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Synthesis and antimicrobial evaluation of some Schiff bases and their metal complexes against bacteria and fungi

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Abstract

Finding novel active compounds to solve the problem of microbial resistance of antibiotic is a matter of urgency. That's why several drugs were produced from many precursors. Schiff bases are a good base for synthesis several antimicrobial compounds . This work investigates biological activities as cytotoxicity and antimicrobial properties of some Schiff base compounds which synthesized by coupling reaction between two aromatic amines namely: aminoantipyrine, and 4-aminophenol by two aldehydes namely: vanillin and gluteraldehyde. Metal complexes of the obtained four Schiff bases were prepared throughout reaction with copper and ferric ions. FTIR, atomic absorption spectroscopy and ^{1}H-NMR measurements. microbial evaluation of Schiff bases and metal complexes was tested against various microorganisms including: gram +ve and gram -ve bacterial strains utilizing the diameter of inhibition zone, and minimum inhibitory concentration procedures. Showing that the cytotoxic effect of metal complexes is more than the ligand form . Furthermore, Ferric metal complexes exhibited significant inhibition than the copper complexes, which was attributed to the ability of oxidation-reduction tendency of Fe^{3+} ions than Cu^{2+}. The gram genera of the bacterial strains played a significant role on their resistivity towards the tested antimicrobial compounds, own to the nature of their cellular membranes.

Keywords: Schiff base; metal complexes; antimicrobial activity; cytotoxic assessment; gram-positive bacteria; gram-negative bacteria.

1. INTRODUCTION

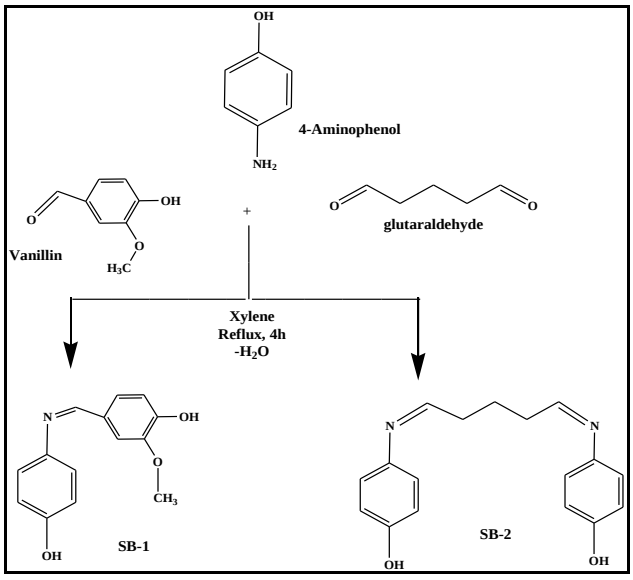
Metal complex compounds show different characteristic properties. Depending on coordination bond between metal ion to which they are bound and nature of metal ion and ligand. Metal complexes have various application in many fields. Schiff bases also known as imines or azomethines are used for complex formation. imine group -N=CH- in Schiff base has a big role in explanation of some operation in biological system [1] . flexibility and different structure of Schiff bases and their complexes make them easy to formed and studied [2]. They could be synthesized from Pyrazolone, amino acids, amino sugar, aromatic aldehydes, etc [3-7]. Biological activity of imine derivatives like

antiviral, antifungal, antimicrobial, anti-tumor and anticancer [8-10]. Schiff bases and their derivatives are known in medicines [11-13].various surveys have investigated the relation between metal ions and their complexes as Carcinogenic and bacteriostatic active compounds [14-16]. It was seen that biological activity increased by chelating with metal ions [17].

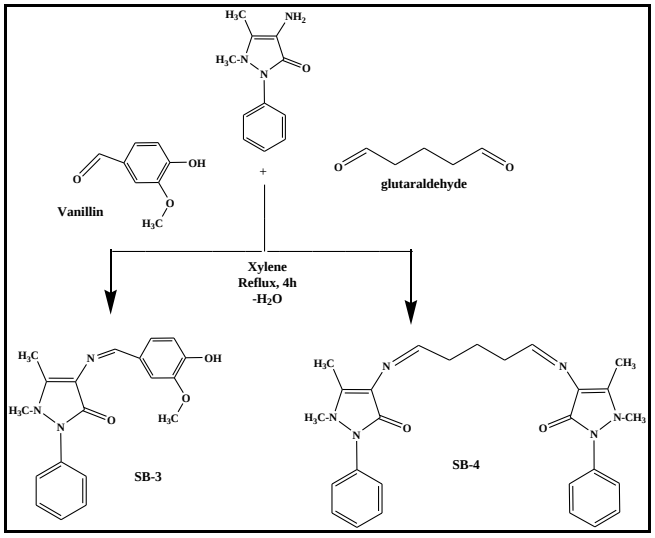
2. Experimental section

2.1 Synthesis of Schiff base

The coupling reaction has occurred between two aldehydes namely: vanillin and gluteraldehyde and two amine derivatives namely: 4-aminophenol and 4-aminoantipyrene in an equimolar ratio (0.1 mole) of the two reactants, solvent is xylene (100 ml) in one necked flask connected by a Dean-stark connection, and 0.1wt% dehydrating agent (*p*-toluene sulfonic acid). The reaction medium was agitated at reflux temperature (135 ^{o}C) until 1.8 mL of H_2O was obtained. Then, the product was obtained after evaporating the solvent. The product was further purified by washing with hot bidistilled water to remove the used catalyst and excess reactants, followed by drying at 70 ^{o}C under vacuum for 24 h to obtain **SB1-4**, Yield= 85-92% ***(Schemes 1, 2)***.



Scheme 1: Synthesis of 4-aminophenol Schiff base derivatives SB1-2.

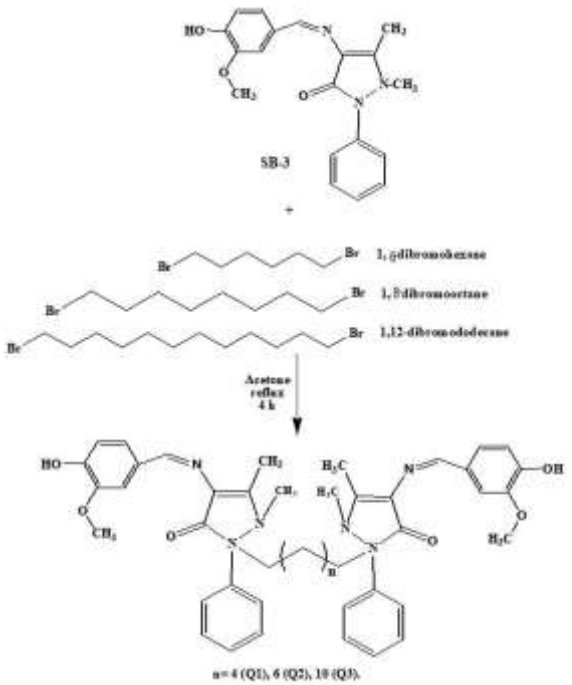


Scheme 2: Synthesis of 4-aminoantipyrene Schiff base derivatives SB3-4.

2.2 Synthesis of the targeted diquaternary biocides

A Quaternization reaction was performed between the prepared Schiff base product (**SB**) and three dibromo alkanes, namely: 1,6-bromohexane, 1,8-bromooctane, and 1,12-bromododecane at 1:2 molar ratio, respectively, in an appropriate amount of

acetone as a solvent for 4hr . then the reaction medium was settled to precipitate the desired diquaternary products **Q1-3**. Filtration, washing by diethyl ether then drying for 24 hr at 40 ^{o}C. The products were designated as **Q1-3** for the hexyl, octyl, and dodecyl derivatives, Yield= 85-82, 83% ***(Scheme 3)***.



Scheme 3: Synthesis of diquaternary biocides (Q1-3).

2.2 Synthesis of SB-4/Fe^{3+} and SB-4/Cu^{2+}

Preparation of Schiff bases metal complexes by the reaction between SB-4 and $FeCl_3$ and $CuSO_4$ salts. In a typical reaction, 0.1 mole of SB-4 was dissolved in ethyl alcohol (50 mL) and 0.1 mole of $FeCl_3$ and/or $CuSO_4$ was dissolved in ethyl alcohol (50 mL). The two solutions of SB-4 and metal salts were mixed in 250 mL on neck flask and refluxed for 12 h, and then left to cool to room temperature. The products were filtered and washed several times using ethyl alcohol to remove the unreacted compounds, and left to dry under vacuum at 40 ^{o}C for 24 h. The obtained metal complexes were designated as SB4-Fe and SB4-Cu in yield % of 72% and 69%, respectively.

2.3 Surface and interfacial tension measurements

at 25 ^{o}C, freshly prepared **Q1-3** dicationic solutions in 0.001-10 mM concentration were tested in bidistilled water utilizing a Kruss-K6 tensiometer to measure Surface tension. While paraffin oil and (0.1% concentration) of surfactant [18] were performed to measure the interfacial tension.

2.4 Anti-microbial assay

Anti-microbial evaluation was performed for prepared diquaternary (**Q1-3)** and metal complexes towards *Staphylococcus aureus* (NCTC-7447), *E. coli* (NCTC-1041), *Bacillus subtillus* (NCIB-3610), *Pseudomonas aeruginosa* (NCIB-9016), and *Desulfomonas pigra*, a popular species of SRB. The fungistatic activity was

investigated using *Candida albicans and Aspergillus niger*..

antimicrobial activities against fungus and bacteria were tested using the agar well diffusion technique [19]. The bacteria cultures were incubated in a nutrient agar medium, whereas the fungal cultures were grown in a malt medium. The bacteria were cultured in broth media for 24 h. In the case of fungi, the broth medium was cultured for 48 hours before being filtered through a fine coating of antiseptic Sintered Glass G2 to eliminate mycelia particles before being utilized for inoculation.

At 40 ^{o}C ,50 ml of agar medium was inoculated by (1.0) ml inoculating agent . Poured agar onto 120 mm Petri plates and let cool to ambient temperature. Utilizing antiseptic tubes, in agar plates, wells were cut and loaded to the agar's surface with 0.1 mL of the tested compounds (5 mg/mL dimethyl formamide). Incubated for 24 hr at 30 ^{o}for bacteria and 48hr for fungus. average score collected from three separate runs has been used to determine each sample's zone of inhibition.

2.5 Minimum inhibition concentration (*MIC*)

Biological activity was expressed in terms of minimum inhibition concentration (MIC). MIC is the minimal concentration of biocides that can inhibit the detectable growing of microorganisms after incubation for 24 hours. MICs were estimated using the dilution technique. In typical procedures, the prepared biocide was dissolved in different concentrations. An aliquot of the different biocides solutions, 1 mL in volume, was placed in agar media (14 mL). The final concentrations of the tested biocides were 500-6 μg/mL.

3. Results and Discussion

3.1 Characterization

The chemical structures of the prepared Schiff bases of 4-aminoantipyrene was confirmed using elemental analyses and FTIR, as follows:

Schiff base characterization

Elemental analysis: SB-1: *Calc.:* C=69.22%; H=5.38%, N = 5.77%, *Found:* C=68.31%, H=5.22%, N=5.62%. **SB-2:** *Calc.:* C=72.33%, H=6.42%, N=9.91%, *Found:* C=70.84%, H=6.14%, N=9.46%. **SB-3:** *Calc.:* C=67.63%, H=5.67%, N=12.47%, *Found:* C=65.93%, H=5.46%, N=11.88%. **SB-4:** *Calc.:* C=68.92%, H=6.44%, N=17.85%, *Found:* C=66.91%, H=6.22%, N=16.54%. **FTIR spectra:** FTIR spectra of the prepared four Schiff bases (**SB1-4**) were showed significant absorption bands representing the fundamental functional groups which formed during the coupling reactions of the amine and carbonyl groups at: 31oo-35oo cm^{-1} (O-H, N-H stretching) [20], C-H

aliphatic (symmetric and asymmetric stretching at 2862, 2924 cm^{-1} [21], 1658 cm^{-1} (C=C conjugated) [22], 1650 cm^{-1} (-C=N- azomethine) [23](***Figure 1***: representative for the prepared Schiff base derivatives).

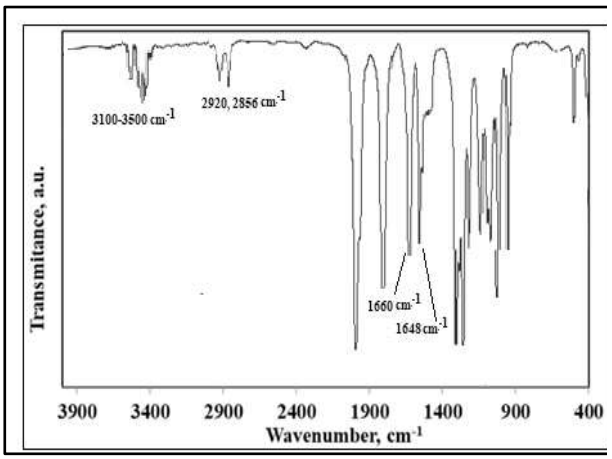


Figure 1: FTIR spectra of SB-3.

Diquaternary compounds characterization

The prepared diquaternary derivatives (**Q1-3**) were characterized using elemental analysis, FTIR, and ^{1}H-NMR spectroscopy.

Elemental analysis: Q1: *Calc.:* C=56.5%, H=5.1%, N= 9%, Br=18%, *Found* C=56%, H= 5%, N =9%, Br=18%; **Q2**: *Calc.:* C=58%, H=5.1%, N =9%, Br =17%, *Found:* C=56%, H=4%, N=7%, Br=16%; **Q3**: *Calc.:* C=59%, H=6%, N=9%, Br=16%, *Found:* C=57%, H=5%, N=7%, Br=14% **FTIR spectra** showed significant bands corresponding to the present functional groups at: 3100-3500 cm^{-1} (-OH, -NH stretching), 3025 cm^{-1} (C-N^{+} stretching) confirming the formation of diquaternary products, 2862, 2932cm^{-1} (symmetric and asymmetric stretching of C-H aliphatic), 1668 cm^{-1} (C=C conjugated), 1647 cm^{-1} (-C=N- azomethine) ***(Figure 2)***. ^{1}H-NMR: δ(ppm)=1.73 ppm (s, 6H, $\underline{CH_3}$-C=C), 1.85 ppm (**Q1**: m, 8H, (-C$\underline{H_2}$-)$_4$; **Q2**: m, 12H, (-C$\underline{H_2}$-)$_6$, **Q3**: m, 20H, (-C$\underline{H_2}$-)$_{10}$), 2.45 ppm (s, 6H, C$\underline{H_3}$-N), 3.71 ppm (s, 6H, C$\underline{H_3}$-O), 5.1 ppm (m, 2H, $\underline{H}$-O-Ar), 6.61 ppm (m, 4H, *m*$\underline{H}$-C-Ar), 6.76 ppm (m, 6H, *o,p*$\underline{H}$-C-Ar), 8.1 ppm (s, 2H, $\underline{H}$-C=N-azomethine).

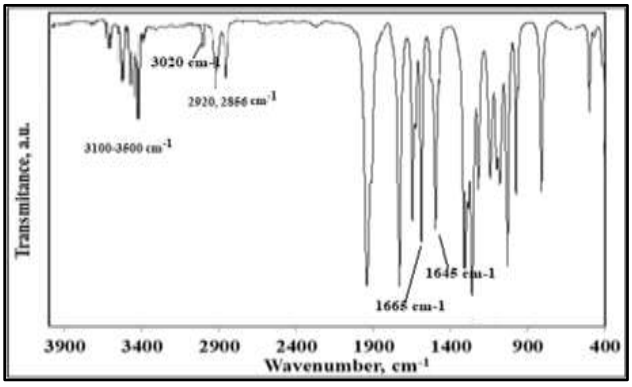


Figure 2: FTIR spectra of diquaternary (Q1).

3.2 Surface Tension and Critical Micelle Concentration

Figure 3 relationship between surface tension (γ) and -log concentration (C) of the prepared diquaternary biocides at 25 ^{o}C. It is noticeable that γ *vs.* –log C relation is notable by two distinct zones. One in a reduced concentration range and distinguished by a rapid decrease in surface tension values. (CMC) is produced

by the concentration at the intersection of these two locations (CMC). Furthermore, the greater reduction in surface tension values in ***Figure 3*** demonstrates that these diquaternary compounds have excellent surface activity. This is owing to the surfactant molecules' capacity to considerably reduce surface tension. ***Figure 3*** demonstrates the importance of the lengths of **Q1-3** hydrophobic chains in determining the surface tension magnitude of their solutions. This effect is caused by a greater contact between the nonpolar chains (hydrophobes) and the polar medium. To reduce that interaction, the molecules are guided towards the air-water contact, which significantly reduces surface tension. As seen in ***Figure 3***, the length of the hydrophobic chain has a major influence on CMC values within a similar homologous chain. As the hydrophobic chain length rises, the critical micelle concentration values of **Q1-3** derivatives decrease. This result was described in some reported studies [24,25]. The CMC value of the dodecyl derivative is the lowest (**Q3**).

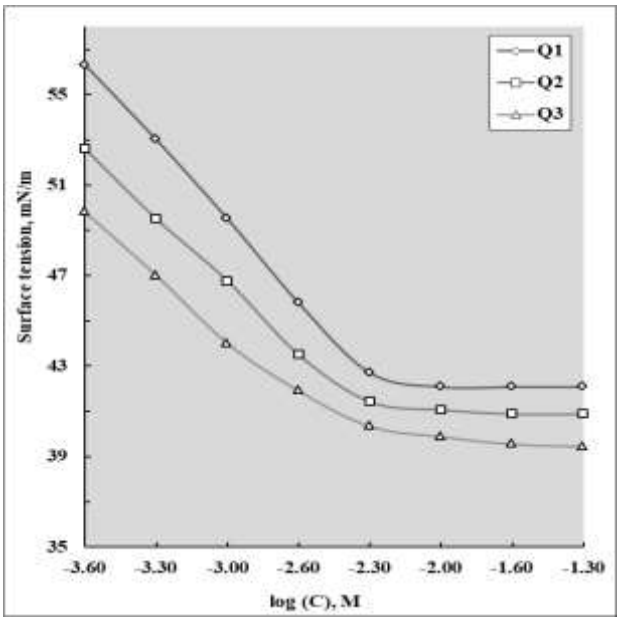


Figure 3: Surface tension-log concentration of the prepared diquaternary derivatives (Q1-3) at 25 ºC.

according to Eq. 1:

$$\pi_{cmc} = \gamma_o - \gamma_{cmc} \quad (1)$$

The efficiency values (π_{cmc}) of the prepared diquaternary surfactants showed high surface activity. π_{cmc} value also showed improved surface activity than that of quaternary homologs with identical hydrophobic tails [26] . This impact might be attributed to the distinctive adsorption properties of compounds at interfaces. hydrophobic spacer tails promote adsorption in interfaces that extremely lower surface tension but increase efficacy. While effectiveness (pC_{20}) is described as the concentration of surfactant which can reduce 20 mN/m from surface tension of bidistilled water, taken from surface tension profile as concentration-related to 51.2 mN/m. It appears that effectual amphiphiles have lesser π_{cmc} values. The π_{cmc} values of **Q1-3** surfactants displayed relatively low values ranging from 0.525-0.416 mM compared with the quaternary surfactants with identical hydrophobic tails [27]. The values of π_{cmc} and pC_{20} of the prepared surfactants (**Q1-3**) illustrated their potential as effectual interfacial agents in numerous uses that required great depression in the surface tension (***Table 1***). These results were illustrated in several reports [28,29]. These uses involve phase transfer catalysis, nucleic acid solubilization, gene extraction, food additives, pharmaceuticals, household products, and antimicrobial substances.

(Γ_{max}) is the surfactant concentration at the saturation of the surface interface near the critical micelle concentration. Γ_{max} is a perfect predictor of efficacy of surfactant adsorption at the water-air interface. Γ_{max} of the prepared surfactants was estimated utilizing the Gibbs equation (Eq. 2), ***Table 1***:

$$\Gamma_{max} = [\partial\gamma/\partial \log C] / [3x2.303RT] \quad (2)$$

While A_{min} (minimum surface area) estimated from the following equation (Eq. 3):

$$Amin = \frac{1}{NA.\Gamma max} \quad (3)$$

Where N_A is constant and referred to several Avogadro.

Larger hydrophobes provide high surface pressure ($\partial\gamma/\partial \log C$), which relates to increased surfactant molecule concentration at the interface. The increased surface concentration is because of the hydrophobe-water interface (repulsion forces) that improved due to the value reduction in HLB, which raised the surfactant molecules at the interface and therefore increased Γ_{max} as seen in ***Table 1***. Raising the surface concentration (surface pressure, $\partial\gamma/\partial \log C$) leads to enhance number of surfactant molecules at interface, causing crowding & decreasing

accessible area at the interface for each molecule. The results in ***Table 1*** show that extending the length of the hydrophobic molecules reduces the accessible area for surfactant compounds at the interface (A_{min}).

3.3 Standard free energy of adsorption and micellization (ΔG_{ads}, ΔG_{mic})

the free energy of adsorption (ΔG_{ads}) and micellization (ΔG_{mic}) were estimated using Rosen's approach (Eqs. 4-5) [26].

$$\Delta G_{mic} = -RT \ln (CMC) \quad (4)$$

$$\Delta G_{ads} = \Delta G_{mic} - (6.023 \times 10^{-1} \pi_{cmc} \cdot A_{min}) \quad (5)$$

where, R= 8.31×10^{7} erg/ mol·K, T is the absolute temperature, π_{cmc} efficiency and A_{min} lowest surface area.

minus value of ΔG_{ads} and ΔG_{mic} ***(Table 1)*** suggests that both micellization and adsorption processes are occurring spontaneously at 25 ^{o}C. Comparison between ΔG_{ads} and ΔG_{mic} values of the prepared surfactants showed the greater negatives of ΔG_{ads} suggesting the amphiphiles' proclivity for adsorption. But, at the same time exhibit a good tendency towards micellization.

Table 1: Critical micelle concentration (CMC), effectiveness (π_{cmc}), efficiency (PC_{20}), maximum surface excess (Γ_{max}) and minimum surface area (A_{min}), free energy changes of adsorption (ΔG_{ads}) and micellization (ΔG_{mic}) of Q1-3 surfactants at 25 ^{o}C

Compound	CMC, M/L	π_{cmc}, mN/m	PC_{20}, M/L	Γ_{max}, mol/cm^2. 10^{-8}	A_{min}, nm^2	ΔG_{ads}, Kj/mole	ΔG_{mic}, Kj/mole
Q1	0.000525	36	0.0000050	7.87	2.11	-22.94	-18.86
Q2	0.000495	34	0.0000071	8.21	2.02	-23.31	-19.29
Q3	0.000416	33	0.0000089	8.33	1.99	-24.18	-20.11

3.4 Cytotoxic activity of prepared compounds

The bacterial cell membrane is thought to be made up of phospholipids and particular amino acids. The cellular membrane's functioning is primarily the dissemination of the constituents required for biological processes and the excretion of the wastes created. The selective permeability determines the regulation of the two processes. The charged amino acids (teichoic acid derivatives) in the outer cellular membrane govern the entering or exiting of the polar species into or out of the cells, whereas phospholipids and peptidoglycans play this role for nonpolar materials [30]. When the preferential permeability of the cell membranes is damaged the vital biological processes, result in death for the microorganisms. Bacterial and fungal biocides achieved their lethal role on the microorganisms by

breaking and/or destroying the high selectivity of the cellular membranes. This behavior commonly occurs in the case of cationic biocides. anti-microbial effectiveness was measured by the inhibition zone diameter method of the produced dicationic biocides against several microorganisms (*E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtillus*, and *Desulfomonus pigra*) was high as depicted in ***Table 2***. The inhibitory effects of **Q1-3** were increased by increasing their spacer chain length, and the highest inhibitory zone diameter was obtained for **Q3** biocide against *E. coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* at 17.5, 22.0, 23.2, and 27.8 mm, referring to the used reference (cetyl trimethyl ammonium bromide-CTABr, 12.3 mm), respectively. These results were in comparison with the reported results of SRB bacteria using cationic biocides [31,32].

Several variables including structural and interfacial characteristics, contribute to the excellent antibacterial activity of cationic surfactants. The benzene ring nucleus, the aliphatic hydrocarbon chains, azomethine groups, and positively charged head groups (N^+) are all structural elements. Low effectiveness, efficiency, low surface area, and high surface concentration, are examples of interfacial factors [33]. The existence of aliphatic chains promotes adsorption of biocides onto the cell membranes . Because of the matching behavior between the aliphatic chains of their molecules and the nonpolar chains which constituted the bacterial lipid layers. The existence of positive charges at the biocide molecules (**Q1-3**) is attached to the negatively charged teichoic acid derivatives that participated in the cellular membranes. Furthermore, the highly interfacial activities of the biocides facilitate the contact between the external components and the cellular membrane, while suppressing the selective permeability. As a result, the microorganisms' biochemical reactions and metabolic pathways are affected, resulting in the death of microorganisms [34]. **Q3** displayed the highest efficiency against the tested bacterial strains. That was ascribed to its greater efficacy values as well as a higher maximum surface excess. Higher efficiency values suggest a proclivity for adsorption at various surfaces, including bacterial membranes. Furthermore, the improved surface excess demonstrated the presence of the adsorbed **Q3** molecules at high concentrations at the interfaces. The antibacterial properties of **Q1-3** biocides were shown to be effective against sulfur-reducing bacteria (*Deulfomonus pigra*). in ***Table* 2** This might be attributed to the SRB bacterial strain's resistance to harsh

factors in the environment due to the stiffness of their cell membranes.

Table 2: Bactericidal activity of the synthesized Q1-3 biocides

Derivative	Inhibition zone diameter, mm				
	E. coli	***Salmonella typhi.***	***Staphylococcus aur.***	***Bacillus sub.***	***Deulfomonus pigra***
SB-3	13	13	13	14	13
Q1	13.0	14.0	15.0	16.7	14.2
Q2	16.8	18.2	17.0	22.5	16.5
Q3	17.5	22.0	23.2	27.8	19.1
CTABr	12.3	12.3	12.3	12.3	11.0

The antifungal behavior of **Q1-3** biocides against *Candida albicans* and *Aspergillus niger* were illustrated in ***Table 3***. The recorded inhibition zones ranged between 15.7 and 25.4 mm, referring to the used reference (Grisofulvine, 11.6 mm), indicating their high cytotoxic activities towards the examined fungus. The inhibition diameters values revealed that cytotoxic efficacies of **Q1-3** are significantly associated with their interfacial characteristics, mainly their efficacy and maximum surface excess. The cytotoxic efficiencies of **Q1-3** biocides were demonstrated to have an excellent inhibitory propensity against various bacterial species and fungi. The potencies of these biocides can be referred to as the presence of azomethine groups (-N=C-) and diquaternary ($-N^+---N^+-$) groups in these molecules. The existence of these groups promotes the adsorption of the molecule at the microorganism's outer membranes, while the existence of bromide ions (counter ions) allows them to pass readily across these membranes. As a result, the biological response in the cells is severely harmed, which leads to cell mortality.

Table 3: Fungicidal activity of the synthesized Q1-3 biocides

Derivative	Inhibition zone diameter, mm *	
	Aspergillus niger	***Aspergillus flauv***
SB-3	14.5	14.2
Q1	15.7	16.3
Q2	19.2	18.2
Q3	24.5	25.4
Grisofulvine	11.6	11.6

3.5 Minimum inhibitory concentration (*MIC*)

Minimum inhibition concentrations (*MIC*) of the prepared biocides **Q1-3**, and cetyl trimethyl ammonium bromide (CTABr) were listed in ***Table 4.*** MIC values of CTABr ranged between 20 and 600 μM. Comparing the results of MICs of the tested compounds and the reference biocide (CTABr) revealed their higher efficacies compared to CTABr for combat SRB [35]. By increasing the spacer chain length in biocides , the efficiency towards the different types of bacterial cells increased . **Q1** showed the lowest efficiency towards the bacterial strains in a

concentration range of 50-200 μM. While **Q3** performed the maximum efficiency with the lower concentration ranges of 6-20 μM. The mode of action of the cationic biocides upon the different germs is generally preceded via an adsorption mechanism. In this mechanism, the biocides adsorb onto the negative centers on the cellular membranes. The adsorption leads to deducing cellular osmotic stability and outflow of biological constituents in the cells [36]. Several proposed mechanisms can explain the effect on the microorganisms based on the type of the bacterial strains (gram +ve or gram -ve) including impermeable coat formation on the bacterial membranes, penetration of smaller biocides molecules into the cells, and their interaction by the oppositely charged sites [37,38] in the cell, and inhibition of bacterial growth.

It is clear that *P. aeruginosa* and *S. typhiumurium* species exposed higher resistivity towards the prepared biocides and also against the used reference. That can be attributed to the nature of the chemical composition of their cellular membranes. It is reported that gram-negative bacteria are more resistant to biocides than gram + ve bacteria, due to the types of constituents in the cellular membranes of each type [39]. The lipopolysaccharides and proteins in the gram-negative bacterial cell membrane limit the biocide molecules' penetration into the bacterial cells. Consequently, their diffusion into these types of cells required sufficient acceptability between the hydrophobic-hydrophilic balance (*HLB*) of the biocide molecules and the cellular membrane constituents. The prepared cationics were monitored for their toxicity for sulfate-reducing bacteria (*D. pigra*), (***Table 4***). The data showed their comparatively higher efficacies against SRB bacteria. SRB bacteria (anaerobic bacteria) released H_2S gas in oilfields due to their ability to reduce sulfur-containing compounds in crude oil. The *MIC* values of the prepared cationic biocides showed acceptable efficacies against SRB. (***Table 4*)** show increasing of the chain length of the synthesized surfactants increases their biocidal activities against SRB bacteria.

Table 4: Minimum inhibitory concentration values, *MIC*[a] (μM) of the synthesized biocides Q1-3 against different bacterial strains

Biocides	Bacteria					
	***S. aureus* ATCC 29213**	***B. subtilis* ATCC 55422**	***E. coli* ATCC 25922**	***P. aeruginosa* ATCC 27853**	***S. typhiumurium* ATCC 27948**	***Desulfomonas pigra* ATCC 29098**
SB-3	200	100	200	>600	>600	100
Q1	50	50	200	600	> 600	200
Q2	50	20	100	500	> 600	100
Q3	20	6	20	400	> 600	50
CTABr	20	50	100	300	600	400

[a] The data is a mean of five replicates with relative error ~7%.

Biological activity of metal complexes

Table 5 showed the antifungal and antibacterial activities of copper and ferric complexes of SB-4 presented acceptable efficacies against SRB. Metal complexes of Schiff bases showing anti-microbial activity than Schiff bases ligand,

Compounds	Fungi		Bacteria				
	Asp. niger	***Asp. Flavu.***	***E. coli***	***Salmonella typhi.***	***Staphylococcus aur.***	***Bacillus sub.***	***Deulfomonus pigra***
SB-4/Fe^{3+}	27	30	19	20	16	22	***16***
SB-4/Cu^{2+}	26	28	24	26	23	28	***18***
Reference	11.6	11.6	12.3	12.3	12.3	12.3	12.3

Table 5: Biological activity of SB-4/Cu^{2+}, SB-4/Fe^{3+} complexes

4. Conclusion

The chemical structures of the diquaternary cationic surfactants showed a high influence on their surface activities. The critical micelle concentration, effectiveness, and maximum surface excess decreased by increasing alkyl spacers, while minimum surface area was increased. Inhibition zone diameter evaluation showed increased inhibition area by increasing surface activity of biocides. Q3 showed the highest area of inhibition against the tested bacterial strains. sulfate-reducing bacteria was highly inhibited by applying biocides compared to the traditional biocides. The prepared biocides Q1-3 showed promising results due to their comparatively higher efficacies against SRB bacteria. The MIC values of the prepared cationic biocides

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