstructure surface was denoted as superhydrophobic if the water bounced when the contact angles were equal to or greater than 151°.[82] Crick and Parkin studied the behavior of water droplets when dropped at the height of 20 mm at different contact angles of 95, 151, and 175°.[83] They found that the maximum number of bounces occurred at contact angle of 175° (Figure 3). This unique water repellency experiment was used to predict the potential reduction of bacterial adhesion on the tested superhydrophobic surfaces.

EFFECT OF MATERIAL PROPERTIES ON BACTERIAL ADHESION

Studies are underway on surface modification techniques such as antibacterial coatings, chemical modifications, and surface grafting that have been applied on material surfaces to impede

TABLE II
APPLICATIONS OF FABRICATED SUPERHYDROPHOBIC SURFACES

Type	Application	Technique	Bacterial strain(s)	Outcome	References
Fluorinated silica colloid superhydrophobic surface	Antibacterial	A synthesized mixture of nanostructured fluorinated silica colloids, fluoroalkoxysilane, and backbone silane	*S. aureus*, *P. aeruginosa*	Reduction of *S. aureus* by 99.0% and *P. aeruginosa* by 98.2%	Privett et al. (2011)[75]
Silver-coated NPs superhydrophobic surface	Antibacterial	Silver NPs precipitated onto superhydrophobic surfaces fabricated with ceramic nanotopography and flurosilane hydrophobication by spin coating	*L. paracasei*, *S. marcescensi*, *P. fluorescens*	88% of bacteria were killed	Heinonen et al. (2013)[76]
Superhydrophobic surface casted by SEBS	Antibacterial, antifouling	SEBS dissolved in solvent mixtures of xylene and decanol	*E. coli*	No *E. coli* found on the superhydrophobic surface of SEBS, whereas there were many *E. coli* cells on the original SEBS	Ye et al. (2014)[77]
Submicrometer and micrometer patterned polyurethane biomaterial	Antibacterial	Polyurethane urea textured with an ordered array of submicrometer- and micrometer-sized patterns	*S. epidermis*	Inhibition of *S. epidermis* adhesion	Xu and Siedlecki (2014)[78]
Nanoporous and nanopillared aluminium surface	Antibacterial	Electropolished specimens submerged in oxalic acid to form nano-porous aluminium surface; nanoporous surface specimens etched in H_3PO_4	*S. aureus*, *E. coli*	Reduction of *S. aureus* by 99.9% and *E. coli* by 99.4%	Hizal et al. (2017)[79]

TABLE II
CONTINUED

Type	Application	Technique	Bacterial strain(s)	Outcome	References
Fabricated zinc oxide fabrics	Antibacterial, self-cleaning	Zinc oxide NPs loaded on cotton fabrics by spin coating	*Salmonella* Typhimurium, *K. pneumoniae*, *E. coli*, *Bacillus subtilis*	Largest zone of inhibition on *K. pneumonia* compared with non-coated fabric and standard reference antibiotic, gentamicin	Shaban et al. (2018)[80]
Superhydrophobic titania nanotube	Antibacterial	Titanium sheets fabricated to titania nanotube arrays by anodization	*P. aeruginosa*, *S. aureus*	Minimal bacterial attachment after 24 h and no biofilm was formed	Bartlet et al. (2018)[81]

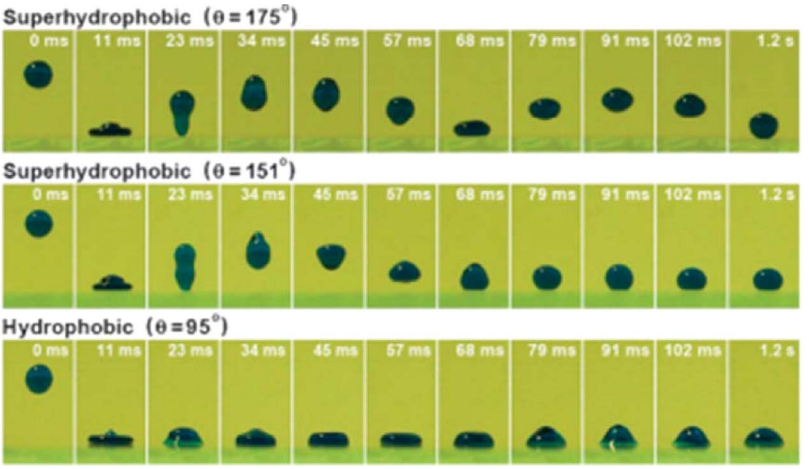

FIG. 3. — Images of a water droplet bouncing at a contact angle of 95, 151, and 175°.[83]

bacterial growth. These techniques modify the surface charge, surface energy, wettability, surface topography, and other techniques, making it possible to kill bacteria.

SURFACE CHARGE

Many particles obtain surface electric charges in the aq environment as it is responsible for the distribution of ions in the surrounding interfacial region, which often leads to an increase in the concentration of counterions close to the surface.[71] Like most natural surfaces, bacteria in aq suspension carry a net negative charge, especially during the early stationary phase of cell growth.[83,84] Because of electric double layer repulsion, bacterial adhesion is generally reduced upon contact with these like-charged surfaces and is more favorable toward the oppositely charged surfaces. For example, a study showed that the adherence of bacteria was reduced on negatively charged acrylic acid, whereas bacterial adhesion increased on a positively charged dimethylaminoethyl methacrylate surface.[83]

SURFACE ENERGY

Intermolecular and interfacial attractive forces are influenced by surface free energy. It was asserted that hydrophobic material with lower surface energy could decrease bacterial adhesion for easier cleaning.[71] For example, a study showed that a hydrophobic material with a surface energy that ranged between 20 and 30 mNm^{-1} had potential in reducing bacterial adhesion.[85] In another study, results showed that minimal *E. coli* adhesion was achieved on the Ni-P-polytetrafluroethylene coatings with free surface energy ranging from 21 to 29 mNm^{-1}.[71,86]

WETTABILITY

Hydrophobicity and hydrophilicity of surface materials have been studied to determine their influences on bacterial adhesion, known as wettability. Water contact angle measurements are commonly used to investigate the hydrophobicity and hydrophilicity of material surfaces.[87] Reports indicate that bacterial cells adhering onto polymer surfaces present a moderate wettability when the contact angle of water falls from 40 to 70°.[71,88] A study reported that *S. aureus* adhesion on

methyl-terminated self-assembled monolayers (SAMs) was the highest, followed by carboxylic-terminated SAMs and hydroxylic-terminated SAMs. It was lowest on SAMs terminated with ethylene oxide–bearing surfaces (EG_3).[83] This could be due to the property of EG_3 that undergoes water nucleation to provide a stable interfacial water layer that prevents the bacteria–surface interaction.[89] Moreover, some material may alter its hydrophilicity when exposed to the environment for the long term. For example, $Ti(OH)_4$, which is hydrophilic and found in titania nanotubes fabricated by anodization, may experience oxidation and form a more stable product, TiO_2, that is more hydrophobic.[90]

SURFACE TOPOGRAPHY

The advent micro- or nano-fabrication topography of a material surface plays a vital role in bacterial attachment.[87,91,92] For example, a study showed that *S. aureus* cells were retained in 0.5-μm pits, *P. aeruginosa* cells were retained in 1-μm pits, and some daughter *C. albicans* cells were retained in 2-μm pits.[93] In another study, *S*. aureus exhibited a twofold increase compared with the poorly colonized *P. aeruginosa* on titanium thin film surfaces.[92] This could be due to the different membrane rigidity of bacterial cells, a deciding factors for cell morphology.[92,94]

OTHER MATERIAL PROPERTIES

Apart from the common properties mentioned above, other material properties that could affect the interaction between bacteria and surfaces include modification of surface coating and surface roughness.[83,87] A few studies have suggested that the surface should be altered with peptide and nonsteroidal anti-inflammatory coatings to impede bacterial adhesion.[83,95,96] Another study showed bacterial adhesion and biofilm formation on polymeric surfaces instead of ultra-smooth surfaces. This could be due to the irregularities on the polymeric surfaces that promote a greater surface area for bacterial colonies to grow.[71,83]

COMMERCIALLY AVAILABLE ANTIMICROBIAL GLOVES

Antimicrobial gloves for surgical, examination, and food processing purposes have been marketed to prevent the transmission of microbes. Ansell became the first company to successfully launch the surgical and examination antimicrobial glove called GAMMEX® Latex Powder-Free with AMT by using antimicrobial approaches.[97] It is a tri-layer glove consisting of an inner mechanical layer, a middle layer that contains the drop-like antimicrobial agent chlorhexidine gluconate, and an anti-stick overcoat outer layer. A microscopic image of GAMMEX Powder-Free with AMT is illustrated in Figure 4.

The inner surface of the sterilized natural rubber latex (NRL) glove was coated with the antimicrobial coating chlorohexidine gluconate (Figure 4A) to provide a protective layer to the user in case of glove breaching.[97] The antimicrobial agent releases slowly to maintain a microbe-free environment.[18] This release is reflected from the results showing that the glove had the ability to kill more than 99% of hepatitis C virus surrogate virus and HIV-1 strain MN in just 1 min. In addition, the glove was capable of killing up to 99.999% of clinically relevant bacteria categorized as Gram negative (*Bacteroides fragilis*, *E. coli*, *K. oxytoca*, and *Proteus mirabilis*) and Gram positive (*A. baumannii* and *E. faecium*), thereby proving that the gloves indeed have antimicrobial properties. Furthermore, there was an additional thin layer (Figure 4B) on the antimicrobial coating made up of an anti-stick overcoat that could prevent the stickiness of the inner surface and ease donning.[97] The authors also tested the glove on human skin following the Standard Test Method for Human Repeat Insult Patch Testing for Medical Gloves, ASTM Standard D 6355-07, by comparing it against a

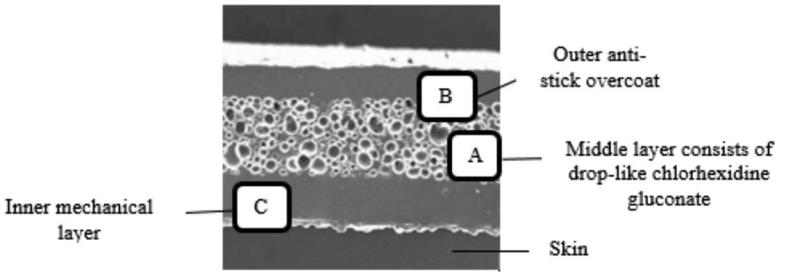

FIG. 4. — Illustration of trilayer GAMMEX Powder-Free with AMT antimicrobial glove.[97]

deionized water control. The results showed that the Gammex Powder-Free gloves were less irritating compared with deionized water. However, these antimicrobial gloves could only protect the wearer from microbe infection should breaching occur; they did not necessarily prevent the transmission of pathogens.

Next, Ansell invented an antimicrobial glove called Gammex Nitrile Antibacterial, a non-sterile nitrile glove coated with the antibacterial coating with a formulation containing 0.5–3% PHMB on the exterior surface; this glove was designed by a group of medical researchers from Ansell, Malaysia.[98] This invention is mainly targeted to healthcare personnel. The antibacterial properties of the gloves were determined against four clinically relevant Gram-positive bacteria, namely *E. faecalis*, *E. coli*, *S. aureus*, and *S. epidermidis*, and four Gram-negative bacteria, namely *A. baumannii*, *K. pneumoniae*, *P. aeruginosa*, and *S. marcescens*. Six of the eight bacterial species showed a net log reduction of more than 4, ~99.99% within exposure time of 1 min; *P. aeruginosa* and *S. marcescens* took longer to reach more than 4. The results (Table III) show that Gammex Nitrile Antibacterial glove is fast acting in terms of its antibacterial properties; thus, it is effective in infection control.

The authors further conducted a study according to the ASTM Draft method to evaluate the bacterial contact transfer between the antibacterial-treated examination gloves and the contact surfaces compared with a control glove without antibacterial coating. The results showed more than 4-log reduction for the antimicrobial gloves compared with the control. Unlike the NRL gloves, nitrile gloves can protect the wearer from latex allergy, giving an additional highlight to the examination of antimicrobial gloves.[99] Although the treated gloves have antimicrobial activities, the log reduction value is insufficient to reflect the effect of antimicrobial gloves in the presence of a high amount of microorganisms because the risk of infection to the patient during a surgical procedure may still be there even with bioburden as low as 100 colony-forming units (CFUs).[100–102]

Another game-changing technology is the use of photosensitizer as an active ingredient coated on the non-leaching antimicrobial gloves invented by Hartalega.[103] Upon exposure to light, the photosensitizer becomes activated and releases reactive oxygen species, mainly singlet oxygen. This singlet oxygen then oxidizes the bacterial proteins and lipids, thereby causing the death of the microbes. Depending on its killing mechanism, the development of this antimicrobial glove plays a crucial role in hospital settings, especially to healthcare workers in reducing the spread of HAIs. The bacterial efficacy of Hartalega's antimicrobial glove was tested according to the ASTM Standard D 7907 antimicrobial test method. It is usually used for the identification of bactericidal activity on the surface of medical examination gloves.[104] According to this standard, the outside or inner layer of the glove surface can be tested for its antimicrobial activities against an initial concertation of 10^8 CFU/mL bacteria. There are four specific calibration bacterial strains used in ASTM Standard D 7907: *S. aureus*, *E. faecalis*, *P. aeruginosa*, and *K. pneumoniae*.[104] Bacteria of VRE and MRSA are

TABLE III
ANTIBACTERIAL PROPERTY OF GAMMEX NITRILE ANTIBACTERIAL GLOVE[a]

Species	Log reduction			
	1 min	2 min	5 min	10 min
Gram-negative bacteria				
A. baumannii	>6	>6	>6	>6
K. pneumoniae	6.0	>6	>6	5.9
P. aeruginosa	0.7	1.6	3.8	4.4
S. marcescens	1.4	3.1	>6	5.9
Gram-positive bacteria				
E. faecalis	>6	>6	>6	>5.9
E. coli	4.4	>6	>6	>6
S. aureus	>6	>6	>6	>6
S. epidermis	>6	>6	>6	>6

[a] Adapted from "Table 2: In Vitro kill-rate results for Gammex® Nitrile Antibacterial Glove" in *Latex & Synthetic Polymer Dispersions*.[98]

also included in the test. Notably, Hartalega's antimicrobial glove is effective in killing these antibiotic-resistant microbes. The antibacterial test conducted by the authors showed an effective killing efficiency of at least 99.946% in just a short span of 5 min, and efficacy could increase to 99.999% later. The potential antimicrobial activities of Hartalega's antimicrobial glove against fungi and viruses, which are commonly found in clinical environments, remain unknown.

Based on the current literature, there is a limited choice of antimicrobial glove for application in hospital and surgical settings, and this limitation has driven the microbiologists' interest to investigate, develop, or improve the current limitations of the antimicrobial glove to reduce the transmission of pathogens or microorganisms during an examination or surgical procedure.

CURRENT LIMITATIONS AND FUTURE ASPECTS OF ANTIMICROBIAL GLOVE DEVELOPMENT

As mentioned, biocides could be impregnated or covalently deposited on a medical or surgical glove to reduce HAIs via pathogen cross-transmission. In addition, a protective antimicrobial glove could also be applied to prevent the spread of microorganisms responsible for laboratory-acquired infections.[105–107] The incidence of laboratory-acquired infections is not rare and has been reported previously.[107–111] Although gloving is beneficial, some users may experience allergic reactions. A few studies related to contact dermatitis, a condition frequently exhibited by sensitive healthcare workers after wearing surgical gloves, have been published.[112,113] For example, chlorhexidine or a mixture of chlorhexidine added into the polymer matrix (such as natural rubber) may induce a hypersensitivity reaction, as summarized by Calogiuri et al.[114] In addition, an antibacterial-coated glove containing quaternary ammonium salts, especially benzalkonium chloride, may pose a risk of allergic contact dermatitis (ACD) to certain individuals. Studies examining the cause of ACD in users after being exposed to quaternary ammonium salts have been reported previously.[113,115–118] The emergence of resistance toward quaternary ammonium salts or chlorhexidine has also been documented previously.[119–124] For example, *L. monocytogenes* possesses efflux pumps to confer its resistance against quaternary ammonium salts. This efflux-based system is also used by *Staphylococcus* spp. in mediating resistance to quaternary ammonium salts.[125] Carson et al.

reported that several staphylococci detected from non-clinical environments showed decreased susceptibility to benzalkonium chloride.[125] Importantly, some Gram-negative bacteria were detected to be chlorhexidine-resistant strains.[126,127] Because of these problems, research groups have been interested in the development of gloves coated with PHMB and the characteristics of PHMB.[128–130] Literature supporting the use of PMMA NPs, such as PMMA-chitosan, has also expanded rapidly, as evidenced by both reviews and research data.[51,60,131–134] Overall, this is because of their low cytotoxicity and because they may be less likely to develop resistance. In addition, they show a high antimicrobial activity against a broad range of bacteria. However, most of the antimicrobial effects were tested by using vegetative forms of bacteria; thus, relevant data for their biocidal effects or anti-adherence properties against endospores remain scarce. The cross-contamination of endospores could also contribute to antimicrobial resistance by widely disseminating the resistance genes.[135,136] Furthermore, endospores usually sustain longer than vegetative bacteria under harsh environmental conditions. Hence, there is a potential risk for glove contamination in healthcare workers who have touched an infected patient (particularly a *C. difficile*–infected individual) or an environmental surface colonized by endospores.[137–139] Moreover, there are many endospore-forming bacteria that could be found from non-clinical environments. For example, high levels of genotypic diversity of *Clostridium* spp. and *Bacillus* spp. endospores are found on farms, whereas some bacterial species are found in farm animals, and they all carry antimicrobial resistance genes.[140–143] Thus, the implementation of gloving merely focusing on the healthcare environment is insufficient to globally minimize the spread of pathogens that harbor antibiotic-resistant genes. Of note, there is an emergence of antimicrobial-resistant strains originated from poultry to the human population. For example, colistin-resistant genes (*mcr-1*) that originated from livestock were found in hospitals.[144–146] A study also demonstrated that MRSA could spread between animals and humans and that the MRSA strain isolated from the pig and pig handler could be the same clone of MRSA.[147] Consequently, it is suggested to emphasize the guidelines or policies for poultry workers to use appropriate antimicrobial glove use. This adherence may lower the risks of microbial cross-transmission of antibiotic-resistant strains from animals to humans.

Glove perforation and sharp injuries are some other common occupational hazards for healthcare workers, especially during orthopedic surgical procedures.[148] The single-layer latex glove can be as thin as 0.25 mm, and with repetitive handling of power tools, exposure to sharp bones, and penetration of deep cavities is prone to perforations in orthopedic surgery.[149] In many cases, the glove may be punctured in such a manner that the perforation is not perceived by the wearer. Previous documentation estimated that double gloving can minimize the risk of intraoperative blood exposure and be considered as an effective "barrier enhancement" strategy, particularly when the perforation is due to a sharp object such as a suture needle.[8] Regrettably, tiny punctures on the inner glove are observed even when double gloves are used.[150] A recent review mentioned that glove perforation happens in all surgical procedures, ranging from 19% in gynecologic surgeries to 78% in emergent surgical procedures.[151,152] Because of the unnoticed glove perforation, routine glove changing within a 2-h cycle has been practiced by some healthcare workers.[153]

Apart from glove perforation, there is a high possibility that the penetration of antimicrobial substances into the microorganism is hindered in the presence of biofilms. Biofilms are functionally complex structures with varying distributions of cells and cell aggregates in an extracellular polymeric substance matrix that serves as a protective medium for the growth of microorganisms adhering to a solid surface.[154] Cells grown in biofilms express different properties than planktonic cells, with the main difference being the increased microbial resistance to antimicrobial agents commonly used in clinical practice.[155] Despite the scientifically proven antimicrobial activity of chlorhexidine, microorganisms contained in a biofilm structure also become resistant to this

antimicrobial disinfectant. Theoretically, chlorhexidine is not able to act against the microorganism in biofilms, because it cannot transpose the molecules in the biofilm to reach biofilm bacterial wall, because chlorhexidine's mode of action involves disruption of the cell membrane.[156] However, chlorhexidine was proven to be effective against *S. aureus* and *C. albicans* in biofilms status.[14] Thus, further research is needed to investigate biofilm compositions, the mechanism of how chlorhexidine and other antimicrobial agents penetrate the cell wall, and the identification of combination biocides to develop a synergistic mechanism of biofilm inhibition to eliminate the microorganisms present in the biofilm.

As mentioned, the antimicrobial glove serves as a functional barrier to prevent the transmission of microorganisms between patients and healthcare workers or from a contaminated object to patients or healthcare workers. Unfortunately, existing studies did not further investigate the risk of microorganisms transferred from a patient to antimicrobial gloves to another patient or a surface such as surgical devices or implants. Although transference of microorganisms from a test surface back to a living subject is considered an unethical and immoral act, the transfer of microorganisms from test surfaces to other surfaces has been determined in controlled experimental studies. For example, Montville and Schaffner conducted laboratory experiments to determine inoculum size as a possible factor influencing bacterial percent transfer rates.[157] Contrary to expectations, their study showed that the rate of bacterial transfer was slower when the inoculum size on the source was increased compared with when the inoculum size on the source was lower. This showed that inoculum size could have a significant effect on measured bacterial cross-contamination rates between surfaces. Their findings were supported by their study on a meta-analysis of the published literature on the effectiveness of antimicrobial soaps.[158,159] Their analysis showed that there was a clear, statistically significant connection between inoculum size and percent transfer for all cross-contamination activities, provided the results were well above the detection limit, and preferably with inoculation methods that mimic natural contamination. This odd phenomenon has posed significant implications for a researcher to account for the effect of inoculum size as a possible factor influencing the percent transfer rate in determining cross-contamination rates.[155,158,159] Other factors such as surface topography and moisture content of the glove must also be taken into consideration to determine the bacterial transfer rates between a patient and an object surface and from object-surface to object-surface.

More fundamental experiments must be designed carefully to evaluate the antimicrobial activity of newly developed antimicrobial agents and anti-adhesion materials. Published data should include descriptions of the following: (1) initial microbial loadings or concentrations; (2) log reductions (or percent killed); (3) how long it takes for reductions to occur; (4) growth and recovery media (if applicable); (5) detection or test method (e.g., liquid or surface disinfection, MIC); and (6) strain of bacteria used, because different strains of the same species may have orders-of-magnitude different susceptibilities. These details are critical to accurately determine the antimicrobial effectiveness of agents and materials.

CONCLUSION

Antimicrobial gloves need to be designed carefully to accommodate the needs of patients and healthcare workers as an effective barrier to cross-contamination. The fabrication of novel antimicrobial gloves impregnated with various antimicrobial agents was critically reviewed herein. Chlorhexidine gluconate has been widely used as a common antimicrobial agent. The lack of efficacy of this chemical in inhibiting biofilm formation of bacteria has stimulated the development of some innovative mixtures of chlorhexidine and other antiseptics. The fabrication of novel antimicrobial gloves impregnated with chlorhexidine mixtures such as chlorhexidine and quaternary ammonium salts, gardine (brilliant green dye and chlorhexidine), and gendine (gentian

violet and chlorhexidine) has also been reported. Furthermore, some innovative antimicrobial agents such as water-soluble gas chlorine dioxide, polymeric disinfectant poly(hexamethylene biguanide) hydrochloride (PHMB), aq-based magnesium fluoride nanoparticles (MgF_2-NPs), positively charged poly(methyl methacrylate)-*N*,*N*,*N*-trimethylated chitosan (PMMA-TMC) NPs, and electrospun trimethylated chitosan-loaded polyvinyl alcohol (TMC-PVAl) were comprehensively reviewed for their potential as antimicrobial agents for glove applications. The principles of killing microbes must be understood to effectively select antimicrobial agents in designing antimicrobial gloves.

Recent advances on surface modification techniques such as antibacterial coatings, chemical modifications, and surface grafting applied on material surfaces were also summarized herein. The applications of fabricated superhydrophobic surfaces as antibacterial surface coatings on medical gloves were discussed. Further discussion on the techniques used to modify the surface charge, surface energy, wettability, and surface topography of the glove materials and their potential to kill bacteria or prevent bacterial adhesion were given.

The chemicals and coating techniques used in fabricating commercially available antimicrobial gloves were briefly introduced. Current limitations on antimicrobial glove development were outlined. Studies on allergenic contact dermatitis exhibited by sensitive healthcare workers after wearing surgical gloves coated with antimicrobial agents were provided. Issues on the susceptibility of some common bacterial strain toward antimicrobial resistance toward antimicrobial agents were highlighted. Future aspects of antimicrobial development should cover the development of a customized or personalized antimicrobial glove for different surgical procedures and medical examinations. Researchers also should design experiments carefully to take into account factors such as inoculum size, surface topography, and moisture content of gloves in determining the cross-contamination rates between patient and object surface and object-surface to object-surface.

ACKNOWLEDGEMENTS

This work was supported by Malaysia Rubber Board (grant S17STL0663) and International Medical University (grant R 210/2018).

REFERENCES

[1]R. M. Klevens, J. R. Edwards, C. L. Richards, T. C. Horan, R. P. Gaynes, D. A. Pollock, and D. M. Cardo, *Public Health Rep*. **122**, 160 (2007).

[2]N.-O. Hübner, A.-M. Goerdt, N. Stanislawski, O. Assadian, and C.-D. Heidecke, *BMC Infect. Dis*. **10**, 192 (2010).

[3]J. Leitgeb, R. Schuster, B. N. Yee, P. F. Chee, J.-C. Harnoss, P. Starzengruber, M. Schäffer, and O. Assadian, *BMC Surg*. **15**, 81 (2015).

[4]J. A. Al-Tawfiq and P. A. Tambyah, *J. Inf. Public Health* **7**, 339 (2014).

[5]D. Pittet, S. Hugonnet, S. Harbath, P. Mourouga, V. Sauvan, S. Touveneau, and T. V. Perneger, *Lancet* **356**, 1307 (2000).

[6]E. Girou, S. H. Chai, F. Oppein, P. Legrand, D. Ducellier, F. Cizeau, and C. Brun-Buisson, *J. Hosp. Infect*. **57**, 162 (2004).

[7]E. S. McBryde, L. C. Bradley, M. Whitby, and D. L. McElwain, *J. Hosp. Infect*. **58**, 104 (2004).

[8]C. D. Salgado, *Am. J. Infect. Control* **36**, S175.e5 (2008).

[9]E. Yip and P. Cacioli, *J. Allergy Clin. Immunol*. **110**, S3 (2002).

[10]J. Tanner and H. Parkinson, *Cochrane Database Syst Rev*. **19**, CD003087 (2009).

[11]D. E. Fry, W. E. Harris, E. N. Kohnke, and C. L. Twomey, *J. Am. Coll. Surg*. **210**, 325 (2010).

[12]M. L. Hemani and H. Lepor, *Rev. Urol*. **11**, 190 (2009).

[13]S. M. Weber, C. A. Hargunani, and M. K. Wax, *Head Neck J. Sci. Spec*. **28**, 649 (2006).

[14]P. C. Bonez, C. F. Dos Santos Alves, T. V. Dalmolin, V. A. Agertt, C. R. Mizdal, C. Flores Vda, J. B. Marques, R. C. Santos, and M. M. Anraku de Campos, *Am. J. Infect. Control* **41**, e119 (2013).

[15]F. J. Sun, F. Qu, Y. Ling, P. Mao, P. Xia, H. P. Chen, and D. S. Zhou, *Future Microbiol*. **8**, 877 (2013).

[16]K. Toté, T. Horemans, D. Vanden Berghe, L. Maes, and P. Cos, *Appl. Environ. Microbiol*. **76**, 3135 (2010).

[17]H. Lamfon, S. R. Porter, M. McCullough, and J. Pratten, *J. Antimicrob. Chemother*. **53**, 383 (2004).

[18]G. Daeschlein, A. Kramer, A. Arnold, A. Ladwig, G. R. Seabrook, and G. E. Edmiston, Jr., *Am. J. Infect. Control* **39**, 98 (2011).

[19]O. Assadian, A. Kramer, K. Ouriel, M. Suchomel, M.-L. McLaws, M. Rottman, D. Leaper, and A. Assadian, *Surg. Infect. (Larchmt)* **15**, 43 (2014).

[20]M. Simões, M. O. Pereira, and M. J. Vieira, *Water Res*. **39**, 5142 (2005).

[21]C. Ferreira, A. M. Pereira, M. C. Pereira, L. F. Melo, and M. Simões, *J. Antimicrob. Chemother*. **66**, 1036 (2011).

[22]R. J. Lambert, G. W. Hanlon, and S. P. Denyer, *J. Appl. Microbiol*. **96**, 244 (2004).

[23]R. Krikorian, A. Lozach-Perlant, A. Ferrier-Rembert, P. Hoerner, P. Sonntag, D. Garin, and J. M. Crance, *J. Hosp. Infect*. **66**, 339 (2007).

[24]R. A. Reitzel, T. L. Dvorak, R. Y. Hachem, X. Fang, Y. Jiang, and I. Raad, *Am. J. Infect. Control* **37**, 294 (2009).

[25]R. Reitzel, J. Rosenblatt, Y. Jiang, R. Hachem, and I. Raad, *Am. J. Infect. Control* **42**, 55 (2014).

[26]A. M. Maley and J. L. Arbiser, *Exp. Dermatol*. **22**, 775 (2013).

[27]P. Bakker, H. Van Doorne, V. Gooskens, and N. F. Wieringa, *Int. J. Dermatol*. **31**, 210 (1992).

[28]S. Mani and R. N. Bharagava, *Rev. Environ. Contam. Toxicol*. **237**, 71 (2016).

[29]G. Chaiban, H. Hanna, T. Dvorak, and I. Raad, *J. Antimicrob. Chemother*. **55**, 51 (2005).

[30]H. Hanna, P. Bahna, R. Reitzel, T. Dvorak, G. Chaiban, R. Hachem, and I. Raad, *Antimicrob. Agents Chemother*. **50**, 3283 (2006).

[31]R. Hachem, R. Reitzel, A. Borne, Y. Jiang, P. Tingkey, R. Uthamanthil, J. Chandra, M. Ghannoum, and I. Raad, *Antimicrob. Agents Chemother*. **53**, 5145 (2009).

[32]M. Barza, *Clin. Infect. Dis*. **38**, 857 (2004).

[33]S. T. Wellinghoff, J. J. Kampa, S. A. Barenberg, P. N. Gray, and M. D. Lelah, U.S. Patent 6,277,408 B1 (to Southwest Research Institute and Bernard Technologies, Inc.), August 21, 2001.

[34]S. T. Wellinghoff, J. J. Kampa, S. A. Barenberg, P. N. Gray, and M. D. Lelah, U.S. Patent 6,605,304 B1 (to Bernard Technologies, Inc. and Southwest Research Institute), August 12, 2003.

[35]S. T. Wellinghoff, J. J. Kampa, M. D. Leah, S. A. Barenberg, P. N. Gray, and H. Dixon, U.S. Patent 7,273,567 B1 (to MicroActive Corp.), September 25, 2007.

[36]S. B. Young and P. Setlow, *J. Appl. Microbiol*. **95**, 54 (2003).

[37]C. I. Noss, F. S. Hauchman, and V. P. Olivieri, *Water Res*. **20**, 351 (1986).

[38]F. S. Hauchman, C. I. Noss, and V. P. Olivieri, *Water Res*. **20**, 357 (1986).

[39]N. C. Burton, A. Adhikari, Y. Iossifova, S. A. Grinshpun, and T. Reponen, *J. Air Waste Manag Assoc*. **58**, 647 (2008).

[40]Lenntech. "Disinfectants Chlorine Dioxide," 2021, https://www.lenntech.com/processes/disinfection/chemical/disinfectants-chlorine-dioxide.htm#ixzz6Ez4RIem6. Accessed January 2, 2020.

[41]M. K. Bador, V. Rai, M. Y. Yusof, W. K. Kwong, and O. Assadian, *J. Hosp. Infect*. **90**, 248 (2015).

[42]L. Leitgeb, R. Schuster, A.-H. Eng, B.-N. Yee, Y.-P. Teh, V. Dosch, and O. Assadian, *Antimicrob. Resist. Infect. Control* **2**, 27 (2013).

[43]T. Koburger, N. O. Hübner, M. Braun, J. Siebert, and A. Kramer, *J. Antimicrob. Chemother*. **65**, 1712 (2010).

[44]P. Gillbert and L. E. Moore, *J. Appl. Microbiol*. **99**, 703 (2005).

[45]J. Lellouche, A. Friedman, J.-P. Lellouche, A. Gedanken, and E. Banin, *Nanomedicine* **8**, 702 (2012).

[46]A. Gedanken, *Chem. Eur. J*. **14**, 3840 (2008).

[47]J. H. Bang and K. S. Susclick, *Adv. Mater.* **22**, 1039 (2010).

[48]J. Lellouche, E. Kahana, S. Elias, A. Gedanken, and E. Banin, *Biomaterials* **30**, 5969 (2009).

[49]A. L. Neal, *Ecotoxicology* **17**, 362 (2008).

[50]A. Mai-Prochnow, M. Clauson, J. Hong, and A. B. Murphy, *Sci. Rep.* **6**, 38610 (2016).

[51]D. R. Bhumkar, H. M. Joshi, M. Sastry, and V. B. Pokharkar, *Pharm. Res.* **24**, 1415 (2007).

[52]N. Kanjanathaworn, C. Kaewsaneha, D. Polpanich, K. Jangpatarapongsa, and P. Tangboriboonrat, *Polym. Polym. Compos.* **20**, 197 (2012).

[53]E. I. Rabea, M. E. Badawy, C. V. Stevens, G. Smagghe, and W. Steurbaut, *Biomacaromolecules* **4**, 1457 (2003).

[54]N. Vallapa, O. Wiarachai, N. Thongchul, J. Pan, V. Tangpasuthadol, S. Kiatkamjornwong, and V. P. Hoven, *Carbohyd. Polym.* **83**, 868 (2011).

[55]T. Xu, M. Xin, M. C. Li, H. L. Huang, and S. Zhou, *Carbohyd. Polym.* **81**, 931 (2010).

[56]W. Sun, W. Tian, Y. Zhang, J. He, S. Mao, and L. Fang, *Nanomedicine* **8**, 460 (2012).

[57]M. N. J. Haas, Ravi Kumar, G. Borchard, U. Bakowsky, and C. M. Lehr, *AAPS PharmSciTech.* **6**, E22 (2005).

[58]W. Anancharungsuk, W. Taweepreda, S. Wirasate, R. Thonggoom, and P. Tangboriboonrat, *J. Appl. Polym. Sci.* **115**, 3680 (2009).

[59]A. Sruanganurak, K. Sanguansap, and P. Tangboriboonrat, *Colloids Surf. A Physicochem. Eng. Asp.* **289**, 110 (2006).

[60]A. Sruanganurak and P. Tangboriboonrat, *Colloids Surf. A Physicochem. Eng. Asp.* **301**, 147 (2007).

[61]W. Anancharungsuk, D. Polpanich, K. Jangpatarapongsa, and P. Tangboriboonrat, *Colloids Surf. B Biointerfaces* **78**, 328 (2010).

[62]F. W. Perrella and A. A. Gaspari, *Methods* **27**, 77 (2002).

[63]M. Wu, J. Mclntosh, and J. Liu, *J. Occup. Health* **58**, 138 (2016).

[64]T. Vongsetskul, P. Wongsomboon, P. Sunintaboon, S. Tantimavanich, and P. Tangboriboonrat, *Polym. Bull.* **72**, 2285 (2015).

[65]K. N. Kongtogiannopoulos, A. N. Assimopoulou, I. Tsivintzelis, C. Panayiotou, and V. P. Papageorgiou, *Int. J. Pharm.* **409**, 216 (2011).

[66]B. L. Fletcher, T. E. McKnight, J. D. Fowlkes, D. P. Allison, M. L. Simpson, and M. J. Doktycz, *Synth. Met.* **157**, 282 (2007).

[67]V. Beachley and X. J. Wen, *Mater. Sci. Eng. C* **29**, 663 (2009).

[68]M. Thanou, B. I. Florea, M. Geldof, H. E. Junginger, and G. Borchard, *Biomaterials* **23**, 153 (2002).

[69]D. Raafat, K. V. Bargen, A. Haas, and H.-G. Sahl, *Appl. Environ. Microbiol.* **74**, 3764 (2008).

[70]M. Kong, X. G. Chen, K. Xing, and H. J. Park, *Int. J. Food Microbiol.* **144**, 51 (2010).

[71]H. Katsutoshi and M. Shinya, *Biochem. Eng. J.* **48**, 424 (2010).

[72]X. X. Zhang, L. Wang, and Levänen, *RSC Adv.* **3**, 12003 (2013).

[73]J. T. Simpson, S. R. Hunter, and T. Aytug, *Rep. Prog. Phys.* **78**, 086501 (2015).

[74]Y. Y. Yan, N. Gao, and W. Barthlott, *Adv. Colloid Interface Sci.* **169**, 80 (2011).

[75]B. J. Privett, J. H. Youn, S. A. Hong, J. Y. Lee, J. H. Han, J. H. Shin, and M. Schoenfisch, *Langmuir* **27**, 9597 (2011).

[76]S. Heinonen, J.-P. Nikkanen, J. Laakso, M. Raulio, O. Priha, and E. Levänen, *IOP Conf. Ser. Mater. Sci. Eng.* **47**, 012064 (2013).

[77]W. Ye, Q. Shi, J. W. Hou, J. Jin, Q. F. Fan, S.-C. Wong, X. Xu, and J. Yin, *J. Mater. Chem B* **2**, 7186 (2014).

[78]L. C. Xu and C. A. Siedlecki, *Biomed. Mater.* **9**, 035003 (2014).

[79]F. Hizal, N. Rungraeng, J. Lee, S. Jun, H. J. Busscher, H. C. van der Mei, and C. H. Choi, *ACS Appl. Mater. Interfaces* **9**, 12118 (2017).

[80]M. Shaban, F. Mohamed, and S. Abdallah, *Sci. Rep.* **8**, 3925 (2018).

[81]K. Bartlet, S. Movafaghi, L. P. Dasi, A. K. Kota, and K. C. Popat, *Colloids Surf. B Biointerfaces* **166**, 179 (2018).

[82]C.-H. Xue, J. Chen, W. Yin, S.-T. Jia, and J.-Z. Ma, *Appl. Surf. Sci.* **258**, 2468 (2012).

[83]C. R. Crick and I. P. Parkin, *Chem. Commun*. **47**, 12059 (2011).

[84]M. Katsikogianni and Y. F. Missirlis, *Eur. Cell Mater*. **8**, 37 (2004).

[85]H. Tuson and D. B. Weibel, *Soft Matter* **9**, 4368 (2013).

[86]Y. Yuan, M. P. Hays, P. R. Hardwidge, and J. Y. Kim, *RSC Adv*. **7**, 14254 (2017).

[87]C. I. Pereni, Q. Zhao, Y. Liu, and E. Abel, *Colloids Surf. B Biointerfaces* **48**, 143 (2006).

[88]W. Orapiriyakul, P. S. Young, L. Damiati, and P. M. Tsimbouri, *J. Tissue Eng*. **9**, 1 (2018).

[89]Y. Arima and H. Iwata, *Biomaterials* **28**, 3074 (2007).

[90]V. A. Tegoulia and S. L. Looper, *Colloids Surf. B Biointerfaces* **24**, 217 (2002).

[91]D. H. Shin, T. Shokuhfar, C. K. Choi, S. H. Lee, and C. Friedrich, *Nanotechnology* **22**, 315704 (2011).

[92]S. Rozhok, Z. F. Fan, D. Nyamjav, C. Liu, C. A. Mirkin, and R. C. Holz, *Langmuir* **22**, 11251 (2006).

[93]E. P. Ivanova, V. K. Truong, H. K. Webb, V. A. Balin, J. Y. Wang, N. Mohammodi, F. Wang, C. Fluke, and R. J. Crawford, *Sci. Rep*. **1**, 165 (2011).

[94]K. A. Whitehead, J. Colligon, and J. Verran, *Colloids Surf. B Biointerfaces* **41**, 129 (2005).

[95]F. M. Harold, *Curr. Opin. Microbiol*. **10**, 591 (2007).

[96]L. G. Harris, S. Tosatti, M. Wieland, M. Textor, and R. G. Richards, *Biomaterials* **25**, 4135 (2004).

[97]J. K. Baveja, M. D. Willcox, E. B. Hume, N. Kumar, R. Odell, and L. A. Poole-Warren, *Biomaterials* **25**, 5003 (2004).

[98]A. H. Eng, K. L. Lim, L. S. Tang, and D. Lucas, "World's First Surgical Glove with Antimicrobial Coating on Inside Surface," Paper 14, *Proceedings of the International Latex & Synthetic Polymer Dispersions Conference (Latex 2012)*, Kuala Lumpur, Malaysia, March 13–14, 2012, Smithers Rapra Technology, Shropshire, UK, 2012.

[99]A. H. Eng, L. S. Tang, Y. P. Teh, and D. Lucas, "The First Antibacterial Infection Protection Medical Glove," Paper 2, *Proceedings of the International Latex & Synthetic Polymer Dispersions Conference (Latex 2013)*, Kuala Lumpur, Malaysia, Sept 10–11, 2013, Smithers Rapra Technology, Shropshire, UK, 2013.

[100]J. Sawyer and A. Bennett, *Ann. Occup. Hyg*. **50**, 289 (2005).

[101]A. Elemam, J. Rahimian, and W. Mandell, *Clin. Infect. Dis*. **49**, 271 (2009).

[102]C. Nimmo, S. Capocci, I. Honeyborne, J. Brown, J. Sewell, S. Thurston, M. Johnson, T. D. McHugh, and M. Lipman, *Eur. Respir. J*. **46**, 1208 (2015).

[103]T. F. Moriarty, D. W. Grainger, and R. G. Richards, *Eur. Cell Mater*. **12**, 112 (2014).

[104]Hartalega, "AMG antimicrobial gloves FAQs," https://amgantimicrobialglove.com/faqs/#1539586945364-40eb06da-9fa2. Accessed date December 15, 2019.

[105]ASTM Standard D 7907-14, *Annu. Book ASTM Stand*., 09.02 (2014).

[106]A. C. Coelho and J. García Díez, *Front. Bioeng. Biotechnol*. **23**, 56 (2015).

[107]Y. Duman, Y. Yakupogullari, B. Otlu, and M. S. Tekerekoglu, *Am. J. Infect. Control* **44**, 935 (2016).

[108]E. J. Baron and J. M. Miller, *Diagn. Microbiol. Infect. Dis*. **60**, 241 (2008).

[109]E. C. Hayden, *Nature* **473**, 132 (2011).

[110]S. Silver, *FEMS Microbiol Lett*. **362**, 1 (2015).

[111]R. M. Pike, *Health Lab Sci*. **13**, 105 (1976).

[112]J. Siengsanan-Lamont and S. D. Blacksell, *Trop. Med. Infect. Dis*. **3**, 36 (2018).

[113]K. Aalto-Korte, K. Alanko, M. L. Henriks-Eckerman, and R. Jolanki, *Arch. Dermatol*. **142**, 1326 (2006).

[114]K. Sato, Y. Kusaka, N. Suganuma, S. Nagasawa, and Y. Deguchi, *J. Occup. Health* **46**, 165 (2004).

[115]G. F. Calogiuri, E. Di Leo, A. Trautmann, E. Nettis, A. Ferrannini, and A. Vacca, *J. Allergy Ther*. **4**, 4 (2013).

[116]D. A. Basketter, M. Marriott, N. J. Gilmour, and I. R. White, *Contact Dermatitis* **50**, 213 (2004).

[117]S. E. Anderson, H. Shane, C. Long, E. Lukomska, B. J. Meade, and N. B. Marshall, *J. Immunotoxicol*. **13**, 557 (2016).

[118]K. Vanden Broecke, E. Zimerson, M. Bruze, and A. Goossens, *Contact Dermatitis* **71**, 117 (2014).

[119]M. Iwata, H. Tanizaki, H. Fujii, Y. Endo, A. Fujisawa, M. Tanioka, Y. Miyachi, and K. Kabashima, *Acta Dermatol. Venereol*. **95**, 628 (2015).

[120]R. Bragg, A. Jansen, M. Coetzee, W. van der Westhuizen, and C. Boucher, *Adv. Exp. Med. Biol*. **808**, 1 (2014).

[121]G. Sundheim, S. Langsrud, E. Heir, and A. L. Holck, *Int. Bioderterior. Biodegradation* **41**, 235 (1998).

[122]J. V. Martinez-Suárez, S. Ortiz, and V. López-Alonso, *Front. Microbiol* **7**, 638 (2016).

[123]P. Gilbert and A. J. McBain, *Clin. Microbiol. Rev*. **16**, 189 (2003).

[124]A. M. Kropinski, J. Kuzio, B. L. Angus, and Hancock, *Antimicrob. Agents Chemother*. **21**, 310 (1982).

[125]R. T. Carson, E. Larson, S. B. Levy, Marshall and A. E. Aiello, *J. Antimicrob. Chemother*. **62**, 1160 (2008).

[126]P. Gilbert and L. E. Moore, *J. Appl. Microbiol*. **99**, 703 (2005).

[127]N. Luddin and H. M. Ahmed, *J. Conserv. Dent*. **16**, 9 (2013).

[128]G. Kampf, *J. Hosp. Infect*. **94**, 213 (2016).

[129]S. Ali and A. P. R. Wilson, *BMC Infect. Dis*. **17**, 574 (2017).

[130]M. Kahar Bador, V. Rai, M. Y. Yusof, W. K. Kwong, and O. Assadian, *J. Hosp. Infect*. **90**, 248 (2015).

[131]E. E. Creppy, A. Diallo, S. Moukha, C. Eklu-Gadegbeku, and D. Cros, *Int. J. Environ. Res. Public Health* **11**, 8069 (2014).

[132]T. Arpornwichanop, D. Polpanich, R. Thiramanas, T. Suteewong, and P. Tangboriboonrat, *Carbohydr. Polym*. **109**, 1 (2014).

[133]D. Raafat and H. G. Sahl, *Microb. Biotechnol*. **2**, 186 (2009).

[134]E. Marie, K. Landfester, and M. Antonietti, *Biomacromolecules* **3**, 475 (2002).

[135]K. S. Huang, C. H. Yang, S. L. Huang, C. Y. Chen, Y. Y. Lu, and Y. S. Lin, *Int. Mol. Sci*. **17**, 1578 (2016).

[136]G. Tetz and V. Tetz, *Gut Pathog*. **9**, 38 (2017).

[137]C, Paul, Z. Bayrychenko, T. Junier, S. Filippidou, K. Beck, M. Bueche, G. Greub, H. Bürgmann, and P. Junier, *PeerJ* **20**, e4989 (2018).

[138]D. M. Guerrero, M. M. Nerandzic, L. A. Jury, S. Jinno, S. Chang, and C. J. Donskey, *Am. J. Infect. Control* **40**, 556 (2012).

[139]T. Sasahara, R. Ae, M. Watanabe, Y. Kimura, C. Yonekawa, S. Hayashi, and Y. Morisawa, *J. Infect. Chemother*. **22**, 521 (2016).

[140]J. Barra-Carrasco and D. Paredes-Sabja, *Future Microbiol*. **9**, 475 (2014).

[141]E. Bagge, M. Persson, and K. E. Johansoon, *J. Appl. Microbiol*. **109**, 1549 (2010).

[142]F. Van Immerseel, J. De Buck, F. Pasmans, G. Huyghebaert, F. Haesebrouck, and R. Ducatelle, *Avian Pathol*. **33**, 537 (2004).

[143]A. Cloeckaert, M. S. Zygmunt, and B. Doublet, *Front Microbiol*. **8**, 2428 (2017).

[144]W. Witte, *Science* **279**, 996 (1998).

[145]Y. Wang, G. B. Tian, R. Zhang, Y. Shen, J. M. Tyrrell, X. Huang, H. Zhou, L. Lei, H. Y. Li, Y. Doi, Y. Fang, H. Ren, L. L. Zhong, Z. Shen, K. J. Zeng, S. Wang, J. H. Liu, C. Wu, T. R. Walsh, and J. Shen, *Lancet Infect. Dis*. **17**, 390 (2017).

[146]G. B. Tian, Y. Doi, J. Shen, T. R. Walsh, Y. Wang, R. Zhang, and X. Huang, *Lancet Infect. Dis*. **17**, 30266 (2017).

[147]R. Wang, L. van Dorp, L. P. Shaw, P. Bradley, Q. Wang, X. J. Wang, L. Y. Jin, Q. Zhang, Y. Q. Liu, A. Rieux, T. Dorai-Schneiders, L. A. Weinert, Z. Iqbal, X. Didelot, and H. Wang, *Nat. Commun*. **9**, 1179 (2018).

[148]V, Neela, Z. A. Mohd Zafrul, N. S. Mariana, A. van Belkum, Y. K. Liew, and E. G. Rad, *J. Clin. Microbiol*. **47**, 4138 (2009).

[149]A. H. Goldman, E. Haug, J. R. Owen, J. S. Wayne, and G. J. Golladay, *Clin. Orthop. Relat. Res*. **474**, 2513 (2016).

[150]W. Yinusa, Y. H. Li, W. Chow, W. Y. Ho, and J. C. Y. Leong, *Int. Orthop*. **28**, 36 (2004).

[151]S. Thomas, M. Agarwal, and G. Mehta, *Postgrad. Med. J*. **77**, 458 (2001).

[152]C. Lancaster and P. Duff, *Am. J. Obstet. Gynecol*. **196**, e36 (2007).

[153]S. C. Soldá, J. C. Assef, J. G. Parreira, J. A. Perlingeiro, Pde A. Candelária, M. P. Cury, and S. Manzione Tda, *Rev. Assoc. Med. Bras*. **55**, 597 (2009).

[154]Y. Kojima and M. Ohashi, *Ann. Thorac. Surg*. **80**, 1078 (2005).

[155]P. C. Bogino, L. Oliva Mde, F. G. Sorroche, and W. Giordano, *Int. J. Mol. Sci*. **14**, 15838 (2013).

[156]P. S. Stewart, *Microbiol. Spectr*. **3**, 1 (2015).

[157]T. Kuyyakanond and L. B. Quesnel, *FEMS Microbiol. Lett*. **100**, 211 (1992).

[158]R. Montville and D. W. Schaffner, *Appl. Environ. Microbiol*. **69**, 7188 (2003).

[159]R. Montville and D. W. Schaffner, *J. Food Prot*. **74**, 1875 (2011).

[*Received November 2020*]