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Research Article

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Synthesis, reactions and biological evaluation of pentadecanyl benzoxazinone and pentadecanyl quinazolinone derivatives

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ABSTRACT

*New series of fatty chain derivatives ofbenzoxazinones and quinazolinones have been synthesized from the two simple precursors of palmitoyl acid chloride and anthranilic acid. Antibacterial and anti-fungal inhibition effect of all products has been investigated. Compounds**1**, **3**, **8, 12** and **15** showed high inhibitory effect towards gram negative and gram positive bacteria while compounds**3, 6** and **7** exhibitedhigher anti-fungal effect. The structure of all products has been characterised by IR, NMR, Mass spectra and elemental analyses.*

Key words: Benzoxazinones; Quinazolinones, Hydrophobic and hydrophilic compounds; Fatty acids; Anti-microbial.

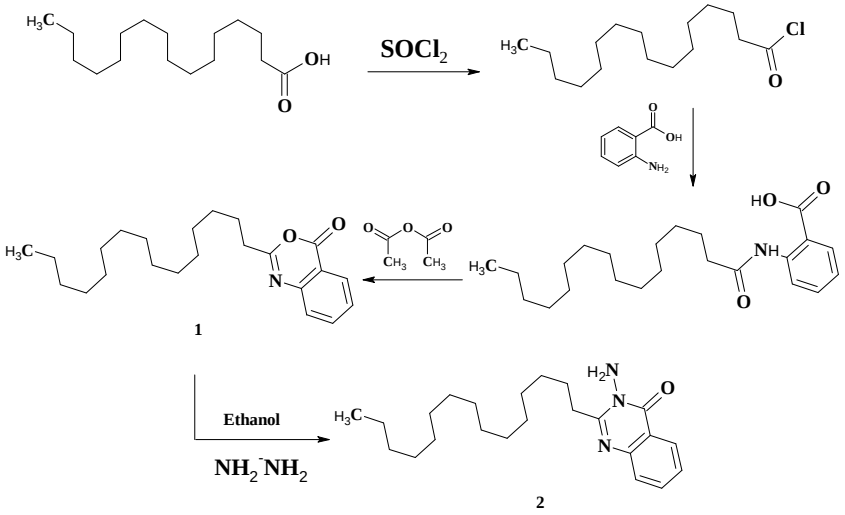
INTRODUCTION

Quinazoline and its derivatives are very important and vital group of chemotherapeutical drugs such as antibacterial[1, 2], antifungal [3], antimicrobial [4], antihistamine [5], anticonvulsant [6], and antiallergy [7]. Most of tetrazoloquinazoline used as inhibitors in treatment of proliferation diseases [8], also quinazolinone and its derivatives exhibited a good activity as anticancer,[9] anti-fibrillatory [10], and antifungi [11, 12]. It was reported that quinazolinone and its derivatives are also used as antimicrobial [13-15], anti-tuberculser agent [16], antimalarial [17], it has a broad activity toward different infectious diseases. So, we use p-quinazolyl benzoic acid as a starting material to synthesis imidazolyl quinazoline, pyrazolyl quinazoline, which expected to have a biological activity towards different selected microorganisms.

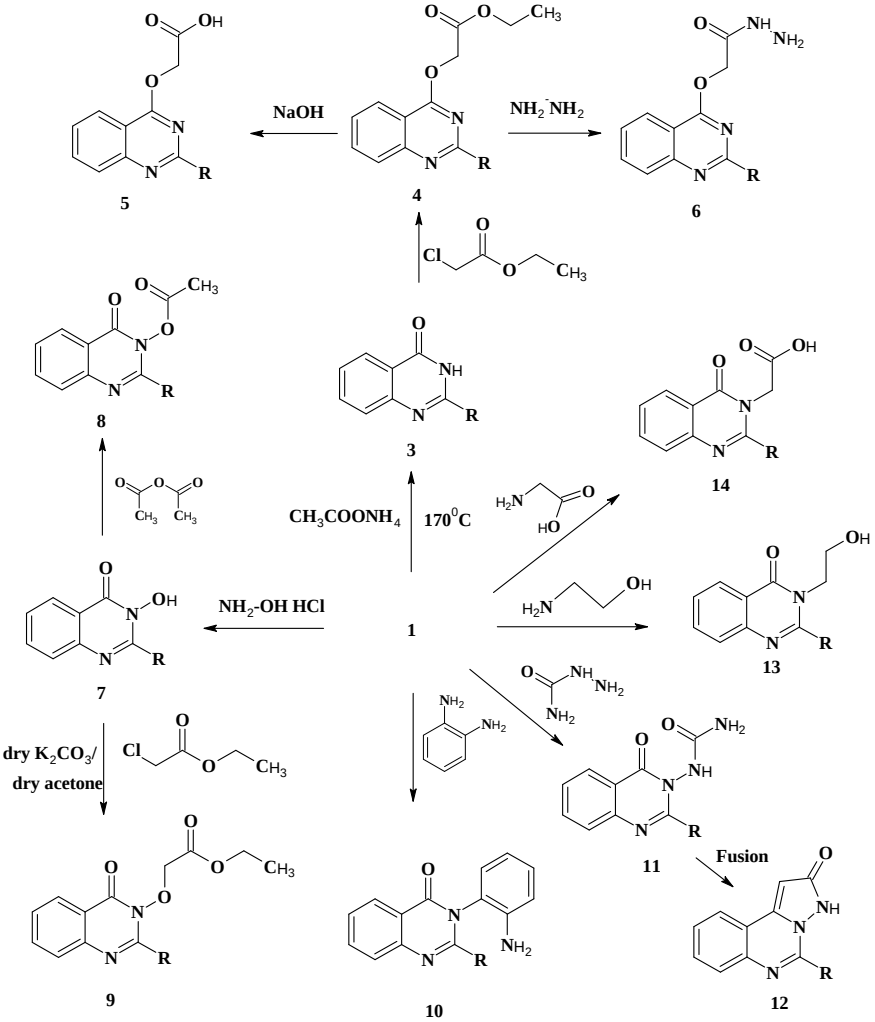
Trizoloquinazoline derivatives are useful for treatment of hypertension, inflammation. Furthermore, itcan be used in a diagnostic application to determine the presence of tumour cells which possess a high concentration of adenosine A3 receptor [18].Tetrazolotrizoloquinazoline derivatives are used as famesyl transferase inhibitors in the treatment of proliferative diseases [19].

Substituted 2-arylquinazolinone derivatives were screened for anti- HIV activity, the HIV-Virus might be anew target for quinazolinone bearing methoxy groups [20].Also 3H-quinazoline-4-ones their derivatives have been reported to possess significant activity as anticancer active agents and anti-metabolites from the group of analogues of the folic acid. They are not only anti-convulsant agents [21, 22]but also been successfully tested as CNS depressants and muscle relaxants [23, 24].Based on the for mentioned facts and extension to our interest in synthesis of biologically active compounds [25-27] we get tempted to concentrate our progress in synthesizing of potential bioactive new quinazolinone derivatives having long aliphatic chain in position 2-as hydrophobic group.

EXPERIMENTAL SECTION



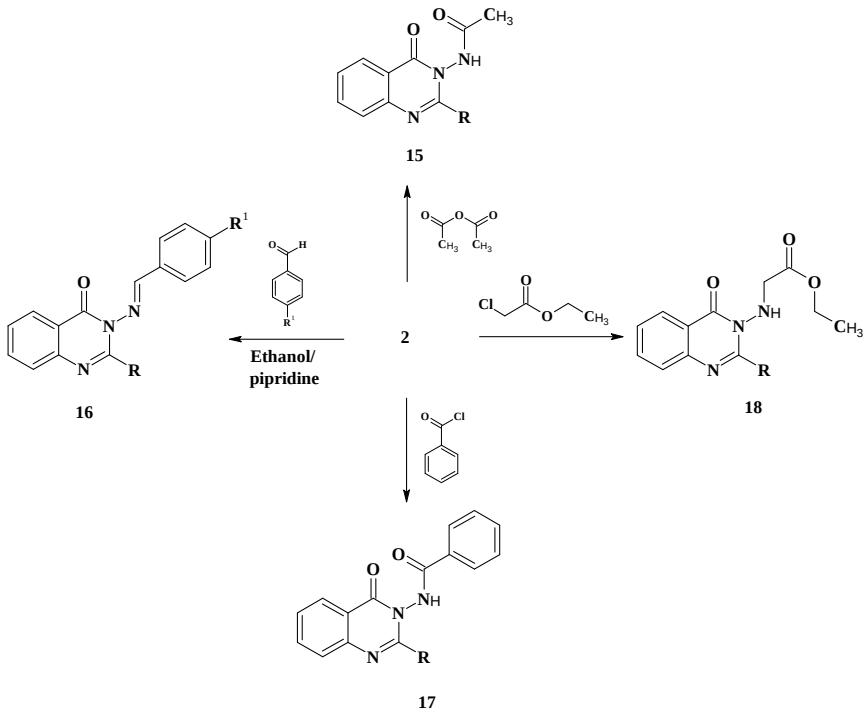
(Scheme 1)



(Scheme 2)

Melting points are uncorrected and determined by the open capillary method using Gallen Kamp melting point apparatus.Spectrophotometer (KBr disk) of the synthesized compounds was recorded on FT/IR-BRUKER, Vector 22(Germany).Microanalyses were carried out by Micro Analytical Unit at Cairo University.[1]HNMR Spectra were recorded in deuterated chloroform (CDCL3) or dimethylsulphoxide (DMSO-d6) on a Varian Germini-200 MHz instrument.Mass Spectra were recorded on HP-MODEL MS-5989A (U.S.A) and/or Shimadzu GCMS-QP-1000EX mass spectrometer at 70e.v.All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F254 (Mark) plates. The physical properties of the synthesized compounds are tabulated in table 1.

The synthesized compounds were tested for biological activities in Botany Department, Faculty of Science, Benha University.



(Scheme 3)

Synthesis of 3,1-benzoxazin-4-one derivative (1):

To a solution of anthranilic acid (0.01mole) in dry acetone, palmitoyl chloride (0.01mole) was added. The mixture was refluxed for 4hrs then concentrated under vacuum. Thesolid product that separated on cold was filtrated off, dried and crystallized from pet-ether (40-60). The pure product was further heated for 6 hrs under reflux in acetic anhydride then concentrated under vacuum. A solid product was obtained on cooling, filtered off and crystallized. IR (KBr), cm^{-1}: νCH aromatic at 3030, νCH aliphatic in the region of (2919-2850) and νC=O (of benzoxazinone) at 1761, νC=N at 1637. MS (EI, 70 eV), m/z (Irel, %):molecular ion peak ($M^{\cdot+}$) at m/z = 358, 1.5% and the base peak at m/z= (160, 100%).

Synthesis of 3- amino-2-pentadecyl-quinazolin-4-one (2):

A mixture of equimolar amount of compound **1**(0.01mole) and hydrazine hydrate (0.01mole) in 50ml ethanol was refluxed for 3hrs. On removing the excess solvent under vacuum a solid product was collected, filtered off, washed by little ethanol, dried then recrystallized from ethanol in pure and good yield (80%). IR (KBr), cm^{-1}:νNH_2 at 3324 and 3285 and νC=O at 1679beside the other bands of the compound.MS (EI, 70 eV), m/z (Irel, %):molecular ion peak ($M^{\cdot+}$+1) at m/z =373, 18.3% and the base peak at m/z= 175, 100%.

Synthesis of 2-pentadecylquinazolin-4-one(3):

Benzoxazinone (0.01mole) was fused with of ammonium acetate (0.04mole) on sand bath above the melting points for 3hrs, then cooled, water is added, the solid product obtained after filtration and crystallized. IR (KBr), cm^{-1}: Absorption bands at 3169 and 3120 due to NH bonded and non-bonded, and 3036, (2918-2850), 1674, and 1615 attributed to νCH aromatic, νCH aliphatic, νC=O, and νC=N groups respectively, beside the characteristic bands of

the quinazoline moiety in region of (1630-1620), (1580-1570), and (1515-1488). MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak ($M^{\cdot+}$) at m/z = 357, 46.2 % and the base peak at m/z=161, 100%.

Table 1: Physical properties of quinazoline compounds 1-18:

No.	M.F.	M.wt	Solvent	Yield %	M.P. (°C)	Analysis data calc/ found %			
						C	H	N	S
1	$C_{23}H_{35}NO_2$	357.53	Pet-ether 40-60	75	47-50	77.27 77.10	9.87 9.58	3.92 4.12	-
2	$C_{23}H_{37}N_3O$	371.56	Ethanol	80	98-100	74.35 74.17	10.04 9.87	11.31 11.57	-
3	$C_{23}H_{36}N_2O$	356.57	Ethanol	80	115	77.48 77.36	10.18 10.12	7.86 7.55	-
4	$C_{27}H_{42}N_2O_3$	442.63	Ethanol	70	63-65	73.26 73.40	9.56 9.62	6.33 6.12	-
5	$C_{25}H_{38}N_2O_3$	414.58	Methanol	70	96-100	72.43 72.19	9.24 8.98	6.76 6.53	-
6	$C_{25}H_{40}N_4O_2$	428.61	Methanol	70	88-90	70.06 69.89	9.41 9.23	13.07 12.96	-
7	$C_{23}H_{36}N_2O_2$	372.28	Ethanol	70	72-75	74.15 74.11	9.74 9.95	7.52 7.33	-
8	$C_{25}H_{38}N_2O_3$	414.58	Mthanol	70	63-65	72.43 72.22	9.24 9.43	6.76 6.81	-
9	$C_{27}H_{42}N_2O_4$	458.63	n-butanol	75	60	70.71 70.56	9.23 9.00	6.11 6.32	-
10	$C_{29}H_{41}N_3O$	447.66	Methanol	80	115	77.81 77.64	9.23 9.43	9.39 9.15	-
11	$C_{24}H_{38}N_4O_2$	414.57	Ethanol	85	97-100	69.93 70.01	9.24 9.17	13.51 13.28	-
12	$C_{24}H_{36}N_4O$	396.57	n-butanol	75	78-80	72.69 72.43	9.15 8.98	14.13 14.33	-
13	$C_{25}H_{40}N_2O_2$	400.60	Benzene	85	120	74.95 75.21	10.06 9.86	6.99 6.79	-
14	$C_{25}H_{38}N_2O_3$	414.58	Ethanol	85	92-95	72.43 72.21	9.24 9.46	6.76 6.44	-
15	$C_{25}H_{39}N_3O_2$	413.60	Ethanol	75	85	72.60 72.46	9.50 9.75	10.16 9.99	-
16	$C_{31}H_{43}N_3O_2$	489.69	Ethanol	85	120	76.03 75.28	8.85 8.60	8.58 8.62	-
17	$C_{30}H_{41}N_3O_2$	475.67	Ethanol	85	87-90	75.75 75.49	8.69 8.87	8.83 8.55	-
18	$C_{27}H_{43}N_3O_3$	457.65	n-butanol	70	73-75	70.86 70.68	9.47 9.23	9.18 9.33	-

Synthesis of 4-ethoxycarbonylmethoxy-2-heptadecyl-quina-zoline (4):

A mixture of compound **3**(0.04mol), anhydrous potassium carbonate (0.04mole) and ethyl chloroacetate (0.04mole) in dry acetone (60 ml) was heated under reflux for 24hrs. The excess solvent was removed under vacuum then poured on cold water, filtered off, washed several times by cold water, dried and crystallized from the appropriate solvent (see table 1).IR (KBr), cm^{-1}: shows νC=O (of ester) at 1743 and νC-O at 1170 beside the other characteristic bands of compound.MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak ($M^{\cdot+}$) at m/z = (443, 8.3 %) and the base peak at m/z = 245, 100 %

Synthesi of (2-pentadecyl-quinazolin-4-yl-oxy) acetic acid (5):

0.01 Mole of compound**4** wasrefluxed with 20% aq. sodium hydroxide solution for 3 hrs. The alkaline solution was acidified with HCl and extracted with ether. On evaporation of ether, a solid product was deposited andrecrystallized.IR (KBr), cm^{-1}: νOH (H-bonded) at 3445, νC=O (acid) at 1712 and νC=N at 1651 in addition to the bands νC-H aliphatic and aromatic of the compound.

Synthesis of 2-pentadecyl-4-hydrazinocarbonylmethoxy-quinazoline (6):

A mixture of compound **4** (0.01mole) and hydrazine hydrate (0.01mole) in ethanol was refluxedfor 3hrs. After cooling, the resulting product was filtered off and recrystallized.IR (KBr), cm^{-1}: exhibits νNH in region of (3396-3200), νC=O at 1675 and νC=N at 1612beside disappearance of carbonyl of ester.

Synthesis of 2-pentadecyl-3-hydroxy-quinazolin-4-one (7):

A mixture of equimolar amount of benzoxazinone **1** (0.01mole) and hydroxyl amine hydrochloride (0.01mole) in dry pyridine (50ml) was heated under reflux for 6 hours then left to cool down and poured into ice/HCl with stirring. The solid product that separated out was filtered off, washed with water, dried and recrystallized from

ethanol.IR (KBr), cm^{-1}: νOH at 3419, νC-H aromatic at 3067, νC-H aliphatic in region of (2918-2850) and νC=O at 1676.MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak ($M^{\cdot+}$) at m/z = 372, 13.9% and the base peak at m/z= 175, 100%.

Synthesis of 3-N-acetoxy-2-pentadecyl-quinazolin-4-one (8):
0.01 Mole of compound **7** was heated under reflux in freshly distilled acetic anhydride (20 ml) for 3hrs. The reaction mixture was left to cool at ambient temperature where a solid product that deposited was filtered off, washed several times with light petroleum ether, dried and recrystallized.IR (KBr), cm^{-1}: shows the absence of hydroxyl group and appearance of νC=O (of ester) at 1714 and νC-O at 1164 beside the other bands of the compound.MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak ($M^{\cdot+}$+1) at m/z = 416, 12.7 % and the base peak at m/z = 176, 100 %.

Synthesis of 3-ethoxycarbonylmethoxy-2-pentadecyl-quina-zolin-4-one (9):
To a solution of compound **7**(0.01mole) in of dry acetone (50ml), ethyl chloroacetate (0.04mole) and anhydrous potassium carbonate (0.04mole) was heated under reflux for 24hrs on water bath. The excess acetone was removed by distillation and the residue was poured into cold water with stirring. The resulting solid was filtered off by Bockner funnel, washed with cold water, dried and purified by crystallized. IR (KBr), cm^{-1}:shows the absenceof hydroxyl group and appearance of carbonyl of ester at 1734, νC=O (of quinazolinone) at 1684 and ν C-O at 1227 beside the other bands of the compound.

Synthesis of 2-pentadecyl-3- (2-amino phenyl)quinazolin-4-one (10):
A solution of 0.01 mole of a compound **1**in 30ml ethanol was added toa solution of 0.01mole of o-phenylene diamine in 20ml ethanol and refluxed. The reaction was monitored by TLC till completion after 3hrs then cooled at room temperature. Excess solvent was removed under vacuum and solid product was deposited. The product was collected on filtration, washed with little cold ethanol, dried then recrystallized from the appropriate solvent. IR (KBr), cm^{-1}:νNH at 3231, νC=O at 1690 and νC=N at 1602.

Synthesis of 2-pentadecyl-quinazolinylurea (11):
To a solution of compound **1** (o.o1mol) in 40ml pyridine, semicarbazide hydrochloride (0.01mole) was added and the reaction mixture was heated under reflux for 6hrs, the crud solid product that separated was filtered off, washed with cold water, dried and recrystallized.IR (KBr), cm^{-1}:shows νNH2, NH at (3358, 3260) and 3155 νC-H aromatic at 3029, νC-H aliphatic in region of (2918-2850) and νC=O at 1690 in addition of other bands of the compound.MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak (M+-3) at m/z = 411, 8.7% and the base peak at m/z = 55, 100 %.

Synthesis of 5-pentadecyl-2-oxo-1,2,4-triazolo[2,3-c]quinazoline (12):
On a sand bath, 0.01 mole of compound **11**was heated above its melting point for 2 hrs.On cooling, the solid product obtainedwas crystallized from n-butanol in a very good yield (78-80%).IR (KBr), cm^{-1}: shows the characteristic bands in region of (1520-1438) due to the triazole ring–skeletal bands vibrationand 1464 in addition of νNH/OH at the region 3386, 3220 and νC=O at 1679.

Synthesis of 3-(2-Hydroxy-ethyl)-2- pentadecyl quinazolin-4-one (13):
A solution of compound **1** (0.01mole) in ethanolamine (20ml) was refluxed for 3 hrs. The excess solvent was removed by evaporation under vacuum and the solid that formed was collected, washed with light petroleum, dried and recrystallized.IR (KBr), cm^{-1}:shows νC=O at 1642, νOH'S at 3296, νC-H'S aromatic at(3095), νC-H'Saliphatic at (2917, 2849).^{1}H-NMR (DMSO- d6) δ, ppm:δ'S at 0.9(t,3H,terminal CH_3), 1.2 (m,26H,13CH_2), 2.1 (t,2H, CH_2), 3.4(t, 2H, CH_2) adjacent to quinazolinone ring, 3.7(t, 2H, CH_2)(N-CH_2), 7.25-7.26 (s,4H,Ar-H), 6(s,1H, OH).

Synthesis of (4-oxo-2-pentadecyl-4H-quinazolin-3-yl)-acetic acid (14):
To a solution 0.01 mole of a compound **1**in 40ml pyridine, 0.01mole glycine was added and the heated under reflux for 4hrs then left to cool at room temperature. The reaction mixture was poured into into ice/HCl to reveal the solid product, which was filtered off, washed with water, dried and crystallized.IR (KBr), cm^{-1}:shows νOH'S (H-bonded) at 3340, νC=O (acid) at 1719.9 , νC=O (of quinazoline) at 1681.3, νC=N'S at 1605 inaddition of the bands νC-H'S aliphatic and aromatic of the compound.

Synthesis of N-(4-oxo-2-pentadecyl-4H-quinazolin-3-yl)acetamide (15):
Compound **2** (0.01mole) was refluxed in acetic anhydride for 3hrs then cooled in fume cupboardand poured on crushed ice. The solid product obtained was filtered off, dried and crystallized.IR (KBr), cm^{-1}:νNH centered at 3427, νC-H aromatic at 3076, νC-H aliphatic at (2920, 2850), and νC=O (of quinazolinone and acetamide) at 1708 and 1672 respectively.MS (EI, 70 eV), m/z (Irel, %):a molecular ion peak ($M^{\cdot+}$+1) at m/z = 415, 7.2% the base peak at m/z=176, 100%.

Synthesis of* 3-[(4-Methoxy- benzylidene)-amino]-2-pentadecyl-3H-quinazolin-4-one *(16):
A mixture ofcompound **2** (0.01mole) and p-methoxybenzaldehyde (0.01mole) in ethanol (50ml) was heated under reflux for 4hrs in the presence of catalytic amount of piperidine. The excess alcohol was removed by evaporation under vacuum. The reaction mixture was left to cool at ambient temperature to furnish the solid product which was filtered off and recrystallized.IR (KBr), cm^{-1}:νC=N'S at 1602, νC=O at 1667 (of quinazolinone),νC-O at 1259 ,and disubstituted benzene at 833.MS (EI, 70 eV), m/z (Irel, %):molecular ion peak ($M^{\cdot+}$+1) at m/z = 491 , 11.3% and the base peak at m/z = 160 , 100%

Synthesis of N-(4-oxo-2-pentadecyl-4H-quinazolin-3-yl) benzamide (17):
To a solution of compound **2** (0.01mole) in dry benzene (40ml) containing a catalytic amount of triethylamine (3drops), benzoyl chloride was added in drop wise. The reaction mixture was refluxed for 2hrs, then cooled at room temperature. The separated solid product was filtered off and crystallized.IR (KBr), cm^{-1}: νC=O at 1671, νC-H aromatic at (3003, 3053), νC-H aliphatic at (2917, 2849),νNH at 3207, and νC=N at 1633.

Synthesi of 3-[ethoxycarbonylmethylamino]-2- pentadecyl- quinazolin -4-one(18):
A mixture of compound **2** (0.01mole), anhydrous potassium carbonate (0.04mole) and ethyl chloroacetate (0.04mole) in dry acetone (60ml) was heated under reflux for 24hrs. The product obtained after removing the excess solvent was poured on cold water, filtered off, washed several times with cold water, dried and crystallized.IR (KBr), cm^{-1}:appearance of carbonyl of ester at 1736, νNH at 3226, νC=O (of quinazolinone) at 1696, νC-O at 1243.

Antibacterial, antifungal and antiyeast activation of the synthesized compounds:
The antimicrobial activities of the synthesized surfactants were determined in vitro using the holeplate and filter paper disc method (Rosen, 1989) which considered the most commonly used technique for determining sensitivity of chemotherapeutic agents. Compounds were dissolved in 10% acetone at different concentrations (125, 250, 500 µg/ml). Agar plates were inoculated uniformly from fresh broth culture of Gram +ve bacteria (Escherichia coli), Gram –ve bacteria (Bacillus subtilis), fungi (Pencicilliumnatatum), and yeast (Candida albicans). The disks were incubated at 28˚C for 24hr, and the formed inhibition zones were diffused into the agar from the disk (this refers to the organism was inhibited by material) and were measured in mm [28-30].

Bacterial media: Nutrient agar and broth (pH 7.0), Peptone (0.5g), Beef extract (0.3g), Agar (15.0g) and distilled water (1000.0ml).

Fungal media: $MgSO_4$ (0.5g); KCl(0.5g); Sucrose (30.0g); $FeSO_4$ (0.01g); $NaNO_3$ (3.0g); K_2HPO_4 (1.0g); Agar (15.0g) and distilled water (1000.0 ml).

Table 2: Antimicrobial activity of some synthesized quinazoline compounds.

Compds	Bacteria				Fungi		Yeast	
	E. coli (-ve)		B.subtilis(+ve)		*P. chrysogenum*		C. albicans	
	A	MIC	A	MIC	A	MIC	A	MIC
1	+++	125	++	250	++	125	+++	125
2	+	125	+	125	+	125	++	125
3	+++	125	++	125	+++	125	+	500
6	+	125	+	250	+++	500	++	125
7	++	125	++	125	+++	250	++	250
8	+++	125	++	250	++	250	+	250
9	++	250	+	250	+	500	+	250
11	+	125	++	250	++	500	+++	125
12	++	250	+++	125	+	250	+	500
13	+	125	+	500	+	250	++	250
15	+++	250	+++	250	+	250	+	125
17	++	250	+	250	+	125	++	250
18	++	125	+	500	+	250	++	250

A = Antimicrobial activity of tested compounds
MIC = Minimum inhibitory concentration
+ < 10 mm slightly active, ++< 20 mm moderately active, +++<30 mm highly active.

RESULTS AND DISCUSSION

Palmitoyl chloride reacted with anthranilic acid in dry acetone to produce anthranilamide derivatives which was cyclized with acetic anhydride to afford 4H,3,1-benzoxazin-4-one**1**. Reaction of 1 with hydrazine hydrate in ethanol with reflux afforded 3-N- amino quinazolinone compound **2**(Scheme 1). The structure of **1** was confirmed by IR-

spectrum which showed νCH aromatic at 3030, νCH aliphatic in the region of (2919-2850) and νC=O (of benzoxazinone) at 1761, νC=N at 1637 cm^{-1} and by Mass spectrum which showed the molecular ion peak (M^{-+}) at m/z = 358, 1.5% and the base peak at m/z= (160, 100%). Compound **2** was proofed by IR which showed the existence of νNH_2 at and 3285 and νC=O at 1679 Cm^{-1} with molecular ion peak at m/z 373 in mass spectrum.

Fusion of 3,1-benzoxazinone **1**with ammonium acetate at 170°C produced 3-N-hydroxy quinazolinone**3**which in turnreacted with ethyl chloroacetateto afford the correspondence ester3-N-ethoxycarbonylmethoxy quinazolin-4-one**4**(Scheme 2).Absorption bands at 3169 and 3120 cm^{-1} due to NH bonded and non-bonded at **3** and the molecular ion peak at m/z = 357 confirmed the structure of **3** while disappearance of NH at compound **4** and observing peaks at νC=O (of ester) at 1743 and νC-O at 1170 cm^{-1}in addition to its molecular ion peak at 443m/z proved the structure of **4**. On reaction of 4 with either sodium hydroxide or hydrazine hydrate furnished the corresponding acid**5** or acid hydrazide **6**respectively.Both compounds **5** and **6** have been confirmed by IR where acidic carbonyl absorption of **5** was shown at 1712Cm^{-1} in addition to the acidic νOH (H-bonded) at 3445 Cm^{-1} while IR of **6**exhibited νNH in region of (3396- 3200) and νC=O at 1675 of amidic carbonyl. Reaction of **1** with hydroxylamine hydrochloride gave 3-hydroxy-quinazolin-4-one**7**which has been acylated with acetic anhydride to give3-N-acetoxy-2-pentadecyl-quinazolin-4-one **8** or reacted with chloro-ethylacetate to give the corresponding ester 3-ethoxycarbonylmethoxy-2-pentadecyl-quina-zolin-4-one **9.** Structures of **8** and **9** have been proved by IR spectra which showed the absorption peaks of carbonyl ester at 1714 and 1734Cm^{-1} respectively in addition to a molecular ion peak at 416m/z for compound **8**. Reaction of 1 with o-phenylene diamiine in ethanol under reflux afforded the product 2-pentadecyl-3-(2-amino phenyl)quinazolin-4-one**10**.Presence of νNH_2in IR at 3231, νC=O at 1690 and νC=N at 1602 cm^{-1}in addition to the elemental analyses of **10** confirmed its structure. Quinazolinyl urea **11** was obtained when 3,1-benzoxazinone **1** was reacted with semicarbazide hydrochloride. On fusion of the last compound **11**over its melting point produced triazolo quinazoline derivatives **12**. IR of **11** showed νNH2 and NH at 3358 and 3260Cm^{-1} respectively and C=) at 1690Cm^{-1} in addition to molecular ion peak at 411m/z in mass spectrum. The characteristic vibration bands of triazole ring-skeleton [31] in**12** have been observed in region of 1520-1438Cm^{-1} and 1464 cm^{-1} in addition to νNH/OH at the region 3386, 3220Cm^{-1} and νC=O at 1679.1 cm^{-1}.Direct reaction of **1** with ethanolamine or with glycine in pyridine solution under reflux afforded the corresponding N-substituted quinazolinone compounds **13** and **14** respectively (Scheme 2). Alcoholic hydroxyl absorption of **13** was observed in IR at 3296Cm^{-1} and at 6ppm of ^{1}H-NMR in addition to two chemical shifts of two alcoholic CH_2 at 2.1 and 3.4ppm respectively. The IR of **14** exhibited νOH'S (H-bonded) at 3340, νC=O (acid) at 1719.9 and νC=O (of quinazoline) at 1681.3Cm^{-1}.

Acetylation of 3- amino-2-pentadecyl-quinazolin-4-one**2**in acetic anhydride afforded the formation of N-(4-oxo-2-pentadecyl-4H-quinazolin-3-yl)acetamide**15**while Schiff's base **16** was obtained on treatment of **2** with p-anisaldehyde in ethanol under reflux (Scheme 3). IR of **15** revealedνNHwas centered at 3427, and νC=O (of quinazolinone and acetamide) at 1708 and 1672Cm^{-1} respectively in addition to the molecular ion peak on its mass was at 415m/z. In compound **16**, the IR exhibited νC=N'S at 1602, νC=O at 1667 (of quinazolinone) and νC-O at 1259Cm^{-1}in addition to its molecular ion peak at mass spectra was at 491m/z. When 2 was allowed to react with the halogenated compounds e.g benzoyl chloride and chloro ethylacetate in presence of Lewis base as catalyst, the corresponding products N-(4-oxo-2-pentadecyl-4H-quinazolin-3-yl) benzamide **17** and 3-[ethoxycarbonylmethylamino]-2- pentadecyl- quinazolin -4-one**18** were obtained. IR showed νNH at 3207 for **17** and carbonyl of ester at 1736, νNH at 3226, νC=O (of quinazolinone) at 1696, νC-O at 1243 were observed on compound **18**.

Biological activity:

Some of the prepared compounds were tested for their antimicrobial activities against test organisms as represented gram (+ve and –ve) bacteria **(**Bacillus subtilies and Escherichia coli**)**, antifungal activity against (Pencillium notatum) and antiyeast activity against (Candida albicans), are given in (table 2). In general, the data revealed that all the tested compounds are highly active against both gram (+ve) and gram (–ve) bacteria except compounds **2**, **9** and **13**.Compounds benzoxazinone **1**, quinazolinone **3**, 3-N-acetoxy quinazoline **8**, triazoloquinazoline **12** and quinazolinonyl acetamide derivative **15**have exhibited the highest inhibitory effect towards bacteria, and compounds quinazolinone **3,** quinazolinyl acetic acid hydrazide **6**and 3-hydroxy quinazolinone **7**, were the most active compounds towards fungi. Compounds of benzoxazinone**1** and quinazolinyl urea derivative **11** showed the most active compounds towards yeast.

Thus it is clear that these compounds were effective and inhibited the growth of all tested microorganisms.

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