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Synthesis of polymerizable quaternary ammonium bromides and their efficacy against pathogenic and food spoilage bacteria

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ABSTRACT

Despite rigorous cleaning and sanitization protocols, food manufacturing facilities can harbor persistent microorganisms that can cause post processing contamination leading to food safety and food spoilage issues. Of particular concern are 'growth niches', regions within a manufacturing facility more likely to accumulate water and debris because they are outside the zones of routine cleaning and sanitization. Such growth niches present a challenge in controlling post-processing microbial contamination which can affect the safety and shelf life of foods and beverages. In recent years, researchers have explored using antimicrobial and nonfouling coatings to control microbial persistence and cross contamination. A challenge in identifying effective coatings is the limited research on efficacy of antimicrobial monomers (suitable for polymerization into antimicrobial coatings) on microorganisms relevant in food safety and spoilage. In this work, we synthesize and characterize the efficacy of five antimicrobial quaternary ammonium bromide (QAB) monomers against pathogenic and food spoilage organisms. The QAB monomers are end-capped with dihydroxy moieties suitable for subsequent polymerization into antimicrobial polyurethanes and polyesters. N,N-bis(2-hydroxyethyl)-N-methyl-N-R-1-ammonium bromides (R= -octan {C8QAB}, -decan {C10QAB}, -dodecan {C12QAB}, -hexadecan {C16QAB}, -octadecan {C18QAB}) were synthesized and characterized using spectral techniques (Fourier transform infrared spectroscopy and nuclear magnetic resonance spectroscopy). Minimum inhibitory concentrations were determined against relevant food safety and food spoilage bacteria *Listeria monocytogenes*, *Salmonella* Typhimurium, *Escherichia coli,* and *Pseudomonas poae*. Sixteen and eighteen carbon length QAB monomers inhibited growth of *L. monocytogenes* and *P. poae* at a concentration of 3 ppm, while sixteen carbon length QAB monomerinhibited growth of *Salmonella* Typhimurium at 26 ppm and against *Escherichia coli* at 13 ppm. Quaternary ammonium compounds capped with polymerizable end groups such as those reported here offer an opportunity to reduce persistence and cross-contamination of food pathogens and food spoilage bacteria with particular relevance in growth niches outside of routine cleaning and sanitization regimens.

1. Introduction

Microbial contamination of food remains a critical issue to human health, food safety, and food spoilage (Scallan et al., 2011). As per WHO estimates, 600 million people, globally, acquire foodborne illness upon consuming contaminated food and 420,000 die annually (World Health Organization, 2022). The United States Centers for Disease Control estimates 48 million people in the United States alone fall ill from foodborne illness, 128,000 may be hospitalized, and 3000 may die annually (Scallan et al., 2011)(Hoffmann et al., 2015). In addition to the public health concern, foodborne disease presents an economic burden to the U.S. estimated at over $15.5 billion USD (Hoffmann et al., 2015). The economic burden of foodborne illness in low- and middle-income countries as reported by the 2019 World Bank report with an annual estimated productivity loss of $95.2 billion USD (World Health Organization, 2022) and an annual cost of treating foodborne illness of $15 billion USD (Gorton & Stasiewicz, 2017). Beyond the food safety implications, microbial contamination and spoilage of foods contribute to food waste and loss. Indeed, it has been reported that 25% of all foods produced globally are lost due to spoilage, much of this due to microbial spoilage, with a corresponding annual economic impact of $162 billion USD (Petruzzi et al., 2017; World Health Organization, 2022).

While there are many potential routes of microbial contamination from production to retail (Alegbeleye et al., 2018; Chatterjee &

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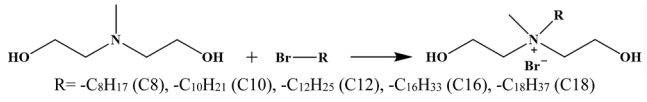
Abraham, 2018), post-processing contamination by food contact and non-contact materials in food production facilities remains a major hurdle in reducing the economic, public health, and environmental impact of microbial food contamination (Karanth et al., 2023; Werner et al., 2019a).

Routine cleaning and sanitization of surfaces is standard practice in combatting cross-contamination in food production facilities (U.S. Department of Agriculture, 2023; U.S Food and Drug Administration, 2017). Following debris removal and cleaning, chlorine, peroxyacetic acid, iodine, and quaternary ammonium compounds are commonly used as surface sanitizers. Quaternary ammonium compounds (QAC, 'quats') are common antimicrobial agents and are incorporated in surfactants (Montefusco-Pereira et al., 2020), dyes (Vereshchagin et al., 2021a), hair care products (C. Zhang et al., 2015a), dental restoratives (Makvandi et al., 2018), cosmetic formulations (Okeke et al., 2023; Vereshchagin et al., 2021b), contact lens solutions (Mooney et al., 2020), fabric softener (Jan et al., 2017a) and many more applications in which controlling microbial growth is essential. QACs first found use within the medical field in the early 20th century (Domagk, 1935) and are now used in many industries, including as a sanitizing agent in food processing. Generally, monomeric QACs consist of a central cationic nitrogen (N^+) bonded to four additional groups that can be hydrogen or alkyl chains (with at least one hydrophobic chain) with the possibility of additional functionality. QACs contain a halogen anion (X^-), which is often chloride or bromide when used as industrial sanitizers. QACs in which the halogen is a bromide are referred to as Quaternary Ammonium Bromides (QAB). The mechanism of antibacterial action, though thoroughly studied, remains not completely understood. It is widely theorized that the positively charged nitrogen associates with the negatively charged acidic hydrophobic phospholipid layer of microorganism cell membrane via electrostatic attraction, allowing the hydrophobic alkyl chain to penetrate the phospholipid membrane. As the hydrophobic tail interdigitates into the hydrophobic membrane core, at lower concentrations, the interactions of the membrane and alkyl chain increases the surface pressure of the membrane which decreases the membrane fluidity and phase transition temperature causing the cells to lose osmoregulatory capability and leakage of low molecular weight material leading to the degradation of proteins and nucleic acids and eventually cell lysis (Gilbert & Moore, 2005; Kwaśniewska et al., 2020; Tischer et al., 2012). To summarize, the antimicrobial activity of QAC essentially relies on their interaction with the cell membrane, leading to the disruption of membrane integrity and a subsequent release of cellular content. (Buffet-Bataillon et al., 2012; F. Liu et al., 2013).

The bactericidal activity of QACs and its lipophilicity (from the n-alkyl chain length) are reported to be related (Gilbert & Moore, 2005). The alkyl chain length impacts the hydrophobicity and the degree of quaternization; the longer alkyl chain brings higher hydrophobicity and a lower degree of quaternization (Lin et al., 2021). It has been found that optimal alkyl chain length is between 12 and 16 carbons, but the structure of the cell, being either Gram positive or Gram negative, determines which chain length is most effective (Bragg et al., 2014; Gerba, 2015). Quaternary ammonium compounds are inexpensive, biodegradable under aerobic conditions, have low toxicity to humans, excellent antimicrobial and surface-active properties (Osimitz & Droege, 2023; C. Zhang et al., 2015b). For these reasons, QACs are produced in such high volumes for use in sanitizers and home cleaning products (Bureau of Indian Standards, 2023). They are on the U.S. Environmental Protection Agency high production volume chemical list which tracks the safe manufacturing and testing of chemicals (Tezel & Pavlostathis, 2011). With the widespread use of solubilized QACs, there is subsequent widespread environmental exposure and quaternary ammonium compound residues have been documented in marine and freshwater environments, wastewater, sediment, and soil (Jan et al., 2017b). The substantial environmental existence of QACs and increased use in disinfection practices (Okeke et al., 2023) renders them a potential risk to environmental and public health by creating antimicrobial resistance, which continues to be a major issue in fighting bacterial infections and contamination (Centers for Disease Control, U, 2019). As most QAC surface sanitizers do not require rinsing post application, it allows for prolonged contact between bacteria and QAC potentially exposing the microbial community to subinhibitory concentrations aiding natural selection, survival of the clones resistant to higher Minimum Inhibitory Concentration (MIC) of antimicrobial agents (Bragg et al., 2014; FAO; WHO, 2023; Jan et al., 2017b; Møretrø et al., 2017). In addition to microbial resistance, migration into food in food industries is also a matter of concern (Bento de Carvalho et al., 2023). A potential means to reduce the overuse and subsequent environmental contamination of free antimicrobial compounds, while maintaining their performance in reducing microbial contamination, is to immobilize the QACs by covalently binding them or polymerizing them to or in a surface applied coating. Once chemically bound, antimicrobial agents are not immediately washed away and can display longer term antimicrobial functionality than traditional antimicrobial spraying of surfaces. Contact active antimicrobials are of high applicative interest as they offer potential sustainable and operational advantages as the antimicrobial agent is not released while still retaining their effectiveness after multiple usages (Elena & Miri, 2018) Therefore, this approach allows for curtailing the amount of active agents required to prevent microbial growth (Elena & Miri, 2018). Many researchers have developed methods to bind antimicrobial agents like metal nanoparticles (Fernández et al., 2008; Knetsch & Koole, 2011; Kraśniewska et al., 2020; Monteiro et al., 2009; Rai et al., 2009), N-halamines (Barnes et al., 2007; PP. 0, 2628; Bastarrachea & Goddard, 2015; Denis-Rohr et al., 2015; Qiao et al., 2017), chitosan (Benkocká et al., 2018, 2019; Mesgari et al., 2021; Xu et al., 2018; H. Zhang et al., 2019) and quaternary ammonium compounds to different surfaces and within polymers. Quaternary ammonium compounds have been polymerized into polyurethanes, polyethyleneimines, and polyesters (Daniels et al., 2016; Dong et al., 2018; Gharibi et al., 2019; He et al., 2016; Hu et al., 2019; Matsukizono & Endo, 2015; Peng et al., 2018; B. Zhang & Jiang, 2018; P. Zhang et al., 2018). Yagci et al. (2011) developed antimicrobial polyurethane coatings by covalently binding quaternary ammonium compounds and a hydroxyl end capped liquid oligoester to the polymer network via the addition of a polyisocyanate crosslinker and showed antimicrobial activity against both gram-positive and gram-negative bacteria. Zhu et al. (2021) reported achieving inactivation of airborne bacteria for a self-decontaminating air filter by embedding a filler made by grafting a layer of antibacterial polymeric quaternary ammonium compound (QAC) onto the surface of a metal-organic framework into electrospun nanofibers. Grover et al. (2016) immobilized acylase into polyurethane films to generate non-leaching biocatalytic coatings capable of resisting formation of biofilms and showing potential for prevention of medical device related infections. Ping et al. (2018) developed a low bio-fouling membrane for water and wastewater treatment by grafting quaternary ammonium compounds onto polyvinyl fluoride (PVDF) membrane using surface-initiated activators regenerated by electron transfer atom – transfer radical polymerization (ARGET ATRP). Lehui Ren et al. (2020) reported on membranes developed with improved hydrophilicity, permeability, antibacterial activity and stability to create antibiofouling membranes for wastewater treatment by grafting quaternary ammonium compounds (QACs) onto polyvinylidene fluoride (PVDF) membranes.

While many studies have reported incorporation of QACs into materials of varying chemistries, few studies on quaternary ammonium compound monomers assess their efficacy against spoilage and pathogenic microorganisms relevant in food manufacturing.

In this study, we report on synthesis of dihydroxy end-capped quaternary ammonium monomers which can be polymerized via condensation reaction with isocyanates to form antimicrobial polyurethanes or polycarboxylic acids to form antimicrobial polyesters. We synthesized five dihydroxy functionalized quaternary ammonium bromides of varying alkyl chain lengths with the aim to identify the effect of alkyl



Scheme 1. Synthesis and final structure of quaternary ammonium bromides (QAB) where R is differing alkyl chain length C8, C10, C12, C16, or C18.

chain length on minimum inhibitory concentration against pathogenic and spoilage organisms common in food processing environments. Identification of the most effective alkyl chain length of polymerizable quaternary ammonium bromides against Gram-negative *Salmonella* Typhimurium and *Escherichia coli* and Gram-positive *Listeria monocytogenes* pathogens and the Gram-negative *Pseudomonas poae* spoilage organism expands the current literature of polymerizable QAC development and provides important research towards translation of these technologies to food safety and spoilage interventions.

2. Materials and methods

2.1. Materials

N-methyldiethanolamine (MDEA), bromoalkanes (1-bromooctane, 1-bromodecane, 1-bromododecane, 1-bromohexadecane, 1-bromooctdecane), 200 proof ACS reagent grade ethanol, petroleum ether, deuterated dimethylsulfoxide (dDMSO), tetramethylammonium bromide were sourced from Millipore Sigma (Burlington, MA, USA). Skim Milk Powder, Tryptic Soy Agar (TSA), Brain Heart Infusion Broth (BHI), biological agar, and Mueller Hinton Broth (MHB) were purchased from Thermo Fisher Scientific (Fairlawn, NJ, USA). Phosphate buffered saline was purchased from VWR Scientific (Radnor, PA, USA).

2.2. Synthesis

Methyldiethanolamine (MDEA) (20 mmol) and individual bromoalkanes (20 mmol) were added to 15 ml ethanol in a round bottom flask equipped with positive flow of nitrogen and a reflux condenser[34]. Reaction was stirred for 24 h at 80 °C. After 24 h, the reaction was allowed to cool to room temperature (20 °C) followed by rotoevaporating (Heidolph, Schwabach, Germany) to remove residual ethanol. The resulting product was washed twice with 3 ml petroleum ether to purify residual monomers. Volatiles were removed by rotoevaporation. Product was recrystallized from ethanol and left at − 20 °C for 24 h. Crystals were removed and washed with − 20 °C ethanol in a Buchner funnel and dried in a desiccator over anhydrous calcium carbonate for 24 h. The following dihydroxy quaternary ammonium bromides were synthesized: *N,N*-bis(2-hydroxyethyl)-*N*-methyleoctan-1-aminium bromide (C8QAB), *N,N*-bis(2-hydroxyethyl)-*N*-methyledecan-1-aminium bromide (C10QAB), *N,N*-bis(2-hydroxyethyl)-*N*-methyledodecan-1-aminium bromide (C12QAB), *N,N*-bis(2-hydroxyethyl)-*N*-methylehexadecan-1-aminium bromide (C16QAB), *N,N*-bis(2-hydroxyethyl)-*N*-methyleoctadecan-1-aminium bromide (C18QAB) (Scheme 1).

2.3. Nuclear magnetic resonance (NMR)

^{1}H NMR and ^{13}C NMR spectra of dihydroxy quaternary ammonium bromides dissolved in dimethylsulfoxide-d_6 were collected using a Bruker AV500 (Bruker, Billerica, MA, USA). Spectra were analyzed using Mnova 14 (Mestrelab Research, Santiago, Spain).

2.4. Attenuated total reflectance fourier transform infrared (ATR-FTIR) spectroscopy

Dihydroxy quaternary ammonium bromide chemistries were characterized using attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy. Spectra were collected using an IRTracer-100 FTIR spectrometer (Shimadzu Scientific Instruments, Inc., Kyoto, Japan) equipped with diamond ATR crystal. Spectra were collected using Happ-Genzel apodization (32 scans per spot, with a resolution of 4 cm^{-1}). Ambient air was used as background and spectra were subject to baseline correction and analyzed using OriginPro Version 2019b (OriginLab Corporation, Northampton, MA, USA) and KnowItAll Software (BioRad Laboratories, Hercules, CA).

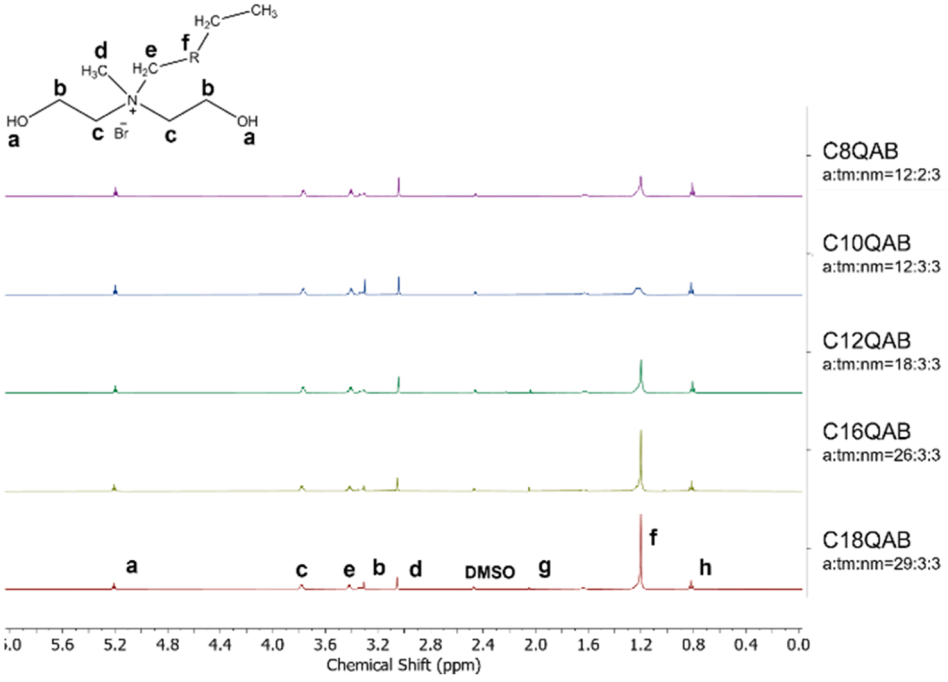


Fig. 1. ^{1}H NMR spectra of synthesized QAB with varying alkyl chain lengths. Ratio of peak integration for alkyl chain: terminal methyl: N-methyl (noted a:tm:nm in the legend to the right). Spectra collected in C2H6OS-d6 (500 MHz).

2.5. Minimum inhibitory concentration

Listeria monocytogenes (FSL C1–0053) and *Pseudomonas poae* (FSL R10–0084) environmental isolate were provided by the Cornell Food Safety Lab (Cornell University, Ithaca, NY, USA). *Salmonella enterica* serovar Typhimurium (ATCC® 14028™) and *Escherichia* coli (ATCC® 25922™) was purchased from American Type Culture Collection (ATCC, Manassas, VA, USA). Overnight bacterial cultures were grown in 40 g L^{-1} of TSB for *Listeria monocytogenes*, *Salmonella* Typhimurium, and *Escherichia coli* or 100 g L^{-1} Skim Milk Broth for *Pseudomonas poae* at 30 °C while shaking at 90 rpm(Bastarrachea & Goddard, 2016; Hung et al., 2018; Werner et al., 2019b). Overnight cultures were streaked on TSA for *L. monocytogenes* and *S. enterica* and BHI for *P. poae*. Minimum inhibitory concentrations were determined using broth microdilution methods as described in Wiegand et al(Wiegand et al., 2008). Direct suspension of overnight colonies into sterile MHB was used to prepare the starting inoculum. Bacterial concentration of starting inoculum was adjusted to reach 1.5×10^8 log (CFU ml^{-1}) based on optical density at 600 nm according to a standard plate count and optical density growth curve. Each synthesized quaternary ammonium compound and tetramethylammonium bromide was combined with sterile MHB to form test concentrations. Inoculated and non-inoculated broth *without* inclusion of quaternary ammonium compounds served as growth and sterility controls, respectively. Minimum inhibitory concentration analyses were performed in 96-well polypropylene microtiter plates over 24 h at 37 °C with polystyrene cover and damp paper towels to reduce evaporation. The absorbance of wells before and after 24 h was read at 600 nm using a Synergy Neo2 Hybrid Multi-Mode Reader (Biotek Instruments, Winooski, VT, USA). The final minimum inhibitory concentration was determined to be the concentration one dilution higher than the well with an increase of at least 0.010 in absorbance after incubation, or the concentration when no bacterial growth is observed.

3. Results and discussion

3.1. Synthesis

In this study, quaternary ammonium bromides (QAB) containing alkyl chain lengths 8, 10, 12, 16, and 18 carbons were synthesized via the Menshutkin reaction in which the tertiary amine reacts with an alkyl bromide to form a quaternary ammonium salt. Scheme 1 illustrates the synthesis route in which R represents different alkyl chain lengths. Alkyl chain length is known to influence the antimicrobial activity of quaternary ammonium compounds due to differing interaction with bacterial cell membranes corresponding to differing alkyl chain length (Kwaśniewska et al., 2020). Commercial quaternary ammonium sanitizers used in food processing facilities often utilize a blend of alkyl chain lengths between 12 carbons and 16 carbons to maximize antimicrobial efficacy, therefore chain lengths 8–18 are explored in this study(Møretrø et al., 2017).

3.2. QAB characterization

Structural confirmation was carried out via ^{1}H NMR with hydrogen atoms assigned a letter *a* through *h* on spectra and the representative chemical structure (Fig. 1). The –OH (a) appears at δ = 5.52 ppm. There are four different formations of $–CH_2–$ located at 3.82 ppm (c), 3.45 ppm (e), 3.37 ppm (b), and 1.67 ppm (g). Two distinct methyl groups appear at 3.09 ppm (d) which correspond to $N–CH_3$ and the $–CH_3$ found at 0.85 ppm (h). The distinctive difference between compounds is the alkyl chain $–CH_2–CH_2–$ attributed to peak f from 1.24 ppm to 1.27 ppm. The intensity of the signal increases when longer alkyl chains are present in the compound. Though C10QAB appears to have a truncated intensity for peak f, the ratio of peak integrations between the alkyl chain, the N-methyl, and the terminal methyl (a:tm:nm) continue to increase with the increase of carbon chain length. Peaks c, e, b, and d shift up field due to the bond with the central N whereas f, g, and h are downfield (Fig. 1).

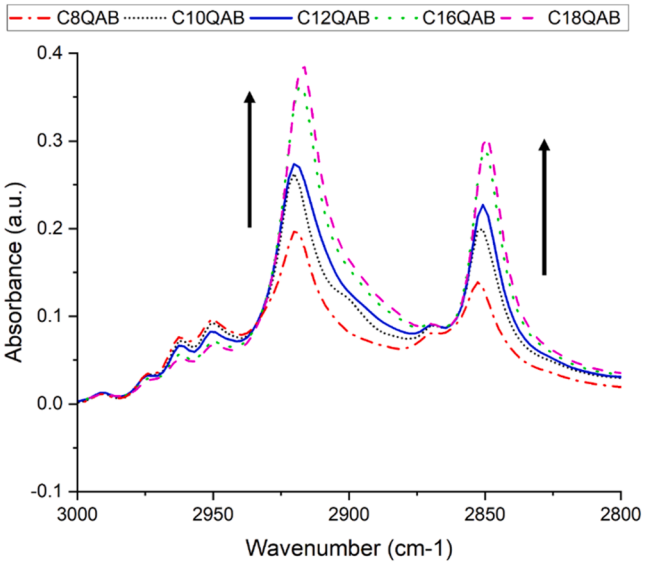


Fig. 2. FTIR spectra of quaternary ammonium bromides (QAB) between 2800 and 3000 cm^{-1} showing increasing absorbance of C-H stretching of alkane with increasing alkyl chain length.

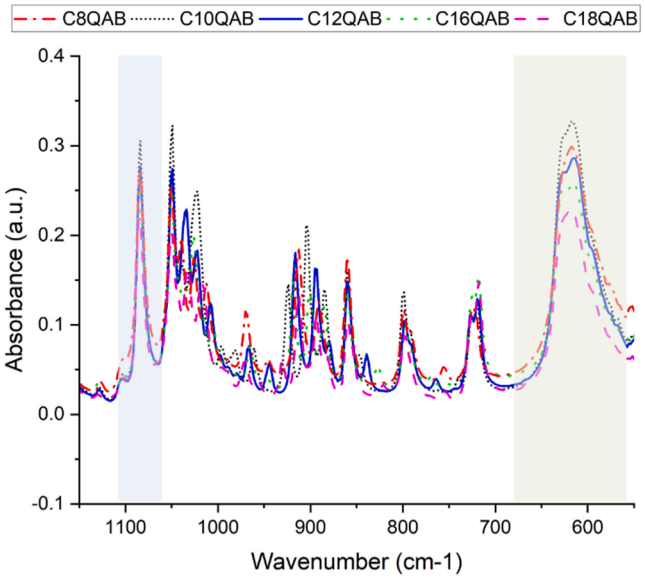


Fig. 3. FTIR spectra of QAB between 550 and 1150 cm^{-1} with highlighted regions showing formation of N^+– C asymmetric stretching (blue) and N^+–C symmetric stretching (green).

Fourier-transform infrared spectroscopy (FTIR) was utilized to characterize the chemistry of the monomers by identifying key functional groups. Absorbance at 3280 cm^{-1} representing hydroxyl group stretching indicates dihydroxy functionalization of the synthesized QAB. A corresponding increase of absorbance at 2920 cm^{-1} and 2850 cm^{-1}, representing alkyl stretching, is characteristic of the increasing length of quaternary ammonium bromide alkyl chain (Fig. 2). Absorbance at 1085 cm^{-1} and 620 cm^{-1} represent quaternized ammonium symmetric and asymmetric stretchings. Importantly, these bands are not present in starting reagent spectra, indicating successful formation of quaternized ammonium (Fig. 3). Absorbance at 1085 cm^{-1} corresponds to quaternized ammonium asymmetric stretching and the absorbance located at 620 cm^{-1} corresponds to quaternized ammonium symmetric stretching.

Table 1
Minimum inhibitory concentrations (MIC) of synthesized quaternary ammonium bromides and control quaternary ammonium bromides against *Listeria monocytogenes*, *Salmonella* Typhimurium, *Escherichia coli*, and *Pseudomonas poae*.

	MIC (ppm)*Listeria monocytogenes*	MIC (ppm)*Salmonella* Typhimurium	MIC (ppm)*Escherichia coli*	MIC (ppm)*Pseudomonas poae*
QAB Control	> 160	> 160	> 160	> 160
C8QAB	> 160	> 160	> 160	> 160
C10QAB	80	160	> 160	> 160
C12QAB	26	80	80	3
C16QAB	3	26	13	3
C18QAB	3	26	40	3

3.3. Minimum inhibitory concentration

Minimum inhibitory concentration (MIC) is the lowest concentration of tested quaternary ammonium compound needed to prevent the growth of a microorganism (Wiegand et al., 2008). The minimum inhibitory concentration of an antimicrobial substance is an important characteristic to determine because exposing bacteria to sub-lethal levels can promote antimicrobial resistance. Quaternary ammonium bromide compounds at concentrations ranging from 3 ppm to 160 ppm (1:2 and 1:3 dilution ratio used) were tested for this study as preliminary experimentation showed MIC to be above 2 ppm for all compounds. Synthesized antimicrobial quaternary ammonium bromide monomers (QAB) and control QAB (tetramethylammonium bromide) were tested against three pathogenic food systems relevant bacteria: *Listeria monocytogenes*, *Salmonella* Typhimurium, and *Escherichia coli*. In addition, a common dairy spoilage bacterium, *Pseudomonas poae*, was selected to determine effectiveness against non-pathogenic spoilage environmental isolates. C16QAB and C18QAB possess the lowest MIC for all four organisms (Table 1). Against both *L. monocytogenes* and *P. poae*, C16QAB and C18QAB had MIC of 3 ppm. However, against Gram-negative *S. enterica* and *E. coli,* C16QAB and C18QAB had higher MICs. C16QAB and C18QAB had MICs of 26 ppm against *S. enterica* and 13 ppm and 40 ppm against *E. coli* (Table 1). This phenomenon of lower efficacy of QACs against Gram-negative bacteria has been reported previously by Liu et al. (2015) with *Bacillus subtilis, Staphylococcus aureus* (Gram-positive bacteria), and *Escherichia coli* (Gram-negative bacteria), and by Harney et al. (2009) with *Staphylococcus aureus* and *Escherichia coli*. Additionally, it has been reported that the composition of the outer layers of a bacterial cell assist with limiting the uptake of antimicrobial compounds (Tischer et al., 2012). The higher MIC for *S. enterica* and *E. coli* can be attributed to the outer lipid membrane associated with Gram-negative bacteria, while *L. monocytogenes* and *P. poae* are both Gram positive and lack the outer lipid membrane, allowing for the mid to long alkyl chains to penetrate and disrupt cell function (Tischer et al., 2012). Interestingly, *E. coli* was less susceptible to the longest alkyl chain compound, C18QAB and required a high concentration for inhibition (40 ppm). These observations are similar to those made by Liu et al. in which *E. coli* displayed no inhibition when exposed to n- octadecyl quaternary ammonium chloride during zone of inhibition testing. MIC for C8QAB and the control tetramethylammonium bromide was above the highest tested ppm (160 ppm). The control QAB does not contain a long alkyl chain, but instead has only methyl groups. This further suggests the presence of the alkyl chain included in the reported, synthesized QABs is critical to its antimicrobial modality and efficacy. Minimum inhibitory concentration results indicate that quaternary ammonium compounds with long carbon chains possess higher antimicrobial activity, which is consistent with previous studies by Liu et al. (2015) who reported higher antibacterial efficacy of n-hexadecyl chlorinated quaternary ammonium compounds against *Staphylococcus aureus, Bacillus subtilis,* and *Escherichia coli* and Harney et al. (2009) who reported that quaternary ammonium bromides with n-octyl alkyl groups were more effective against *Staphylococcus aureus and Escherichia coli* compared to n-hexyl quaternary ammonium bromide compounds.

4. Conclusions

The chemistry discussed herein produced a dihydroxy end-capped antimicrobial quaternary ammonium compound suitable for subsequent polymerization reactions into antimicrobial polymer coatings. Antimicrobial efficacy was demonstrated against gram-positive and gram-negative organisms with relevance to food spoilage and safety. Quaternary ammonium bromide monomers or varying alkyl chain length were tested against bacteria relevant to food spoilage and safety. The terminal dihydroxy groups of the monomers can react with either isocyanates and carboxylic acids to produce antibacterial polyurethane or polyester polymer coatings and materials suitable for preventing cross-contamination of spoilage and pathogenic microorganisms in food production facilities. On-going work in synthesizing and applying antimicrobial coatings and demonstrating performance under real processing conditions will support translation of these monomers into food manufacturing applications. Characterizing the efficacy of antimicrobial monomers of other chemistries will help expand the toolbox of available moieties for research in controlling persistence of spoilage and pathogenic microorganisms in hard to clean growth niches. Such antimicrobial monomers have application beyond food systems in dental, marine, and biomedical applications as well. Characterization of synthesized antimicrobial monomers to include both chemical characterization and performance against system relevant microorganisms, as done here, is essential in demonstrating potential efficacy in a real end-use application. This work thus expands on the existing published literature by offering a systems focused framework for design and synthesis of antimicrobial monomers.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

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