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Synthesis of some new substituted azetidinonyl and thiazolidinonyl quinazolon-4(3H)-ones as potential non-steroidal anti-inflammatory and analgesic agents

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ABSTRACT: A series of 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(substituted benzylidene) acetohydrazides (5a-5l) have been synthesized via condensation of 2-(5-(6-Bromo-2-methyl-4-oxaquinazolin-3 (4H)-yl)-4H-1,2,4-triazole-3-ylthio)acetohydrazide (4) with different aromatic aldehydes. Cycloaddition of thioglycolic acid with 5a-5l yielded 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(substituted benzylidene)-4-oxothiazolidin-3-yl) acetamides (6a-6l) while compound 5a-5l on treatment with chloro-acetylchloride in the presence of triethylamine are converted into 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro-2-(substituted benzylidene)-4-oxoazetidin-1-yl) acetamides (7a-7l).The structure of all the newly synthesized compounds have been confirmed by elemental analysis and spectral studies (IR, ^{1}H-NMR and mass spectroscopy).Compounds 5a-5l,6a-6l and 7a-7l have been evaluated for their anti-inflammatory and analgesic activity and were compared with the standard drug phenylbutazone. The most active compound of this series is 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2,6-dichloro benzylidene)-4-oxoazetidin-1-yl) acetamide (7g).

KEYWORDS: Thiazolidinonyl quinazolinone; Azetidinonyl quinazolinone; anti-inflammatory activity; Analgesic activity; acute toxicity.

INTRODUCTION

Quinazolinone nucleus has been gaining prominence due to the fact that its derivatives have been found to possess wide spectrum of activities like anti-becterial[1,2] analgesics[3] , anticonvulsant[4] and anti-inflammatory[5-8]. However, we have also reported substituted quinazolinone[9,10] derivatives as potent anti-inflammatory and analgesic inhibitors. Substitution pattern by different aryl or heteroaryl moieties at 2/3 position [11,12] of quinazolinone nucleus markedly influence anti-inflammatory activities. Moreover, Thiazolidinones[13-15] Azetidinones[16,17] and Triazole[18,20] are other important pharmacodynamic heterocyclic nuclei which when incorporated in different heterocyclic templates have been reported to possess potent anti-inflammatory activity. In the light of the above observation we have synthesized a new series of quinazolinone derivatives by incorporating the Triazole, Thiazolidinone and Azetidinone moieties at 3rd position of the quinazolinone nucleus. All the compounds have been screened for their anti-inflammatory, analgesic and ulcerogenic activities.

CHEMISTRY

The started compound 5-Bromo anthranilic acid has been synthesized according to the method of wheeler (1910). Compound 6-Bromo-2-methyl-4H-benzo [1,3]oxazin-4-one (1) have also been prepared by known method of Bogert et al (1907). Reaction of 5-amino-4H-1,2,4-triazole-3-thiol in dried pyridine with 6-Bromo-2-methyl-4H-benzo[1,3]oxazin-4-one carried out to obtain compound (2), which on reaction with chloro acetyl chloride resulted into 2-(5-(6-Bromo-2-methyl-4-oxaquinazolin-3(4H)-1,2,4-triazole-3-ylthio) acetyl chloride (3). Compound (3) when refluxed with 99% hydrazine hydrate in absolute ethanol yielded 2-(5-(6-Bromo-2-methyl-4-oxaquinazolin-3 (4H)-yl)-4H-1,2,4-triazole-3-ylthio) acetohydrazide (4).

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Compound (5a-5l) have been synthesized by condensation of compound (4) with various aromatic aldehydes in the presence of 2% NaOH solution. Addition of thioglycolic acid in the presence of anhydrous $ZnCl_2$ followed by cyclisation in compounds (5a-5l) introduced the Thizolidinone moiety in these compounds i.e. 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(Substituted benzylidene)-4-oxothiazolidin-3-yl) acetamides (6a-6l), while compounds 5a-5l when refluxed with chloro acetyl chloride in the presence of triethyl amine resulted into compounds 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro-2-(Substituted benzylidene)-4-oxoazetidin-1-yl) acetamides (7a-7l).

PHARMACOLOGY

The experiment were performed with albino rats of Charles-Foster strain of either sex, excluding pregnant females, of 60 to 90 days weighing 100 to 120 g. Food (chaw pallet) and water was given to the animals *ad libitum*. The test compounds were dissolved in propylene glycol. Indomethacin and phenylbutazone were used as reference drugs for the comparison of anti-inflammatory, analgesic and ulcerogenic activity.

Anti-inflammatory activity against carrageenan-induced rat's paw oedema

This study was done by following the procedure of Winter et al. [1962]. The rats were divided into three groups (control, drug treated, and standard, drug of six animals each. A freshly prepared suspension of carrageenan (1% in 0.9% saline) 0.05 ml. was injected under the planter aponeurosis of the right hind paw of each rat. Test compounds and standard drug were administered orally to the animals of drug treated groups and the standard drug group, respectively 1h before the carrageen an injection. The paw volume of each rat was measured before 1 and after 3 h of carrageenan treatment with the help of a plethymometer. The percent anti-inflammatory activity was calculated according to the formula given below-

Percentage of inhibition of oedema = $(1-V_t/V_c) \times 100$

Where, V_t and V_c are the mean increase in paw volume of rats of the treated and the control group, respectively. Results obtained were statistically analyzed.

Analgesic activity

Following the method of Berkowitz et al. [1977] performed this activity. This method is based on the property of the test compound to antagonize the phenyl quinone-induced pain syndrome in mice. Groups of five mice were injected intraperitonely with 0.25 ml of a 0.02% solution of phenylquinone in ethanol (5%) 1 h after of oral administration of the test compound. The number of writhes induced in each mouse was counted for 5 min (between 5 and 10 min) after injection of an irritant. The analgesic effect was expressed as percent protection in comparison to control.

% protection = (1-mean no. of writhes in mice of test groups/mean number of writhes in mice of control group) x 100

Ulcerogenic activity

Ulcerogenic liabilities of newly synthesized compounds were checked with method of Verma et al [1981]. Albino rats were fasted for 24 h prior to drug administration. All animals were sacrificed 8 h after drug treatment, and their stomachs and small intestines were microscopically examined to assess the incidence of hyperemia, shedding of epithelium, Petechial and frank hemorrhages and erosion or discrete ulceration with or without perforation. The presence of any one of these criteria was considered to be an evidence of ulcerogenic activity.

Acute Toxicity study

The test compounds were investigated for their acute toxicity (ALD_{50}) in albino mice, according to the method of Smith [1960]. The test compounds were given orally at different dose levels in separate groups of animals. After 24 h of drug administration, percent mortality in each group was observed. ALD_{50} was calculated from the data obtained.

Pharmacological result and discussion

All the newly synthesized compounds were studied for their anti-inflammatory activity against carrageenan-induced oedema. All the compounds were tested at a dose of 50 mg/kg given orally. The results of the study have shown in **table-I, II, & III.** All the compounds of this series **(5a-5l), (6a-6l)** and **(7a-7l)** have shown varying degree of anti-inflammatory activity (10.12-45.76%). The active compounds of this series **6g** and **7g** were found to possess more potent anti-inflammatory activity in the comparison of phenyl butazone. The compound **6g** i.e. which substituted with chloro group at 2,6,-position have shown 40.69% of inhibition of oedema. The compound **5a,** which possessed chloro group at 2^{nd}-position has shown least activity i.e., 10.12%. The compound **(6g)** 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-

(2,6-dichloro benzylidene)-4-oxothiazolidin-3-yl) acetamide and **(7g)** 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio)-N-(3-chloro-2-(2,6-dichloro phenyl)-4-oxoazetidin-1-yl) acetamide, have shown the better anti-inflammatory activity i.e. 40.69 and 45.76% at a dose of 50 mg./kg.p.o. as compared to phenyl butazone, **figure-I** showed the bar diagram of anti-inflammatory activity at three graded doses (25, 50, and 100 mg/kg p.o.) of compounds **6g**, **7g** and phenyl butazone. At all the three dose levels compounds **6g**, **7g** showed more inhibitory activity than that of phenyl butazone.

The newly synthesized compounds of the present series showed analgesic activity varying from 8.35-42.37 %. The active compound of this series **6g** and **7g** were found to possessed better analgesic activity i.e. (38.54 and 42.37 %) at the dose of 50 mg/kg p.o. Considering, potentiality of compound **6g** and **7g**, these were studied in details at three graded doses 25, 50 and 100 mg/kg p.o. The compound **7g** have shown better analgesic activity at all three graded doses of 25, 50 and 100 mg/kg p.o as compared to phenyl butazone **Figure-IV**

Compound **6g** and **7g** were also tested for their ulcerogenic activity and found to be less ulcerogenic liability as compared to phenyl butazone. UD_{50} of compound **6g** is 165.5 mg/kg i.p. and compound **7g** is 195.5 mg/kg i.p. UD_{50} of phenyl butazone is 66.6 mg./kg. i.p.

Approximate lethal dose (ALD_{50}) of all compounds of the present series showed > 1000 mg/kg. p.o. The compound **6g** and **7g** have exhibited > 1400 mg./kg. p.o., it indicates a good safety margin.

EXPERIMENTAL

All reagents and solvents were generally used as received from the commercial supplier. Reactions were routinely performed in oven-dried borosil glassware. The melting points of compounds were determined in open capillaries with the help of thermionic melting point apparatus and were uncorrected. The progress of the reaction is monitored by TLC and product are purified through recrysttalization and purity of the compounds was checked by thin layer chromatography (TLC) performed on silica gel G coated plate of 0.5 mm thickness. The eluent was a mixture of different polar and nonpolar solvents in different proportions, and spots were visualized under iodine chamber. The IR spectra were recorded on Perkin Elmer 881 FTIR spectrophotometer ($\bar{\nu}_{max}$ in cm^{-1}). The ^{1}H-NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Brucker DRX-400/300 FTNMR instrument. Mass spectra were determined on JEOL JMS-D-300 instrument.

Elemental and spectral analyses of the compounds were obtained from sophisticated, Analytical Instrumentation Facility Chandigarh, Punjab and CDRI, Lucknow, India.

6-Bromo-2-methyl-4H-benz[1,3]oxazine-4-one (1)

Yield 90%, m.p.176 ºC, IR max/cm-^{1} 2998, 2915, 1685, 1565, 1245,725; ^{1}H-NMR ($CDCl_3$) δ in ppm: 7.90–7.38 (m, 3H, Ar-H), 1.73 (s, 3H, CH_3), Compound 1 (Found: C, 37.84; H, 02.20; N, 16.97; Calc. for : $C_9H_6NO_2Br$,C, 37.99; H, 2.18;N, 16.88 %).

MS: $[M]^+$ at m/z 240.

6-Bromo-3-(5-mercapto-4H-1,2,4-triazole-3-yl)-2-methyl quanazolin-4(3H)-one (2)

To a solution of 5-amino-4H-1,2,4-triazole-3-thiol (0.01 mole) in dried Pyridine (100 ml.) 6-bromo-2-methyl-4H-benzo[d][1,3] oxazin-4-one (0.02 mole) was added. The reaction mixture was refluxed separately for 6-8 hr. Excess of solvent was removed and the residue was neutralized with HCl. The solid separated out, filtered, washed and recrystallized from methanol.

Yield 87%, m.p.216 ºC, IR max/cm-^{1} 3358, 3045, 2920, 1625, 1562, 1485, 735; 1H-NMR

(CDCl3) in ppm: 10.23 (s,1H,SH exchangeable with D_2O), 9.67 (s,1H,NH of triazole ring, exchangeable with D_2O), 7.97-7.42 (m,3H,Ar-H), 1.82 (s,3H,CH_3). Compound **2** (Found: C, 29.25; H, 2.40; N, 20.54; Calc. for : $C_{11}H_8SN_5$ OBr ,C, 39.07; H, 2.38;N, 20.71 %). MS:[M]+ at m/z 338

2-(5-(6-Bromo-2-methyl-4-oxaquinazolin-3(4H)-1,2,4-triazole-3-ylthio) acetyl chloride (3)

6-Bromo-3-(5-mercapto-4H-1,2,4-triazole-3-yl)-2-methyl quinazolin-4(3H)-one (0.01 mole) in dry THF (100 ml.) was added a solution of chloro acetyl chloride (0.02 mole) in dry THF (200 ml.) at OºC drop by drop along with manual stirring for 2hr. The reaction mixture was further stirred for 2-4 hr. on the mechanical stirrer and excess of solvent was distilled off, cooled and poured onto ice. The solid thus obtained, filtered and recrystallized from methanol.

Yield 82%, m.p.225 ºC, IR max/cm-^{1} 3357, 3046, 2932, 1632, 1620, 1553, 1487,732; ^{1}H-NMR ($CDCl_3$) δ in ppm: 9.68 (s, 1H, NH of triazole ring exchangeable with D_2O), 7.91–7.40 (m, 3H, Ar-H), 2.68 (s, 2H, -CH_2CO-), 1.85 (s, 3H, CH_3), Compound 3 (Found: C, 37.84; H, 02.20; N, 16.97; Calc. for : $C_{13}H_9S_5O_2ClBr$,C, 37.99; H, 2.18;N, 16.88 %).

MS: $[M]^+$ at m/z 415.

2-(5-(6-Bromo-2-methyl-4-oxaquinazolin-3 (4H)-yl)-4H-1,2,4-triazole-3-ylthio) acetohydrazide (4)

2-(5-(6-Bromo-2-methyl-4-oxaquionazolin-3(4H)-1,2,4-triazole-3-ylthio) acetyl chloride (0.01 mole) and hydrazine hydrate (99 %) (0.01 mole) in absolute ethanol (50 ml.) was refluxed for 10-12 hr. and the completion of reaction were monitored by TLC. The excess of solvent was distilled off. The reaction mixture was poured onto ice; the product thus obtained was recrystallized by ethanol.

Yield 77%, m.p.234 ºC, IR max/cm-^{1} 3355, 3052, 2924, 1650, 1625, 1555, 1495,1238,743; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 9.64 (s,1H, NH of triazole ring exchangeable with D_2O) 7.92-7.41 (m,3H,Ar-H), 4.45 (s, 2H, $NHNH_2$), 3.12 (hump.1H,CONH exchangeable with D_2O), 2.70 (s,2H,SCH_2CO), 1.90 (s,3H,CH_3).Compound 4 (Found: C, 37.82; H, 02.98; N, 23.96; Calc. for : $C_{13}H_{12}SN_7O_2Br$,C, 38.06; H, 2.95;N, 23.89 %).

MS: $[M]^+$ at m/z 410.

2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-chloro benzylidene) acetohydrazide (5a)

A mixture of 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3 (4H)-yl)-4H-1,2,4-triazole-3-ylthio) acetohydrazide (0.01 mole) and 2-chloro benzaldehyde (0.01 mole) in methanol (50 ml.) were refluxed for 7hr, in the presence of few drops of glacial acetic acid. The progress and completion of reaction were checked by TLC. The reaction was distilled off, cooled and then poured into ice water, filtered, washed with water and dried. The solid thus obtained were recrystallized from ethanol.

Yield 72%, m.p.196 ºC, IR max/cm-^{1} 3360, 3050, 2920, 1725, 1710, 1680, 1620,1560,1490,1235,740,710; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.85 (s, 1H, = CH-Ar), 7.92-7.36 (m, 7H, Ar-H), 7.15 (ss, 1H of triazole nucleus exchangeable with D_2O), 3.10 (hump, 1H, CONH exchangeable with D_2O), 2.64 (s, 2H, SCH_2CO), 2.12 (s, 3H, CH_3 attached to quinazolinone ing).Compound 5a (Found: C, 45.27; H, 02.85; N, 18.47; Calc. for : $C_{20}H_{15}SN_7O_2ClBr$,C, 45.09; H, 2.84;N, 18.40 %).

MS: $[M]^+$ at m/z 533.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(4-chloro benzylidene) acetohydrazides (5b)

Yield 67%, m.p.201 ºC, IR max/cm-^{1} 3350,3040,2915,1735,1718,1690,1605,1568,1484,1230,734,705 ; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.82 (s,1H,=CH-Ar), 7.90-7.35 (m, 7H, Ar-H), 7.13 (ss, 1H of triazole nucleus, exchangeable with D_2O),3.07 (hump, 1H, CONH exchangeable with D_2O),2.61 (s, 3H, SCH_2CO), 2.10 (s, 3H, CH_3 attached to quinazolin ring).Compound 5b (Found: C, 45.27; H, 02.85; N, 18.47; Calc. for : $C_{20}H_{15}SN_7O_2ClBr$: C, 45.09; H, 2.84;N, 18.40 %).

MS: $[M]^+$ at m/z 533.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-bromo benzylidene) acetohydrazides (5c)

Yield 65%, m.p.222 ºC, IR max/cm-^{1} 3354,3040,2922,1740,1715,1695,1612,1565,1480,1225,730,700; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.86 (s,1H,=CH-Ar), 7.95-7.37 (m, 7H, Ar-H), 7.17 (ss, 1H of triazole nucleus, exchangeable with D_2O), 3.12 (hump, 1H, CONH exchangeable with D_2O), 2.66 (s, 3H, SCH_2CO), 2.15 (s, 3H, CH_3 attached to quinazolin ring).Compound 5c (Found: C, 41.78; H, 02.63; N, 17.05; Calc. for : $C_{20}H_{15}SN_7O_2ClBr_2$: C, 41.62; H, 2.62;N, 16.98 %).

MS: $[M]^+$ at m/z 577.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(4-bromo benzylidene) acetohydrazides (5d)

Yield 63%, m.p.242 ºC, IR max/cm-^{1} 3350,3035,2920,1730,1720,1685,1610,1570,1485,1233,730,710 ; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.84 (s,1H,=CH-Ar 7.92-7.38 (m, 7H, Ar-H), 7.15 (ss, 1H of triazole nucleus, exchangeable with D_2O),), 3.08 (hump, 1H, CONH exchangeable with D_2O),2.67 (s, 3H, SCH_2CO), 2.18 (s, 3H, CH_3 attached to quinazolin ring)Compound 5d (Found: C, 41.78; H, 02.63; N, 17.05; Calc. for : $C_{20}H_{15}SN_7O_2ClBr_2$: C, 41.62; H, 2.62;N, 16.98 %).

MS: $[M]^+$ at m/z 577.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2,4-dichloro benzylidene) acetohydrazides (5e)

Yield 60%, m.p.220 ºC, IR max/cm-^{1} 3345,3042,2920,1720,1710,1677,1620,1554,1480,1220,735,710; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.67 (s,1H,=CH-Ar), 7.85-7.15 (m, 6H, Ar-H), 7.10 (ss, 1H of triazole nucleus, exchangeable with D_2O),2.95 (hump, 1H,

CONH exchangeable with D_2O),2.52 (s, 3H, SCH_2CO), 1.98 (s, 3H, CH_3 attached to quinazolin ring).Compound 5e (Found: C, 42.78; H, 02.48; N, 17.21; Calc. for : $C_{20}H_{14}SN_7O_2Cl_2Br$: C, 42.35; H, 2.49;N, 17.28 %).

MS: $[M]^+$ at m/z 567.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2,4-dibromo benzylidene) acetohydrazides (5f)

Yield 55%, m.p.248 ºC, IR max/cm-^{1} 3350,3050,2925,1730,1720,1680,1622,1560,1480,1225,735,710; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.68 (s,1H,=CH-Ar), 7.96-7.22 (m, 6H, Ar-H), 7.08 (ss, 1H of triazole nucleus, exchangeable with D_2O),3.05 (hump, 1H, CONH exchangeable with D_2O), 2.60 (s, 3H, SCH_2CO), 2.04 (s, 3H, CH_3 attached to quinazolin ring).Compound 5f (Found: C, 36.46; H, 02.14; N, 14.88; Calc. for : $C_{20}H_{14}SN_7O_2Br_3$: C, 36.61; H, 2.15;N, 14.94 %).

MS: $[M]^+$ at m/z 656.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2,6-dichloro benzylidene) acetohydrazides (5g)

Yield 65%, m.p.228 ºC, IR max/cm-^{1} 3335,3050,2975,1715,1705,1665,1610,1540,1470,1240,738,700; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.59 (s,1H,=CH-Ar), 7.77-7.11 (m, 6H, Ar-H), 6.95 (ss, 1H of triazole nucleus, exchangeable with D_2O),2.88 (hump, 1H, CONH exchangeable with D_2O),2.43 (s, 3H, SCH_2CO), 1.89 (s, 3H, CH_3 attached to quinazolin ring).Compound 5g (Found: C, 42.18; H, 02.48; N, 17.21; Calc. for : $C_{20}H_{14}SN_7O_2Cl_2Br$: C, 42.35; H, 2.49;N, 17.28 %).

MS: $[M]^+$ at m/z 567.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2,6-dibromo benzylidene) acetohydrazides (5h)

Yield 55%, m.p.252 ºC, IR max/cm-^{1} 3340,3045,2925,1720,1710,1685,1620,1565,1485,1232,740,702 ; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.64 (s,1H,=CH-Ar), 7.90-7.19 (m, 6H, Ar-H), 7.04 (ss, 1H of triazole nucleus, exchangeable with D_2O),3.00 (hump, 1H, CONH exchangeable with D_2O), 2.55 (s, 3H, SCH_2CO), 2.01 (s, 3H, CH_3 attached to quinazolin ring). Compound 5h (Found: C, 36.46; H, 02.14; N, 14.88; Calc. for : $C_{20}H_{14}SN_7O_2Br_3$: C, 36.61; H, 2.15;N, 14.94 %).

MS: $[M]^+$ at m/z 656.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-methoxy benzylidene) acetohydrazides (5i)

Yield 61%, m.p.197 ºC, IR max/cm-^{1} 3365,3060,2930,1735,1720,1690,1630,1570,1495,1240,750,725; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.88 (s,1H,=CH-Ar), 7.96-7.38 (m, 7H, Ar-H), 7.19 (ss, 1H of triazole nucleus, exchangeable with D_2O),3.13 (hump, 1H, CONH exchangeable with D_2O), 2.74 (s, 3H, SCH_2CO), 2.31 (s, 3H, CH_3 attached to quinazolin ring) .Compound 5i (Found: C, 47.93; H, 3.44; N, 18.63; Calc. for : $C_{21}H_{18}SN_7O_3Br$: C, 47.74; H, 3.43;N, 18.56%).

MS: $[M]^+$ at m/z 528.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(4-methoxy benzylidene) acetohydrazides (5j)

Yield 63%, m.p.188 ºC, IR max/cm-^{1} 3370,3066,2940,1745,1725,1638,1575,1490,1250,745,720; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.80 (s, 1H, = CH-Ar), 7.98-7.41 (m, 7H, Ar-H), 7.24 (ss, 1H of triazole nucleus exchangeable with D_2O), 3.15 (hump, 1H, CONH exchangeable with D_2O), 2.70 (s, 3H, SCH_2CO), 2.36 (s, 3H, CH_3 attached to quinazolinone ing).Compound 5j (Found: C, 47.55; H, 3.42; N, 18.49; Calc. for : $C_{21}H_{18}SN_7O_3Br$: C, 47.74; H, 3.43;N, 18.56%).

MS: $[M]^+$ at m/z 528.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-methyl benzylidene) acetohydrazides (5k)

Yield 58%, m.p.176 ºC, IR max/cm-^{1} 3375,3070,2950,1750,1735,1645,1580,1495,1260,755,730; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.86 (s,1H,=CH-Ar), 7.98-7.48 (m, 7H, Ar-H), 7.29 (ss, 1H of triazole nucleus, exchangeable with D_2O),3.18 (hump, 1H, CONH exchangeable with D_2O), 2.92 (s, 3H, SCH_2CO), 2.42 (s, 3H, CH_3 attached to quinazolin ring) .Compound 5k (Found: C, 49.43; H, 3.55; N, 19.22; Calc. for : $C_{21}H_{18}SN_7O_2Br$: C, 49.23; H, 3.54;N, 19.14%).

MS: $[M]^+$ at m/z 512.

(E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(4-methyl benzylidene) acetohydrazides (5l)

Yield 56%, m.p.182 ºC, IR max/cm-^{1} 3380,3065,2945,1755,1740,1650,1575,1490,1265,750,730; ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.90 (s,1H,=CH-Ar), 8.02-7.50 (m, 7H, Ar-H), 7.34 (ss, 1H of triazole nucleus, exchangeable with D_2O) 3.23 (hump, 1H, CONH exchangeable with D_2O), 2.88 (s, 3H, SCH_2CO), 2.46 (s, 3H, CH_3 attached to quinazolin ring) .Compound 5l (Found: C, 49.03; H, 3.53; N, 19.02; Calc. for : $C_{21}H_{18}SN_7O_2Br$: C, 49.23; H, 3.54;N, 19.14%).

MS: $[M]^+$ at m/z 512.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2-chloro benzylidene)-4-oxothiazolidin-3-yl) acetamide (6a) :

To a solution of the compound **(5a)** 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(2-chlorobenzaldehyde) acetohydrazide (0.01 mole) in ethanol (50 ml.), thioglycolic acid (0.02 mole) were added drop wise in presence of anhydrous zine chloride and the reaction mixture were refluxed for 10 hr. The completion of reaction was checked by TLC. The excess of methanol were distilled off. The cooled residual mass were diluted with ice-water, filtered washed with water, dried and recrystallized from methanol.

Yield 55%, m.p.206 ºC, IR max/cm-^{1} 3355, 3050, 2935, 2840, 1745, 1730, 1715,1685,1620,1570,1485,1230,745,715,695; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.90-7.40 (m, 7H, Ar-H), 7.25 (ss, 1H, of triazole nucleus exchangeable with D_2O), 6.75 (s, 1H, -CH-Ar), 3.42 (s, 2H, CH_2 of thiazolidinone ring), 3.15 (hump, 1H, CONH exchangeable with D_2O), 2.70 (s, 2H, S CH_2CO), 2.15 (s, 3H, CH_3 attached to quinazolinone ring). Compound 6a (Found: C, 43.71; H, 02.83; N, 16.10; Calc. for $C_{22}H_{17}N_7O_3S_2BrCl$: C, 43.44; H, 02.82;N, 16.16 %).

MS: $[M]^+$ at m/z 607.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(4-chloro benzylidene)-4-oxothiazolidin-3-yl) acetamide (6b) :

Yield 50%, m.p.211 ºC, IR max/cm-^{1} 3340, 3035, 2930, 2825, 1750, 1725, 1710,1675,1610,1560,1475,1220,735,705,685; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.95-7.45 (m, 7H, Ar-H), 7.30 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.78 (s, 1H, -CH-Ar), 3.48 (d, CH_2 of thiazolidinone), 3.20 (hump, 1H, CONH exchangeable with D_2O),2.80 (s,2H,SCH_2CO), 2.20 (s, 3H, CH_3 attached to quinazolin ring). Compound 6b (Found: C, 43.71; H, 02.83; N, 16.22; Calc. for $C_{22}H_{17}N_7O_3S_2BrCl$: C, 43.54; H, 02.82;N, 16.16 %).

MS: $[M]^+$ at m/z 607.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2-bromo benzylidene)-4-oxothiazolidin-3-yl) acetamide (6c) :

Yield 48%, m.p.217 ºC, IR max/cm-^{1} 3345, 3040, 2935, 2830, 1750, 1730, 1715,1685,1615,1565,1480,1215,740,710,695; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.99-7.40 (m, 7H, Ar-H), 7.35 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.82 (s, 1H, -CH-Ar), 3.55 (d, CH_2 of thiazolidinone), 3.24 (hump, 1H, CONH exchangeable with D_2O),2.84 (s,2H,SCH_2CO), 2.26 (s, 3H, CH_3 attached to quinazolin ring). Compound 6c (Found: C, 40.41; H, 02.62; N, 15.11; Calc. for $C_{22}H_{17}N_7O_3S_2Br_2$: C, 40.57; H, 02.63;N, 15.05 %).

MS: $[M]^+$ at m/z 651.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(4-bromo benzylidene)-4-oxothiazolidin-3-yl) acetamide (6d) :

Yield 45%, m.p.228 ºC, IR max/cm-^{1} 3335, 3035, 2930, 2825, 1750, 1725, 1715,1680,1610,1560,1470,1210,735,710,680; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.92-7.35 (m, 7H, Ar-H), 7.32 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.84 (s, 1H, -CH-Ar), 3.44 (s, CH_2 of thiazolidinone), 3.22 (hump, 1H, CONH exchangeable with D_2O),2.80 (s,2H,SCH_2CO), 2.32 (s, 3H, CH_3 attached to quinazolin ring).Compound 6d (Found: C, 40.41; H, 02.62; N, 15.11; Calc. for $C_{22}H_{17}N_7O_3S_2Br_2$: C, 40.57; H, 02.63;N, 15.05 %).

MS: $[M]^+$ at m/z 651.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2,4-dichloro benzylidene)-4-oxothiazolidin-3-yl) acetamide (6e) :

Yield 49%, m.p.230 ºC, IR max/cm-^{1} 3340, 3030, 2915, 2820, 1745, 1725, 1710,1670,1605,1550,1460,1205,730,705,675; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.85-7.37 (m, 6H, Ar-H), 7.28 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.73 (s, 1H, -CH-Ar), 3.40 (d, CH_2 of thiazolidinone), 3.01 (hump, 1H, CONH exchangeable with D_2O),2.70 (s,2H,SCH_2CO), 2.10 (s, 3H, CH_3 attached to quinazolin ring).Compound 6e (Found: C, 41.36; H, 02.50; N, 15.35; Calc. for $C_{22}H_{16}BrCl_2N_7O_3S_2$: C, 41.20; H, 02.51;N, 15.29 %).

MS: $[M]^+$ at m/z 641.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2,4-dibromo benzylidene)-4-oxothiazolidin-3-yl) acetamide (6f) :

Yield 43%, m.p.258 ºC, IR max/cm-^{1} 3345, 3030, 2915, 2820, 1740, 1725, 1715,1670,1610,1555,1470,1215,740,715,685; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.94-7.41 (m, 6H, Ar-H), 7.14 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.82 (s, 1H, -CH-Ar), 3.48 (d, CH_2 of thiazolidinone), 3.05 (hump, 1H, CONH exchangeable with D_2O),2.78 (s,2H,SCH_2CO), 2.15 (s, 3H, CH_3 attached to quinazolin ring). Compound 6f (Found: C, 36.04; H, 02.22; N, 13.38; Calc. for $C_{22}H_{16}N_7O_3S_2Br_3$: C, 36.18; H, 02.21;N, 13.43 %).

MS: $[M]^+$ at m/z 730.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2,6-dichloro benzylidene)-4-oxothiazolidin-3-yl) acetamide (6g) :

Yield 46%, m.p.238 ºC, IR max/cm-^{1} 3335, 3025, 2905, 2810,1730, 1715,1700,1660,1595,1545,1455,1200,725,705,670; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.75-7.25 (m, 6H, Ar-H), 7.05 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.60 (s, 1H, -CH-Ar), 3.30 (d, CH_2 of thiazolidinone), 3.00 (hump, 1H, CONH exchangeable with D_2O),2.88 (s,2H,SCH_2CO), 2.04 (s, 3H, CH_3 attached to quinazolin ring). Compound 6g (Found: C, 41.36; H, 2.50; N, 15.35; Calc. for $C_{22}H_{16}BrCl_2N_7O_3S_2$: C, 41.20; H, 2.51;N, 15.29 %).

MS: $[M]^+$ at m/z 641.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2,6-dibromo benzylidene)-4-oxothiazolidin-3-yl) acetamide (6h) :

Yield 41%, m.p.248 ºC, IR max/cm-^{1} 3345, 3045, 2920, 2820, 1740, 1725, 1710,1675,1620,1550,1460,1215,740,715,690; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.85-7.35 (m, 6H, Ar-H), 7.15 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.71 (s, 1H, -CH-Ar), 3.41 (d, CH_2 of thiazolidinone), 3.08 (hump, 1H, CONH exchangeable with D_2O),2.96 (s,2H,SCH_2CO), 2.15 (s, 3H, CH_3 attached to quinazolin ring). Compound 6h (Found: C, 36.04; H, 2.22; N, 13.38; Calc. for $C_{22}H_{16}N_7O_3S_2Br_3$: C, 36.18; H, 02.21;N, 13.43 %).

MS: $[M]^+$ at m/z 730.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2-methoxy benzylidene)-4-oxothiazolidin-3-yl) acetamide (6i) :

Yield 48%, m.p.192 ºC, IR max/cm-^{1} 3365, 3065, 2935, 2835, 1750, 1730, 1715,1685,1625,1565,1490,1240,750,720,695; ^{1}H-NMR ($CDCl_3$) δ in ppm:7.90-7.40 (m, 7H, Ar-H), 7.29 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.78 (s, 1H, -CH-Ar), 3.47 (d, CH_2 of thiazolidinone), 3.33 (hump, 1H, CONH exchangeable with D_2O),3.06 (s,2H,SCH_2CO), 2.40 (s, 3H, CH_3 attached to quinazolin ring).Compound 6i (Found: C, 45.67; H, 3.34; N, 16.33; Calc. for $C_{23}H_{20}N_7O_4S_2Br$: C, 45.85; H, 3.35;N, 16.27 %).

MS: $[M]^+$ at m/z 602.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(4-methoxy benzylidene)-4-oxothiazolidin-3-yl) acetamide (6j) :

Yield 45%, m.p.183 ºC, IR max/cm-^{1} 3375, 3070, 2945, 2840, 1765, 1750, 1730,1690,1640,1575,1500,1250,760,730,705; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.95-7.45 (m, 7H, Ar-H), 7.35 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.83 (s, 1H, -CH-Ar), 3.49 (d, CH_2 of thiazolidinone), 3.25 (hump, 1H, CONH exchangeable with D_2O), 3.10 (s,2H,SCH_2CO), 2.50 (s, 3H, CH_3 attached to quinazolin ring).Compound 6j (Found: C, 45.67; H, 3.34; N, 16.33; Calc. for $C_{23}H_{20}N_7O_4S_2Br$: C, 45.85; H, 3.35;N, 16.27 %).

MS: $[M]^+$ at m/z 602.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(2-methyl benzylidene)-4-oxothiazolidin-3-yl) acetamide (6k) :

Yield 40%, m.p.181 ºC, IR max/cm-^{1} 3380, 3075, 2950, 2850, 1770, 1760, 1740,1695,1650,1580,1510,1265,770,735,715; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.99-7.48 (m, 7H, Ar-H), 7.40 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.89 (s, 1H, -CH-Ar), 3.54 (d, CH_2 of thiazolidinone), 3.32 (hump, 1H, CONH exchangeable with D_2O), 3.14 (s,2H,SCH_2CO), 2.54 (s, 3H, CH_3 attached to quinazolin ring).Compound 6k (Found: C, 47.29; H, 3.45; N, 16.68; Calc. for $C_{23}H_{20}N_7O_3S_2Br$: C, 47.10; H, 3.44;N, 16.72 %).

MS: $[M]^+$ at m/z 586.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(4-methyl benzylidene)-4-oxothiazolidin-3-yl) acetamide (6l) :

Yield 42%, m.p.187 ºC, IR max/cm-^{1} 3375, 3070, 2945, 2840, 1765, 1755, 1735,1690,1640,1575,1500,1260,760,730,710; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 8.05-7.55 (m, 7H, Ar-H), 7.46 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.95 (s, 1H, -CH-Ar), 3.62 (d of thiazolidinone), 3.37 (hump, 1H, CONH exchangeable with D_2O), 3.22 (s,2H,SCH_2CO), 2.60 (s, 3H, CH_3 attached to quinazolin ring).Compound 6l (Found: C, 47.29; H, 3.45; N, 16.68; Calc. for $C_{23}H_{20}N_7O_3S_2Br$: C, 47.10; H, 3.44;N, 16.72 %).

MS: $[M]^+$ at m/z 586.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro-2-(2-chloro benzylidene)-4-oxoazetidin-1-yl) acetamide (7a) :

To a solution of the compound **(5a)** 2-(5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio)-N-(2-chloro benzylidene) acetohydrazide (0.01 mole), chloro acetyl chloride were added drop wise with constant stirring in presence of triethyl amine (0.02 mole) at 0-5ºC . The reaction mixture was further refluxed for 8hr. The completion of reaction was checked by TLC and excess of ethanol was distilled off. The resulting residual mass were cooled, poured into ice water, filtered, washed with water, dried and recrystallized from methanol.

Yield 40%, m.p.215 ºC, IR max/cm-^{1} 3360, 3065, 2925, 1745, 1725, 1715, 1685,1625,1565,1490,1225,745,715; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.95-7.32 (m,7H,Ar-H), 7.21 (ss, 1H, of triazole nucleus exchangeable with D_2O), 6.74 (d, 1H, -CH-Ar), 3.92 (d, 1H, -CHCl of Azetidinone ring), 3.08 (hump,1H,CONH exchangeable with D_2O), 2.62 (S, 2H, SCH_2CO), 2.12 (S,3H,CH_3 attached to quinazolinone ring).Compound 7a (Found: C, 43.19; H, 02.62; N, 16.18; Calc. for : $C_{22}H_{16}N_7O_3SBrCl_2$,C, 43.37; H, 02.65;N, 16.09 %).

MS: $[M]^+$ at m/z 609.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro-2-(4-chloro benzylidene)-4-oxoazetidin-1-yl) acet-amide (7b) :

Yield 35%, m.p.221ºC, IR max/cm-^{1} 3360, 3060, 2930, 1735, 1720, 1710,1680,1620,1570,1495,1225,747,718; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.88-7.42 (m, 7H, Ar-H), 7.17 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.78 (d, 1H, CH-Ar), 3.90 (d, 1H, CH-Cl of Azetidinone ring), 3.08 (hump, 1H, CONH exchangeable with D_2O), 2.60 (s, 2H, SCH_2CO), 2.18 (s, 3H, CH_3 attached to quinazolin ring).Compound 7b (Found: C, 43.18; H, 2.64; N, 16.17; Calc. for $C_{22}H_{16}N_7O_3SBrCl_2$: C, 43.37; H, 2.65;N, 16.09 %).

MS: $[M]^+$ at m/z 609.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2-bromo benzylidene)-4-oxoazetidin-1-yl) acet-amide (7c) :

Yield 30%, m.p.213ºC, IR max/cm-^{1} 3355, 3058, 2920, 1743, 1730, 1720,1680,1635,1560,1490,1230,743,710; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.90-7.45 (m, 7H, Ar-H), 7.19 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.70 (d, 1H, CH-Ar), 3.84 (d, 1H, CH-Cl of Azetidinone ring), 3.10 (hump, 1H, CONH exchangeable with D_2O), 2.53 (s, 2H, SCH_2CO), 2.07 (s, 3H, CH_3 attached to quinazolin ring).Compound 7c (Found: C, 40.51; H, 2.48; N, 15.08; Calc. for $C_{22}H_{16}N_7O_3SBr_2Cl$: C, 40.42; H, 2.47;N, 15.00 %).

MS: $[M]^+$ at m/z 654.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(4-bromo benzylidene)-4-oxoazetidin-1-yl) acet-amide (7d) :

Yield 32%, m.p.221ºC, IR max/cm-^{1} 3348, 3050, 2925, 1738, 1730, 1715,1673,1635,1560,1485,1215,748,718; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.85-7.40 (m, 7H, Ar-H), 7.20 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.74 (d, 1H, CH-Ar), 3.88 (d, 1H, CH-Cl of Azetidinone ring), 3.05 (hump, 1H, CONH exchangeable with D_2O), 2.58 (s, 2H, SCH_2CO), 2.14 (s, 3H, CH_3 attached to quinazolin ring).Compound 7d (Found: C, 40.48; H, 2.48; N, 15.09; Calc. for $C_{22}H_{16}N_7O_3SBr_2Cl$: C, 40.42; H, 2.47;N, 15.00 %).

MS: $[M]^+$ at m/z 654.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2,4-dichloro benzylidene)-4-oxoazetidin-1-yl) acet-amide (7e)

Yield 28s%, m.p.237ºC, IR max/cm-^{1} 3365, 3068, 2930, 1740, 17330, 1720,1685,1625,1575,1495,1230,740,720; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.90-7.42 (m, 6H, Ar-H), 7.11 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.62 (d, 1H, CH-Ar), 4.05 (d, 1H, CH-Cl of Azetidinone ring), 2.90 (hump, 1H, CONH exchangeable with D_2O), 2.40 (s, 2H, SCH_2CO), 2.00 (s, 3H, CH_3 attached to quinazolin ring).Compound 7e (Found: C, 41.18; H, 2.31; N, 15.21; Calc. for $C_{22}H_{15}N_7O_3SBrCl_3$: C, 41.05; H, 2.35;N, 15.23 %).

MS: $[M]^+$ at m/z 644.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2,4-dibromo benzylidene)-4-oxoazetidin-1-yl) acet-amide (7f)

Yield 30%, m.p.253ºC, IR max/cm-^{1} 3345, 3055, 2924, 1745, 1725, 1710,1670,1625,1565,1480,1230,745,716; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.80-7.38 (m, 6H, Ar-H), 7.15 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.43 (d, 1H, CH-Ar), 4.00 (d, 1H, CH-Cl of Azetidinone ring), 2.94 (hump, 1H, CONH exchangeable with D_2O), 2.48 (s, 2H, SCH_2CO), 2.04 (s, 3H, CH_3 attached to quinazolin ring).Compound 7f (Found: C, 36.22; H, 2.05; N, 13.30; Calc. for $C_{22}H_{15}N_7O_3SClBr_3$: C, 36.07; H, 2.06;N, 13.38 %).

MS: $[M]^+$ at m/z 733.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2,6-dichloro benzylidene)-4-oxoazetidin-1-yl) acet-amide (7g)

Yield 33%, m.p.234ºC, IR max/cm-^{1} 3372, 3070, 2920, 1745, 1730, 1720,1680,1625,1570,1485,1225,735,712; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.85-7.42 (m, 6H, Ar-H), 7.00 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.50 (d, 1H, CH-Ar), 3.94 (d, 1H, CH-Cl of Azetidinone ring), 3.00 (hump, 1H, CONH exchangeable with D_2O), 2.35 (s, 2H, SCH_2CO), 2.05 (s, 3H, CH_3 attached to quinazolin ring).Compound 7g (Found: C, 41.16; H, 2.33; N, 15.28; Calc. for $C_{22}H_{15}N_7O_3SBrCl_3$: C, 41.05; H, 2.35;N, 15.23 %).

MS: $[M]^+$ at m/z 641.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2,6-dibromo benzylidene)-4-oxoazetidin-1-yl) acet-amide (7h)

Yield 29%, m.p.243ºC, IR max/cm-^{1} 3350, 3060, 2920, 1748, 1725, 1715,1675,1610,1560,1470,1220,750,720; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.77-7.35 (m, 6H, Ar-H), 7.06 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.58 (d, 1H, CH-Ar), 3.98 (d, 1H, CH-Cl of Azetidinone ring), 3.11 (hump, 1H, CONH exchangeable with D_2O), 2.42 (s, 2H, SCH_2CO), 1.98 (s, 3H, CH_3 attached to quinazolin ring).Compound 7h (Found: C, 36.25; H, 2.05; N, 13.29; Calc. for $C_{22}H_{15}N_7O_3SClBr_3$: C, 36.07; H, 2.06;N, 13.38 %).

MS: $[M]^+$ at m/z 733.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2-methoxy benzylidene)-4-oxoazetidin-1-yl) acet-amide (7i)

Yield 26%, m.p.204ºC, IR max/cm-^{1} 3340, 3045, 2960, 1740, 1725, 1715,1680,1605,1570,1460,1225,715,695; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.85-7.42 (m, 7H, Ar-H), 7.20 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.62 (d, 1H, CH-Ar), 3.72 (d, 1H, CH-Cl of Azetidinone ring), 3.40 (hump, 1H, CONH exchangeable with D_2O), 2.50 (s, 2H, SCH_2CO), 2.10 (s, 3H, CH_3 attached to quinazolin ring).Compound 7i (Found: C, 45.80; H, 3.15; N, 16.13; Calc. for $C_{23}H_{19}N_7O_4SClBr$: C, 45.67; H, 3.17;N, 16.21 %).

MS: $[M]^+$ at m/z 605.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(4-methoxy benzylidene)-4-oxoazetidin-1-yl) acet-amide (7j)

Yield 23%, m.p.184ºC, IR max/cm-^{1} 3330, 3040, 2950, 1745, 1725, 1710,1670,1600,1570,1460,1230,720,690; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.90-7.48 (m, 7H, Ar-H), 7.25 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.69 (d, 1H, CH-Ar), 3.76 (d, 1H, CH-Cl of Azetidinone ring), 3.35 (hump, 1H, CONH exchangeable with D_2O), 2.60 (s, 2H, SCH_2CO), 2.22 (s, 3H, CH_3 attached to quinazolin ring).Compound 7j (Found: C, 45.51; H, 3.16; N, 16.13; Calc. for $C_{23}H_{19}N_7O_4SClBr$: C, 45.67; H, 3.17;N, 16.21 %).

MS: $[M]^+$ at m/z 605.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(2-methyl benzylidene)-4-oxoazetidin-1-yl) acet-amide (7k)

Yield 25%, m.p.186ºC, IR max/cm-^{1} 3350, 3040, 2920, 1740, 1730, 1710,1680,1615,1560,1480,1225,740,705; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.95-7.50 (m, 7H, Ar-H), 7.34 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.81 (d, 1H, CH-Ar), 3.70 (d, 1H, CH-Cl of Azetidinone ring), 3.38 (hump, 1H, CONH exchangeable with D_2O), 2.72 (s, 2H, SCH_2CO), 2.35 (s, 3H, CH_3 attached to quinazolin ring).

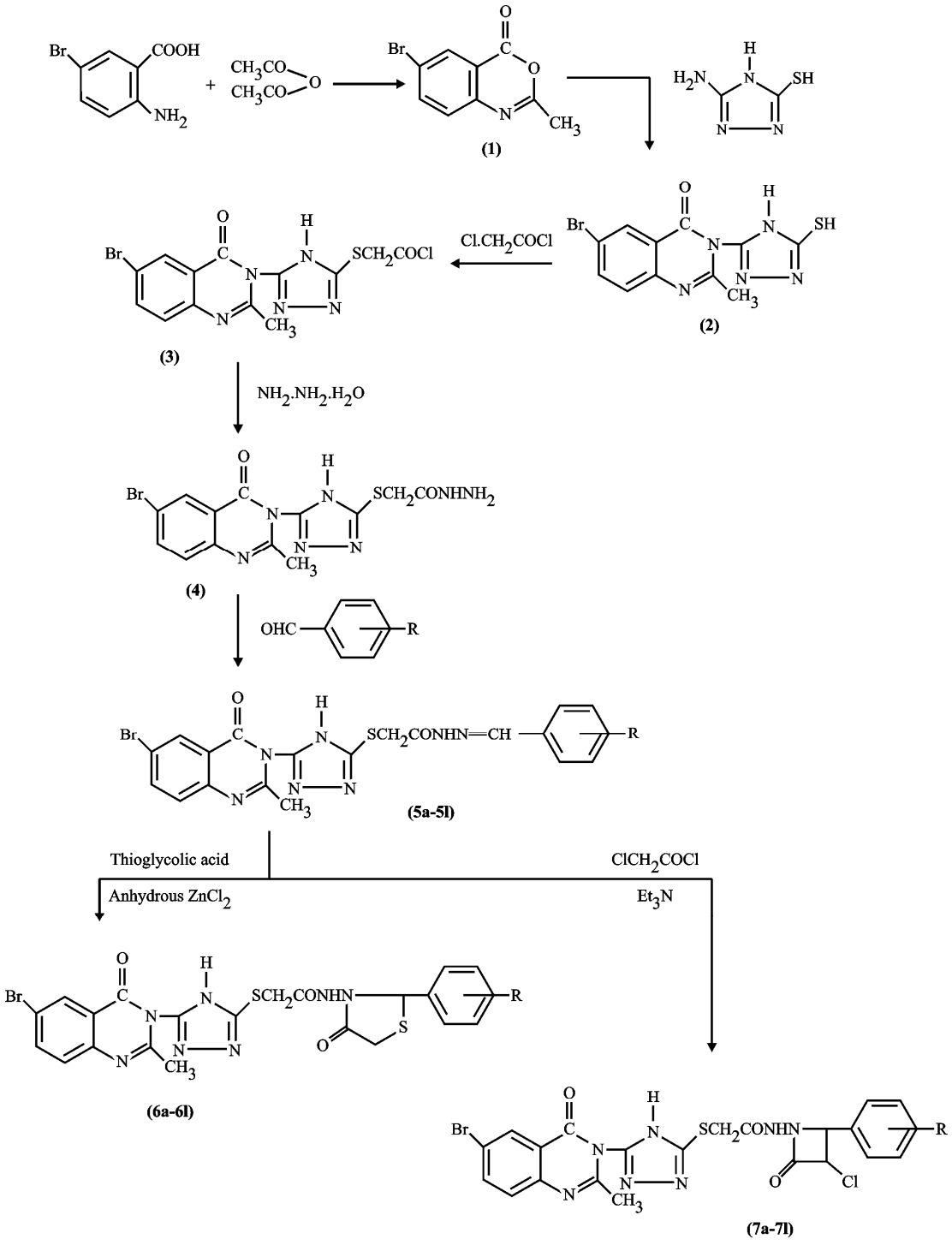
Compound 7k (Found: C, 46.80; H, 3.26; N, 16.69; Calc. for $C_{23}H_{19}N_7O_3SBrCl$: C, 46.91; H, 3.25;N, 16.65 %).

MS: $[M]^+$ at m/z 589.

2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro(4-methyl benzylidene)-4-oxoazetidin-1-yl) acet-amide (7l)

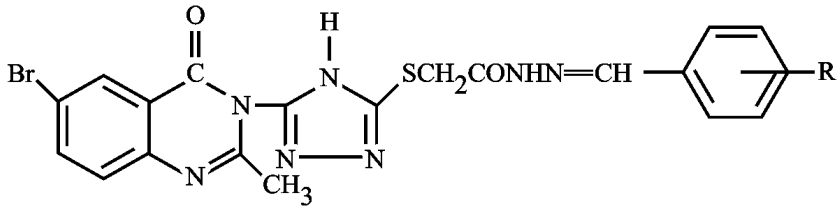
Yield 30%, m.p.191ºC, IR max/cm-^{1} 3340, 3040, 2928, 1745, 1735, 1715,1670,1625,1565,1470,745,710; ^{1}H-NMR ($CDCl_3$) δ in ppm.: 7.98-7.52 (m, 7H, Ar-H), 7.37 (ss, 1H of triazole nucleus, exchangeable with D_2O), 6.94 (d, 1H, CH-Ar), 3.73 (d, 1H, CH-Cl of Azetidinone ring), 3.45 (hump, 1H, CONH exchangeable with D_2O), 2.86 (s, 2H, SCH_2CO), 2.48 (s, 3H, CH_3 attached to quinazolin ring).Compound 7l (Found: C, 46.75; H, 3.27; N, 16.68; Calc. for $C_{23}H_{19}N_7O_3SBrCl$: C, 46.91; H, 3.25;N, 16.65 %).

MS: $[M]^+$ at m/z 589.


Br
COOH
NH2
CH3CO
CH3CO
O
(1)
H2N
SH
Cl.CH2COCl
SCH2COCl
(2)
(3)
NH2.NH2.H2O
SCH2CONHNH2
(4)
OHC
R
SCH2CONHN=CH
(5a-5l)
Thioglycolic acid
Anhydrous ZnCl2
ClCH2COCl
Et3N
SCH2CONHN
(6a-6l)
(7a-7l)
Cl
CH3

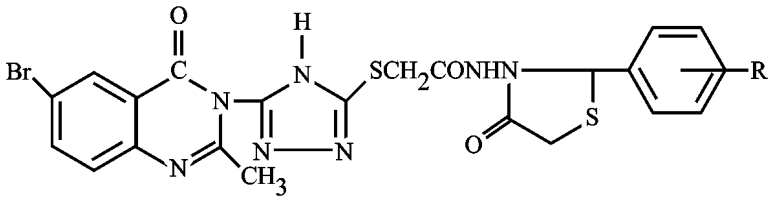
Scheme - I

Table-I: Physical and analytical data of (E)-2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazole-3-ylthio)-N-(substituted benzylidene) acetohydrazides (5b-5l)



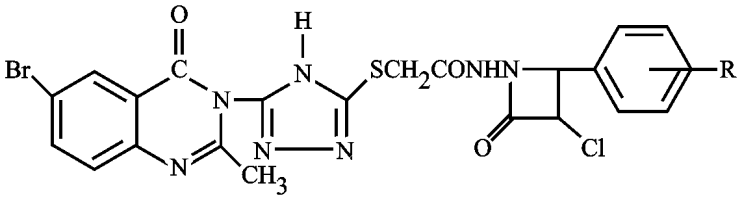
Comp.	R	M.P. (ºC)	Yield (%)	Recrysta-llization solvent	Molecular formula	Elemental analysis (%)					
						C %		H %		N %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
5b	4-Cl	201	67	Ethanol	$C_{20}H_{15}SN_7O_2ClBr$	45.09	45.27	2.84	2.85	18.40	18.47
5c	2-Br	222	65	Acetone	$C_{20}H_{15}SN_7O_2ClBr_2$	41.62	41.78	2.62	2.63	16.98	17.05
5d	4-Br	242	63	Benzene	$C_{20}H_{15}SN_7O_2ClBr_2$	41.62	41.78	2.62	2.63	16.98	17.05
5e	2,4-Cl_2	220	60	Methanol	$C_{20}H_{14}SN_7O_2Cl_2Br$	42.35	42.18	2.49	2.48	17.28	17.21
5f	2,4-Br_2	248	55	DMF Water	$C_{20}H_{14}SN_7O_2Br_3$	36.61	36.46	2.15	2.14	14.94	14.88
5g	2,6-Cl_2	228	65	Ethanol	$C_{20}H_{14}SN_7O_2Cl_2Br$	42.35	42.18	2.49	2.48	17.28	17.21
5h	2,6-Br_2	252	55	Benzene	$C_{20}H_{14}SN_7O_2Br_3$	36.61	36.46	2.15	2.14	14.94	14.88
5i	2-OCH_3	197	61	Acetone	$C_{21}H_{18}SN_7O_3Br$	47.74	47.93	3.43	3.44	18.56	18.63
5j	4-OCH_3	188	63	Methanol	$C_{21}H_{18}SN_7O_3Br$	47.74	47.55	3.43	3.42	18.56	18.49
5k	2-CH_3	176	58	Ethanol	$C_{21}H_{18}SN_7O_2Br$	49.23	49.43	3.54	3.55	19.14	19.22
5l	4-CH_3	182	56	Ethanol	$C_{21}H_{18}SN_7O_2Br$	49.23	49.03	3.54	3.53	19.14	19.02

Table-II: 2-[5-(6-Bromo-2-methyl-4-oxoquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(substituted benzyli-dene)-4-oxothiazolidin-3-yl) acetamides (6b-6l)



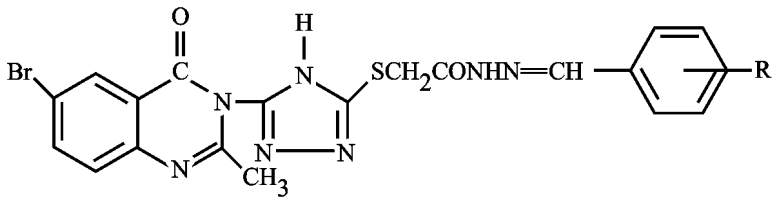
Comp.	R	M.P. (ºC)	Yield (%)	Recrysta-llization solvent	Molecular formula	Elemental analysis (%)					
						C %		H %		N %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
6b	4-Cl	211	50	Acetone	$C_{22}H_{17}N_7O_3S_2BrCl$	43.54	43.71	2.82	2.83	16.16	16.22
6c	2-Br	217	48	Benzene	$C_{22}H_{17}N_7O_3S_2Br_2$	40.57	40.41	2.63	2.62	15.05	15.11
6d	4-Br	228	45	DMF Water	$C_{22}H_{17}N_7O_3S_2Br_2$	40.57	40.41	2.63	2.62	15.05	15.11
6e	2,4-Cl_2	230	49	Ethanol	$C_{22}H_{16}BrCl_2N_7O_3S_2$	41.20	41.36	2.51	2.50	15.29	15.35
6f	2,4-Br_2	258	43	Benzene	$C_{22}H_{16}N_7O_3S_2Br_3$	36.18	36.04	2.21	2.22	13.43	13.38
6g	2,6-Cl_2	238	46	Ethanol	$C_{22}H_{16}BrCl_2N_7O_3S_2$	41.20	41.36	2.51	2.50	15.29	15.35
6h	2,6-Br_2	248	41	Acetone	$C_{22}H_{16}N_7O_3S_2Br_3$	36.18	36.04	2.21	2.22	13.43	13.38
6i	2-OCH_3	192	48	Benzene	$C_{23}H_{20}N_7O_4S_2Br$	45.85	45.67	3.35	3.34	16.27	16.33
6j	4-OCH_3	183	45	Ethanol	$C_{23}H_{20}N_7O_4S_2Br$	45.85	45.67	3.35	3.34	16.27	16.33
6k	2-CH_3	181	40	DMF Water	$C_{23}H_{20}N_7O_3S_2Br$	47.10	47.29	3.44	3.45	16.72	16.68
6l	4-CH_3	187	42	Acetone	$C_{23}H_{20}N_7O_3S_2Br$	47.10	47.29	3.44	3.45	16.72	16.68

Table-III: 2-[5-(6-Bromo-2-methyl-4-oxcquinazolin-3(4H)-yl)-4H-1,2,4-triazol-3-ylthio]-N-(3-chloro-2-(substituted phenyl)-4-oxoazetidin-1-yl) acetamides (7b-7l)



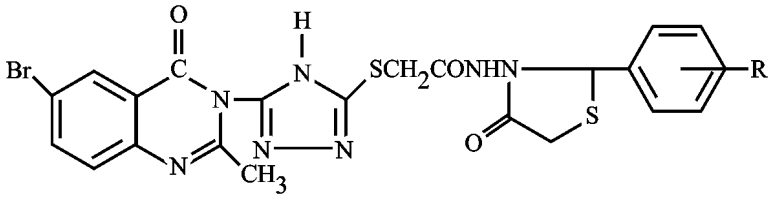
Comp.	R	M.P. (ºC)	Yield (%)	Recrysta-llization solvent	Molecular formula	Elemental analysis (%)					
						C %		H %		N %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
7b	4-Cl	221	35	Benzene	$C_{22}H_{16}N_7O_3SBrCl_2$	43.37	43.18	2.65	2.64	16.09	16.17
7c	2-Br	213	30	Acetone	$C_{22}H_{16}N_7O_3SBr_2Cl$	40.42	40.51	2.47	2.48	15.00	15.08
7d	4-Br	221	32	Methanol	$C_{22}H_{16}N_7O_3SBr_2Cl$	40.42	40.48	2.47	2.48	15.00	15.09
7e	2,4-Cl_2	237	28	Ethanol	$C_{22}H_{15}N_7O_3SBrCl_3$	41.05	41.18	2.35	2.31	15.23	15.21
7f	2,4-Br_2	253	30	Methanol	$C_{22}H_{15}N_7O_3SClBr_3$	36.07	36.22	2.06	2.05	13.38	13.30
7g	2,6-Cl_2	234	33	Acetone	$C_{22}H_{15}N_7O_3SBrCl_3$	41.05	41.16	2.35	2.33	15.23	15.28
7h	2,6-Br_2	243	29	Benzene	$C_{22}H_{15}N_7O_3SClBr_3$	36.07	36.25	2.06	2.05	13.38	13.29
7i	2-OCH_3	204	26	Methanol	$C_{23}H_{19}N_7O_4SClBr$	45.67	45.80	3.17	3.15	16.21	16.13
7j	4-OCH_3	184	23	Methanol	$C_{23}H_{19}N_7O_4SClBr$	45.67	45.51	3.17	3.16	16.21	16.13
7k	2-CH_3	186	25	DMF Water	$C_{23}H_{19}N_7O_3SBrCl$	46.91	46.80	3.25	3.26	16.65	16.69
7l	4-CH_3	191	30	Benzene	$C_{23}H_{19}N_7O_3SBrCl$	46.91	46.75	3.25	3.27	16.65	16.68

Table-IV: Anti-inflammatory, analgesic and toxicity data of compounds (5a-5j)



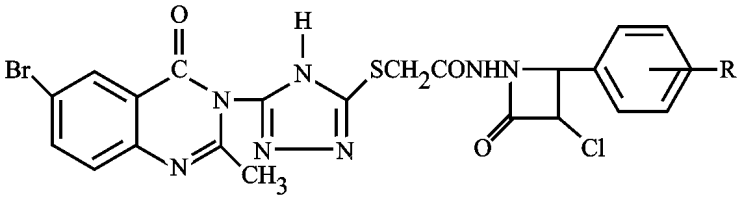
Comp.	R	Anti-Inflammatory Activity		Analgesic Activity		UD_{50} (mg./kg. i.p.)	Acute Toxicity ALD_{50} (mg./kg. p.o)
		Dose (mg./kg. p.o.)	% Inhibition of oedema	Dose (mg./kg. p.o.)	% Protection		
5a	2-Cl	50	10.12*	50	08.35*	-	> 1000
5b	4-Cl	50	16.15*	50	14.27*	-	> 1000
5c	2-Br	50	17.38*	50	15.26*	-	> 1000
5d	4-Br	50	18.76*	50	16.52*	-	> 1000
5e	2,4-Cl_2	50	14.82*	50	12.38*	-	> 1000
5f	2,4-Br_2	50	13.52*	50	11.40*	-	> 1000
5g	2,6-Cl_2	50	15.18*	50	13.45*	-	> 1000
5h	2,6-Br_2	50	12.92*	50	10.19*	-	> 1000
5i	2-OCH_3	50	16.65*	50	14.60*	-	> 1000
5j	4-OCH_3	50	14.38*	50	12.52*	-	> 1000
5k	2-CH_3	50	17.72*	50	15.14*	-	> 1000
5l	4-CH_3	50	13.23*	50	11.38*	-	> 1000

Table-V: Anti-inflammatory, analgesic and toxicity data of compounds (6a-6j)



Comp	R	Anti-Inflammatory Activity		Analgesic Activity		UD_{50} (mg./kg. i.p.)	Acute Toxicity ALD_{50} (mg./kg. p.o)
		Dose (mg./kg. p.o.)	% Inhibition of oedema	Dose (mg./kg. p.o.)	% Protection		
6a	2-Cl	50	21.18**	50	18.64*	-	> 1000
6b	4-Cl	50	26.47**	50	24.60**	-	> 1000
6c	2-Br	50	27.58**	50	24.38**	-	> 1000
6d	4-Br	50	28.24**	50	26.92**	-	> 1000
6e	2,4-Cl_2	50	30.19**	50	29.53**	-	> 1000
6f	2,4-Br_2	50	22.49**	50	20.63**	-	> 1000
6g	2,6-Cl_2	25 50 100	19.30** 40.69*** 71.62***	25 50 100	16.93** 38.54*** 62.39***	165.50	> 14000
6h	2,6-Br_2	50	26.83**	50	24.48**	-	> 1000
6i	2-OCH_3	50	23.39**	50	22.11**	-	> 1000
6j	4-OCH_3	50	25.63**	50	22.40**	-	> 1000
6k	2-CH_3	50	27.16**	50	25.61**	-	> 1000
6l	4-CH_3	50	22.36**	50	20.81*	-	> 1000

Table-VI: Anti-inflammatory, analgesic and toxicity data of compounds (7a-7j)



Comp.	R	Anti-Inflammatory Activity		Analgesic Activity		UD_{50} (mg./kg. i.p.)	Acute Toxicity ALD_{50} (mg./kg. p.o)
		Dose (mg./kg. p.o.)	% Inhibition of oedema	Dose (mg./kg. p.o.)	% Protection		
7a	2-Cl	50	30.68**	50	27.30**	-	> 1000
7b	4-Cl	50	34.27***	50	32.62***	-	> 1000
7c	2-Br	50	36.56***	50	34.54***	-	> 1000
7d	4-Br	50	37.52***	50	35.48***	-	> 1000
7e	2,4-Cl_2	50	35.63***	50	32.62***	-	> 1000
7f	2,4-Br_2	50	32.45**	50	30.59**	-	> 1000
7g	2,6-Cl_2	25 50 100	20.82** 45.76*** 75.30***	25 50 100	18.25** 42.37*** 65.48***	195.50	> 14000
7h	2,6-Br_2	50	33.37***	50	30.54***	-	> 1000
7i	2-OCH_3	50	31.28**	50	29.40**	-	> 1000
7j	4-OCH_3	50	34.22***	50	32.16***	-	> 1000
7k	2-CH_3	50	32.35**	50	29.27**	-	> 1000
7l	4-CH_3	50	35.53***	50	33.61***	-	> 1000
Phenyl butazone		25 50 100	17.50** 38.80*** 68.60***	25 50 100	15.80** 36.50*** 60.50***	66.60	

**P < 0.05; **P < 0.01; ***P <0.001*

Propylene glycol standard for control group

REFERENCES

[1] Alagarsamy V.; Mahukumar V.; Pavalarani N.; Vasanthanathan P.; Rivathi R., Synthesis, analgesic, anti-inflammatory and antibacterial activities of some novel 2,3-disubstituted quinazolin-4(3H)-ones, *Biol. Pharm. Bull*., **2003**, 26(4): 557-559.

[2] Alagarsamy V.; Rajesh R.; Rameseshu M.; Vijay K.S.; Ramseshu K.V. and Duraiananda K.T., Synthesis, analgesic, anti-inflammatory and antibacterial activities of some novel 2-methylthio-3-substituted quinazolin-4-(3H)-ones, *Biol. Pharm. Bull*.; **2004**, 27(5): 652-656.

[3] Amin, K.M.; Kamel M.M.; Anwar M.M.; Khedr M.; Syam Y.M.: Synthesis, biological evaluation and molecular doking of novel series of spiro {(2H, 3H) quinazoline 2,1-cyclohexan] -4 (1H)-one derivatives, *Eur J.med. chem* .**2010**, 45(6) : 2117-2131.

[4] James F Wolf.; Terry L Ratham.; Merk E Sleevi.; James A Campbell.; Thomas & Greenwood, J Med Chem., 33(1) 1990, 16.

[5] Srivastava, M.; Salahuddin, M.D.; Santra Kumar, S.M.; Synthesis and anti-inflammatory activity of some novel 3-(6-substituted-1, 3, benzothiol-2-yl)- 2 [{(4- substituted phenyl) amino} methyl] quinazolins-4 (3H)- ones: *Eur. J. Med. chem.*, **2009**, 6:1055-1062

[6] Alagarsamy V.; Soloman V.R.; Dhanabal K., Synthesis and pharmacological evaluation of some 3-phenyl-2-substituted-3H-quinazolin-4-one as analgesic, anti-inflammatory agents, *Bio-Org. Med. Chem*.; **2007**, 15(1): 235-241.

[7] Bekhit, A.A.; Habib, N.S.; Park, Ji Young: Synthesis of some thiazolyl and thiadiazolyl derivatives of 4-(3H)-quinazolinone as anti-inflammatory, anti-microbial agents: *Bolletino Chemico Farmaceutico,* **2004,** 143(1): 34-39.

[8] Kumar, Ashok; Rajput, C. S.: Synthesis and anti-inflammatory activity of some newer quinazolins 4-ones derivatives: Eur. J. Med. Chem**. 2009,** 44(1): 83-90.

[9] Kumar, Ashok; Sharma, Shalabh; Kiran, Bajaj; Shipra, Sharma; Hemant, Panwar; Tripti, Singh and Srivastava V.K.: Some new 2,3,6-tri substituted quinazolinones as potent anti-inflammatory, analgesic and COX II inhibitors : *Bioorganic and Medicinal Chemistry,* **2003**, 11: 5293-5299.

[10] Alagarsamy V.; Soloman V.R.; Dhanabal K., Synthesis and pharmacological evaluation of some 3-phenyl-2-substituted-3H-quinazolin-4-one as analgesic, anti-inflammatory agents, *Bio-Org. Med. Chem*.; **2007**, 15(1): 235-241.
[11] Singh, Inder Pal; Saxena, A.K.; Sinha, J.N.; Bhargava, K.P.; Shanker, K.: Synthesis and anti-inflammatory activity of 2-substitutedphenethyl-3-substitutedphenyl-4(3H)-quinazolinones: *Indian J. Chem*., **1984**, 23B (6): 592-594.
[12] Khilil M.A.; Soliman R.; Fargaly A M & Bekhit A A, Arch pharm (Weinheim,Ger.),327(1),**1994**,27.
[13] Vagdevi H.M.; Vaidya V.P.; Latha K.P.; Padmashali B., Synthesis and pharmacological examination of some thiazolidinone derivatives of naphtho-[2,1-b] furan. *Indian J. Pharma. Sci*.; **2006**, 68 (6): 719-725.
[14] Ottana R.; Maccari R.; Barreca M.L.; Bruno G.; Rotondo A.; Rossi A.; Chiricosta G.; Paola R.D.; Sautebin L.; Cuzzocrea S.; Vigorita M.G., 5-arylidene-2-imino-4-thiazolidinones: Design ad synthesis of novel anti-inflammatory agents. *Bio-org. Med. Chem*.; **2005**, 13 (13): 4243-4253.
[15] Yadav R; Srivastava S.D and Srivastava S.K.: Synthesis, anti-microbial and anti-inflammatory activities of 4-oxothiazolidines and their-5-arylidenes: *Indian J. Chem.* **2005**, 44B: 1262-1266.
[16] Tandon, Manju; Kumar, Piyush; Tandon, P.; Bhalla, T.N.; Bhargava, K.P.; Bharthwal, J.P.: Some new azetidinones as possible anti-inflammatory, analgesic and anti-proteolytic agents: *Acta, pharm. Jygosl,* **1983,** 33(2): 93-102.
[17] Doherty, James B.; Finke, Paul E.; Dorn, Conrad P.; Maccoss, Malcolm; Durette, Philippe L.; Mills, Sander G.; Shah, Shrenik K.; Lanza, Thomas J.; Sahoo, Soumya P.: Substituted azetidinones as anti-inflammatory and anti-degenerative agents : *Chem. Abstr.,* **1994**, 121(25): 300749y.
[18] El-shehry; M.F.; Abu-Hushem. A.A.; El-Telbani E.M.: 3-((2,4- dichlorophenoxy methyl)-1,2,4-triazolo (Thiadiazoles and Thiadiazines) as anti-inflammatory and molluscicidal agents. *Euro J. Med. chem.* **2010**, 45, 5, 1906-1911.
[19] Karegoudar P.; Prasad D.J.; Ashok M.; Mahalinga M.; Poojary B.; Holla B.S., Synthesis, antimicrobial and anti-inflammatory activities of some 1,2,4-triazole [3,4-b] [1,3,4] thiadiazoles and 1,2,4-triazolo [3,4-b] [1,3,4] thiadiazines bearing trichlorophenyl moiety. *Eur.J. Med. Chem*.;**2008**. 43: 808-815.
[20] Goksen U.S.; Kelekei N.G.; Goktas O.; Koysal yavuz,; Kilic E,; Isik S.; Aktay G and Ozalp M : 1-acylthiosemicarbezides, 1,2,4-triazole-5(4H)-thiones, 1,3,4-thiadiazoles and hydrazones containing 5-methyl-2-benzoxazolin- ones : Synthesis, analgesic, anti-inflammatory and anti-microbial activities: *Bio-org and Med, chem,*. : **2007**, 15 (17) : 5738-5751.
[21] Bogert M.T.; and Soil H.A.; *J. Am. Chem. Soc.* **1907**, 29:517.
[22] Winter C. A ; Risley E. A.; and Nuss G. W. : Carrageenan induced oedema in hind paw of the rat an as assay for anti-inflammatory drugs. *Proc. Soc. Exp. Biol. N. Y.* **1962**, 111, 544-550.
[23] Smith Q. E.: Pharmacological Screening Tests Progressive, Medicinal Chemistry, **1960,** Vol. I. Butterworth's, London.1-32.