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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL 2-PHENYLQUINAZOLIN-4(3H)-ONE DERIVATIVES

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Abstract- A series of 3-((E)-5-(substitutedbenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one (V)1-12 have been synthesized. In order to establish optimization of different parameters of chemical transformation, that is the reaction pathway for each step and reaction conditions in the each step, in the present paper, different solvents and catalysts were used. The structures of the synthesized compounds were assigned on the basis of elemental analysis, IR, 1H NMR and 13C NMR spectral data. All the newly synthesized compounds were screened against various strains of bacteria and fungi.

Keywords- Quinazoline, 2-phenylquinazolin-4(3H)-one, Antimicrobial activity, 4-thiazolidinones

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Introduction

The rapid rise in bacterial resistance to the traditional antibiotics such as penicillin's [1] and tetracycline [2] has encouraged a continuing search for new classes of compounds with novel modes of anti-bacterial activity. The quinazolinones have emerged as antimicrobial agents of an immense interest because of their broad spectrum of *in-vitro* activity and their *in-vivo* chemotherapeutic activity [3,4].

Quinazolin-4(3H)-ones with substitution at position3, has been reported to be associated with anti-microbial properties [5]. Examples of these substitutions were substituted phenyl ring moieties [6], bridged phenyl rings [7,8], heterocyclic rings [9] and aliphatic systems [10].

Quinazoline derivatives represent one of the most active classes of compounds possessing a wide spectrum of biological activity. They are widely used in pharmaceuticals and agrochemicals; for example, fluquinconazole fungicide for the control of agriculture diseases Several reports have been published on the biological activity of quinazoline derivatives, including their bactericidal, herbal and antitumour activity Thus, their synthesis has been of great interest in the elaboration of biologically active heterocyclic compounds[11] Novel non-steroidal progesterone receptor antagonists with a 3-phenylquinazoline-2,4-dione/2-phenylisoquinoline- 1,3-dione skeleton were developed and their structure-activity relationships were investigated[12]. 2-phenylquinazoline analogues have shown to possess anti-prion[13], antiviral and cytotoxic [14], topoisomerase-I inhibitors[15], antibacterial activities[15] etc.

Similarly, various 4-thiazolidinones [16] have attracted considerable attention as they are also endowed with a wide range of pharmaceutical activities including anaesthetic [17], anticonvulsant [18], antibacterial (19] and antiviral [20]. Furthermore, drug research and development have led to the discovery of new pharmacologically active agents, including imidoxy [21] compounds such as succinimidoxy [22]. 4-Thiazolidinones may be considered as phosphate bioisosteres and therefore inhibit the bacterial enzyme MurB which is involved in the biosynthesis of peptidoglycan layer of the cell wall [23]. In addition, some thiazolidinones were recently reported as novel inhibitors of mycobacterial rhamnose synthetic enzymes [23]. This new approach is believed to be selective as rhamnose is not found in humans, but is essential for mycobacterial cell wall synthesis in animals [24].

Looking to the medicinal importance of quinazolinone and thiazolidinone, we report here the synthesis of new class of heterocyclic molecules in which both of these moieties are present and try to develop potential bioactive molecules. The structures of the compounds synthesized were assigned on the basis of elemental analysis, IR, 1H NMR, 13C NMR and Mass spectral data. These compounds were evaluated for their antimicrobial screening on different strains of bacteria and fungi.

Experimental Part

Materials and Physical Measurements

General Procedures. Laboratory Chemicals were supplied by Merck Ltd. Melting points were determined by the open tube capillary method and are uncorrected. The purity of the compounds was

monitored by thin layer chromatography (TLC) plates (silica gel G) in the solvent system n-hexane: ethyl acetate (V/V = 1:3). The spots were observed by exposure to iodine vapour or by UV light. The IR spectra were obtained on a Perkin-Elmer 1720 FT-IR spectrometer (KBr pellets).The 1H NMR and 13C NMR spectra were recorded on a Bruker Avance II 400 spectrometer using TMS as the internal standard in DMSO. Elemental analysis of the newly synthesized compounds was carried out on Carlo Erba 1108 analyzer.

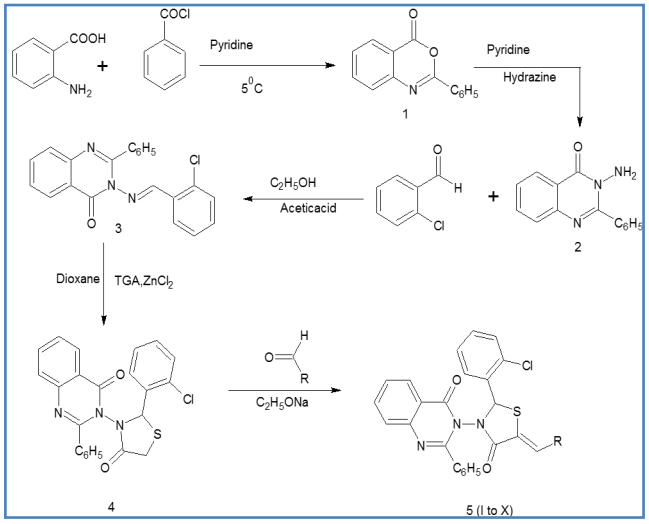


Fig. 1- Synthesized Compounds (1 to 5 $_{1 \text{ to } X}$)

Preparation Methods and Physical Data of Synthesized Compounds (1 to 5 $_{1 \text{ to } X}$)

Procedure for the Synthesis of 3-{[(*E*)-(2-chlorophenyl) methylidene]amino}-2-phenylquinazolin-4(3*H*)-one

To a solution of the 2-chlorobenzaldehyde (1.0 mmol) in ethanol (15 mL) was added 3-amino-2-phenyl-4(3H)-quinazolinone (1.0 mmol) and a few drops of glacial acetic acid was added. The reaction mixture was refluxed for 3-8 h and the course of the reaction was monitored by TLC [n-hexane/ethyl acetate (V/V =1:2)] to its completion. The reaction mixture was cooled. The crude product was recrystallized from 95% ethanol to give the intermediate compound- (III). Yield 73%, m.p. 178°C; IR (KBr, cm^{-1}) m: 3051, 1650 (quinazolinone ring, Benzene ring Ar-H), 3072 (CH stretching), 1671 (C,O stretching), 1605, 1580 (C,N stretching), 1562-1439 (C,C, quinazolinone ring, benzene ring), 838 (C-Cl stretching). 1H NMR (DMSO): d (ppm):7.4-7.9(m 4H quinazolinone), 7.2-7.6(m, 4H, Ar-H) 8.1 (s, 1H, ,CH group), 7.29.7.62(m, 5H, Ar-H)

Anal. Calcd for $C_{24}H_{15}ClN_4O$: C, 70.16; H, 3.68; N, 13.64. Found: C, 70.22; H, 3.74; N, 13.67.

Procedure for the Synthesis of 3-(2-(2chlorophenyl)-4-oxothiazolidin-3yl)-2-phenylquinazolin-4(3H)-one

To a solution of compound-(III) (0.01 mol) in 1,4-dioxane (50 ml) was added mercapto acetic acid (0.01 mol) with stirring and a little amount of anhydrous $ZnCl_2$ was added. The mixture was refluxed for 10-12 hrs., after the completion of the reaction, it was cooled and the excess solvent distilled and poured into sodium bicarbonate solution to neutralize it. The solid product was filtered, washed with cold water. The resulting light brown colour product was obtained. The completion of the reaction was checked by TLC [n-hexane/ethyl acetate (V/ V=1:3)]. The crude product was recrystallized from 95% ethanol to give the intermediate compound-(IV). Yield 73%, m.p. 178°C; IR(KBr, cm cm^{-1}) m: 3052, 1650 (quinazolinone ring, benzene ring Ar-H), 1677, 1686 (C,O stretching), 1609, 1582 (C,N stretching), 1564-1448 (C,C, quinazolinone ring, benzene ring), 849 (C-Cl stretching): 1H NMR (DMSO): d (ppm): 3.38-3.28 (s, 1H, CH2 group), 7.4-7.9(m 4H quinazolinone), 7.2-7.6(m, 4H, Ar-H) 8.1 (s, 1H, ,CH group), 7.29.7.62(m, 5H, Ar-H) Anal. Calcd for Molecular Formula = $C_{23}H_{17}N_3O_2S$: C, 69.15; H, 4.29; N, 10.52 Found: C, 69.42; H, 3.58; N, 11.12.

General Procedure for the Synthesis of 5 $_{I\text{-}X}$

Compound-(IV) (0.01 mol) was taken in ethanol (25 ml) and substituted aromatic aldehydes (0.01 mol) wer slowly added to it with stirring and a catalytic amount of sodium ethoxide was added. The reaction mixture was refluxed for 6-7 hrs., after the completion of the reaction, the product came out and excess amount of solvent was distilled out and the crude product was filtered off and washed with ethanol, dried and recrystallized in ethanol. The completion of the reaction was checked by TLC [n-hexane/ethyl acetate (V/V = 1:3)] to give the final product **5 $_{I\text{-}X}$**.

3-((*E*)-5-(2-nitrobenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 62%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (,CH stretching), 1675, 1681 (C,O stretching),

1605, 1589 (C-N stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3065 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.29-8.14 (m, 4H nitro benzene)7.24 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone),7.2-715(m,, 4H, Ar-H) 7.2-7.6(m, 4H, Ar-H) 7.94 (s, 1H, ,CH group), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),. ^{13}C NMR (DMSO) d (ppm): 133.5, 122.4, 151.3,120.9, 128.8, 127.4, 164, 161, 128.7, 52.2, 164.4, 129.3, 125.2, 136.1, 132.5, 129.6, 120.3, 148.3, 121.3, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 128.9, 130.2, 128.9, 126.1. Anal. Calcd for C33H20Cl2N4O2S: C, 65.24; H, 3.31; N, 9.22. Found: C, 65.32; H, 3.35; N, 9.30.

3-((*E*)-5-(3-nitrobenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 68%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (,CH stretching), 1675, 1681 (C,O stretching), 1605, 1589 (C-N stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3055 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.29-8.23 (m, 4H nitro benzene) 6.79 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.5 1(m,, 4H, Ar-H) 7.2-7.6(m, 4H, Ar-H) 7.94 (s, 1H, ,CH group), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),. ^{13}C NMR (DMSO) d (ppm): 164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 129.3, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 125.2, 136.1,121.3, 148.3, 120.3, 129.6, 132.5. Anal. Calcd for Molecular Formula = $C_{30}H_{19}ClN_4O_4S$:Composition: C, 63.55; H, 3.38; N(9.88%). Found: C, 63.32; H, 3.35; N, 9.30.

3-((*E*)-5-(4-nitrobenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 62%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (,CH stretching), 1675, 1681 (C,O stretching), 1605, 1589 (C-N stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3043 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.56-8.14 (m, 4H nitro benzene) 6.82 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H) 7.94 (s, 1H, ,CH group), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N). ^{13}C NMR (DMSO) d (ppm): 133.5, 122.4, 151.3, 120.9, 128.8, 127.4, 164,161, 128.7, 52.2, 164.4, 129.3, 125.2, 141.3, 127.3, 121, 147.6, 121, 127.3, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 126.1, 128.9, 130.2, 128.9, 126.1. Anal. Calcd for Molecular Formula = $C_{30}H_{19}ClN_4O_4S$: Composition = C, 63.55; H, 3.38; N, 9.88. Found: C, 63.32; H, 3.35; N, 9.56.

3-((*E*)-5-(4-methylbenzylidene)-2-(2-chlorophenyl)-4-oxothiazoli -din-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 63%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (CH stretching), 1675, 1681 (C,O stretching), 1605, 2950 (-CH3 stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3052 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.01-7.29 (m, 4H 4-methyl benzene), 6.68 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N), 2.35 (s, 3H, CH_3). ^{13}C NMR (DMSO) d (ppm): 164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 129.3, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 125.2, 132.2,126.3, 129, 137.6, 129, 126.3, 24.3, Anal. Calcd for Molecular Formula = $C_{31}H_{22}ClN_3O_2S$: Composition =C, 69.46; H, 4.14; N, 7.84. Found: C, 63.32; H, 3.35; N, 9.56.

3-((*E*)-5-(2-chlorobenzylidene)-2-(2-chlorophenyl)-4-oxothiazoli -din-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 70%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (,CH stretching), 1675, 1681 (C,O stretching), 1605, 845 (C-Cl stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3049 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.01-7.29 (m, 4H 4-methyl benzene), 6.68 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),7.08-7.24(m, 4H Ar-Cl). ^{13}C NMR (DMSO) d (ppm):133.5, 122.4, 151.3, 120.9, 128.8, 127.4, 164, 161.0, 128.7, 52.2,164.4, 129.3, 125.2, 133.1, 127.8, 126.8, 129.4, 128.8, 131.2, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 126.1, 128.9, 130.2, 128.9, 126.1. Anal. Calcd for Molecular Formula = $C_{30}H_{19}Cl_2N_3O_2S$. Composition =C, 64.75; H,3.44; N, 7.55, Found: C, 64.32; H, 3.35; N, 8.66.

3-((*E*)-5-(4-hydroxybenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 60%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (,CH stretching), 1675, 1681 (C,O stretching), 1605, 845 (C-Cl stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3082 (CH stretching), 5.39 (s, 1H, -OH group), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.01-7.29 (m, 4H 4-methyl benzene), 6.68 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),7.08-7.24(m, 4H Ar-Cl). ^{13}C NMR (DMSO) d (ppm):164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 129.3,1.5.3, 133.1, 128.9, 128.6, 126.9, 129.2, 125.2, 127.8, 127.8, 115.8, 157.7, 115.8, 127.8. Anal. Calcd for Molecular Formula = $C_{30}H_{20}ClN_3O_3S$.

Composition = C,66.97; H, 3.75; N, 7.81, Found: C, 66.39; H, 3.75; N, 7.66.

3-((*E*)-5-(3-hydroxybenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 65%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3073 (CH stretching), 1675, 1681 (C,O stretching), 1605, 845 (C-Cl stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3082 (CH stretching), 5.39 (s, 1H, -OH group), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.01-7.29 (m, 4H 4-methyl benzene), 6.68 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),7.08-7.24(m, 4H Ar-Cl). ^{13}C NMR (DMSO) d (ppm):164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 129.3,1.5.3, 133.1, 128.9, 128.6, 126.9, 129.2, 125.2, 127.8, 127.8, 115.8, 157.7, 115.8, 127.8. Anal. Calcd for Molecular Formula = $C_{30}H_{20}ClN_3O_3S$.

Composition = C,66.97; H, 3.75; N, 7.81, Found: C, 66.49; H, 3.78; N, 7.56.

3-((*E*)-5-(2-hydroxybenzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 68%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3062, 1654 (quinazolinone ring, benzene Ar-H), 3073 (CH stretching), 1675, 1681 (C,O stretching), 1605, 845 (C-Cl stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3082 (CH stretching),, 768, 692 (mono substituted benzene ring). 1H NMR (DMSO): d (ppm): 7.01-7.89 (m, 4H 4-methyl benzene), 6.78 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N),7.08-7.24(m, 4H Ar-Cl). ^{13}C NMR (DMSO) d (ppm):164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 126.3,1.5.3, 134.1, 128.9, 128.6, 126.9, 129.2, 125.2, 127.8, 127.8, 115.8, 157.7, 115.8, 127.8. Anal. Calcd for Molecular Formula = $C_{30}H_{20}ClN_3O_3S$.

Composition = C,66.97; H, 3.75; N, 7.81, Found: C, 66.59; H, 3.76; N, 7.56.

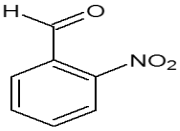
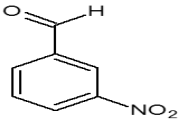
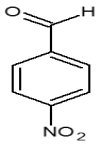
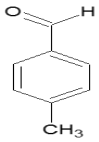
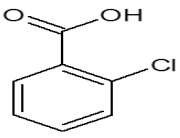
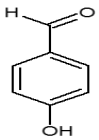
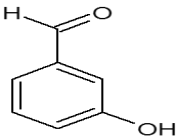
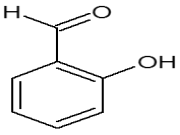
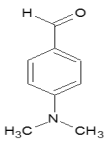
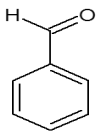
3-((*E*)-5-(4-(dimethylamino)benzylidene)-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 74%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3062, 1654 (quinazolinone ring, benzene Ar-H), 3073 (CH stretching), 1675, 1681 (C,O stretching), 1605, 845 (C-Cl stretching), 1568-1445 (C=C, quinazolinone ring, benzene ring), 3082 (CH stretching), 2810-2819 (dimethyl amino stretching), 768, 692 (mono substituted benzene ring). 1H NMR (DMSO): d (ppm): 7.01-7.89 (m, 4H 4-methyl benzene), 6.78 (s, 1H, CH group), 7.4-7.9(m

4H quinazolinone), 5.00 (s, 1H, -OH group), 7.0-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.00 (s, 1H, -OH group), 5.92 (s, 1H, S -CH-N),7.08-7.24(m, 4H Ar-Cl) 2.85 (s, H. CH_3-N-CH_3). ^{13}C NMR (DMSO) d (ppm):164,161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9, 126.1, 52.2, 164.4, 129.3,105.3, 133.1, 128.9, 128.6, 126.9,129.2, 125.2, 124.7, 127.3, 114.2, 148.8, 114.2, 127.3, 40.3. Anal. Calcd for Molecular = $C_{32}H_{25}ClN_4O_2S$

Composition = C, 68.02; H,4.46; N, 9.91, Found: C, 68.39; H, 4.36; N, 9.58.

Table 1- Antimicrobial activity of the final synthesized compounds 5 i-x

S. No	Compound	R	Minimum inhibitory concentration for bacteria µg / ml -/+ SD				Minimum inhibitory concentration for fungi µg / ml -/+ SD		
			Gram positive		Gram negative				
			E. coli	*P. aeruginosa*	*S. aureus*	*S. pyogenus*	*C. albecans*	*A. niger*	*A. clavatus*
1	5 i		250 ± 2.64	250±3.01	250±3	250±3.01	200 ±4.16	500±3.50	500± 3.20
2	5 ii		100±3	250±3.43	500± 4.06	100 ± 3.48	250± 3.05	1000±2.7	100 ± 3.25
3	5 iii		150± 2.28	25±1.05	100± 3.62	200±4.12	500± 4.12	100±3.05	1000±3.21
4	5 iv		100±3.04	200±4	250±2.62	250±2.64	250±2.06	500±3.51	500±3.44
5	5 v		100±4.45	250±2.04	500±3.04	500±4.56	500±4.02	100±3.60	1000±3.51
6	5 vi		200±2.54	250±2.48	250±3.55	500±4.55	100±4.04	100±3.05	500±3.46
7	5 vii		500±3	50±2.54	500±4.12	250±3.14	100±3.49	500±2.08	100±3.05
8	5 viii		100±3.49	100±4.46	200±4.14	250±3.66	500±4.04	500±2.08	100±3.05
9	5 ix		50±2.52	200±2.38	100±3.56	100±4.88	500±3	100±3.51	500±3.21
10	5 x		500±4.67	50±2.51	250±3.18	100±4.62	500±3.51	1000±3.02	100±3.51
	Ampicillin		100±4	100±4.02	250±4.04	100±3.51	-	-	-
	Griseofulvin		-	-	-	-	500±2.64	100±3	100±3.46

3-((*E*)-5-benzylidene-2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-2-phenylquinazolin-4(3H)-one

Yield, 77%, off yellow crystalline solid, mp 292-293°C. IR (KBr, cm cm^{-1}) m: 3057, 1650 (quinazolinone ring, benzene Ar-H), 3080 (CH stretching), 1675, 1681 (C,O stretching),, 1568-1445 (C=C, quinazolinone ring, benzene ring), 3052 (,CH stretching), 845 (C-Cl stretching), 768, 692 (mono substituted benzene ring 1H NMR (DMSO): d (ppm): 7.14-7.30 (m, 5H 4-methyl benzene), 6.68 (s, 1H, CH group), 7.4-7.9(m 4H quinazolinone), 7-7.15 1(m, 4H, Ar-H), 7.29.7.62(m, 5H, Ar-H), 5.92 (s, 1H, S-CH-N), 2.35 (s, 3H, CH_3). ^{13}C NMR (DMSO) d (ppm): 164, 161, 120.9, 128.8, 127.4, 133.5, 122.4, 151.3, 128.7, 126.1, 128.9, 130.2, 128.9,126.1, 52.2, 164.4, 129.3, 105.3, 133.1, 128.9, 128.6, 126.9, 129.2, 125.2, 135.2, 126.4, 128.7, 128, 128.7, 126.4. Anal. Calcd for Molecular Formula = $C_{30}H_{20}ClN_3O_2S$. Composition = C, 69.02;H, 3.86; N, 8.05. Found: C, 69.21; H, 3.77; N, 8.56.

Results and Discussion

Synthesis

Intermediate compound 1 and compound 2 were prepared by procedure mention in literature procedures [25]. The reaction conditions for the synthesis of (II) were optimized in various solvents at different temperatures and different time. The results were observed and data was reported in [Table-1]. In step-(II), ethanol was used as a solvent and refluxed at 78°C, reaction was completed in 4 h and yield was found to be 24%. When we used isopropanol as a solvent and at 85°C temperature for 4 hrs., we found that 31% yield was obtained in step II. Pyridine was used as a solvent and reaction mixture was refluxed at 116°C for 3 hrs., we found that 87% yield was obtained. Thus for the synthesis of intermediate compound 2, pyridine is considered to be appropriate solvent and higher temperature (more than 100°C) was the perfect parameter for step-2. Further synthesis of the derivatives was done as per the procedure mention in 2.2.3.

Antimicrobial Activity

Minimum Inhibitory Concentration for bacteria (MICb) of all the synthesized compounds was determined against four different strains, viz two Gram positive bacteria (*Staphylococcus aureus* and *S. pyogenes* and two Gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) compared with standard drug. Ampicillin by broth dilution method [26]. For Antifungal activities, minimum inhibitory concentration for fungi (MICf) of all the synthesized compounds was determined against *Candida albicans*, *Aspergillus niger* and *A. clavatus* organisms were compared with standard drugs Greseofulvin by same method, which showed 100 lg/ml MICf against all fungi used for the antifungal activity.

Antibacterial Activity

From screening results, final compound 5_{ix} possesses very good activity against *E. coli*. Compounds 5_{ii}, 5_{iv}, 5_{v} and 5_{viii} were good active against *E. coli* compared with standard

ampicillin. Final compound 5_{iii} possesses an excellent activity against *P. aeruginosa* and compound 5_{vii} possesses very good activity against *P. aeruginosa*, while compound 5_{viii} possesses good activity against *P. aeruginosa* as compared to standard ampicillin. Final compounds 5_{viii} and 5_{ix}possesses very good activity against *S. aureus*, while compounds 5_{i}, 5_{iv}, 5_{vi}, 5_{viii} and 5_{x} possesses good activity against *S. aureus* as compared to standard ampicillin. Final compounds 5_{ii}, 5_{viii} and 5_{ix} are considered as good active against S. pyogenus as compared to ampicillin. The remaining compounds of the entire series possesses only moderate to poor antibacterial activity.

Antifungal Activity

Antifungal screening data showed that final compounds 5_{vi} and 5_{vii} possesses very good activity against *C. albecans*, while compounds 5_{i}, 5_{iii} and 5_{iv} possess good activity against *C. albecans* as compared to the standard griseofulvin. Compounds 5_{iii}, 5_{v}, 5_{vi} and 5_{ix} possesses good activity against *A. niger* as compared to the standard griseofulvin. Compounds 5_{iii}, 5_{vii}, 5_{viii} and 5_{x} possesses good activity against *A. clavatus* as compared to the standard griseofulvin.

Conclusion

Some of the newly synthesized compounds exhibited promising antibacterial activities against *E. coli*, *S. aureus*, *P. aerug*inosa and *S. pyogenus*. Some exhibited very good antifungal activity against *C. albicans*, *A. niger* and *A. clavatus*. Compounds 5_{vii} and 5_{x} possessed very good activity against both bacterial and fungal species. It seems that the methyl group at para position and hydroxy group at second position are very significant for activity against both bacterial and fungal species. These results make novel quinazolinone derivatives interesting lead molecules for further synthetic and biological evaluation.

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