Research Article **CODEN: AJPAD7** **ISSN: 2321-0923**

Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry

Journal home page: www.ajpamc.com

SYNTHESIS AND PHARMACOLOGICAL INVESTIGATION OF SOME NOVEL 3-(4-FLUOROPHENYL)-2-SUBSTITUTED- QUINAZOLIN-4(3*H*)-ONE

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ABSTRACT

Pharmacologically quinazolines possess diverse activities like anticonvulsant, analgesic, antiparkinson's, sedative, hypnotic, muscle relaxant, enzyme inhibiting, antiviral, antibacterial, antifungal, antimicrobial, antitumour, anti-inflammatory, cardiovascular, antihelminthic, (infestations of parasitic worms such as tape worm or hook worm), antimalarial, antitubercular, antihistaminic, antiulcer and hypoglycaemic activities. A series of novel 3-(4-fluorophenyl) -2-substituted quinazolin-4(3*H*)-ones were synthesized by the reaction of 3-(4-fluorophenyl)-2hydrazinyl quinazolin-4(3*H*)-one with various dithiocarbamates. The compounds were tested for their antimicrobial activity using Ciprofloxacin as reference standard. The results of the microbial activity indicate that the test compounds inhibit the microbial growth of bacteria. Compound 4-(4-fluorophenyl)-1-(3-(4-fluorophenyl)-4oxo-3,4-dihydroquinazolin-2-yl)thiosemicarbazideemerged as the most potent compound of the series when compared to the reference standard Ciprofloxacin.

KEYWORDS

Quinazolin, 4-fluoro aniline, Ciprofloxacin, Antimicrobial activity and Anti-tuberculosis activity.

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INTRODUCTION

The chemistry of quinazoline compounds[1] has more than centuries old history however the intense search for biologically active substances[2] in this series began only in the last few decades. Evolution of quinazolines began only with discovery of febrifugine, a quinazolinone alkaloid[3], and possessing anti-malarial potential from the Chinese plant aseru (*Dichroafebrifuga Lour*), which served as an impetus for initiation of the research on quinazolin[4]. Quinazolinones are the oxidized form

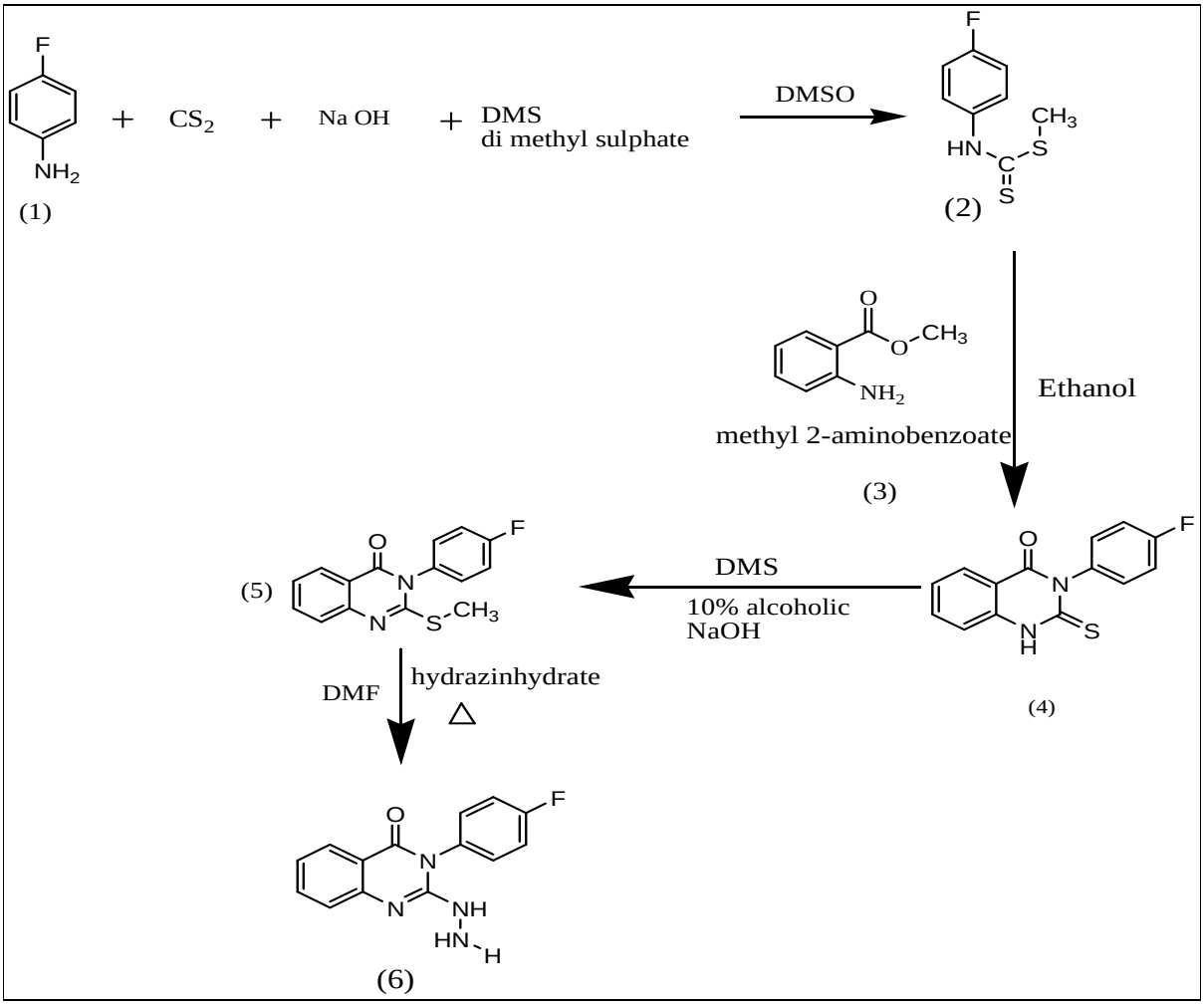
of quinazolines, and as such are also part of the quinoline alkaloids[5]. Both naturally occurring and synthetic quinazolines and quinazolinones have attracted wide spread attention due to the diverse range of pharmacological activities[6]. These structures are defined by the location of the oxygen and the hydrogen on the nitrogen (-NH), and the commonly accepted numbering for quinazolines and quinazolinones is described using the quinazoline structure[7]. Hence in the present study a series of 3-(4-fluorophenyl)-2-substituted- quinazolin-4(3*H*)-ones, The title compounds were synthesized by the reaction of 3-(4-fluorophenyl)-2hydrazinyl quinazolin-4(3*H*)-one with various dithiocarbamates[8]. The starting material, 3-(4-fluorophenyl)-2hydrazinyl quinazolin-4(3*H*)-one from 4-fluoro aniline by a multistep synthesis[9].All the title compounds were tested for their antimicrobial activity using Ciprofloxacin by Zone of inhibition.

EXPERIMENTAL

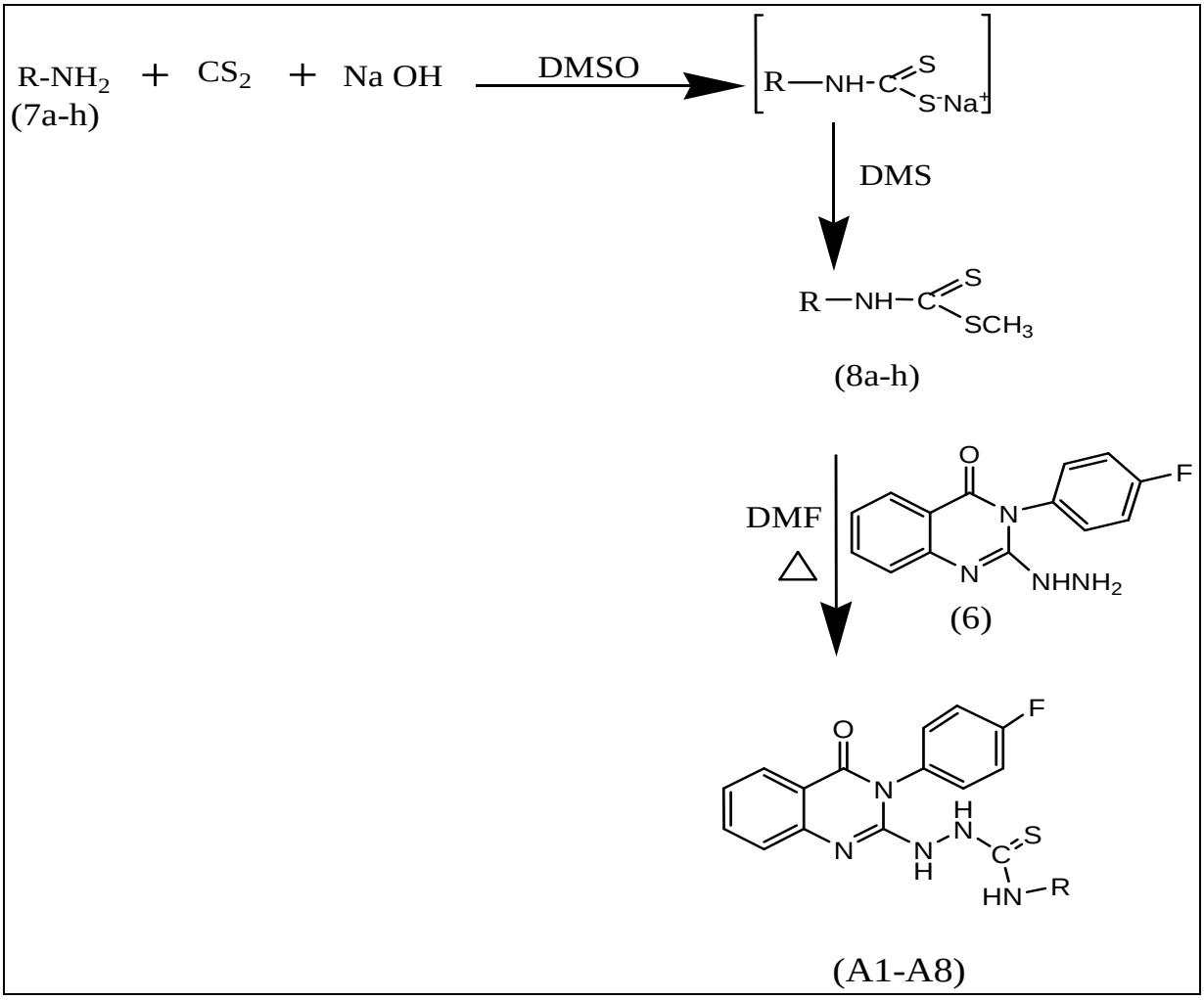
Scheme

The title compounds were synthesized by the following synthetic route depicted in the following.

Step 1: Synthesis of 2-hydrazino-3-(4-flurophenyl)-3*H*-quinazolin-4-one



Step 2: Synthesis of 3-(4-fluorophenyl)-2-substituted-quinazolin-4(3*H*)-ones.



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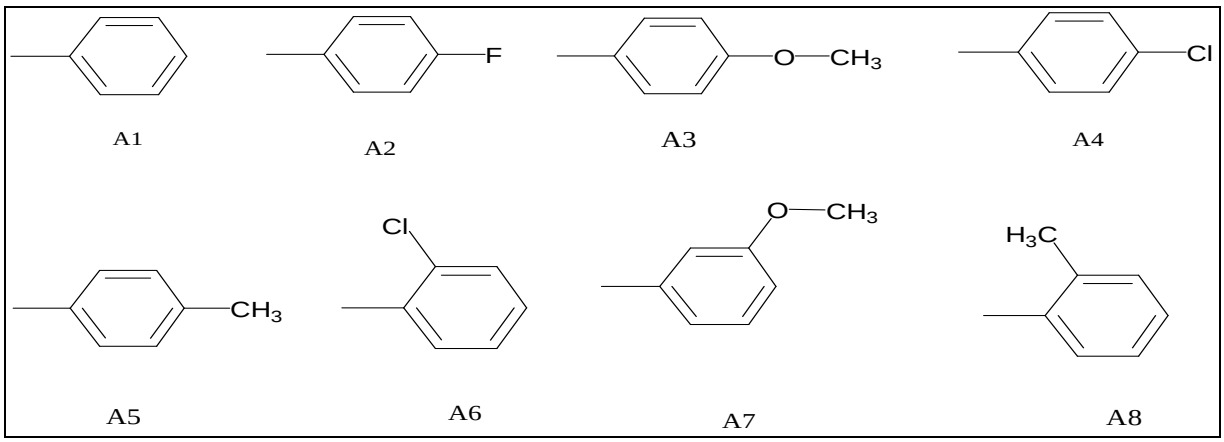


EXPERIMENTAL PROCEDURE

Synthesis of 3-(4-flurophenyl)-2-thioxo-2, 3-dihydro-1*H*-quinazolin-4-one (4)

A solution of 4-fluro aniline (**1)** (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol. Methyl anthranilate (0.01mol) and the above prepared N-(4-flurophenyl)-methyl dithiocarbamic acid (0.01mol), were dissolved in ethanol (20ml). To this anhydrous potassium carbonate (100 mg) was added and refluxed for 23 h. The reaction mixture was cooled in ice and the solid separated was filtered and purified by dissolving in 10% alcoholic sodium hydroxide solution and re-precipitated by treating with dilute hydrochloric acid. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol.

Molecular formula: $C_{14}H_9FN_2OS$, Molecular weight:272.297, Yield: 83%, Mp: 253-255°C.

IR (KBr) cm^{-1}:3242 (NH), 1666 (C=O), 1218 (C=S) cm^{-1},^{1}H NMR ($CDCl_3$) δ ppm: 7.13-8.51 (m, 8H,ArH), 10.12 (br s, 1H, NH), Mass (m/z):272 (M^+).

Synthesis of 3-(4-flurophenyl)-2-methylsulfanyl-3*H*-quinazolin-4-one (5)

The 3-(4-flurophenyl)-2-thioxo-2,3-dihydro-1*H*-quinazolin-4-one.(4)(0.01mol)was dissolved in 40 ml of 2% alcoholic sodium hydroxide solution. To this dimethyl sulphate (0.01 mol) was added drop wise with stirring. The stirring was continued for 1 h, the reaction mixture was then poured into ice water. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol-chloroform (75:25).

Molecular formula: $C_{15}H_{11}FN_2OS$, Molecular weight: 286.324Yield: 81%,M p:153-155 °C, IR (KBr) cm^{-1}:1682 (C=O), 1603 (C=C) cm^{-1}^{1}H NMR ($CDCl_3$) δ ppm: 2.11 (s, 3H, SCH_3), 6.92-8.35 (m, 8HArH).Mass (m/z): 286 (M^+).

Synthesis of 2-hydrazino-3-(4-flurophenyl)-3*H*-quinazolin-4-one (6)

The 3-(4-flurophenyl)-2-methylsulfanyl-3*H*-quinazolin-4-one.(5) (0.01 mol) was dissolved in ethanol (25ml). To this hydrazine hydrate (99%) (0.1 mol) and anhydrous potassium carbonate (100 mg) was added and refluxed for 35 h. The reaction mixture was cooled and poured into ice-water. The solid obtained (6) was filtered, washed with water, dried and recrystallized from chloroform-benzene (25:75) mixture.

Molecular formula: $C_{14}H_{11}FN_4O$, Molecular weight: 270.262Yield:72%.M p:174-176 °C.IR (KBr) cm^{-1}:3310, 3226 ($NHNH_2$), 1680 (C=O) cm^{-1}.^{1}H NMR ($CDCl_3$) δ ppm: 4.50 (s, 2H,NH_2),7.32–8.35(m,8H,ArH), 8.62 (s, 1H, NH),Mass (m/z):270 (M^+).

Synthesis of 1-(3-(4-fluorophenyl)-4-oxo-3, 4-dihydroquinazolin-2yl)-4-phenylthiosemicarbazide (A1)

A solution of aniline (7a) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8a) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(phenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8a) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid (A1) obtained was filtered, dried and recrystallized from DMF.

Molecular formula: $C_{22}H_{16}FN_5OS$, Molecular weight: 405.448, R_f valu:0.259 (Benzene: Chloroform: Methanol) (2:1:0.3)Yield:92%Melting point:278^{O}C,IR (KBr) cm^{-1}:3338, 3286 (NH), 1666 (C=O), 1582 (C=C), 1256(C=S), 1136 (C-F), 822 (C-Cl) cm^{-1}.

Synthesis of 4-(4-fluorophenyl)-1-(3-(4-fluorophenyl)-4oxo-3, 4-dihydroquinazolin-2-yl)thiosemicarbazide (A2)

A solution of 4-fluoro aniline (7b) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8b) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(4-fluorophenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8b) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid obtained (A2) was filtered, dried and recrystallized from DMF.

Molecular formula:$C_{17}H_{15}F_2N_5OS$, Molecular weight:423.439, R_f value:05820 (Benzene: Chloroform: Methanol)(2:1:0.3)Yield:80%,Melting point:230^{O}C,IR (KBr) cm^{-1}:3340, 3288 (NH), 1664 (C=O), 1588 (C=C), 1260(C=S), 1138 (C-F), 824 (C-Cl) cm^{-1}.

Synthesis of 1-(3-(4-fluorophenyl)-4-oxo-3, 4-dihydroquinazolin-2-yl)-4-(4-methoxyphenyl)thiosemicarbazide (A3):

A solution of 4-methoxy aniline (7c) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8c) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(4-methoxyphenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8c) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid (A3) obtained was filtered, dried and recrystallized from DMF.

Molecular formula: $C_{22}H_{18}FN_5O_2S$, Molecular weight: 435.474, R_f value:0.85 (Benzene: Chloroform: Methanol)(2:1:0.3)Yield:84%,Melting poin:220^{O}CIR (KBr) cm^{-1}:1684(C=O), 1602(C=C), 1218(C=S), 1100(C-F), 1037 (C-O-C) cm^{-1}. 3319, 3227(NH), ^{1H} NMR ($CDCl_3$) δ ppm: 3.71(s, 3H, OCH_3), 6.91-8.47 (m, 12H, Ar-H), 8.60(br s, 1H, NH), 9.31 (br s, 1H, NH), 10.48 (br s, 1H, NH)

Synthesis of 4-(4-chlorophenyl)-1-(3-(4-fluorophenyl)-4-oxo-3, 4-dihydroquinazolin-2-yl)thiosemicarbazide (A4)

A solution of 4-chloro aniline (7d)(0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8d) was filtered, washed with water, dried and recrystallized from ethanol. The compound (6) (2.g, 0.01 mol) and the above prepared N-(4-chlorophenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8d) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid (A4) obtained was filtered, dried and recrystallized from DMF.

Molecular formula:$C_{21}H_{15}ClFN_5OS$,Molecular weight:439.893,R_f value:0.2777 (Benzene: Chloroform: Methanol) (2:1:0.3).Yield:88 %, Melting point:262^{O}C, IR (KBr) cm^{-1}:3288, 3203 (NH), 1682 (C=O), 1610 (C=C), 1258(C=S), 1122 (C-F), 751 (C-Cl) cm^{-1}.^{1}H NMR ($CDCl_3$) δ ppm: 6.94-8.31 (m, 12H, Ar-H), 8.60 (br s, 1H, NH), 8.99 (br s, 1H, NH), 10.28 (br s, 1H, NH), Mass: 439 (M^{+}), 441 (M^{+2}).

Synthesis of 1-(3-(4-fluorophenyl)-4-oxo-3, 4-dihydroquinazolin-2yl)-4-p-tolylthisemicarbazide (A5)

A solution of 4-methyl aniline(7e) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8e) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(4-methylphenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8e) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid obtained (A5) was filtered, dried and recrystallized from DMF.

Molecular formula:$C_{22}H_{18}FN_5OS$,Molecular weight:419.475, R_f value: 0.3333 (Benzene : Chloroform: Methanol)(2:1:0.3),Yield:75%,Melting point:225^{O}CIR (KBr) cm^{-1}:3342, 3278 (NH), 1662 (C=O), 1586 (C=C), 1262 (C=S), 1132 (C-F), 826 (C-Cl) cm^{-1}.

Synthesis of 4-(2-chlorohenyl)-1-(3-(4-fluorophenyl)-4-oxo-3,4-dihydroqunazolin-2-yl)thiosemicarbazide (A6)

A solution of 2-chloro aniline (7f) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8f) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(2-chlorophenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8f) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid obtained (A6) was filtered, dried and recrystallized from DMF.

Molecular formula:$C_{21}H_{15}ClFN_5OS$, Molecular weight: 439.893, R_f value 0.8518 (Benzene:Chloroform:Methanol)(2:1:0.3), Yield: 70%, Meltingpoint: 275^{O}C, IRKBr)cm^{-1}:3335, 3283 (NH), 1650 (C=O), 1599 (C=C), 1264 (C=S), 1137 (C-F), 818 (C-Cl) cm^{-1}.^{1}H NMR ($CDCl_3$) δ ppm: 7.09-8.27 (m, 12H, Ar-H), 8.39 (br s, 1H, NH), 8.65 (br s, 1H, NH), 10.70 (br s, 1H, NH), Mass: 439 (M^+), 441 (M^{+2})

Synthesis of 1-(3-(4-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2yl)-4-(3-methoxyphenyl)thiosemicarbazide (A7)

A solution of 3-methoxy aniline (7g)(0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8g) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(3-methoxyphenyl)- methyl dithiocarbamic acid (1.83g, 0.01 mol) (8g) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid obtained (A7) was filtered, dried and recrystallized from DMF.

Molecular formula: $C_{22}H_{18}FN_5O_2S$, Molecular weight: 435.475, R_f value: 0.8135 (Benzene: Chloroform: Methanol)(2:1:0.3)Yield:80%,Melting point:190^{O}CIR (KBr) cm^{-1}:3340, 3280 (NH), 1660 (C=O), 1599 (C=C), 1260(C=S), 1130 (C-F), 820 (C-Cl) cm^{-1}.

Synthesis of 1-(3-(4-fluorophenyl)-4-oxo-3, 4-dihydroquinazolin-2-yl)-4-o-tolylthiosemicarbazide (A8)

A solution of 2-methyl aniline (7h)(0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained (8h) was filtered, washed with water, dried and recrystallized from ethanol.

The compound (6) (2.g, 0.01 mol) and the above prepared N-(2-methylphenyl)-methyl dithiocarbamic acid (1.83g, 0.01 mol) (8h) were dissolved in DMF, potassium carbonate (100 mg) was added as catalyst and refluxed for 35 h (until the methyl mercaptam evolution ceases). After completion of the reaction, the reaction mixture was poured into crushed ice. The solid obtained (A8) was filtered, dried and recrystallized from DMF.

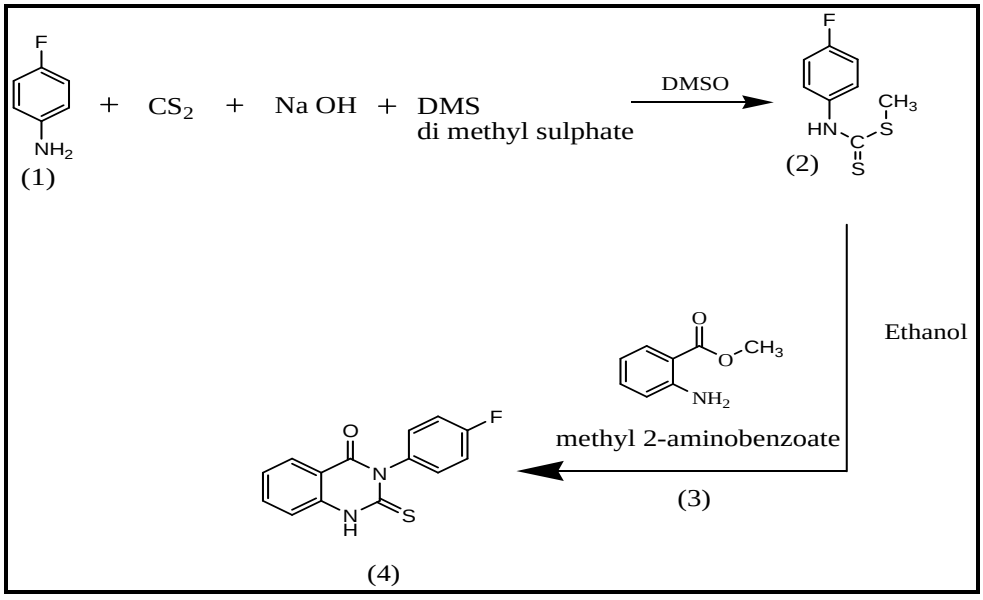
Molecular formula: $C_{22}H_{18}FN_5OS$Molecular weight: 419.475, R_f value:0.333 (Benzene: Chloroform: Methanl(2:1:0.3)Yield:86%,Melting point:240^{O}CIR (KBr) cm^{-1}:3338, 3270 (NH), 1655 (C=O), 1580 (C=C), 1250(C=S), 1135 (C-F), 818 (C-Cl) cm^{-1}.

RESULTS AND DISCUSSION

Synthesis of 3-(4-flurophenyl)-2-thioxo-2, 3-dihydro-1*H*-quinazolin-4-one (4)

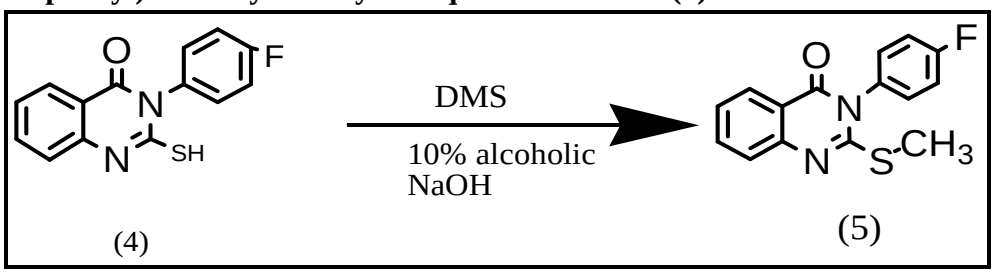
A solution of 4-fluro aniline (1) (0.02 mol) in dimethyl sulphoxide (10ml) was stirred vigorously. To this was added carbon disulphide (1.6ml; 0.026 mol) and aqueous sodium hydroxide 1.2 ml (20 molar solutions) drop wise during 30 min with stirring. Dimethyl sulphate (0.02 mol) was added gradually keeping the reaction mixture stirring in freezing mixture for 2 h. The reaction mixture was then poured into ice water. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol.

Methyl anthranilate (0.01mol) and the above prepared N-(4-flurophenyl)-methyl dithiocarbamic acid (0.01 mol), were dissolved in ethanol (20ml). To this anhydrous potassium carbonate (100 mg) was added and refluxed for 23 h. The reaction mixture was cooled in ice and the solid separated was filtered and purified by dissolving in 10% alcoholic sodium hydroxide solution and re-precipitated by treating with dilute hydrochloric acid. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol.



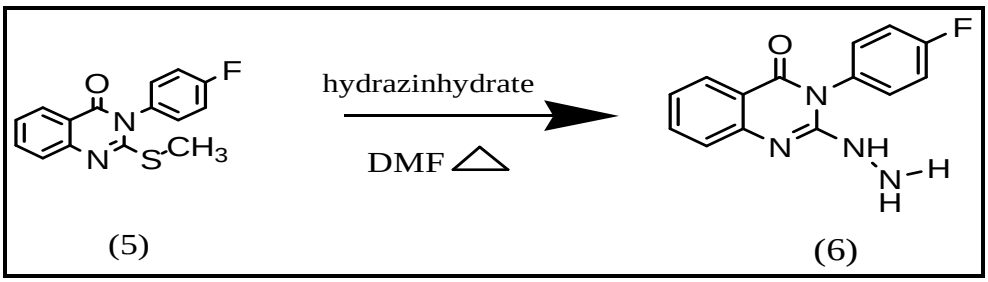
The IR spectrum of (4)show intense peaks at 3242 cm^{-1} for cyclic thiourea (NH), 1666 cm^{-1} for carbonyl (C=O) and 1218 cm^{-1} for thioxo (C=S) stretching. ^{1}HNMR spectrum of (4) showed singlet at δ 10.12 ppm due to fluoro group; for aromatic (8H) protons a multiplet at δ 7.13-8.51 ppm and a singlet at δ 10.12 ppm indicating the presence of NH. MS (m/z) 272 (M^{+}).

Synthesis of 3-(4-flurophenyl)-2-methylsulfanyl-3*H*-quinazolin-4-one (5)



The IR spectrum of (5) showed disappearance of NH and C=S stretching signals of the compound (4).It showed a peak of carbonyl (C=O) stretching at 1682cm^{-1}. C=C at 1602. The ^{1}HNMR spectrum of compound (5) showed singlet at 2.1 δ ppm due to fluoro group, singlet at 2.1 δ ppm due to fluoro group, multiplet at 6.9-8.35 δ ppm due to aromatic protons. MS (m/z) 286 (M^{+}).

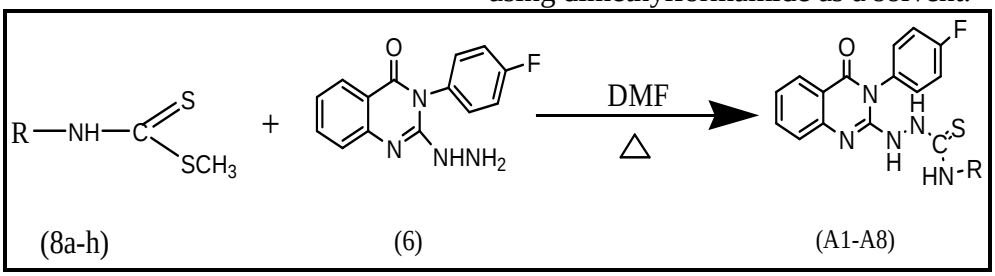
Synthesis of 2-hydrazino-3-(4-flurophenyl)-3*H*-quinazolin-4-one (6)



IR spectrum of (6) showed disappearance of C-S signals of the starting material. It showed a peak of carbonyl (C=O) stretching at 1680 cm^{-1}, 3310, 3226 (NH-NH_2).The ^{1}HNMR spectrum of compound (6) showed singlet at 4.50 δ ppm due to fluoro group, singlet at 8.62 δ ppm amino group, multiplet at 7.32-8.35 δ ppm due to aromatic protons, singlet at 8.92 δ ppm due to secondary amino group.MS (m/z) 270 (M^{+}).

Synthesis of 3-(4-fluorophenyl)-2-substituted quinazolin-4(3*H*)-ones (A1-A8)

The title compounds A1-A8 were obtained in fair and good yields through the displacement of thiomethyl group with a variety of dithiocarbamates using dimethylformamide as a solvent.



The formation of title compounds is indicated by the appearance of peaks due to 3 secondary amino groups at 3442 cm^{-1}, 3354 cm^{-1}, 3229 cm^{-1} in the IR spectra of the compounds. It also showed a peak for carbonyl (C=O) around 1667 cm^{-1}. The ^{1}H NMR spectra of the title compounds showed peaks for substituents at C-2 and a single around 8.48 δ ppm due to NH, a multiplet at 7.13-7.71 δ ppm was observed for aromatic protons, singlet at 3.93 δ ppm due to fluoro group.

Antibacterial activity (Zone of inhibition in 100µg/ml) of (A1-A8)

Table1 No.1: Test compounds A1-A8

S.No	Microorganisms	A1	A2	A3	A4	A5	A6	A7	A8	Standard*
1	S. Aureus	0.9	1.9	.0.8	1.2	0.7	0.9	0.7	1.0	19
2	E. Coli	0.8	2.5	1.2	1.6	1.0	0.8	0.6	0.8	21
3	P. vulgaris	0.6	1.8	1.0	1.9	0.9	1.4	0.5	1.2	19
4	K. pneumoniae	0.4	2.0	0.9	2.0	0.8	0.8	0.5	0.7	21
5	Coagulaszz Negative Staphylococci	0.8	1.5	1	1.8	1.1	1.0	0.6	1.0	20
6	P.aeruginosa	0.7	1.2	0.8	1.5	0.8	0.9	0.8	0.8	22

* Ciprofloxacin used as a reference standard for other bacteria.

Antibacterial activity (zone of inhibition)

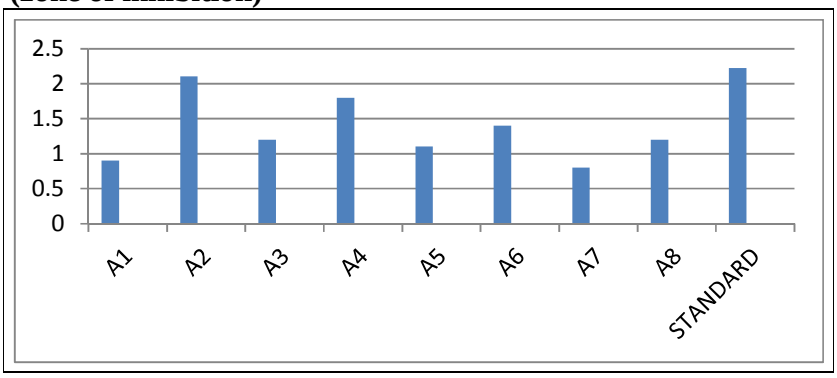


Figure No.1: ↑Zone of inhibition → Compounds (A1-A8)

CONCLUSION

Among the different substituents on the C-2, aryl and heteroaryl substitutents exhibited better activity over the aliphatic substituents. Compounds with electron withdrawing substituents like –Cl and $–NO_2$ showed better activity over the unsubstituted and electron donating substituents. Compounds A2and A4 emerged as the most active compounds of the series. Compound A2 shown most potent activity against *E.Coli, K.pneumoniae. B.subtilis* While the compound A4 showed most potent activity against *S.typhi, E.Coli, P.vulgaris, K.pneumoniae and B.subtilis.*

ACKNOWLEDGEMENT

The authors are thankful to Nethaji Institute of Pharmaceutical Sciences, Somidi, Kazipet, Warangal and MNR College of Pharmacy, Fasalvady, Sanga Reddy, Medak, Telangana, India. For providing necessary facilities to carry out this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Arti V, Joshi H S and Parikh H H. Design, synthesis and antimicrobial activity of 2-methylbenzylamino quinazolin-4(3H)-ones derivatives, *J. Inst. Chem*, 70(6), 1998, 216.
2. Shah B R, Bhatt J J, Patel H H, Undavia N H, Trivedi P B and Desai N C. Synthesis of 2,3-disubstituted-3,1-quinazolin-4(4H)-ones as potential anticancer and anti-HIV agents, *Indian J. Chem*, 34B, 1995, 201.
3. Jantova, S, Hudecova D, Stankovsty S and Ruzotoval H. Antibacterial effect of substituted 4-quinazolylhyd razines and their aryl hydrazones determined by a modified microdilution method, *Folia Microbial Prabha*, 40(6), 1995, 611.

4. Chan J H, Hong J S, Kuper L F, Jeyner S S, Tansik R I and Boytos C M. Selective inhibitors of candida albicans dihydrofolate reductase, Activity and selectivity of 5-(Arylthio)-2,4-diamino quinazolines, *J. Med. Chem*, 38(8), 1995, 3608.
5. Alagarsamy V, Pathak, U S, Sriram D, Pandeya S N and Clercq E De. Anti-HIV and antibacterial activities of some disubstituted quinazolones and their Bio-isostere Disubstituted thieno pyrimidones, *Indian J. Pharm. Sci*, 62(6), 2000, 433.
6. Alagarsamy V, Revathi R, Ramaseshu K V, Rajasekaran S and Clercq E De. Anti-HIV, antibacterial and antifungal activities of some 2,3-disubstituted quinazolin-4(3H)-ones, *Indian J. Pharm. Sci*, 66, 2004, 459.
7. Alagarsamy V, Pathak U S, Venkatesha Perumal R, Meena S, Thirumurugan K, Rajasolomon V and Clercq E De. Anti HIV and antibacterial activites of 2-Subtituted thiadiazolo quinazolines, *Indian J. Pharm. Sci*, 65, 2003, 293.
8. Alagarsamy V, Giridhar R and Yadav M R. Bioorg. Synthesis and pharmacological investigation of novel 1-substituted-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-ones as a new class of H1-antihistaminic agents, *Med. Chem. Lett*, 15(7), 2005, 1877.
9. Alagarsamy V, Rajasolmon V, Parthiban P, Dhanbal K, Murugan S, Saravanan G and Anjana G V. Design and synthesis of 3-(4-ethylphenyl)-2-substituted amino-3H-quinazolin-4-ones as a novel class of analgesic and anti-inflammatory agents, *J. Heterocyclic Chem*, 45, 2008, 709.

Please cite this article in press as: B. Babu Rao, *et al*. Synthesis and Pharmacological Investigation of Some Novel 3-(4-Fluorophenyl)-2-Substituted- Quinazolin-4(3*h*)-One, *Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry*, 3(3), 2015, 145 - 208.