Supporting Information

Novel anionic surfactant-modified chlorhexidine and its potent antimicrobial properties

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1. Structural Characterization via ^{1}H NMR

The representative ^{1}H NMR spectrum is shown in Figure S1. The multiple peaks at 1.4 ppm and 1.55 ppm with the integration of 4.08 and 3.97 are corresponding to H-3, 4 and H-2, 5 proton signals of CHX. The triplet peaks at 3.4 ppm represent H-1 and H-6 with two proton signals each. Two doublet peaks at 6.9 ppm and 7.2 ppm represent the benzene ring protons with the two protons closer to chlorine having a lower chemical shield. Additionally, the dodecyl chain proton signal (-CH_2-) in the ^{1}H NMR was detected at 3.35 ppm and the methyl group of SDS was identified at 3.20 ppm. The result indicates that both dodecyl sulfate and CHX were present in the crystal. To further understand the association between CHX and dodecyl sulfate, the conventional NOESY experiment was performed (Figure S2). The spectrum clearly shows that the methyl group of dodecyl sulfate (3.35ppm) interacts with H-3,4 and H-2,5 of CHX (1.4ppm and 1.55ppm), as evidenced by a cross peak shown in Figure S2. This finding suggests that CHX and dodecyl sulfate are in proximity with each other in crystal structure.

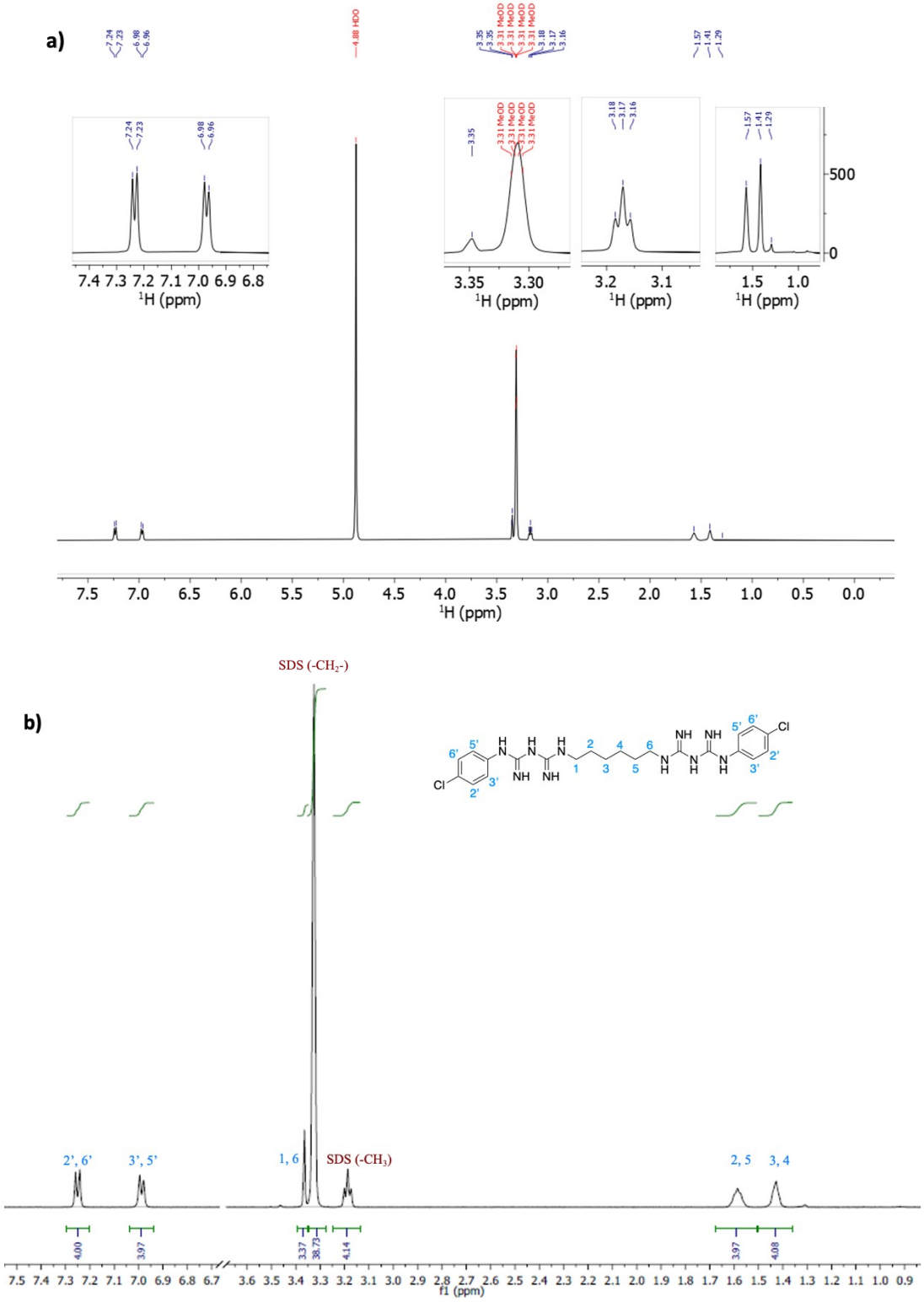

Figure S1. ^{1}H NMR spectrum of full spectrum CHX-DS crystal. (a) full ^{1}H NMR spectrum; (b) ^{1}H NMR spectrum close-up with assigned peaks.

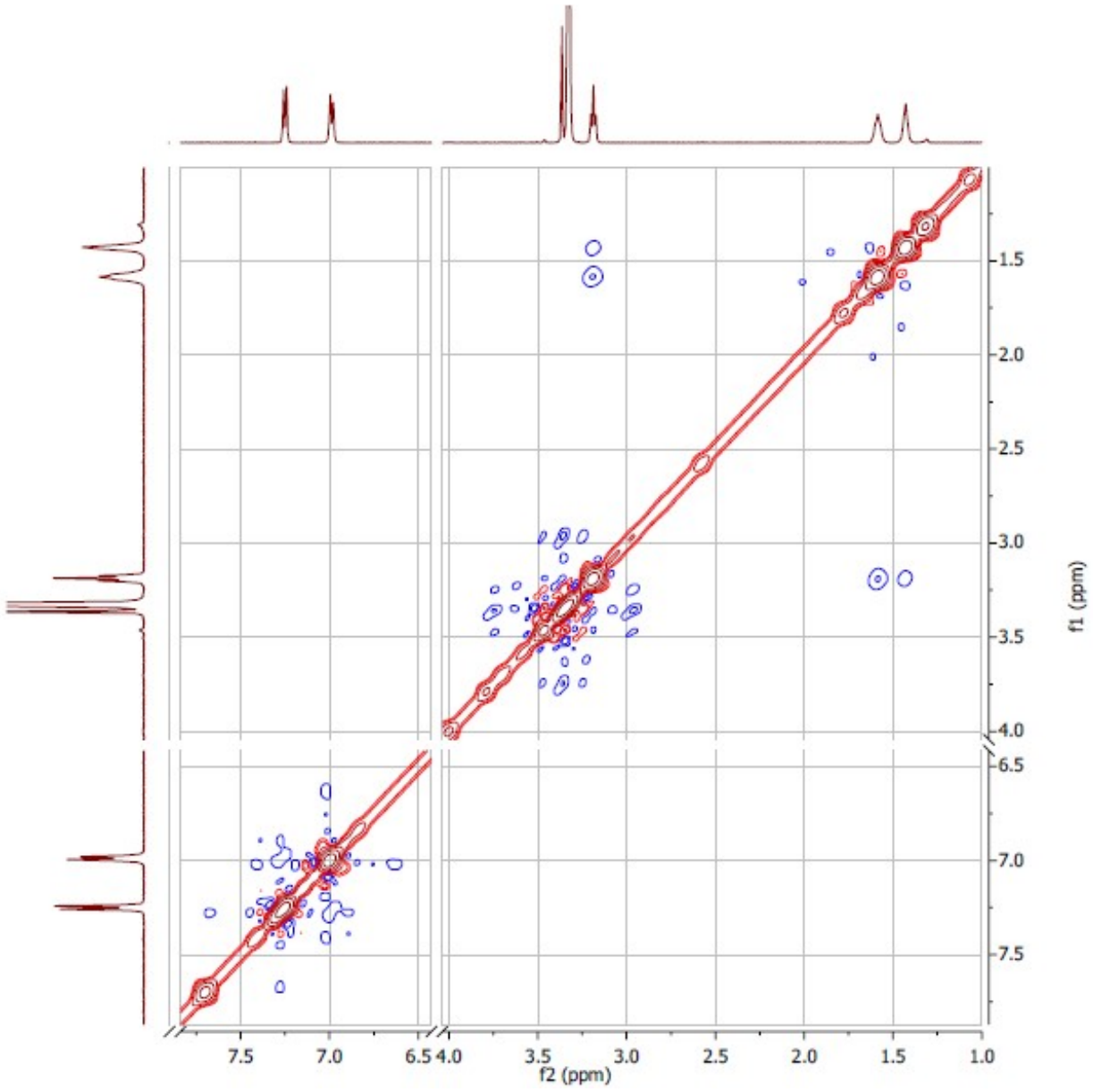

Figure S2. ^{1}H NMR (NOESY) spectrum of CHX-DS crystal.

2. Mass Spectroscopy Method and Results

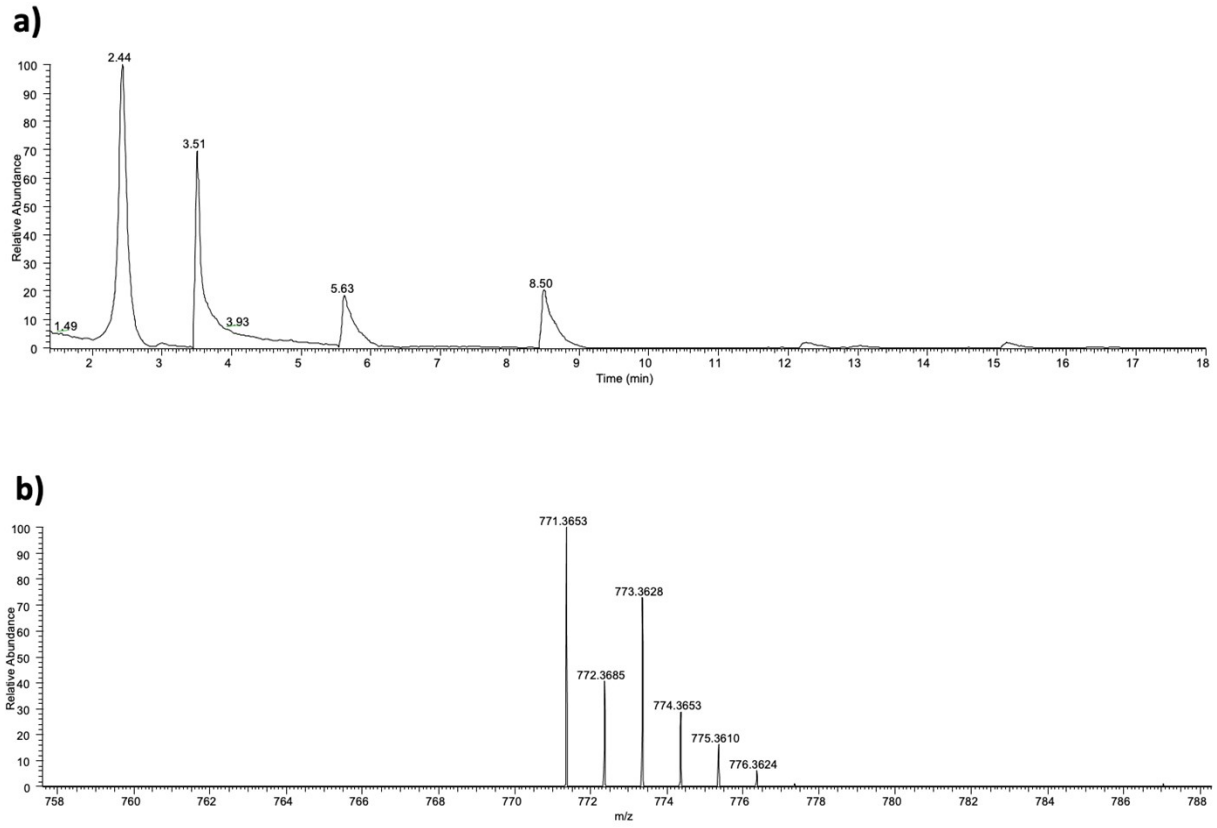

Figure S3. Liquid chromatography mass spectroscopy (LCMS) analysis of CHX-DS. a) Liquid chromatography separation of CHX-DS; b) Mass spectroscopy of CHX-DS.

The mass of 771 - 776 Daltons was identified which corresponds to one CHX coupled with one dodecyl sulfate molecule in positive mode of MS.

3. Crystal structure data

Crystal data and structure refinement, bond lengths, and bond angles for chlorhexidine dodecyl sulfate (CHX-DS) are presented in Tables S1-S3, respectively.

Table S1. Crystal data and structure refinement for CHX-DS.

Identification code	CHX_SDS
Empirical formula	$C_{46}H_{82}Cl_2N_{10}O_8S_2$
Formula weight	1038.23
Temperature/K	99.99
Crystal system	triclinic
Space group	P-1
a/Å	11.6393(3)
b/Å	13.6352(3)
c/Å	18.8400(5)
α/°	70.2440(10)
β/°	78.3980(10)
γ/°	89.769(2)
Volume/Å^3	2749.86(12)
Z	2
ρ_{calc}g/cm^3	1.254
μ/mm^{-1}	2.238
F(000)	1116.0
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	5.1 to 149.476
Index ranges	$-13 \leq h \leq 14$, $-17 \leq k \leq 16$, $-23 \leq l \leq 23$
Reflections collected	34528
Independent reflections	10985 [R_{int} = 0.1176, R_{sigma} = 0.1162]
Data/restraints/parameters	10985/558/726
Goodness-of-fit on F^2	1.134
Final R indexes [I>=2σ (I)]	R_1 = 0.0744, wR_2 = 0.1722
Final R indexes [all data]	R_1 = 0.1038, wR_2 = 0.1815
Largest diff. peak/hole / e Å^{-3}	0.65/-0.42

Table S2. Bond Lengths for CHX-DS.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S01	O005	1.448(2)	C011	C012	1.381(6)
S01	O00A	1.457(2)	C012	C014	1.382(6)
S01	O00B	1.451(3)	C013	C017	1.396(5)
S01	O00C	1.572(2)	C013	C01C	1.391(5)
S02	O006	1.451(2)	C0	C12	1.517(13)
S02	O007	1.447(2)	C017	C019	1.386(6)
S02	O008	1.589(2)	C018	C019	1.384(6)
S02	O009	1.449(2)	C018	C01D	1.384(6)
Cl03	C012	1.746(4)	C01A	C01F	1.524(5)
Cl04	C018	1.744(4)	C01B	C01E	1.518(5)
O008	C010	1.450(4)	C01B	C01F	1.522(5)
O00C	C0	1.52(3)	C01C	C01D	1.387(6)
O00C	C11	1.452(15)	C01E	C01I	1.526(5)
N00D	C00N	1.340(4)	C01G	C01H	1.518(6)
N00D	C00Q	1.461(4)	C01G	C01J	1.513(5)
N00E	C00P	1.356(4)	C01H	C01L	1.520(6)
N00E	C00S	1.414(4)	C01I	C01K	1.529(6)
N00F	C00P	1.337(4)	C01J	C01K	1.526(6)
N00G	C00N	1.349(4)	C1	C4	1.539(13)
N00H	C00R	1.359(5)	C1	C14	1.503(12)
N00I	C00O	1.326(4)	C2	C3	1.534(9)
N00I	C00Z	1.454(4)	C2	C11	1.517(9)
N00J	C00O	1.338(4)	C3	C01T	1.518(9)
N00K	C00O	1.339(4)	C4	C6	1.529(13)

Table S3. Bond Angles for CHX-DS.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O005	S01	O00A	112.94(14)	C011	C012	Cl03	119.0(3)
O005	S01	O00B	114.36(15)	C011	C012	C014	121.1(3)
O005	S01	O00C	102.24(13)	C014	C012	Cl03	119.8(3)
O00A	S01	O00C	107.17(15)	C017	C013	N00M	122.7(3)
O00B	S01	O00A	112.03(14)	C01C	C013	N00M	117.7(3)
O00B	S01	O00C	107.20(15)	C01C	C013	C017	119.5(3)
O006	S02	O008	106.69(13)	C012	C014	C00U	119.5(3)
O007	S02	O006	113.28(14)	C00V	C015	C00W	113.6(3)
O007	S02	O008	102.16(13)	C12	C0	O00C	112.2(19)
O007	S02	O009	114.40(15)	C019	C017	C013	119.7(4)
O009	S02	O006	112.02(14)	C019	C018	Cl04	119.4(3)
O009	S02	O008	107.32(13)	C019	C018	C01D	121.0(4)
C010	O008	S02	116.48(19)	C01D	C018	Cl04	119.6(3)
C0	O00C	S01	122.8(11)	C018	C019	C017	120.0(4)
C11	O00C	S01	113.4(5)	C01F	C01A	C00Y	112.2(3)
C00N	N00D	C00Q	123.1(3)	C01E	C01B	C01F	113.2(3)
C00P	N00E	C00S	127.4(3)	C01D	C01C	C013	120.7(4)
C00O	N00I	C00Z	122.2(3)	C018	C01D	C01C	119.0(4)
C00R	N00K	C00O	123.1(3)	C01B	C01E	C01I	113.5(3)
C00P	N00L	C00N	123.2(3)	C01B	C01F	C01A	114.1(3)
C00R	N00M	C013	126.6(3)	C01J	C01G	C01H	114.5(4)
N00D	C00N	N00G	118.5(3)	C01G	C01H	C01L	114.0(4)
N00D	C00N	N00L	117.1(3)	C01E	C01I	C01K	114.0(3)

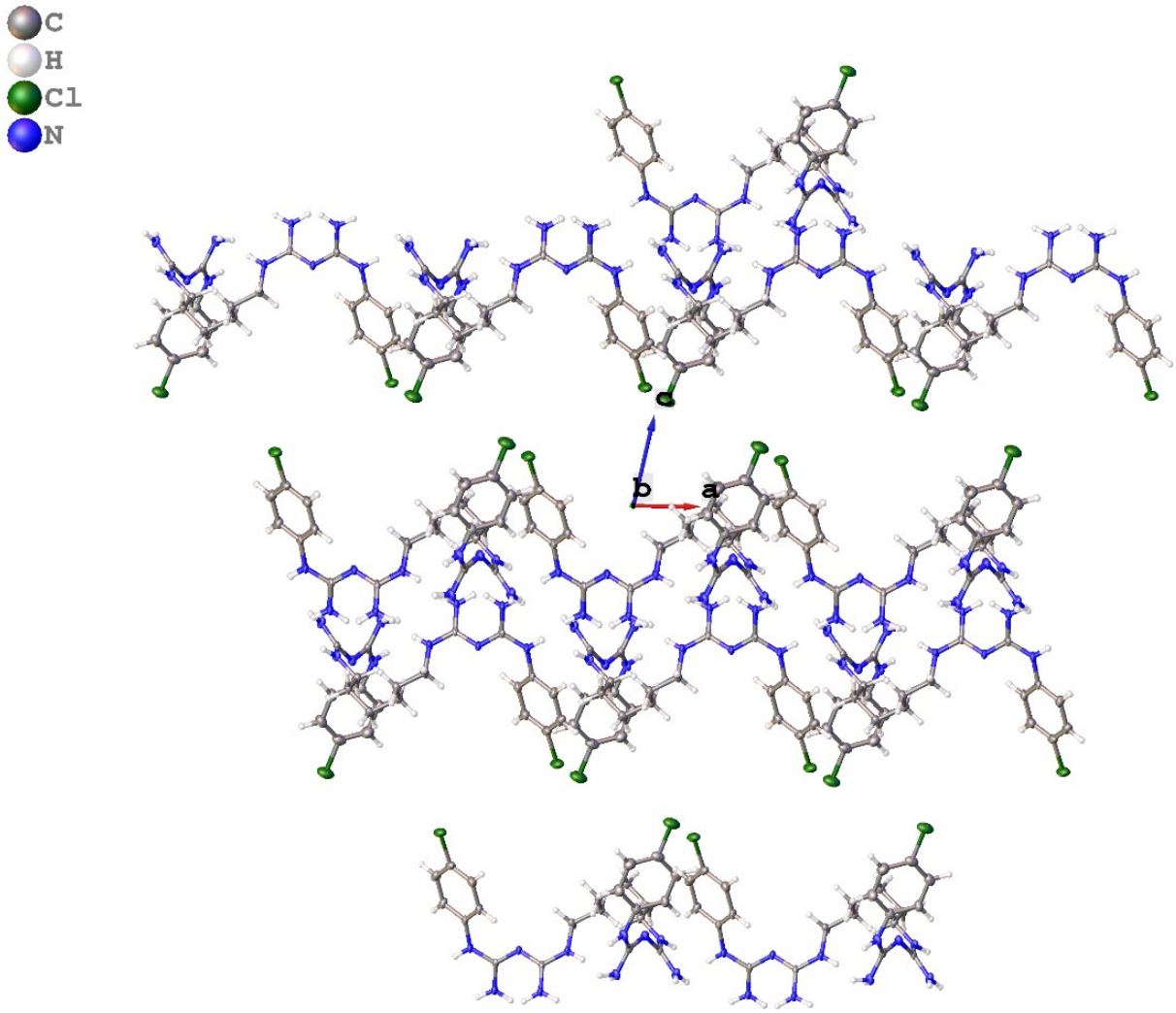

Figure S4. The alternating layers of the CHX coils.

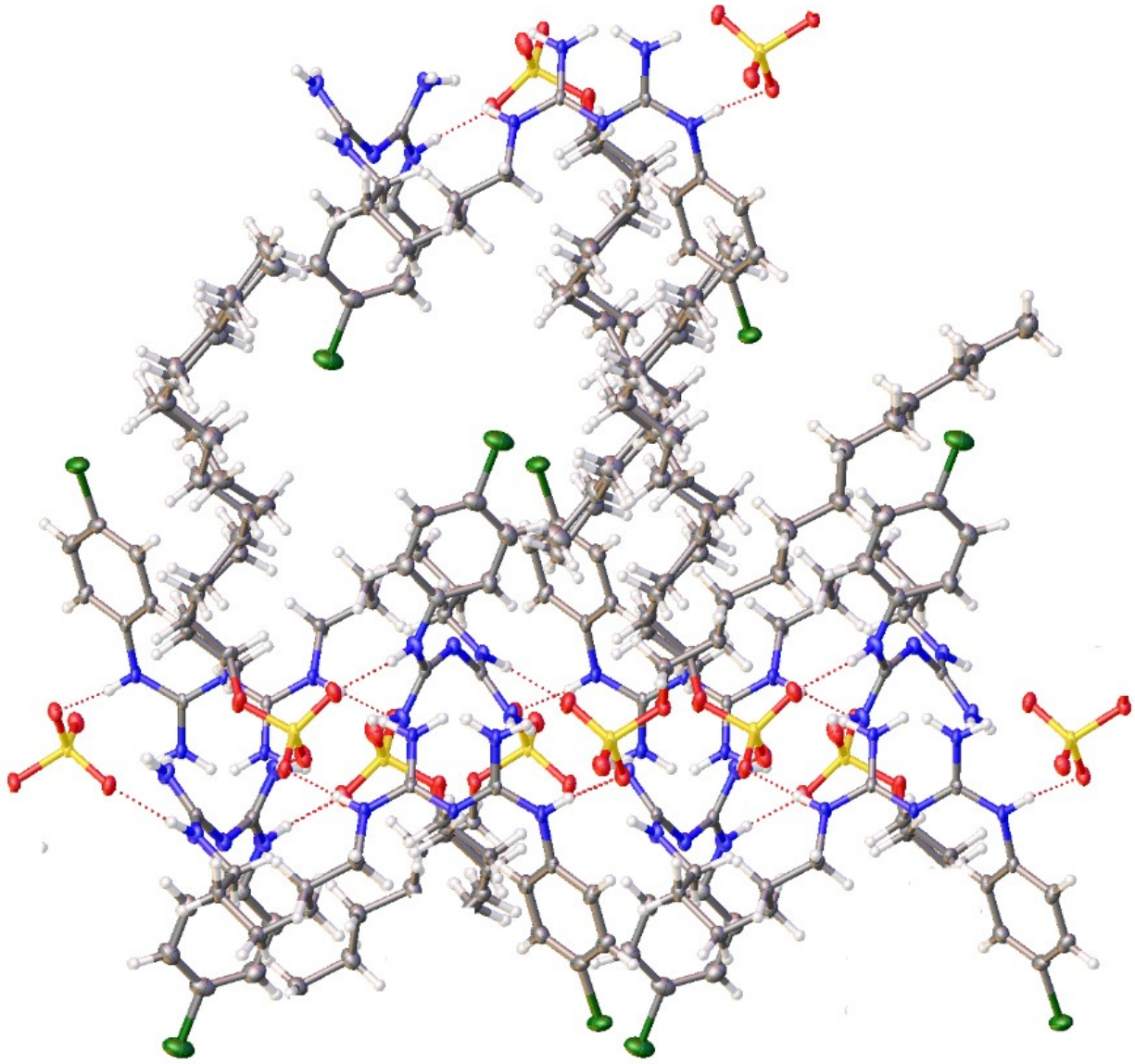

Figure S5. The network formed by H-bonding between the CHX and DS molecules.

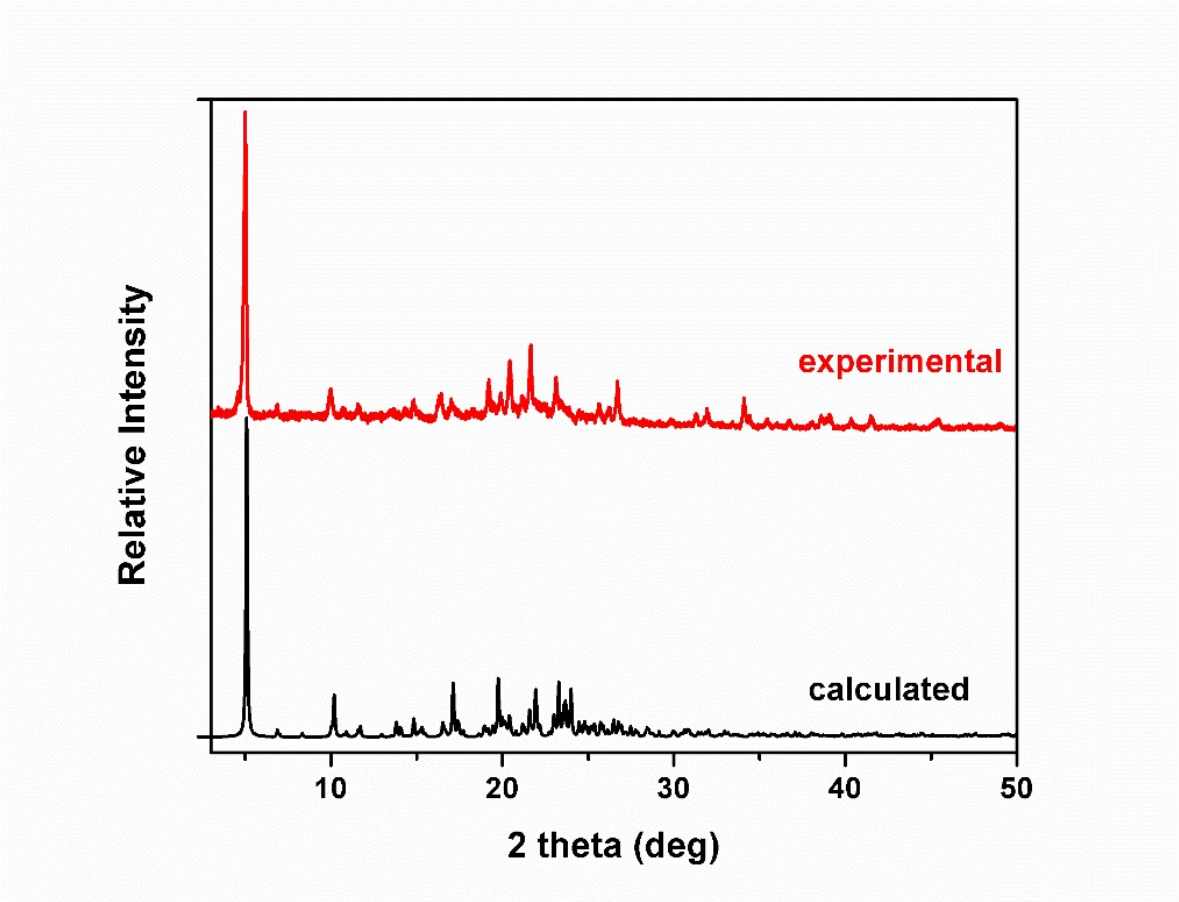

Figure S6. A comparison of the calculated (black) and experimental (red) PXRD pattern for the CHX-DS complex.

4. Volatile Sulfur Compound (VSC) Reduction

Table S4. Samples tested and respective concentrations tested

Sample Description	Concentration (%)
Chlorhexidine dodecyl sulfate (CHX-DS)	0.01
Sodium dodecyl sulfate (SDS)	0.01
Chlorhexidine gluconate (CHG)	0.01
Methanol	0.01

Table S5. Grouping information using Tukey method and 95.0% confidence

C3	N	Mean	Grouping
Methanol	3	11.0822	A
SDS	3	10.7974	A
CHG	3	10.7800	A
CHX-DS	3	10.3956	B

5. PXRD data for CHX-DS@SBA-15

Table S6. The d-spacing calculated for the corresponding 2θ peaks.

2θ	d(Å)
1.14	77.25
2.22	39.75
2.92	30.2

6. Structural Characterization via Scanning Electron Microscopy with Energy Dispersive X-Ray Spectroscopy (SEM-EDX)

The CHX-DS@SBA-15 sample was first coated with Iridium to increase the conductivity during SEM imaging. The SEM images were taken using Zeiss XB540 system, and the EDS spectrum/mapping was obtained by Oxford Xtream EDS system at the accelerating voltage of 10kV and the beam current of 1000 pA.

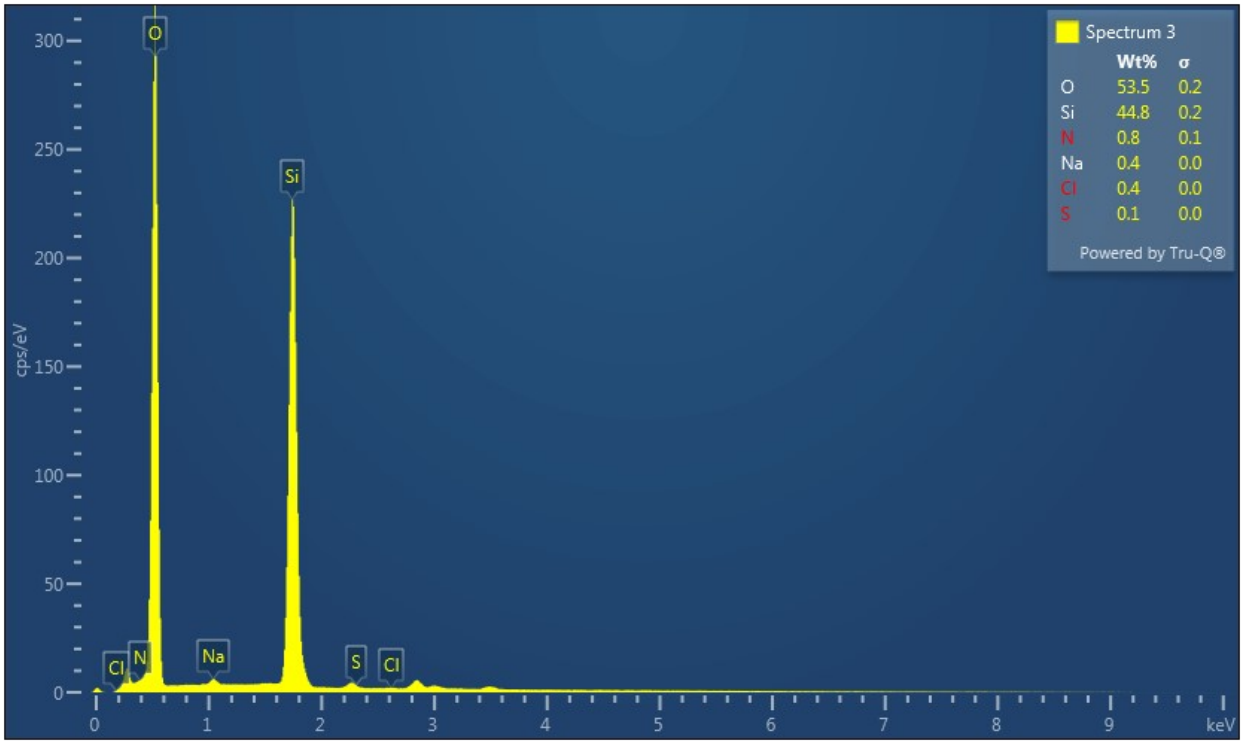

Figure S7. SEM-EDX spectrum of CHX-DS@SBA-15

7. CHX-DS@SBA-15 Release Studies

The release of CHX-DS from CHX-DS@SBA-15 was investigated under static conditions at room temperature in aqueous media at pH 7.0 and acidified to pH 4.0 with HCl. Specifically, 100 mg of CHX-DS@SBA-15 was added to 50 mL, shaken, and allowed to sit over 48 hours. UV-Vis spectroscopy was used to monitor the release. Prior to UV-Vis measurements, the solutions were centrifuged at 10,000 RPM for 20 minutes, and subsequently filtered and added into the quartz cuvettes for analysis. Although chlorhexidine absorption peaks were observed at 231 and 260 nm, however quantification was not possiblep due to broad interference peaks, presumably from the with silica nanoparticles. Analysis was performed using a Lambda 365 UV/Vis Spectrometer (PerkinElmer, Waltham, MA) with spectra collected from a 190-400 nm wavelength.

Quantification of CHX-DS release was attempted by the construction of calibration curves but proved difficult due to broad interference with silica nanoparticles.