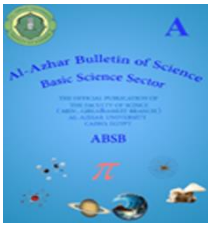
Al-Azhar Bulletin of Science, Section A, Vol. 33, No. 2 (December) 2022, pp. 1-10
http://doi.10.21608/absb.2022.126625.1177

Al-Azhar Bulletin of Science: Section A



THE ANTIMICROBIAL ACTIVITY OF SIX NEW SYNTHESIZED GEMINI SURFACTANTS: THE EFFECT OF SPACER AND ALKYL CHAIN LENGTH

Sharbat A. Baker [a,*], Entsar E. Badr [a], Eman M. Kandeel [a], Nashwa S. Bin-Hudayb [b], Yasmeen M. Mahmood [c]

[a] Department of Chemistry, Faculty of Science (Girls Branch), Al-Azhar University, Postal Code 11754, Cairo, Egypt.
[b] Department of Chemistry, College of Science, Qassim University, Saudi Arabia.
[c] Clinical Pathology Department, Faculty of Medicine, Ain Shams University, Postal code 1181, Cairo, Egypt.
* Corresponding Author: Sharbatbakr.59@azhar.edu.eg

Received: 30 Mar 2022; Revised: 17 May 2022; Accepted: 09 June 2022; Published: 01 Dec 2022

ABSTRACT

New Six cationic Gemini surfactants (GS) with varying alkyl chain lengths and spacer properties were synthesized. The effects of alkyl chain length and spacer characters on antimicrobial activity were investigated. The first group of compounds was known as (2-2'-(ethane-1, 2-diylbis (oxy)) bis (N-(2-alkanamidoethyl)-N, N dimethyl-2-oxoethan-1-aminium)) dichloride, and it had three different alkyl chain lengths (CGSES12, 14 and 16). The general name for the second group was (N_1,N_1,N_3,N_3-tetramethyl-N_1,N_3-bis(2-alkanamidoethyl)propane-1,3-diaminium bromide) with three different alkyl chain lengths, designated as (CGSPS12, 14 and 16).The antimicrobial activity of each surfactant was evaluated by determining the minimum inhibitory concentration (MIC) and the zone of inhibition against six representative organisms: two Gram-positive bacteria; *Staphylococcus aureus* and *Bacillus subtilis*, two Gram-negative bacteria; *Escherichia coli* and *Proteus vulgaris* and two fungi; *Aspergillus fumigates* and *Candida albicans*. The study indicated that all newly synthesized surfactants exhibit antimicrobial activity, but the highest activity was determined for surfactants CGSES12, CGSPS12 i.e. those with the shortest alkyl chain. Remarkably, the lowest MIC value was obtained for CGSES12 against *P.vulgaris* (2 µg/mL). Obviously, the antibacterial activity did not correlate with the length of the spacer. However, the overall antibacterial activity increased with decreasing the length of the alkyl chain. Our data indicated that all synthesized cationic dimeric compounds satisfy the main requirement to be good surfactants, with potential applications as antimicrobials or disinfectants.

Keywords: Antimicrobials; Disinfectants; Cell membrane; Degradation; Surfactants

1. Introduction

Throughout the past few decades many detergent surfactants have been developed. Due to their numerous advantages, Quaternary ammonium compounds (QACs) have been widely used [1]. Their industrial implications include oil recovery, sugar decolorization, fabric softeners and others. Their antibacterial effect is of prime importance in food industry and in hospital settings [2]. They are characterized by high membrane penetration power, long time of residence, low corrosiveness and skin irritation [3]. Thus, they can be used as permeation enhancers of drugs as they promote drug transport through lipid barrier [4], biodeterioration inhibitors in various materials [5] or as cleaning and disinfectant agents [6].

According to Gerba [7], quats are classified into generations, with efficacy increasing in later generations:
First, Benzalkonium, alkyl chains, C12–C18. This was followed by Dialkylmethyl aminos with twin chains. Finally, Bis- Quaternary ammonium compounds (Bis-QACs) with polymeric QACs.

Gemini cationic surfactants (GS) consist of two hydrophobic chains covalently bonded at or approximate to the two hydrophilic head groups by a spacer [8]. The properties of a Gemini surfactant, and therefore its applications are related to its structure, particularly, the nature of the head-group, nature of the spacer chain and its length [9].

Gemini surfactants are considered more effective in comparison to conventional surfactants [10]. This is attributed to high surface activity, low Krafft point, smaller critical micelle concentration (CMC) [11].

In order to use a chemical compound for antimicrobial purposes, it should be highly selective and with low toxicity. The antimicrobial activity of cationic GS is considered good compared to their corresponding monomeric amphiphile [12]. This is attributed to their stability, lower toxicity and their higher effectiveness at killing or inhibiting the growth of microorganisms at low concentrations [13].

There are three major classes of microbes which are viruses, bacteria and fungi. Their interfaces are negatively charged. Cationic surfactants have a high affinity to these interfaces, especially in an alkaline medium [14].

Adsorption to the cell wall, followed by penetration, is the postulated mode of action of quats as antimicrobials. Next, there is an interaction with the cell membrane, which causes it to be disrupted. This results in intracellular material leakage, protein and nucleic acid breakdown, and cell lysis and death [15].

In this study, six cationic Gemini surfactants were synthesized. The impact of different lengths of the alkyl chain and spacer chain on their antimicrobial activities were evaluated by using the agar-well diffusion method and the minimal inhibitory concentration (MIC) against six organisms representative of the three main microbial classes.

2. Materials and Methods

2.1. Gemini surfactants synthesis

2.1.1. Materials

Dodecanoyl, tetradecanoyl chloride and N,N`-dimethyl ethylenediamine were purchased from Sigma-Aldrich (USA). Hexadecanoyl chloride and 1,3- Dibromopropane purchased from across organics. All other solvents were reagent grade. Water used for experiments was deionized water.

2.1.2. Methods

2.1.2.1. Synthesis of (N1,N1,N3,N3-tetramethyl-N1,N3-bis(2-hexadecanamidoethyl)propane-1,3-diaminium bromide) dichloride (CGSPS12-CGSPS16):

(CGSPS12- CGSPS16) were synthesized by the reaction of 1,3 dibromo propane (1.13gm ,0.1 mol) and N.N- dimethyl fatty hydrazide in 2- propanol was refluxed and stirred at 90 c^{o} for 24h. The product was crystalized from acetone/2-propanol.

The structures (CGSPS12- CGSPS16) were proved by IR, H^{1},C^{13} NMR, and MS spectroscopies [16].

2.1.2.2. Synthesis of the gemini surfactants with ester spacer (CGSES12, CGSES14, and CGSES16) was done in three steps:

Step 1: Synthesis of N-(2-(dimethylamino)ethyl)dodecanamide (DAEA12)

Dodecanoyl chloride was added to a solution of N,N-dimethylethylendiamine 2 in anhydrous diethyl ether at 35–40 ◦C, followed by agitation. Then, the solvent was removed under reduced pressure. The subsequent product was washed with water, filtered off as a white solid and recrystallized using absolute ethanol. The final result was vacuum-dried. Tetradecanoyl and Hexadecanoyl derivatives DAEA14; 16 were prepared similarly.

Step 2: Synthesis of the ester spacer (Ethane-1,2-diyl bis(2-chloroethanoate) (ES) The Gao method was used to synthesize ethane-1,2-diyl bis(2-chloroethanoate)

Step 3: Synthesis of 2-2^{-} (Ethane-1,2-diylbis(oxy)) bis(N-(2-alkanamidoethyl)-N,N'-dimethyl-2-oxoethan-1 -aminium) dichloride (CGSES12-CGSES16) as shown in another study by the authors [17].

The structure of synthesized Gemini surfactants was confirmed by different spectroscopic analysis .

FT-IR, ^{1}H-NMR and ^{13}C-NMR MALDI MS techniques: Using a Tescan Shimadzu, Model 8000, Japan, Fourier transform infrared (FT-IR) spectra were obtained within the range 4000–500 cm^{-1}. The ^{1}H NMR spectra are recorded at 20°C on a Bruker NMR spectrometer operating at the ^{1}H resonance frequency of 850 MHz (NMR center, King Abdulaziz University, KSA). Chemical shifts are referenced to $CDCI_3$ as solvent. Mass spectra was carried out on Direct Probe Controller Inlet part to Single Quadropole mass analyzer in Thermo Scientific GC-MS model ISQ LT (The Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar Univeristy, Nasr City, Cairo, Egypt). Further details of the synthesis have been published by the authors in a previous research paper [16,17]

The synthesis of the Gemini surfactants with ester spacer (CGSES12, CGSES14 and CGSES16) and the other Gemini surfactants with propane spacer (CGSPS12, CGSPS14 and CGSPS16) is summarized in **Figure 1.**

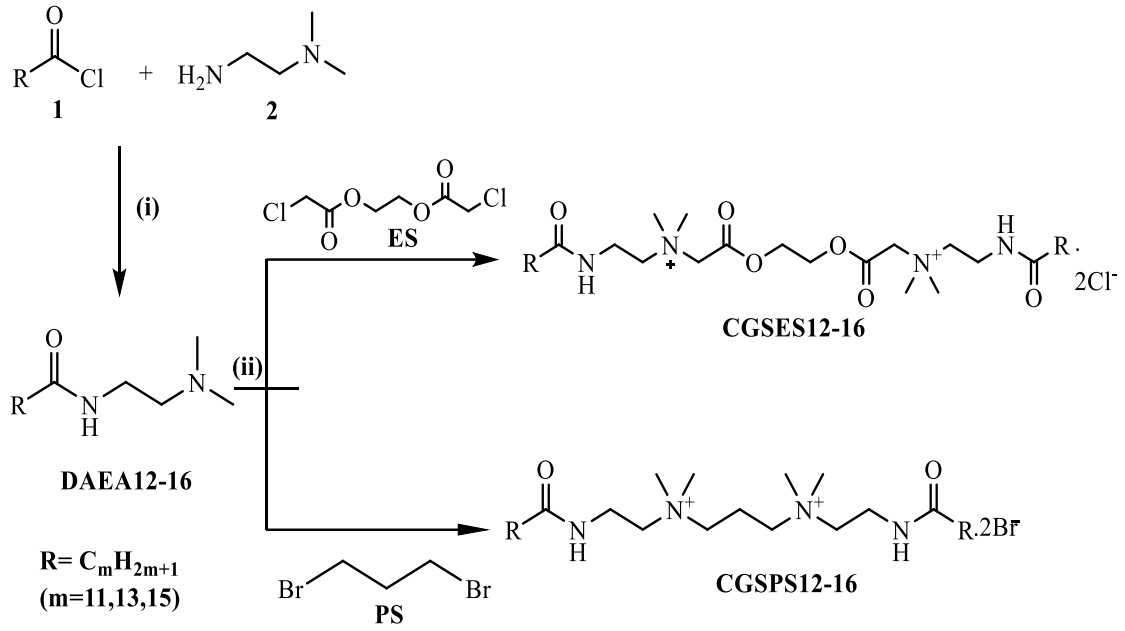


Figure 1. Diethylether anhydrous, 35 - 40 °C, stirring ,2h. (ii) Ethyl acetate, reflux ,24 h. Synthesis of N-(2-(dimethylamino) ethyl) alkanamide (DAEA12-16) and Synthesis of (2-2'-(ethane-1,2-diylbis(oxy))bis(N-(2-alkanamidoethyl)-N,N-dimethyl-2-oxoethan-1-aminium)) dichloride (CGSES12-16).

2.2. Antimicrobial Activity

2.2.1. Materials

Aspergillus fumigates (RCMB 002008), Candida albicans RCMB 005003 (1) ATCC10231, Staphylococcus aureus (RCMB 010010), Bacillus subtilis RCMB 015 (1) NRL B-543, Escherichia coli (RCMB 010052) ATCC25955, Proteus vulgaris RCMB 004 (1) ATCC13315. Sabouraud dextrose agar (HiMedia, M063), Muller-Hinton (HiMedia, M173).

2.2.2. Methods

The antimicrobial activity of the synthesized Gemini surfactants was done according to the guidelines of the Clinical and Laboratory Standards Institute (2019) [18]. Colonies from each strain were grown on an agar plate for 16 to 24 hours. Suspensions from the grown colonies were done using sterile saline. Turbidity was adjusted to 0.5 McFarland. Mueller-Hinton agar plates were inoculated with the suspension using a sterile swab. The compounds were dissolved in dimethyl sulfoxide (DMSO). DMSO was used as a negative control.

The zone of inhibition and the minimum inhibitory concentration (MIC) were measured for each of the respective GS against six strains (Three ATCC strains & three strains from the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Nasr City, Cairo, Egypt). The six strains are a representative group of microorganisms: two fungi: Aspergillus fumigates (RCMB 002008) and Candida albicans RCMB 005003 (1) ATCC10231, two Gram Positive Bacteria: Staphylococcus aureus (RCMB 010010) and Bacillus subtilis RCMB 015 (1) NRL B-543, two Gram Negative Bacteria: Escherichia coli (RCMB 010052) ATCC25955 and Proteus vulgaris RCMB 004 (1) ATCC13315. The evaluation of the antimicrobial activity was done using Sabouraud dextrose agar (HiMedia, M063) for both fungi and Muller-Hinton (HiMedia, M173) for the rest of the organisms. The pH was adjusted to 7.5 throughout. The concentration at which the produced Gemini surfactants were tested was 300 ppm in aqueous medium.

To evaluate the inhibitory action of the GS, the agar plate was inoculated with the selected strain according to Kirby Bauer method [19]. The agar well diffusion method was done in order to detect the zone of inhibition [20]. The surface of the agar plate (100 mm diameter) was inoculated with the colony suspension adjusted to 0.5 McFarland. Wells were created by cutting out 6 mm diameter holes into the agar plates. A volume of 100 µL stock solution of GS, with a dilution of 10 mg/mL was then poured in each well. Incubation of the plates was done at 37 °C for 24 h in case of bacteria and at 25°C for 2–3 days in case of fungi. The clear zone of inhibition around each well was then measured by Vernier calipers. Zones of inhibition are shown in **figures 2, 3 and 4.**

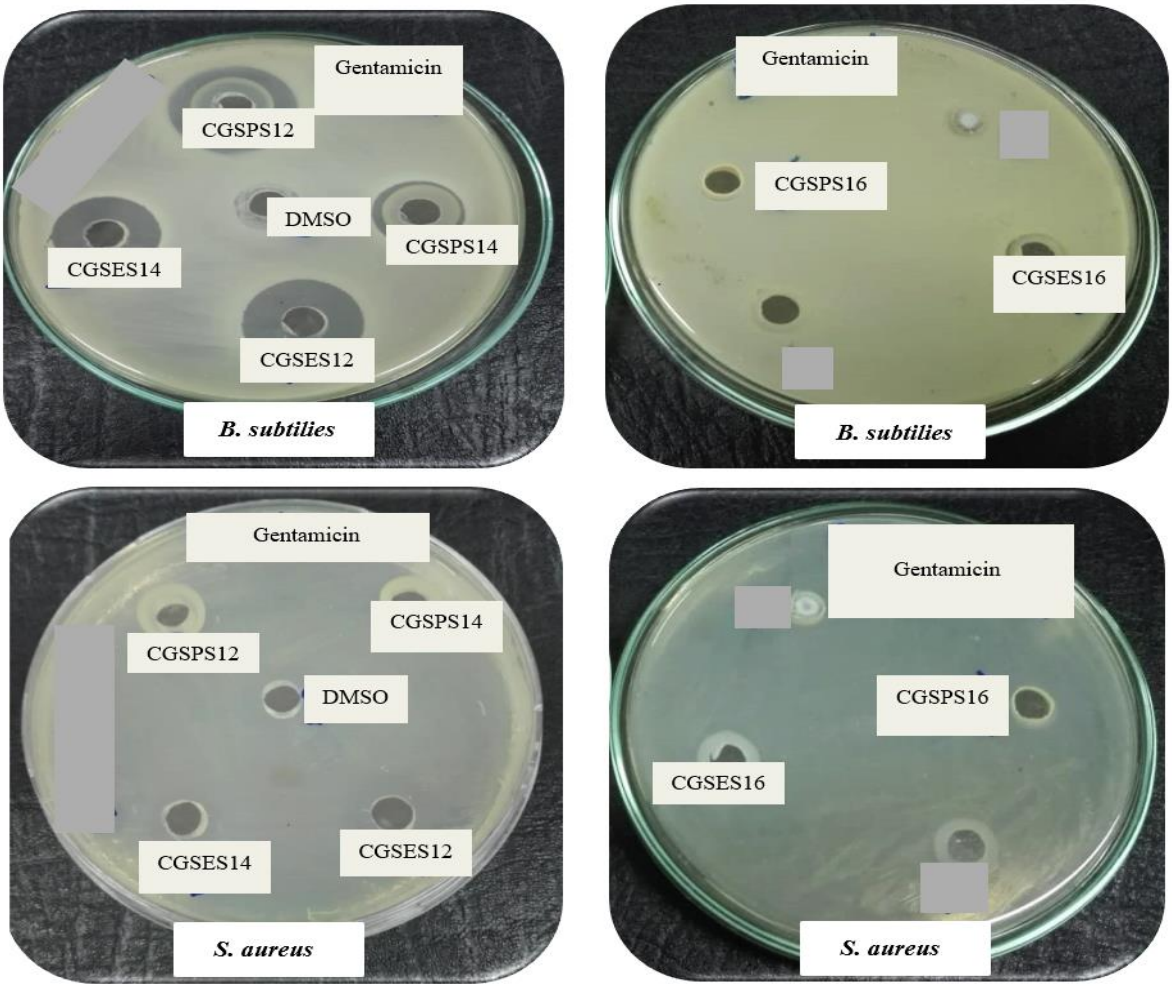


Figure 2. It demonstrates the zones of inhibition of CGSPS12, CGSES12, CGSPS14, CGSES14, CGSPS16, CGSES16, DMSO against *Bacillus subtilis* and *Staphylococcus aureus*, plated on Muller-Hinton agar.

Minimum Inhibitory Concentration Method (MIC) is defined as the lowest concentration of an antimicrobial that inhibits the visible growth of a microorganism after overnight incubation. The MIC of the synthesized GS was evaluated by tube dilution method. Suspensions of the tested strains were prepared (0.5 McFarland turbidity standard). Serial dilutions of the stock solution of each GS were made ranging from 512 μg/mL to 0.25 μg/mL. An equal volume of the prepared microbial suspension was added to each tube. Gentamycin and Ketoconazole were used as positive controls. The lowest concentration (highest dilution) of each GS in the tubes with no visible microbial growth, indicated by the absence of turbidity, was regarded as the MIC [21].

3. Results and Discussion

Six cationic Gemini surfactants with varied lengths of alkyl and spacer chains were produced in this work. The structure of synthesized Gemini surfactants was confirmed by different spectroscopic analysis.

IR, H^1, C^{13} NMR, and MS spectroscopies were used to corroborate the chemical structure of the produced Gemini surfactants (2-2'-(ethane-1,2-diylbis(oxy) bis(N-(2-alkanamidoethyl)-N,Ndimethyl-2-oxoethan-1-aminium) dichloride (CGSES12- CGSES16), as shown in another study by the authors [17].

The structures of the other three produced Gemini surfactants (N_1,N_1,N_3,N_3-tetramethyl-N_1,N_3-bis(2-hexadecanamidoethyl)propane-1,3-diaminium bromide) dichloride (CGSPS12- CGSPS16) were proved by IR, H^1,C^{13} NMR, and MS spectroscopies as shown in a previous study [22].

The prepared cationic surfactants have a high surface activity and a tendency to adsorb at the interface rather than micellize into the bulk of their solutions. Changes in the length of the hydrophobic portion contained in these cationic Gemini

surfactants were discovered to impact the surface activity. The longer the alkyl chain, the lower the CMC. This decreases the adsorption of the surfactant at the air/solution interface and therefore increases the surface tension [23].

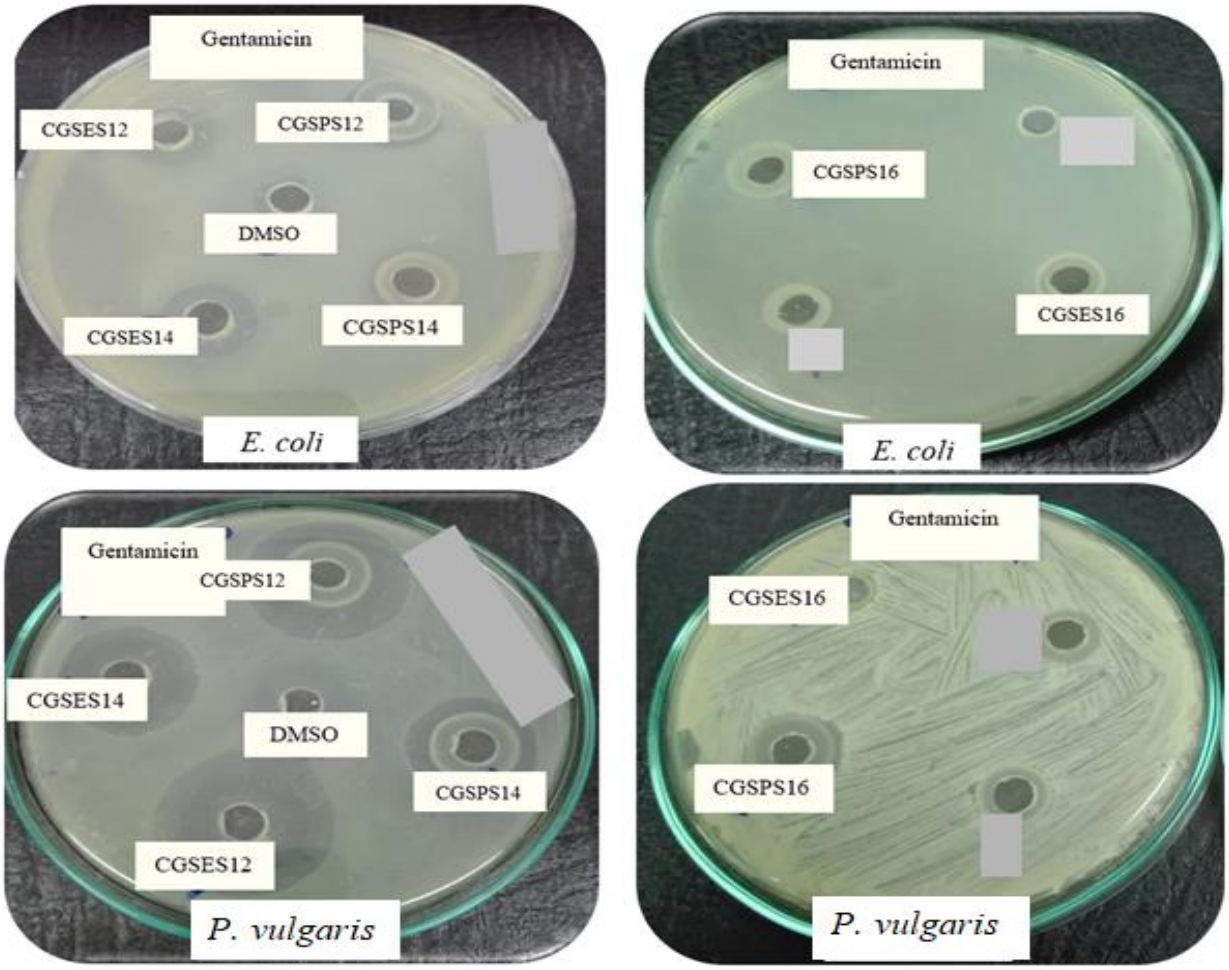


Figure 3: It demonstrates the zones of inhibition of CGSPS12, CGSES12, CGSPS14, CGSES14, CGSPS16, CGSES16, DMSO against *Escherichia coli* and *Proteus vulgaris*, plated on Muller-Hinton agar.

The cell membrane of microorganisms consists mainly of lipids organized in a bilayer, in addition to proteins. The hydrophobicity of the cell membrane is attributed to the lipid bilayer. The cell membrane controls the biological functions of the cell via selective passage of elements known as permeability. Any factor that affects the membrane permeability will interrupt the cell reactions leading eventually to cell death [21]. The cell membrane of microorganisms is more negatively charged than those of eukaryotes. Cationic surfactants adsorb to the negatively charged microbial cell membrane via their positively charged cationic amphiphile [24]. Therefore, the enhanced chemical and physical characteristics of cationic surfactants render them more biocidal compared to conventional single chain surfactants [25].

In *vitro* testing of antibacterial and antifungal activity was done for six different organisms representative of Gram positive, Gram negative bacteria as well as fungi. These organisms are *Escherichia coli*, *Proteus vulgaris*, *Staphylococcus aureus*, *Bacillis subtilis*, *Aspergillus fumigates* and *Candida albicans*. The antimicrobial properties of the examined surfactants were first assessed using agar-well diffusion method. The solutions of each surfactant applied to the wells were found to prevent the growth of all the microorganisms studied. The highest effect was observed for CGSES12 and CGSPS12 surfactants against *P.vulgaris* (30; 28 mm) and Gram-positive bacteria with the maximum zone for CGSPS12 surfactant when tested *on B. subtilities* (23 mm). Gram-positive bacteria *S. aureus* was less responsive to all surfactants, with much smaller zones of inhibited growth (10-15 mm). In addition, we reported a higher antifungal activity of the studied surfactants against *C.albicans* with the largest zone for CGSPS12 (25 mm) than that of A.fumigatus. The results are demonstrated in **figures 5 and 6.**

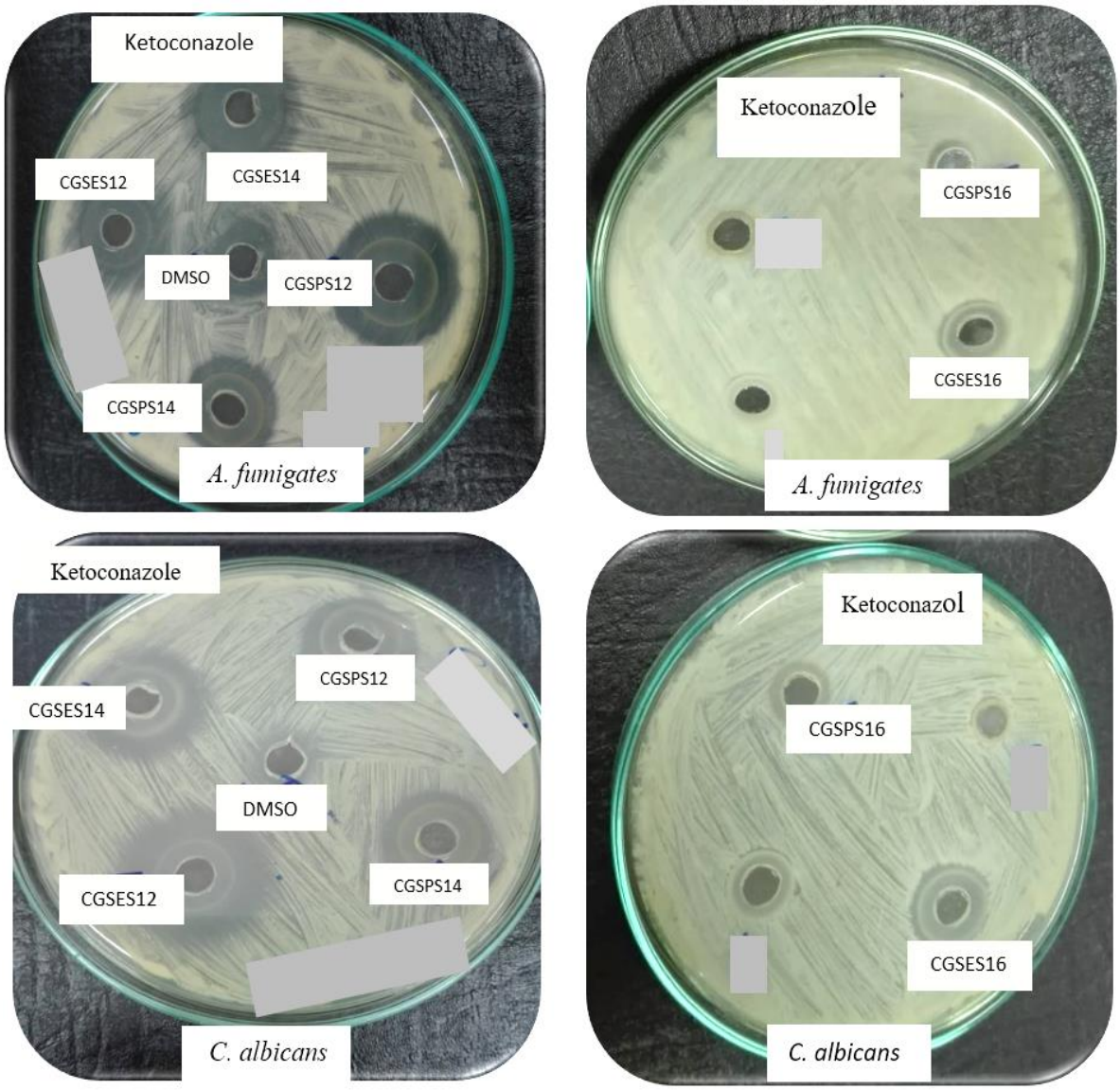


Figure 4. It demonstrates the zones of inhibition of CGSPS12, CGSES12, CGSPS14, CGSES14, CGSPS16, CGSES16, DMSO against Aspergillus fumigatus and Candida albicans, plated on Sabouraud Dextrose agar.

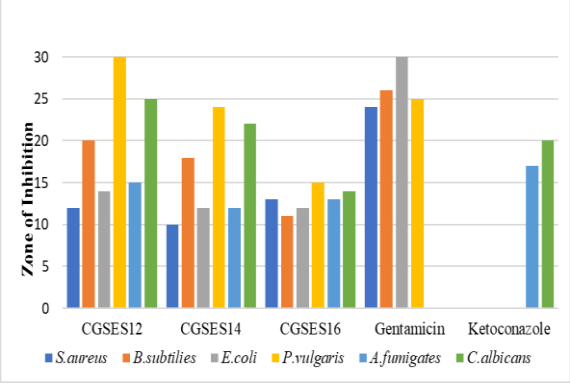


Figure 5. shows the correlation between the zones of inhibition and the alkyl chain length.

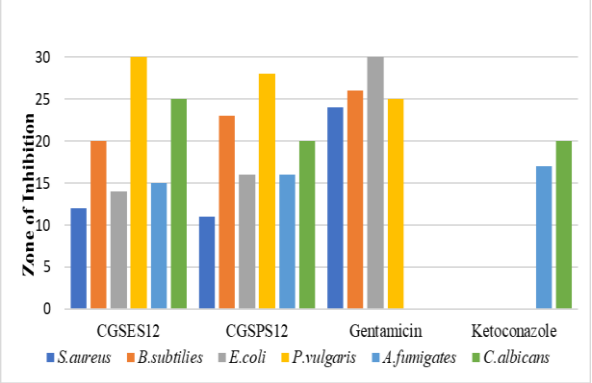


Figure 6. shows the correlation between the zones of inhibition and the type of the spacer.

Furthermore, the antimicrobial properties for all investigated surfactants were measured by detecting the minimum inhibitory concentrations (MICs) for each organism. Remarkably, the lowest MIC value was obtained for CGSES12 against *P. vulgaris* (2 μg/mL). Regarding the MIC results in general, the synthesized surfactants showed the highest activities against *B. subtilies* and *P.vulgaris.* Less sensitivity was observed in case of *E. coli* and *Staph aureus*. The results are listed in **Table 1.**

Table 1: Inhibition zone diameters and minimum inhibition concentrations (MIC) values of synthesized compounds against pathogenic microorganisms.

Compound	Tested Bacteria								Tested Fungi			
	S.aureus (RCMB010010)		*B.subtilies* RCMB 015 (1) (NRL B-543)		*E.coli* (RCMB 010052) (ATCC25955)		*P.vulgaris* RCMB 004 (1) (ATCC13315)		*A.fumigatus* (RCMB 002008)		*C.albicans* RCMB 005003 (1) (ATCC10231)	
	Zone of Inhibition (mm)	MIC (μg/mL)	Zone of Inhibition (mm)	MIC (μg/mL)	Zone of Inhibition (mm)	MIC (μg/mL)	Zone of Inhibition (mm)	MIC (μg/mL)	Zone of Inhibition (mm)	MIC (μg/mL)	Zone of Inhibition (mm)	MIC (μg/mL)
CGSES12	12	128	20	4	14	64	30	2	15	8	25	4
CGSES14	10	512	18	8	12	256	24	4	12	16	22	4
CGSES16	13	32	11	64	12	512	15	128	13	64	14	32
CGSPS12	11	256	23	4	16	32	28	2	16	16	20	8
CGSPS14	10	4	15	32	11	512	20	4	13	64	18	8
CGSPS16	15	32	18	8	14	64	17	512	11	128	13	128
Gentamicin	24	-	26	-	30	-	25	-	-	-	-	-
Ketoconazole	-	-	-	-	-	-	-	-	17		20	

Antimicrobial action of quaternary ammonium compounds has been attributed to microbial cell membranes destruction. Long hydrophobic chains are thought to permeate and damage bacterial cell membranes when they encounter such surfaces [26].

These cationic Gemini surfactants exhibit good antibacterial and antifungal properties. The teichoic acid in the cell wall of Gram-positive bacteria, lipopolysaccharide (LPS) in Gram-negative bacteria, and phospholipids in fungi are all responsible for the cell wall's negativity. Cationic Gemini surfactants electrostatically engage with negative charges on the cell wall. In addition, the cationic Gemini surfactant's hydrophobic group interacts with the hydrophobic end of the phospholipid in the microbial cell membrane. Both types of interaction lead to penetration and disruption. Eventually, degradation of the cell membrane takes place with subsequent leakage of the intracellular components. Therefore, these Gemini surfactants are more effective as disinfectants [1].

The study indicates that all newly synthesized surfactants exhibit antimicrobial activity, but the highest activity was determined for surfactants CGSES12, CGSPS12 i.e., those with the shortest alkyl chain. This can be interpreted by the need for a balance between hydrophobicity and hydrophilicity for optimum antimicrobial activity. Gemini surfactants with longer alkyl chain length are more hydrophobic which reduces water solubility and hinders the permeation of the microbial cell wall, eventually resulting in lower antimicrobial activity [27].

The relationship between the alkyl chain length of cationic surfactants in general and their antimicrobial activity follows a pattern described as “cut-off effect”, rather than a direct linear relevance. In such case, the biological activity increases with longer chain length up to a certain level then the activity is halted[28]. The highest antimicrobial activities have been observed in cationic surfactants of medium alkyl chain length (C12-C14). The activity is lost when the chain length is less than four or more than eighteen [29]. This can be interpreted by the ability of medium chains to disrupt microbial membranes while generating a free volume inside the bacterial membranes [30].

It is also noteworthy that the antimicrobial activity of QACs is affected by the counter anion, namely chloride, bromide or iodide. This is attributed to differences in their solubility and their ability to dissociate and to consequently increase the density of cationic charges [31]. This results in increased interaction with the bacterial surfaces which are negatively charged, and thus leading to more disruption of their membranes [29]. Chloride has the highest ability to do dissociate compared to bromide and iodide which is the lowest in this aspect [32].

4. Conclusions

According to the results of our study, surfactants can be classified as CGSES12, CGSPS12 / CGSES14, CGSPS14 / CGSES16, CGSPS16,

representing those with high, medium, and low antimicrobial potency, respectively. The synthesized Gemini surfactants have high efficiency among other oligomeric surfactants [13,25,33].

According to the tested microorganisms, the antimicrobial activity was the highest against Gram-negative bacteria, followed by fungi and the least against Gram-positive bacteria. These characteristics qualify the Gemini surfactants to be good candidates for widespread commercial uses as disinfectants as well as their possible application in the potentiation of antimicrobial agents.

Conflict of interest:

There is no conflict of interest to declare.

References

[1] Guo S, Sun X, Zou Q, Zhang J, Ni H. Antibacterial activities of five cationic gemini surfactants with ethylene glycol bisacetyl spacers. Journal of Surfactants and Detergents 2014;17:1089–97. https://doi.org/10.1007/s11743-014-1620-3.

[2] Buffet-Bataillon S, Tattevin P, Bonnaure-Mallet M, Jolivet-Gougeon A. Emergence of resistance to antibacterial agents: the role of quaternary ammonium compounds—a critical review. Int J Antimicrob Agents 2012;39:381–9.

[3] Borman S. Surfaces designed to kill bacteria. Chemical & Engineering News 2002;80:36–8.

[4] Silva SMC, Sousa JJS, Marques EF, Pais AACC, Michniak-Kohn BB. Structure activity relationships in alkylammonium C12-Gemini surfactants used as dermal permeation enhancers. AAPS Journal 2013;15:1119–27. https://doi.org/10.1208/s12248-013-9518-y.

[5] Brycki B. Gemini alkylammonium salts as biodeterioration inhibitors. Pol J Microbiol 2010;59:227–31.

[6] Domínguez-Arca V, Sabín J, Taboada P, García-Río L, Prieto G. Micellization thermodynamic behavior of gemini cationic surfactants. Modeling its adsorption at air/water interface. Journal of Molecular Liquids 2020;308. https://doi.org/10.1016/j.molliq.2020.113100.

[7] Gerba CP. Quaternary ammonium biocides: Efficacy in application. Applied and Environmental Microbiology 2015;81:464–9. https://doi.org/10.1128/AEM.02633-14.

[8] Fatma N, Panda M, Kabir-ud-Din, Beg M. Ester-bonded cationic gemini surfactants: Assessment of their cytotoxicity and antimicrobial activity. Journal of Molecular Liquids 2016;222:390–4. https://doi.org/10.1016/j.molliq.2016.07.044.

[9] Zhang L, Jia L, Zhao Z, Yang R, Wang J, Guo X. Synthesis, physiochemical properties, and antimicrobial activities of a novel gemini surfactants with biphenyl and multiple amide groups. Colloids and Surfaces A: Physicochemical and Engineering Aspects 2020;593. https://doi.org/10.1016/j.colsurfa.2020.124628.

[10] Fan Y, Wang Y. Self-assembly and functions of star-shaped oligomeric surfactants. Langmuir 2018;34:11220–41.

[11] Asadov ZH, Ahmadova GA, Rahimov RA, Hashimzade SZF, Abdullayev Y, Ismailov EH, et al. Aggregation and antimicrobial properties of gemini surfactants with mono- and di-(2-hydroxypropyl)ammonium head-groups: Effect of the spacer length and computational studies. Journal of Molecular Liquids 2020;302. https://doi.org/10.1016/j.molliq.2020.112579.

[12] Zhao X, Li Y, Yuan H, Yin J, Hu M. Antibacterial Mechanism of Octamethylene-1,8-Bis(Dodecyldimethylammonium Bromide) Against E. coli. Journal of Surfactants and Detergents 2017;20:717–23. https://doi.org/10.1007/s11743-017-1942-z.

[13] Dani U, Bahadur A, Kuperkar K. Micellization, Antimicrobial Activity and Curcumin Solubilization in Gemini Surfactants: Influence of Spacer and Non-Polar Tail. Colloids and Interface Science Communications 2018;25:22–30. https://doi.org/10.1016/j.colcom.2018.06.002.

[14] Falk NA. Surfactants as Antimicrobials: A Brief Overview of Microbial Interfacial Chemistry and Surfactant Antimicrobial Activity. Journal of Surfactants and Detergents 2019;22:1119–27. https://doi.org/10.1002/jsde.12293.

[15] McDonnell GE. Antiseptics, disinfection, and sterilization. Types, action, and resistance 2007.

[16] Badr EE, Kandeel EM, El-Sadek BM. Novel Gemini Cationic Surfactants Based on N, N-Dimethyl Fatty Hydrazide and 1,3-Dibromopropane: Synthesis, Evaluation of Surface and Antimicrobial Properties. Journal of Oleo Science 2010;59:647–52. https://doi.org/10.5650/jos.59.647.

[17] Bin-Hudayb NS, Badr EE, Hegazy MA. Adsorption and corrosion performance of new cationic gemini surfactants derivatives of fatty amido ethyl aminium chloride with ester spacer for mild steel in acidic solutions. Materials 2020;13:1–28. https://doi.org/10.3390/ma13122790.

[18] Patel JB, Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. n.d.

[19] Bauer AW, Kirby WMM, Sherris JC, Turck M. Antibiotic Susceptibility Testing by a Standardized Single Disk Method. 1966.

[20] Hindler JA, Howard BJ, Keiser JF. Antimicrobial agents and antimicrobial testing. Clinical and Pathogenic Microbiology 2nd Ed Mosby, St Louis 1994:145–96.

[21] Kuperkar K, Modi J, Patel K. Surface-active properties and antimicrobial study of conventional cationic and synthesized symmetrical gemini surfactants. Journal of Surfactants and Detergents

2012;15:107–15. https://doi.org/10.1007/s11743-011-1269-0.
[22] Lu QX, Fu SZ, Yin BL, Sun DZ, Wei Z bin, Ren LH, et al. Study on surface activity and bacteriostasis of a series of gemini cationic surfactants. Journal of Dispersion Science and Technology 2010;31:377–83. https://doi.org/10.1080/01932690903196433.
[23] Badawi AM, Mekawi MA, Mohamed AS, Mohamed MZ, Khowdairy MM. Surface and biological activity of some novel cationic surfactants. Journal of Surfactants and Detergents 2007;10:243–55. https://doi.org/10.1007/s11743-007-1040-8.
[24] Diz M, Manresa A, Pinazo A, Erra P, Infante M. Synthesis, surface active properties and antimicrobial activity of new bis quaternary ammonium compounds. Journal of the Chemical Society, Perkin Transactions 2 1994:1871–6.
[25] Yagci MB, Bolca S, Heuts JPA, Ming W, de With G. Antimicrobial polyurethane coatings based on ionic liquid quaternary ammonium compounds. Progress in Organic Coatings 2011;72:343–7. https://doi.org/10.1016/j.porgcoat.2011.05.006.
[26] Zhu HL, Hu ZY, Ma XM, Wang JL, Cao DL. Synthesis, Surface and Antimicrobial Activities of Cationic Gemini Surfactants with Semi-Rigid Spacers. Journal of Surfactants and Detergents 2016;19:265–74. https://doi.org/10.1007/s11743-015-1777-4.
[27] Balgavý P, Devínsky F. Cut-off effects in biological activities of surfactants. Adv Colloid Interface Sci 1996;66:23–63.
[28] Okazaki1 K, Manabe2 Y, Maeda3 T, Nagamune3 H, Kourai3 H. Quantitative Structure-Activity Relationship of Antibacterial Dodecylpyridinium Iodide Derivatives. vol. 1. 1996.
[29] Gilbert P, Moore LE. Cationic antiseptics: Diversity of action under a common epithet. Journal of Applied Microbiology 2005;99:703–15. https://doi.org/10.1111/j.1365-2672.2005.02664.x.
[30] Jiao Y, Niu L na, Ma S, Li J, Tay FR, Chen J hua. Quaternary ammonium-based biomedical materials: State-of-the-art, toxicological aspects and antimicrobial resistance. Progress in Polymer Science 2017;71:53–90. https://doi.org/10.1016/j.progpolymsci.2017.03.001.
[31] Mynercik D, Devinsky F, Lacko I. Influence of counterions on antimicrobial activity of quaternary ammonium salts. European Journal of Pharmaceutical Sciences 1996:S191.
[32] Murguía MC, Cristaldi MD, Porto A, di Conza J, Grau RJ. Synthesis, surface-active properties, and antimicrobial activities of new neutral and cationic trimeric surfactants. Journal of Surfactants and Detergents 2008;11:41–8.

تأثير الفاصل وطول سلسلة الألكيل على النشاط المضاد للميكروبات في ستة مركبات ذات نشاط سطحى كاتونية جديدة

شربات بكر [1،2] ,انتصار بدر[1] ,إيمان قنديل [1] , نشوى بن هديب [3] ,ياسمين محمود [4]

1. قسم الكيمياء - كلية العلوم بنات - جامعة الأزهر بالقاهرة.
2. قسم الكيمياء - كلية العلوم - جامعة بيشة – بيشة – السعودية.
3. قسم الكيمياء - كلية العلوم - جامعة القصيم – السعودية.
4. قسم الباثولوجيا الإكلينيكية – كلية الطب – جامعة عين شمس بالقاهرة.

الملخص

تم تصنيع ستة مواد خافضة للتوتر السطحي من نوع الكاتيونية الموجبة الجديدة ذات أطوال سلسلة ألكيل متفاوتة وخصائص فواصل مختلفة. تم دراسة تأثير طول سلسلة الألكيل وخصائص الفاصل على النشاط المضاد للميكروبات. عُرفت المجموعة الأولى من المركبات باسم (2-2 '- (إيثان-2،1- داى بس (أكسى) بس (N- (2- ألكانميدو ايثيل) , -N و N داى ميثل -2-أوكسوايثان -1- أمينيم) ثنائي كلوريد ، ولها ثلاثة أطوال مختلفة لسلسلة الألكيل (CGSES12، 14 و 16).(N1، N1، N3، -N3 تيترا ميثيل -N1-N31 بس (2- الكانوميدو ايثيل) بروبان - 1،3 (داى أمونيوم بروميد بثلاثة أطوال مختلفة لسلسلة الألكيل (CGSPS12 و 14 و 16). تم تقييم النشاط المضاد للميكروبات لكل مادة خافضة للتوتر السطحي عن طريق تحديد الحد الأدنى للتركيز المثبط (MIC) ومنطقة التثبيط ضد ستة كائنات تمثيلية: نوعان من البكتيريا موجبة الجرام؛ Staphylococcus aurous و Bacillus subtilis ، نوعان من البكتيريا سالبة الجرام ؛ Escherichia coli و Proteus vulgaris واثنين من الفطريات (Aspergillus fumigates وCandida albicans) . الدراسة إلى أن جميع المواد الخافضة للتوتر السطحي المُصنَّعة حديثًا تظهر نشاطًا مضادًا للميكروبات ، ولكن تم تحديد أعلى نشاط للمواد الخافضة للتوتر السطحي CGSES12، CGSPS12 أي تلك التي تحتوي على أقصر سلسلة ألكيل. بشكل ملحوظ ، تم الحصول على أدنى قيمة MIC لـ CGSES12 من الواضح أن النشاط المضاد للبكتيريا لا يرتبط بطول الفاصل. ومع ذلك ، زاد النشاط الكلي المضاد للبكتيريا مع تقليل طول سلسلة الالكيل.