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Synthesis and Antimicrobial Activity of Some New *S*-Substituted Quinazolinones Containing Different Heterocyclic Rings

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New thiazolidine, azetidine and tetrazole derivatives of 2-mercapto-3-phenyl-4(3*H*)-quinazolinone are synthesized *via* the conversation of ester derivative (**2**) of 2-mercapto-3-phenyl-4(3*H*)-quinazolinone to hydrazide (**3**) by the reaction with hydrazine hydrate followed by Schiff's bases (**4-8**) formation by reaction with different aromatic aldehydes. Finally, Schiff's bases reacted with (2-mercptoacetic acid, monochloroacetyl chloride and sodium azide) to form thiazolidine (**9-13**), azetidine (**14-18**) and tetrazole (**19-23**) derivatives, respectively. The structure of newly synthesized compounds were identified by spectral methods their [FTIR and some of them by ^{1}H NMR, ^{13}C NMR] and measurements some of its physical properties and some specific reactions. Furthermore were studied the effects of the preparing compounds on some strains of bacteria and fungicidal.

Keywords: 4(3*H*)Quinazolinone, Azetidine, Thiazolidine, Tetrazole.

INTRODUCTION

Quinazolines are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties, for example, anticancer[1], antioxidant[2], anti-inflammatory[3], anticonvulsant[4] and antihyperlipidemic[5] activities. 4(3*H*)-quinazolinones are most prevalent, either as intermediates or as natural products in many proposed biosynthetic pathways. This is partly due to the structure being derived from the anthranilates (anthranilic acid or various esters, isatoic-anhydride, anthranilamide and anthranilonitrile) while the 2(1*H*)-quinazolinone is predominantly a product of anthranilonitrile or benzamides with nitriles[6].

2-Azetidinones, 4-thiazolidinones and tetrazoles are the most common and important groups among the small ring hetero cyclic compounds. 2-azetidinones and 4-thiazolidinones are famous antibiotics such as penicillin, cephalosporin and carbapenems are attributed to the presence of 2-azetidinone ring in them. A large number of them possess powerful antimicrobial[7], anti-inflammatory[8] and anticonvulsant[9] and AT1 angiotension-II (AII) receptor[10]. Tetrazole derivatives exhibited various biological activities such as antifungal[11] antiinflammatory[12] analgesic[13] anticancer activities[14].

In view of the importance of the above heterocycles we planned to synthesize new 2-mercapto-3-phenyl-4(3*H*)-quinazolinone derivatives include 4-thiazolidinone 2-azetidinone and tetrazole moieties.

EXPERIMENTAL

Chemicals used in this work are supplied from Merck, BDH, Sigma Aldrich and Fluka companies and are used without further purification. Melting points were recorded using digital Stuart scientific SMP3 melting point apparatus and are uncorrected. FTIR spectra were recorded on SHIMAZU FTIR-8400 Fourier transform infrared spectrophotometer using KBr discs in the (4000-600) cm^{-1} spectral range. ^{1}H NMR and ^{13}C NMR spectra were recorded on Burker 300 MHz using DMSO-d_6 as solvent and TMS as internal reference. Thin layer chromatography (TLC) was carried out using Fertigfollen precoated sheets type polygram Silg and the plates were developed with iodine vapor.

Synthesis of 2-mercpto-3-phenyl-4(3*H*)quinazolinone (1)[15]: A mixture of anthranilic acid (4.114 g, 0.03 mol), phenylisothiocyanate (3.61 mL, 0.03 mol) and triethylamine (3 mL) in (60 mL) absolute ethanol was refluxed for (3 h.). The reaction mixture was cooled at room temperature, then, poured on ice-cold water, stirred and filtered. The precipitate was recrystallized from methanol to give crystals. Physical properties of compound **1** are listed in Table-1.

Synthesis of ethyl 2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-ylthio)propanoate (2)[16]: To mixture of compound **1** (2 g, 0.007 mol) dissolved in (30 mL) methanol in a round bottom flask, potassium hydroxide (0.39 g, 0.007 mol) dissolved in (10 mL) methanol was added to the mixture and heated for

0.5 h. Then, ethyl-2-bromopropanoate (0.9 mL, 0.007 mol) was added and refluxed for 6 h. The reaction mixture was cooled at room temperature, then poured on ice-cold water and filtered. The white precipitate was recrystallized from ethanol to give crystals. Physical properties of compound **2** are listed in Table-1.

Synthesis of 2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-yl thio)propanehydrazide (3)[17]: Compound **2** (2 g, 0.0056 mol) in (15 mL) dimethyl formamide (DMF) as solvent; excess of hydrazine hydrate 99 % was added to the reaction mixture and refluxed for 8 h. Finally, the reaction mixture cooled at room temperature, poured on ice-cold water, stirred and filtered. The precipitate was recrystallized from ethanol and water to give crystals. Physical properties of compound **3** are listed in Table-1.

Synthesis of *S*-isopropanoamido-[1-imino(substituted phenyl)]-2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-ylthio) (4-8)[18]: To a solution of compound **3** (1 g, 0.0029 mol) in 20 mL absolute ethanol as solvent, substituted aromatic aldehyde (0.0029 mol) was added. Then, 4-5 drops of glacial acetic acid were added to the mixture, stirred for about 0.5 h. and refluxed for 5-6 h. Then, the reaction mixture cooled at room temperature, poured on ice-cold water, stirred, the precipitated solid thus obtained was filtered and recrystallized from suitable solvent. Physical properties of compounds **4-8** are listed in Table-1.

Synthesis of *S*-isopropanamido[4-(substituted phenyl)-3-chloro-2-oxo-azetidin-1-yl]-2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-ylthio) (9-13)[19]: A solution of appropriate Schiff-bases (**4-8**) (0.0005 mol) in 10 mL dioxane was added to well-stirred mixture of monochloroacetyl chloride (0.03 mL, 0.0005 mol) and triethyl amine (0.04 mL, 0.0005 mol) in dioxane (5 mL) at 0-5 °C. The mixture was refluxed for 10-15 h and left for 2 days at room temperature. The reaction mixture was then poured into crushed ice, filtered and washed with water. The solid product was dried and recrystallized from suitable solvent. Physical properties of compounds **9-13** are listed in Table-1.

Synthesis of *S*-isopropanamido[2-(substituted phenyl)-4-oxo-thiazolidin-3-yl]-2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-ylthio) (14-18)[20]: To a solution of appropriate Schiff-bases (**4-8**) (0.0005 mol) in tetrahydrofuran (THF) (15 mL); 2-mercaptoacetic acid (0.03 mL, 0.0005 mol) was added. Then, a pinch of anhydrous zinc chloride was added to the mixture and refluxed on water bath for 14-16 h. The separated solid was filtered, dried and recrystallized from suitable solvent to yield products. Physical properties of compounds **14-18** are listed in Table-1.

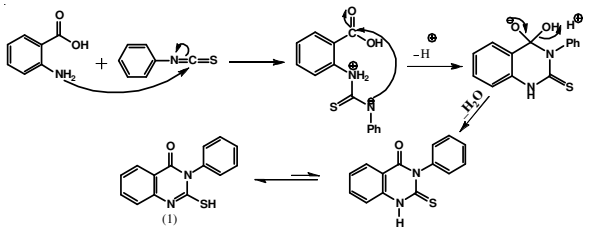
Synthesis of *S*-isopropanamido(5-(substituted phenyl)-1*H*-tetrazol-1-yl)-2-(3-phenyl-4-oxo-3,4-dihydroquinazolin-2-ylthio) (19-23)[21]: To a stirring solution of appropriate Schiff-bases (**4-8**) (0.0005 mol) in (10 mL) of tetrahydrofuran as solvent; sodium azide (0.03 g, 0.0005 mol) in (10 mL) of tetrahydrofuran was added. The mixture was refluxed for 10-14 h. Then, the reaction mixture was cooled at room temperature and the precipitate was filtered, washed with cooled and recrystallized from suitable solvent. Physical properties of compounds **19-23** are listed in Table-1.

Antimicrobial activity test[22]: The test was performed according to the disk diffusion method. Some of the prepared compounds were tested against two strain Gram-positive (*Staphylococcus aura* and *Bacillus*) and two strain Gram-negative bacteria (*Escherichia coli* and *Pseudoman acruginosa*). Also they tested against one strain of yeast (*Candida*). Whattman No. 1 filter paper disk of 5 mm diameter were sterilized by autoclaving for 15 min at 121 °C. The sterile disks were impregnated with different compounds (800 µg/disk). Agar plates were surface inoculated uniformly with 100 °C µL from both culture of tested microorganism. The impregnated disk were placed on the medium suitably spaced a part and the plates incubated at 5 °C for 1 h. to permit good diffusion and then transferred to an incubator at 37 °C for 24 h. The inhibition zones caused by various compounds on the microorganisms were examined. The results are listed in Table-4.

RESULTS AND DISCUSSION

The synthetic sequences for preparation of series of new 2-mercapto-3-phenyl-4(3*H*) quinazolinone linked to thiazolidine, azetidine and tetrazole moieties as in **Scheme- I**.

Compound **1** was prepared by condensing anthranilic acid with phenylisothiocyanate as the following mechanism[23]:



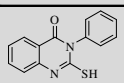
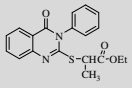
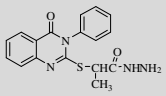
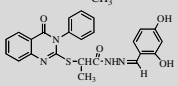
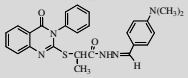
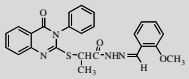
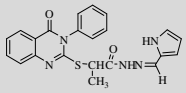
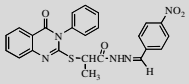
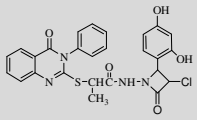
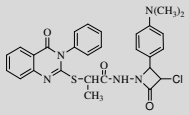
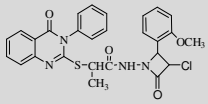
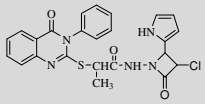
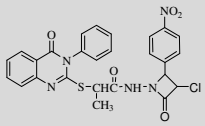
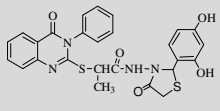
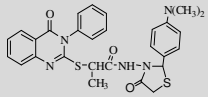
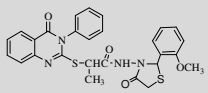
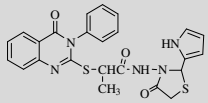
Mechanism of prepared compound **1**

The FTIR spectrum indicated the presence of a ν(N-H) (3244 cm^{-1}) and ν(C=O) (1691 cm^{-1}) of substituted amide[24] as listed in Table-1. Compound **2** was prepared by reaction of compound **1** with ethyl-2-bromo propanoate. The FTIR spectrum indicated that ν(N-H) (2650 cm^{-1}) was disappeared from the spectrum while ν(C-H) aliphatic at (2989 cm^{-1}) and ν(C=O) ester at (1733 cm^{-1}) were appeared (Table-1). ^{1}H NMR spectrum showed triplet signal at δ = (0.82) ppm due to (-CH_2-$C\underline{H}_3$) protons, doublet signal at δ = (1.19) ppm due to (-CH-$C\underline{H}_3$) protons, quartate signal at δ = (2.73) ppm due to (CH) protons, quartate signal at δ = (3.32) ppm due to (-O-CH_2) protons and signals at δ = (7.15-8.10) ppm due to aromatic rings protons as listed in Table-2. ^{13}C NMR spectrum data of compound **2** were listed in Table-3. Also, hydroxamic acid test improved the presence of ester group[25].

Compound **2** reacted with hydrazine hydrate and gave hydrazide compound **3**. FTIR spectrum showed absorption at (3453, 3363 and 3218 cm^{-1}) could be attributed to -NH_2 group asym. and sym. and -NH group stretching band respectively. Also showed shift in the νC=O band from (1733 cm^{-1}) of ester to (1686 cm^{-1}) of amide I . ^{1}H NMR spectrum showed doublet signal at δ = (1.56) ppm due to (-$C\underline{H}_3$) protons, quartate signal at δ = (2.83) ppm due to ($\underline{CH}$) protons, singlet signal at δ = (6.05) ppm due to (-$\underline{NH}_2$) protons, signals at δ = (7.41-8.34) ppm due to aromatic rings protons and singlet signal at δ = (9.72) ppm due to (-$\underline{N}$-$\underline{H}$) proton as listed in Table-2. ^{13}C NMR spectrum data of this compound **3** were listed in Table-3.

Compounds **4-8** were prepared by reaction of hydrazide derivative with different aromatic aldehydes in presence of glacial acetic acid as catalyst. FTIR spectrum of compounds **4-8** showed disappearance of absorptions bands due to

TABLE-1
PHYSICAL DATA AND FTIR SPECTRAL (cm^{1}) OF COMPOUNDS

No	Physical properties				Major FTIR Absorption (cm^{-1})				
	Structures	m.p. (°C)	Yield (%)	Colour	ν(N-H)	ν(C-H) aliph.	ν(C=O)	ν(C=C) arom.	Others
1		296-298	89	Off white	3244	-	1691	1598 1533 1487	ν(C=N) 1622
2		182-184	92	White	-	2989 2935	1733 Ester 1687 Amid	1575 1548 1467	ν(C-O) 1259,1159
3		270-273	62	Grey	3218	2923	1686	1600 1554	ν(NH_2) asym. 3453- Sym. 3363
4		241-243	75	Green	3391	2973	1685	1554 1512	ν(C=N) 1604 ν(O-H) 3421
5		230-231	81	Orange	3232	2947	1689	1554 1531	ν(C=N) 1618
6		208-210	80	Off white	3367	2973	1685	1554 1512	ν(C=N) 1604 ν(C-O) 1253, 1188
7		272-273	86	Green	3374	2996	1883	1556 1512	ν(C=N) 1616
8		248-250	89	Yellow	3400	2995	1687	1554 1512	ν(C=N) 1616 ν(NO_2) asym1458 sym. 1342
9		149-150	78	Milky	3431	2979	1689	1556 1512	ν(C-OH) 3386 ν(C-Cl) 808
10		146-148	74	Brown	3447	2979	1681	1556 1514	ν(C-Cl) 852
11		139-141	76	White	3431	2977	1693	1600 1537	ν (C-O) 1282,1172 ν(C-Cl) 852
12		157-158	87	Black	3438	2977	1689	1554 1537 1512	ν(C-Cl) 854
13		150-151	81	White	3421	2975	1681	1600 1556 1512	ν(NO_2) asym 1456 sym 1390 ν(C-Cl) 858
14		188-190	75	White	3388	2998	1695	1568 1515	ν(C-OH) 3421 ν(C-S) 657
15		185-187	70	Deep orange	3417	2910	1693	1596 1556	ν(C-S) 657
16		138-139	72	Off white	3274	2975	1693	1596 1566	ν(C-O) 1278,1137 ν(C-S) 692
17		206-207	78	Grey	3415	2992	1693	1596 1566	ν(C-S) 692

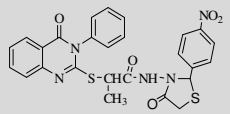
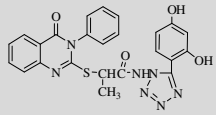
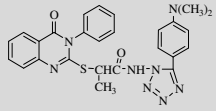
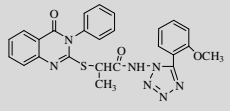
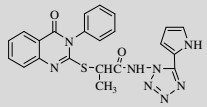
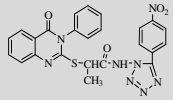
18		191-193	77	Green	3322	2970	1693	1596 1566 1517	$\nu(NO_2)$ asym 1478 sym 1366 ν(C-S) 692
19		270-271	70	Off white	3310	2985	1687	1556	ν(C-OH) 3390 ν(C=N) 1616 ν(N=N) 1512
20		256-258	72	Light Brown	3390	2913	1683	1556 1539	ν(C=N) 1616 ν(N=N) 1513
21		234-235	74	White	3390	2914	1689	1554	ν(C=N) 1600 ν(N=N) 1514 ν(C-O) 1246,1147
22		295-297	79	Dusty	3430	2981	1687	1556	ν(C=N) 1616 ν(N=N) 1512
23		286-287	79	Light green	3390	2969	1689	1554	ν(C=N) 1654 ν(N=N) 1514 $\nu(NO_2)$ asym 1485 sym1342

TABLE-2
^{1}H NMR SPECTRAL DATA (δ ppm) FOR SELECTED COMPOUNDS

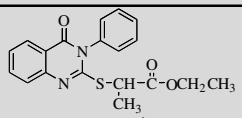
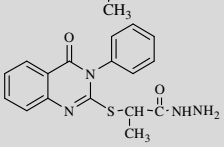
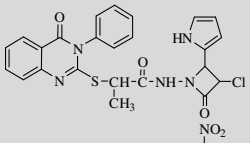
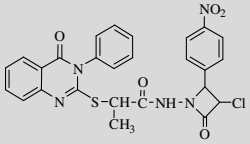
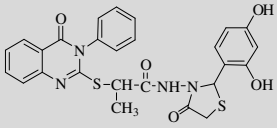
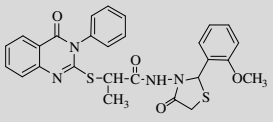
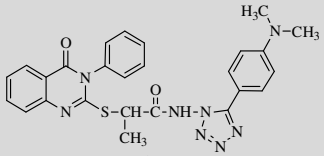
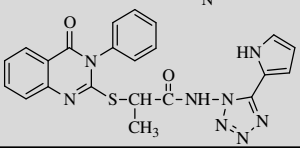
Compound No.	Structures	^{1}H NMR Spectral data (δ ppm)
2		0.82 (b, 3H, -CH_3-$\underline{CH_3}$); 1.19 (d, 3H, -CH-$\underline{CH_3}$); 2.73 (q, 1H, CH); 3.32 (q, 2H, -O-CH_2); 7.15-8.10 (m, 9H, Ar-H)
2		1.56 (d, 3H, CH_3); 2.83 (q, 1H, C-H); 6.05 (s, 2H, NH_2); 7.41-8.34 (m, 9H, Ar-H); 9.72 (s, 1H, N-H)
7		0.97 (d, 3H, CH-$\underline{CH_3}$); 2.85 (q, 1H, C-H); 3.33 (s, 1H, azetidine ring); 4.59 (b, 1H, CH-Cl azetidine ring); 7.30-7.98 (m, 13H, phenyl and pyrrole ring); 8.06 (s,1H, NH pyrrole ring); 9.38(s, 1H, -(CO)-NH-)
8		1.21 (s, 3H, CH-$\underline{CH_3}$); 3.04 (q, 1H, C-H); 3.56 (s, 1H, azetidine ring); 4.42 (d, 1H, CH-Cl azetidine ring); 7.54-8.29 (m, 13H, Ar-H); 9.61(s, 1H, -(CO)-NH-)
9		1,75 (d, 3H, CH-$\underline{CH_3}$); 3.10 (s, 1H, C-H thiazolidine ring); 3.34 (q, 1H, C-H); 3.59 (s, 2H, CH_2-thiazoldine ring); 5.45 (s, 2H, OH); 7.29-8.23 (m, 12H, Ar-H); 9.53(s, 1H, -(CO)-NH-)
11		1.74(d, 3H, CH-$\underline{CH_3}$); 3.20 (s, 1H, C-H thiazolidine ring); 3.37 (q, 1H, C-H); 3.58 (s, 5H, -CH_2-thiazolidine ring overlap with -OCH_3); 7.54-8.22 (m, 13H, Ar-H); 9.56 (s, 1H, -(CO)-NH-)
20		1.25 (d, 3H, -CH-$\underline{CH_3}$); 3.03 (s, 6H, $N(CH_3)_2$); 3.38 (q, 1H, C-H); 7.25-8.23 (m, 13H, Ar-H); 9.54 (s, 1H, -(CO)-NH-)
22		1.25 (d, 3H, CH-$\underline{CH_3}$); 3.33 (q, 1H, C-H); 7.25-7.987 (m, 12H, phenyl and pyrrole ring); 8.24 (s, 1H, N-H pyrrole ring); 9.54 (s, 1H, -(CO)-NH-)

TABLE-3
^{13}CNMR SPECTRAL DATA (δ ppm) FOR SELECTED COMPOUNDS

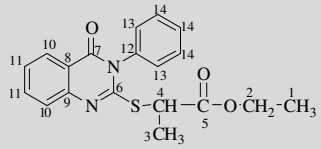
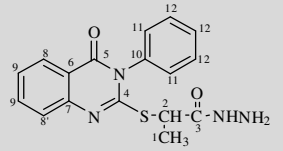
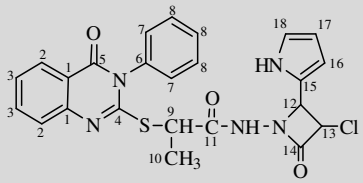
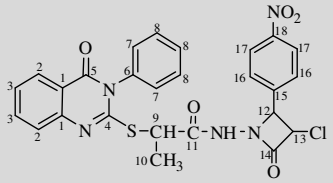
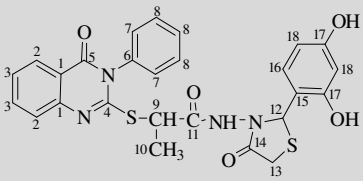
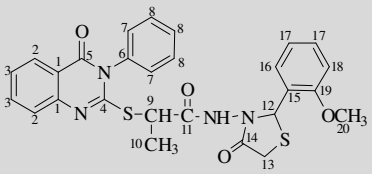
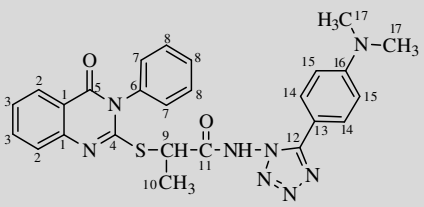
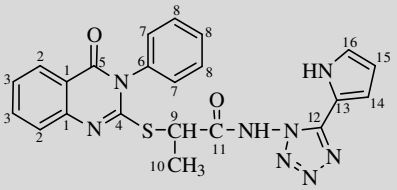
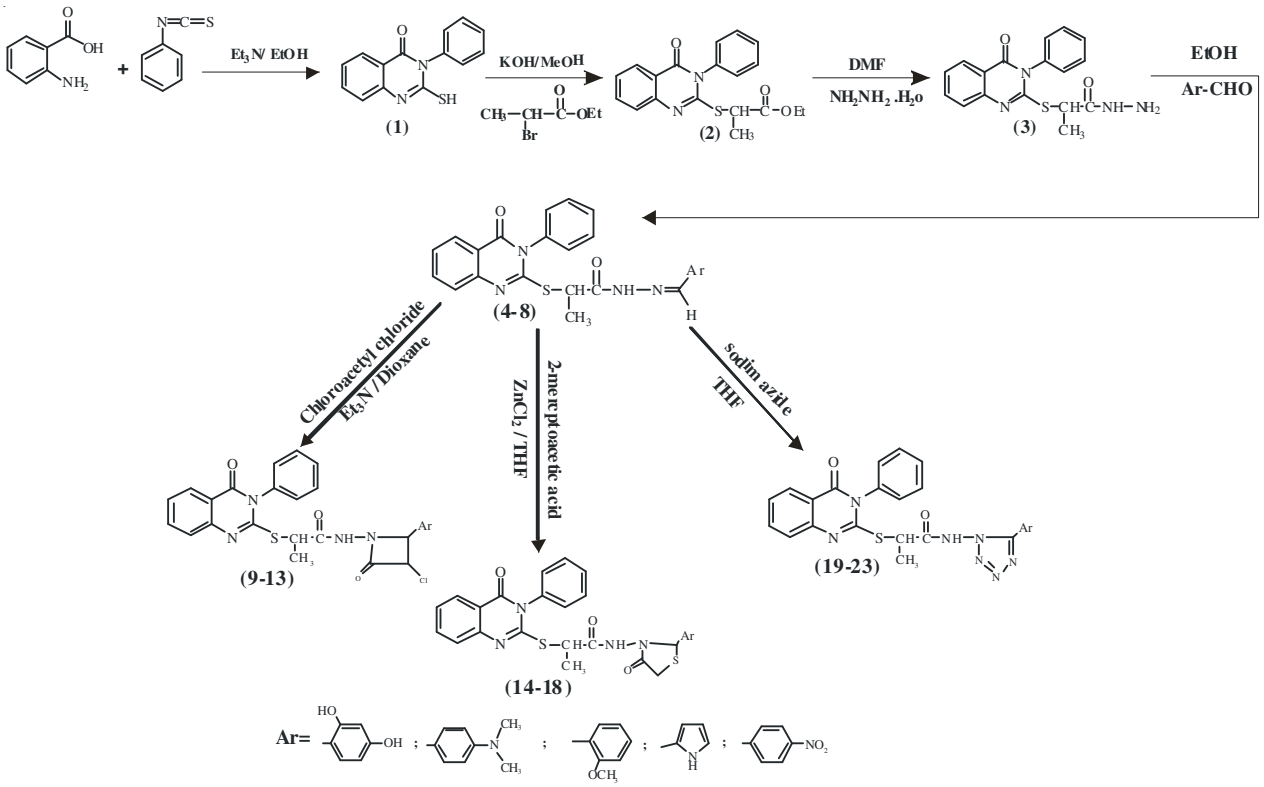
Compound no.	Compound structure	^{13}C NMR spectral data (δ ppm)
2		14.00(C1); 16.58(C3); 44.02(C4); 61.07(C2); 119.54-135.59 (C-8, 9, 10, 11, 12, 13, 14); 147.00 (C6); 160.53(C7); 171.30(C5)
2		11.19(C1); 28.98(C2); 116.63-149.07 (C 6, 7, 8, 8', 9, 10, 11, 12); 155.43 (C4); 160.93(C5); 168.02(C3)
7		8.36(C10); 38.72(C12); 39.27(C9); 45.28(C13); 115.98 (C17); 116.99(C16); 126.91-129.03(C2, C3, C7, C8); 132.82-135.83(C1, C6, C15, C18); 148.44(C4); 158.51(C5); 164.06(C14); 70.52(C11)
8		8.36(C10); 38.72(C12); 39.00(C9); 45.29(C13); 126.89-129.53(C2, C3, C7, C8, C16, C17); 132.82-135.83 (C1,C6, C15, C18); 148.43(C4); 158.50(C5); 164.02(C14); 168.51(C11)
9		10.97(C10), 32.24(C12); 38.97(C9); 44.80(C13); 126.87-129.14 (C2, C3, C7, C8, C16, C18); 132.80-135.80(C1, C6, C15); 148.47(C4, C17); 158.49(C5); 166.92(C14); 170.00(C11)
11		11.97(C10); 30.65(C12); 38.97(C9); 41.07(C13); 59.51(C20); 115.92(C18); 126.89-129.52(C2, C3, C7, C8, C16, C17); 132.80-136.50(C1, C6, C15, C19); 148.48(C4); 158.50(C5); 167.48(C14); 168.45(C11)
20		12.00(C10); 38.96(C9); 41.57(C17); 115.92(C15); 126.85-129.12(C2, C3, C7,C8, C14); 132.83-135.79(C1, C6, C13, C16); 148.45(C4, C12); 158.18(C5); 168,79(C11)
22		11.48(C10); 39.20 (C9); 116.41(C15); 117.46(C14); 127.35-136.28(C1-C8, C13, C16); 148.96(C4, C12); 159.02(C5); 168.02(C11)

TABLE-4
ANTIMICROBIAL ACTIVITY OF THE TESTED PREPARED COMPOUNDS

Compound no.	*Staphylococcus aureus*	*Bacillus subtilis*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Candida*
2	-	8	-	9	-
3	8	-	-	7	-
5	7	-	-	-	-
8	7	-	-	-	-
12	12	9	10	8	-
15	-	-	-	-	-

Solvent: DMSO; [C]: 800 μg/mL; Zone of inhibition: (-) no inhibition zone; (3-6) weak; (7-10) moderate; (11-15) strong



Scheme-I: Preparation of series of new 2-mercapto-3-phenyl-4(3*H*) quinazolinone, thiazolidine, azetidine and tetrazole

ν($NHNH_2$) absorption bands at (3453, 3363 and 3218) cm^{-1} and appearance of ν(NH) absorption bands at (3400-3232) cm^{-1}. The spectrum showed other bands at (1618-1604) cm^{-1} and (1556-1512) cm^{-1} due to ν(C=N) group and ν(C=C) aromatic, respectively. All details of FTIR spectral data of compounds **4-8** are listed in Table-1.

Schiff basses **4-8** in the next steps were cyclized by using three different methods with different reagents. First method includes treatment of Schiff bases **4-8** with chloroacetyl chloride followed by the addition of triethyl amine producing compounds **9-13**. FTIR spectra of compounds **9-13** showed appearance of absorption bands at (1693-1681) cm^{-1}, (1600-1512) cm^{-1} and (858-808) cm^{-1} due to ν(C=O) of carbonyl, ν(C=C) aromatic and ν(C-Cl) group, respectively. All details of FTIR Spectral data of compounds **9-13** are listed in Table-1.

^{1}H NMR spectrum data of compound **7** showed doublet signal at δ = (0.97) ppm due to (CH-C<u>H</u>$_3$) protons, quartet signal at δ = (2.85) ppm due to (C-<u>H</u>) proton, singlet signal at δ = (3.33) due to proton of azetidine ring bearing pyrrole ring, doublet signal at δ = (4.59) ppm due to (C<u>H</u>-Cl) proton, multi signals at δ = (7.30-7.98) ppm due to phenyl and pyrrole ring protons, singlet signal at δ = (8.06) ppm due to NH of pyrrole ring proton and singlet signal at δ = (9.38) ppm due to (-(CO)-N<u>H</u>-) proton. ^{1}H NMR spectral data of compounds **7** are listed in Table-2. ^{13}C NMR spectral data of compounds **7** are listed in Table-3.

While ^{1}H NMR spectrum data of compound **8** showed doublet signal at δ = (1.21) ppm due to (CH-C<u>H</u>$_3$) protons, quartet signal at δ = (3.04) ppm due to (C-<u>H</u>) proton, singlet signal at δ = (3.56) due to proton of azetidine ring bearing substituted phenyl, doublet signal at δ = (4.42) ppm due to (C<u>H</u>-Cl) proton, multi signals at δ = (7.54-8.29) ppm due to aromatic protons and singlet signal at δ = (9.61) ppm due to (-(CO)-N<u>H</u>-) proton. ^{1}H NMR spectral data of compounds **8** are listed in Table-2. ^{13}C NMR spectral data of compounds **8** are listed in Table-3.

The second method to cyclization of Schiff bases (**4-8**) by using mercaptoacetic acid in tetrahydrofuran to give thiazolidinone derivatives (**14-18**). FTIR spectra of compounds **14-18** showed appearance of absorption bands at (1695-1693) cm^{-1}, (692-657) cm^{-1} and (1596-1515) due to ν(C=O) of carbonyl and ν(C-S) bonds of thiazolidine rings, ν(C=C) aromatic, respectively. All details of FTIR spectral data of compounds **14-18** are listed in Table-1.

^{1}H NMR spectrum data of compound **9** showed doublet signal at δ = (1,75) ppm due to (CH-C<u>H</u>$_3$) protons, singlet signal at δ = (3.10) ppm due to (C-H) of thiazolidine ring proton, quartet signal at δ = (3.34) due to (C-H) proton, singlet signal at δ = (3.59) ppm due to (C<u>H</u>$_2$-) thiazolidine ring proton, singlet signal at δ = (5.45) due to (OH) protons, multi signals at δ = (7.29-8.23) ppm due to aromatic protons and singlet signal at δ = (9.53) ppm due to (-(CO)-N<u>H</u>-) proton. ^{1}H NMR spectral data of compound **9** are listed in Table-2. ^{13}C NMR spectral data of compounds **9** are listed in Table-3.

While ^{1}H NMR spectrum data of compound **11** showed doublet signal at δ = (1.74) ppm due to (CH-C<u>H</u>$_3$) protons, singlet signal at δ = (3.20) ppm due to (C-H) of thiazolidine ring proton, quartet signal at δ = (3.37) due to (C-H) proton, singlet signal at δ = (3.58) ppm due to (C<u>H</u>$_2$-) thiazolidine ring protons overlap with (-OC<u>H</u>$_3$) protons, multi signals at δ = (7.54-8.22) ppm due to aromatic protons and singlet signal at δ = (9.56) ppm due to (-(CO)-N<u>H</u>-) proton. ^{1}H NMR spectral data of compound **11** are listed in Table-2. ^{13}C NMR spectral data of compounds **11** are listed in Table-3.

The third method to cyclization of Schiff bases (**4-8**) was by using heating with sodium azide to give tetrazole derivatives. FTIR spectrum of compounds **19-23** showed bands at (1514-1512) cm^{-1} were due to the cyclic (N=N) stretching of tetrazole ring. Also, the FTIR for these compounds appear other absorptions bands at (1689-1683) cm^{-1}, (1654-1600) cm^{-1} and (1556-1539) cm^{-1} due to ν(C=O) amide, ν(C=N) group and ν(C=C) aromatic, respectively. FTIR characteristic data are reported in Table-1.

^{1}H NMR spectrum data of compound **20** showed doublet signal at δ = (1, 25) ppm due to (CH-$\underline{CH_3}$) protons, singlet signal at δ = (3.03) ppm due to ($N(CH_3)_2$) protons, quartet signal at δ = (3.38) due to (C-H) proton, multi signals at δ = (7.25-8.23) ppm due to aromatic protons and singlet signal at δ = (9.54) ppm due to (-(CO)-N$\underline{H}$-) proton. ^{1}H NMR spectral data of compound **20** are listed in Table-2. ^{13}C NMR spectral data of compound **20** are listed in Table-3.

While ^{1}H NMR spectrum data of compound **22** showed doublet signal at δ = (1,25) ppm due to (CH-$\underline{CH_3}$) protons, quartet signal at δ = (3.33) due to (C-H) proton, multi signals at δ = (7.25-7.98) ppm due to phenyl and pyrrole ring protons, singlet signal at δ = (8.24) ppm due to (N-H) proton of pyrrole ring and singlet signal at δ = (9.54) ppm due to (-(CO)-N$\underline{H}$-) proton. ^{1}H NMR spectral data of compound **22** are listed in Table-2. ^{13}C NMR spectral data of compound **22** are listed in Table-3.

Antimicrobial activity: The results of antimicrobial activity are listed in Table-4. The results referred that all synthetic compounds possess moderate activity against certain types of bacteria, while it did not possess any activity against other bacteria and *Candida*. Compound **12** possesses strong activity against *Staphylococcus aureus* while compounds **3**, **5** and **8** possess moderate activity against same bacteria. Compounds **2** and **12** possess moderate activity against *Bacillus subtilis* while *Pseudomonas aeruginosa* was inhibited by compounds **2**, **3** and **12** and showed moderate activity. As far as compound **12** possesses good activity against all types of bacteria

Conclusion

A new class of 4(3*H*) quinazolinone derivatives, different heterocyclic rings oxygen and nitrogen containing in structures has been synthesized a simple and inexpensive method. The prepared compounds identified by spectral methods [FTIR, ^{1}H NMR and ^{13}C NMR], furthermore we were studied the effects of the preparing on four types strains of bacteria and one yeast. Some of the prepared compounds possess moderate to highly activity against for this types of bacteria and yeast in study. The synthesis of further 4(3*H*) quinazolinone derivatives of this novel class is under way.

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