Synthesis of Novel Heterocycles with Antimicrobial and Surface Activity

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A new series of anionic surfactants with dual type of activity antimicrobial and surface activity have been synthesized by reaction of 4*H*-3,1-benzoxazinone **3** and quinazolinethione **10** with nitrogen nucleophiles and activated olefinic compounds. The compounds were evaluated for their surface activity as well as their antimicrobial and biodegradability properties.

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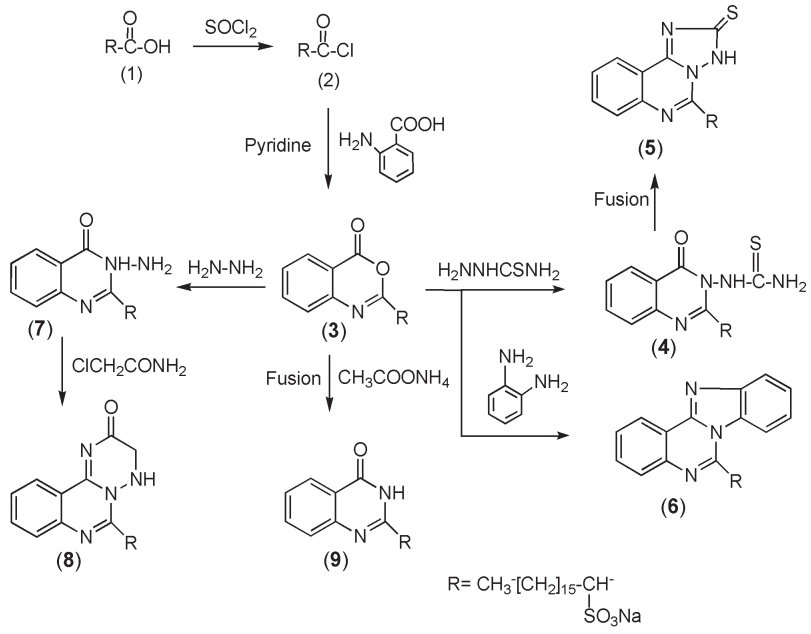
Introduction.

Several anionic surfactants [1,2] containing both the thiophene and pyrrole nucleus as well as a long alkyl chain with a sulphonic or carboxylic hydrophilic groups are reported to possess a wide spectrum of surface activity. Also, the synthesis, characterization, and surface properties of 1-N-L-tryptophan (indol nucleus) glycerol ether and new bis-quaternary pyridinium surfactants were studied [3-5]. Prompted by these observations and in continuation of our investigation on biologically active derivatives among six-membered heterocycles [6,7] it was considered of interest to extend the previous studies [8] to prepare a new series of quinazolone derivatives bearing (long alkyl chain with sulphonic acid hydrophilic center) in a single molecular framework likely to constitute new biologically active anionic surfactants compounds which may serve in the manufacture of drugs, cosmetics, pesticides, and have antibacterial and/or antifungal properties.

Results and Discussion.

The required sodium 1-(4-oxo-4*H*-benzo[*d*][1,3]oxazin-2-yl)heptadecane-1-sulfonate (**3**) was synthesized by refluxing sodium 1-chlorocarbonylheptadecane-1-sulfonate (**2**) with anthranilic acid in boiling pyridine. The reactivity of **3** towards nitrogen nucleophiles was investigated aiming toward the synthesis of novel heterocycles with interesting applications. Thus, the reaction of **3** with thiosemicarbazide in boiling pyridine gave sodium 1-(4-oxo-3-thioureido-quinazolin-2-yl)-heptadecane-1-sulfonate (**4**), which cyclized by fusion above its melting point to yield triazolo-quinazoline derivative **5**. On the other hand, fusion of **3** with *o*-phenylenediamine above its melting point in an oil bath yielded a bridgehead nitrogen compound **6** (Scheme 1). The starting intermediate **3** reacted with hydrazine hydrate to give sodium 1-(3-amino-4-oxo-3,4-dihydro-quinazolin-2-yl)heptadecane-1-sulfonate (**7**). The cyclization of **7** with chloroacetamide in boiling *N*,*N*-dimethylformamide (DMF)

Scheme 1



gave sodium 1-(3-oxo-2,3-dihydro-1*H*-1,4,9,10a-tetraazaphenanthren-10-yl)heptadecane-1-sulfonate (**8**). Also, fusion of **3** with ammonium acetate at 150 °C afforded quinazolinone derivative **9**. The interaction of **9** with phosphorus pentasulphide in dry xylene afforded the quinazolin-3*H*-4-thione derivative **10**.

In the present investigation, the condensation of **10** with thiosemicarbazide using phosphorus oxychloride [9] as the condensing agent gave sodium 1-[4-(5-amino-[1,3,4]thiadiazol-2-yl)quinazolin-2-yl]heptadecane-1-sulfonate (**11**).

However, the reaction of **10** with β-benzoylacrylic acid in dry benzene and in the presence of a few drops of piperidine [10] gave a mercaptoquinazoline derivative **12** which was used to construct another heterocyclic nucleus of biological interest. Thus the reaction of **12** with hydrazine hydrate in boiling ethanol afforded a pyridazinone derivative **13**. Condensation of **12** with hydroxylamine hydrochloride in boiling pyridine yielded the sodium1-[4-(6-oxo-3-phenyl-5,6-dihydro-2*H*-[1,2]oxazin-5-ylsulfanyl)quinazolin-2-yl]heptadecane-1-sulfonate (**14**). Finally, the cyclization of **12** by refluxing in acetic anhydride afforded the furanone derivative **15** (Scheme 2).

Surface Active Properties.

Anionic surface-active agents are very widely distributed throughout science, technology, and everyday life. Examples which at once come to mind are the washing, wetting out textile materials, the preparation of dispersions and emulsions, the application of agricultural and horticultural sprays, and a wide variety of special uses, the number of which is continually increasing. The surface properties (surface and interfacial tension, Kraft point, wetting time, foaming height, and emulsion stability) of purified compounds were investigated at 30 °C in distilled water. The Ca^{++} stability and stability to hydrolysis were also studied. The biodegradability properties were also determined. These surfactants display a substantial surface activity, and comparative study between the structure and activity were carried out.

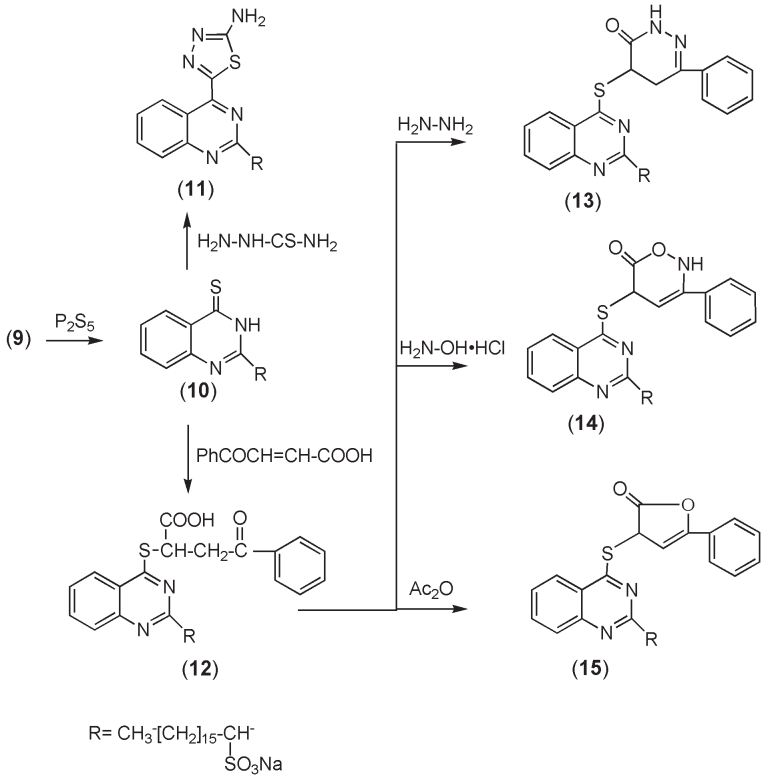
Surface and Interfacial Tension.

The synthesized anionic surfactants with a heterocyclic moiety showed lower values for surface tension and interfacial tension. The results are recorded in Table I. It was found that the decrease of values of surface and interfacial tension might be due to the electrostatic repulsion between the ionized molecules. The results indicate that all the synthesized products have pronounced surface activity.

Kraft Point.

The prepared anionic surfactants were measured at the temperature where 1% dispersion becomes clear on gradual heating. All the synthesized surfactants are freely soluble in

Scheme 2



water at 1 wt % concentration and at any temperature. In some cases, this fact may fail due to the presence of retarding groups in the same molecule. So, in the case of **12** the alkyl groups increase T_{kp} while the carboxy group causes a decrease. In general, Kraft point measurements proved that the higher the molecular weight the higher the Kraft point.

Wetting Time.

Wetting times of the tested surfactants were determined by measuring the sinking time in seconds of a gray cotton skin in the surfactant solution. The results show that the products were very effective wetting agents in distilled water solutions. It is hoped that they will find a wide range of applications in the textile industry.

Foaming Height.

The values of the foaming height were investigated for prepared compounds and the results revealed that the new compounds yield low foam. The low foaming power compounds have application in the dyeing and auxiliary industries.

Emulsion Stability.

Emulsification is one of the most important properties of surfactants. In many textile processes, such as scouring and dyeing, it is necessary to introduce surfactants into the bath to remove oily impurities from the fiber. The emulsion stability of such surfactants was investigated. All the prepared surfactants are good emulsifying agents. They could be useful in dye baths in the textile industry and as emulsion paints.

Ca^{++} Stability.

High calcium stability values show that the prepared compounds can be used in hard water.

Stability Towards Hydrolysis.

The results listed in Table I indicate that the prepared anionic surfactants are moderately stable in basic medium.

Biodegradability.

The biodegradability of the tested compounds after one weak was determined and are listed in Table II. Each experiment was repeated at least three times, and the results are reported as averages of three values. The results indicate that all the compounds undergo substantial degradation.

Antimicrobial Activity.

The antimicrobial activity of the synthesized derivatives was tested using the cup-plate method. All compounds were tested for activity against Gram positive, Gram negative bacteria, and selected fungi. Quantitative assays were carried out for active compounds only. The results are summarized in Table III. Other biological studies are still in progress.

EXPERIMENTAL

Melting points are uncorrected. IR spectra in KBr were measured on a Pye-Uncam SP-1000 infrared spectrophotometer in a KBr disk or nujol. The ^{1}H NMR spectra were obtained on a Varian EM-390-90 MHz spectrometer in DMSO as the solvent. Tetramethylsilane TMS served as an internal reference and chemical shifts are expressed as δ (ppm). Mass spectra were recorded on a G-C/Ms Finning-MAT. Microanalyses were preformed by the Microanalytical Unit at Cairo University, and all the compounds gave satisfactory elemental analyses. Thin layer chromatography (TLC) was carried out on silica gel (MN-Kieselgel G., 0.2 mm thickness) and the plates were scanned under 254 nm ultraviolet light. Antimicrobial and antifungal activity testes were carried out by the microbiology Lab., Faculty of Science, Zagazig University, Benha-branch, Egypt.

Sodium 1-(4-Oxo-4H-benzo[*d*][1,3]oxazin-2-yl)heptadecane-1-sulfonate (**3**).

A solution of acid chloride **2** (5 mmole) and anthranilic acid (5 mmole) in dry pyridine (30 ml) was refluxed for 3 h. The reaction mixture was cooled and poured into cold diluted HCl. The solid that separated was collected by filtration and recrystallized from benzene to give **3**; yield, 75%, mp = 78 °C. IR: ν =3044 (CH aromatic), 2920-2850 (CH in alkyl chain), 1745 (C=O), and 1600 cm^{-1} (C=N). ^{1}H NMR ($CDCl_3$): δ = 0.8 (t, 3H, terminal CH_3), 1.1-1.3 (m, 30 H, CH_2 in alkyl chain), 2.6 (s, 1 H, CH-SO_3Na) and 7.0-7.3 (m, 4 H, ArH). MS: m/z (%) M^++1 = 488 (39.9 %).

Anal. Calcd. for $C_{25}H_{38}NNaO_5S$: C, 61.85; H, 7.85; N, 2.87; S, 6.85%. Found C, 61.89; H, 7.88; N, 2.91; S, 6.88 %.

Sodium 1-(4-Oxo-3-thioureidoquinazolin-2-yl)heptadecane-1-sulfonate (**4**).

A solution of **3** (7 mmole) and thiosemicarbazide (7 mmole) was heated in boiling pyridine (20 ml) under reflux for 3 h then poured into water. The separated solid after concentration and cooling was collected by filtration and crystallized from ethanol to give **4**; yield, 70%. mp = 95 °C. IR: ν = 3348-3185 (NH's), 2920-2850 (CH in alkyl chain), 1664 (C=O), 1589 (C=N) and 1299 cm^{-1} (C=S), besides the characteristic bands of quinazoline nuclei [11] at (1630-1620), (1580-1570) and (1515-1480) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.9 (t, 3 H, terminal CH_3), 1.2-1.5 (m, 30 H, CH_2 in alkyl chain), 2.6 (s, 1 H, CH-SO_3Na), 6.8-7.2 (m, 4 H, ArH), 9.3 (s, 3 H, NH which are exchangeable). MS: m/z (%) M^+ = 544 (54.12%) which fragmented into two distinguishable ion peaks, one corresponding to the quinazoline nucleus at m/z = 179 (21.85 %) and the other to the aliphatic part at m/z = 365 (37%).

Anal. Calcd. for $C_{26}H_{41}N_4NaO_5S$: C, 57.33; H, 7.59; N, 10.29; S, 5.89%. Found C, 57.37; H, 7.62; N, 10.34; S, 5.91 %.

Sodium 1-(2-Thioxo-2,3-dihydro[1,2,4]triazolo[1,5-*c*]quinazolin-5-yl)heptadecane-1-sulfonate (**5**).

Compound **4** (1 gm) was heated above its melting point by fusion in an oil bath for 2 h, then cold water was added, the solid obtained was collected by filtration and crystallized from xylene to give **5**; yield 80%. UV: λ_{max} 283 nm (ε = 3700) attributed to the 1,2,4-triazolo nucleus [12]; mp = 73 °C, IR: ν = 3300 (NH), 2920-2850 (CH in alkyl chain) and 1337 cm^{-1} (C=S). The ^{1}H NMR ($CDCl_3$): δ = 1.1 (t, 3H, CH_3), 1.3-1.5 (m, 30 H, CH_2 in alkyl chain), 2.4 (s, 1H, CH-SO_3Na), 6.9-7.4 (m, 4H, ArH), 9.1 (s, 1H, NH which is exchangeable).

Table I

Surface Properties of the Synthesized Compounds

Compd	Surface tension (dyne/cm) 0.1 m/l	Interfacial tension (dyne/cm) 0.1 m/l	Kraft Point ∞C	Wetting time (sec.)	Emulsion stability (min.)	Foam height (mm)	Ca^{++} stability (ppm)	Stability to hydrolysis (min:sec)
3	30	7.5	14	65	350	225	350	38:5
4	35	8.7	22	120	320	170	1350	44:0
5	35	11.0	18	135	250	220	1240	38:4
6	31	11.4	26	100	340	185	850	34:5
7	31	7.0	17	100	280	190	500	41:2
8	34	10.0	23	115	227	215	1530	35:9
9	32	8.6	14	95	350	180	1300	35:0
10	33	10.2	21	115	280	215	580	37:6
11	34	8.5	24	117	220	215	1060	40:7
12	37	9.0	25	105	310	200	1040	6:2
13	35	10.5	28	125	370	210	1290	48:0
14	32	6.7	26	85	240	205	560	40:
15	30	9.4	25	120	240	210	1420	35:8

Anal. Calcd. for $C_{26}H_{39}N_4NaO_3S_2$: C, 57.54; H, 7.24; N, 10.32; S, 11.82 %. Found C, 57.58; H, 7.28; N, 10.35; S, 11.86 %.

Sodium 1-Benzo[4,5]imidazo[1,2-*c*]quinazolin-6-yl)heptadecane-1-sulfonate (**6**).

Compound **3** (1 gm) was heated with *o*-phenylenediamine above its melting point by fusion in an oil bath for 2 h, then cold water was added, and the solid obtained was collected by filtration and crystallized from xylene to give **6**; yield 76%. mp = 78 °C. IR: ν = 2920-2850 (CH in alkyl chain), 1610 cm^{-1} (C=N). ^1H NMR ($CDCl_3$): δ = 0.8 (t, 3 H, terminal CH_3), 1.2-1.5 (m, 30 H, CH_2 in alkyl chain), 2.5 (s, 1H, CH-SO_3Na) and 6.5-7.2 (m, 8 H, ArH). MS: m/z (%) M^+ +1 = 560 (33.14 %).

Anal. Calcd. for $C_{31}H_{42}N_3NaO_3S$: C, 66.52; H, 7.56; N, 7.51; S, 5.73 %. Found C, 66.55; H, 7.59; N, 7.55; S, 5.76 %.

Sodium 1-(3-Amino-4-oxo-3,4-dihydroquinazolin-2-yl)heptadecane-1-sulfonate (**7**).

A solution of **3** (6 mmole) in dry benzene (30 ml) and hydrazine hydrate (5 mmole) was heated under reflux for 4 h then the mixture was poured into cold water. The precipitated solid was collected by filtration dried and crystallized from ethanol to give **7**; yield 80%, mp = 85 °C. IR: ν = 3300-3200 (NH_2), 2920-2850 (CH in alkyl chain) and 1677 cm^{-1}(C=O). ^1H NMR ($CDCl_3$): δ = 0.85 (t, 3 H, terminal CH_3), 1.1-1.3 (m, 30 H, CH_2 in alkyl chain), 2.7 (s, 1 H, CH-SO_3Na), 8.5-7.8 (m, 4 H, ArH), 5.89 (brs, 2H, NH_2). MS: m/z (%) M^++1 = 502 (34.1 %).

Anal. Calcd. for $C_{25}H_{40}N_3NaO_4S$: C, 59.86; H, 8.04; N, 8.38; S, 6.39 %. Found C, 60.90; H, 8.07; N, 8.42; S, 6.42 %.

Sodium 1-(3-Oxo-2,3-dihydro-1*H*-1,4,9,10a-tetraazaphenanthren-10-yl)heptadecane-1-sulfonate (**8**).

A solution of **7** (8 mmole) and chloroacetamide (8 mmole) was refluxed for 3 h in boiling *N*,*N*-dimethylformamide (30 ml). The mixture was then poured into water, and the precipitated solid was collected by filtration dried and crystallized from ethanol to give **8**; yield 65%. mp = 68 °C. UV: λ_{max} nm (ε) = 330 (450), 314 (1450), 280 (3600), 266 (830) and 255 (600). Bands of this type are found in all fused aromatic aza compounds [13]; IR: ν = 3370 and 3220, 2985, 2850, 1660, 1598 cm^{-1} attributable to (NH) non-bonded and bonded, (CH), (C=O), (C=N). ^{1}HNMR ($CDCl_3$): δ 0.9 (t, 3H, terminal CH_3), 1.1-1.3 (m, 30H, CH_2 in alkyl chain), 2.4 (s, 1 H, CH-SO_3Na), 4.56 (s, 2H, CH_2 of triazine ring), 9.1 (s, 1H, NH which exchangeable) and 6.5-7.1(m, 4H, ArH). MS: m/z; (%) M^++2 = 542 (44.2%).

Table II

Biodegradability of the Prepared Surfactants

Comp	1st day	2nd day	3rd day	4th day	5th day	6th day	7th day
3	44	49	54	65	74	86	-
4	41	50	58	67	75	92	-
5	41	46	62	69	91	-	-
6	39	50	63	75	92	96	98
7	37	46	58	69	82	95	-
8	47	55	66	77	89	97	-
9	38	46	60	71	83	95	-
10	45	58	69	78	87	96	-
11	36	46	55	67	76	88	92
12	47	55	70	82	93	-	-
13	42	56	67	78	89	96	-
14	46	55	67	78	88	95	-
15	48	59	71	80	93	-	-

Anal. Calcd. for $C_{27}H_{41}N_4NaO_4S$: C, 59.98; H, 7.64; N, 10.36; S, 5.93 %. Found C, 60.01; H, 7.68; N, 10.39; S, 6.97 %.

Sodium 1-(3-Oxo-3,4-dihydroquinazolin-2-yl)heptadecane-1-sulfonate (**9**).

A mixture of **3** (6 mmole) and ammonium acetate (8 mmole) was fused in as oil bath at 170 °C for 2 h, then poured into water. The separated solid after concentration and cooling was collected by filtration and crystallized from ethanol to give **9**; yield 76%; mp = 77 °C. IR: ν = 3325 (NH), 2910-2850 (CH in alkyl chain), 1589 (C=N) and 1349 cm^{-1} (C=S). ^1H NMR ($CDCl_3$): δ = 1.1 (t, 3H, CH_3), 1.3-1.5 (m, 30 H, CH_2 in alkyl chain), 2.6 (s, 1H, CH-SO_3Na), 6.9-7.4 (m, 4H, ArH), 9.1 (s, 1H, NH which is exchangeable).

Anal. Calcd. for $C_{25}H_{39}N_2NaO_4S$: C, 61.70; H, 8.08; N, 5.76; S, 6.59 %. Found C, 61.74; H, 8.11; N, 5.80; S, 6.62 %.

Table III

Activity (A) and Minimum Inhibitory Concentration (MIC)

Compd.	*Bacillus sublitis*		Escherichia coil		*Aspergillus niger*		*Candida albicam*	
	A	MIC	A	MIC	A	MIC	A	MIC
3	+	250	-	125	++	250	++	125
4	++	125	+	250	++	250	+	250
5	++	250	-	125	+	125	++	250
6	+	250	+	250	-	125	+	125
7	++	250	+	250	+	250	++	250
8	++	125	+	250	++	125	+	250
9	+	250	++	250	+	125	+	125
10	++	125	++	250	++	125	++	125
11	++	125	+	125	++	250	+	250
12	++	250	++	250	++	250	++	125
13	+++	250	+	125	++	250	+++	250
14	++	125	++	250	+	125	++	250
15	++	250	++	250	++	250	+++	250

A; Antimicrobial activity of tested compounds; the width of the zone of inhibition indicates the potency of antimicrobial activity, (-) no antimicrobial activity, (+) weak activity with diameter equal to (0.5-0.7cm), (++) moderate activity with the diameter zone equal to (1.0-1.2cm), (+++) marked activity with the diameter zone equal to (1.6-1.8cm); MIC; Minimum inhibition concentration.

Origin of Cultures.

Botany Department, Faculty of Science, Benha University, Egypt.

Sodium 1-(3-Thioxo-3,4-dihydro-quinazolin-2-yl)heptadecane-1-sulfonate (**10**).

A mixture of **9** (5 mmole) and phosphorus pentasulphide (5 mmole) in dry xylene (50 ml) was heated under reflux for 1 h then the solution was concentrated. The product was obtained by filtration and recrystallized from xylene to give **10**; yield 75%; mp = 68 °C. IR: ν = 3260 (NH), 2920-2850 (CH in alkyl chain), 1587 (C=N) and 1325 cm^{-1} (C=S). ^1H NMR ($CDCl_3$): δ = 0.8 (t, 3 H, terminal CH_3), 1.2-1.5 (m, 30 H, CH_2 in alkyl chain), 2.6 (s, 1 H, CH-SO_3Na), 6.5-7.2 (m, 4 H, ArH) and 9.1(s, 1 H, NH, which is exchangeable).

Anal. Calcd. for $C_{25}H_{39}N_2NaO_3S_2$: C, 59.73; H, 7.82; N, 5.57; S, 12.76 %. Found C, 59.77; H, 7.85; N, 5.60; S, 12.79 %.

Sodium 1-[4-(5-Amino-[1,3,4]thiadiazol-2-yl)quinazolin-2-yl]heptadecane-1-sulfonate (**11**).

A mixture of **10** (5 mmole) and thiosemicarbazide (5 mmole) and phosphorus oxychloride (5 mmole) was warmed at 60 °C for 1 h and the temperature was raised to 90 °C for an additional 2 h. The contents were poured onto crushed ice, cooled to10 °C, pH adjusted to 8-10 *M* NaOH, and the resulting solid was crystallized from DMF to give **11**; yield 70 %. mp = 60 °C. IR: ν = 3200 (NH), the bands of thiadiazole nucleus were at 1620, 1210, 1075 and 980 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.85 (t, 3 H, terminal CH_3), 1.2-1.5 (m, 30 H, CH_2 in alkyl chain), 2.45 (s, 1 H, CH-SO_3Na), 6.7-7.6 (m, 4 H, ArH) and 3.4 (s, 2 H, NH_2, which is exchangeable). MS: m/z (%) M^+ = 569 (69%).

Anal. Calcd. for $C_{27}H_{40}N_5NaO_3S_2$: C, 56.92; H, 7.08; N, 12.29; S, 11.26 %. Found C, 59.96; H, 7.12; N, 12.33; S, 11.29 %.

Sodium 4-Oxo-4-phenyl-2-[2-(1-sulfoheptadecyl)quinazolin-4-ylsulfanyl)butanoic Acid (**12**).

A solution of **10** (5 mmol) and β-benzoylacrylic acid (5 mmole) and few drops of pyridine in dry benzene (50 ml) was left at room temperature for 48 h, the reaction mixture was concentrated under reduced pressure and the cold mixture was washed with light petroleum ether. The solid that was obtained was crystallized from xylene to give **12**; yield 85%; mp = 108 °C, IR: ν = 3450 (OH) and 1705, 1680 cm^{-1} (C=O of acid and ketone). ^1H NMR ($CDCl_3$): δ = 0.95 (t, 3 H, CH_3), 1.1-1.4 (m, 30 H, CH_2 in alkyl chain), 2.4 (s, 1 H, CH-SO_3Na), 5.9 (d, 2H, CH=*CH_2*), 4.3 (t, 1H, *CH*=CH_2), 7.9-8.7 (m, 9 H, ArH) and 10.5 (s, 1 H, OH). MS: m/z (%) M^+ = 678 (69%).

Anal. Calcd. for $C_{35}H_{47}N_2NaO_6S_2$: C, 61.92; H, 6.98; N, 4.13; S, 9.45 %. Found C, 61.95; H, 7.01; N, 4.17; S, 9.49 %.

Sodium 1-[4-(3-Oxo-6-phenyl-2,3,4,5-tetrahydropyridazin-4-ylsulfanyl)quinazolin-2-yl]heptadecane-1-sulfonate (**13**).

A mixture of **12** (5 mmole) and hydrazine hydrate (5 mmole) in ethanol (40 ml) was heated under reflux for 5 h at which time the solution was concentrated. The product was obtained by filtration and recrystallized from ethanol to give **13**; yield 78%; mp = 65 °C. IR: ν = 3370 (NH), 1675 (CO of pyridazinone) and 1590 cm^{-1} (C=N). ^1H NMR ($CDCl_3$): δ = 0.8 (t, 3 H, CH_3), 1.1-1.4 (m, 30 H, CH_2 in alkyl chain), 2.35 (s, 1 H, CH-SO_3Na), 4.4 (s, 2H, CH_2), 4.89 (s, 1H, methine proton), 7.5-8.7 (m, 9 H, ArH) and 9.5 (br.s, 1 H, NH, exchangeable). MS: m/z (%), M^+= 674 (59%).

Anal. Calcd. for $C_{35}H_{47}N_4NaO_4S_2$: C, 62.29; H, 7.02; N, 8.30; S, 9.50 %. Found C, 62.32; H, 7.06; N, 8.33; S, 9.52 %.

Sodium 1-[4-(6-Oxo-3-phenyl-5,6-dihydro-2*H*-[1,2]oxazin-5-ylsulfanyl)quinazolin-2-yl]heptadecane-1-sulfonate (**14**).

A mixture of **12** (5 mmole) and hydroxylamine hydrochloride (5 mmole) in pyridine (20 ml) and a few drops of water was heated under reflux for 12 h. The reaction mixture was poured onto ice cold HCl. The product was obtained by filtration and recrystallized from ethanol to give **14**; yield 65%; mp = 83 °C, IR: ν = 1720 cm^{-1} attributed to carbonyl of cyclic ether. ^1H NMR ($CDCl_3$): δ = 1.1 (t, 3 H, CH_3), 1.3-1.5 (m, 30 H, CH_2 in alkyl chain), 2.6 (s, 1 H, CH-SO_3Na), 4.1 (s, 2H, CH_2), 4.92 (s, 1H,

methine proton), 6.9-7.5 (m, 9 H, ArH).

Anal. Calcd. for $C_{35}H_{46}N_3NaO_5S_2$: C, 62.20; H, 6.86; N, 6.22; S, 9.49 %. Found C, 62.22; H, 6.89; N, 6.25; S, 9.52 %.

Sodium 1-[4-(3-Oxo-6-phenyl-3,4-dihydro-2*H*-furan-4-ylsulfanyl)-quinazolin-2-yl]heptadecane-1-sulfonate (**15**).

A mixture of **12** (5 mmole) in acetic anhydride (20 ml) was heated under reflux for 4 h. The product separated upon addition to cold 50% ethanol (20 ml), and was collected by filtration and recrystallized from ethanol to give **15**; yield 65%; mp = 79 °C. IR: ν = 1765 cm^{-1} attributed to lactone carbonyl. ^1H NMR ($CDCl_3$): δ = 0.95 (t, 3 H, CH_3), 1.2-1.4 (m, 30 H, CH_2 in alkyl chain), 2.4 (s, 1 H, CH-SO_3Na), 4.97 (s, 1H, methine proton), 5.6 (s, 1 H, CH) and 6.5-7.9 (m, 9 H, ArH). MS: m/z (%), M^++1 = 662 (34%).

Anal. Calcd. for $C_{35}H_{46}N_2NaO_5S_2$: C, 63.51; H, 7.01; N, 4.23; S, 9.69 %. Found C, 63.54; H, 7.05; N, 4.27; S, 9.72 %.

The Surface Active Properties.

Surface and interfacial tension [14], Kraft point [15], wetting time [16], foaming [17], emulsification properties [18], Ca^{++} stability [19], and stability to hydrolysis [20] were determined.

Biodegradability.

The percentage of biodegradability was measured according to Eter et al [21].

Biological Activity.

Antimicrobial activity of the prepared compounds was tested via a modification of the cup-plate method [22].

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