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SYNTHESIS AND BIOLOGICAL EVALUATION OF QUINOLINE DERIVATIVES BEARING THIAZOLIDINONES SCAFFOLDS AS POTENT ANTI-INFLAMMATORY AND ANALGESIC AGENTS

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ABSTRACT Some new thiazolidinones substituted quinoline derivatives **(6a-g)** have been synanti-inflammatory and analgesic activities have been evaluated by using carragennan induced rat paw edema model and Eddy's hot plate method respectively. Acetanilide (**1**) was allowed to react with Vilsmeier-Haack reagent (DMF + $POCl_3$) to form 2-chloroquinoline-3-carbaldehyde (**2**). The compound (**2**) was treated with p-toluenesulphonic acid (PTSA) and sodium azide (NaN_3) to yield tetrazolo[1,5-1] quinoline-4-carbaldehyde **(3)**. The nucleophilic reaction between formyl group and amino group of various substituted amine **(4a-g)** gave corresponding Schiff base intermediates **(5a-g)**. Final thiazolidinones analogues **(6a-g)** were obtained from Schiff base intermediates **(5a-g)** by the reaction with thioglycolic acid and solvent DMF in presence of catalytic amount of aluminium chloride.

KEYWORDS Analgesic activity, Anti-inflammatory, Quinoline, Schiff base, Thiazolidinones, Vilsmeier-Haack reaction

INTRODUCTION

Inflammation is a serious clinical problem and marker of many pathological states such as rheumatoid arthritis, gout, osteoarthritis and Alzheimer's disease (AD)[1]. Throughout inflammation the body reacts to different injuries by assembling leukocytes and local fluids which ultimately eliminate the noxious stimulus. In pathological conditions, the inflammatory cells do not properly repair the development of persistent damaged tissue[2,3]. However, toxicity and poor tolerance to current therapeutic agents are dose-limiting factors. This has led to a rising in development of compounds with a safe anti-inflammatory profile.

Quinoline frameworks is part of several natural and synthetic compounds which exhibit a variety of biological activities such as antituberular[4], antibacterial[5,6], anti-inflammatory[7], antioxidant[8], antimalarial, diuretic, clastogenic, antimicrobial[9,10], antitubulin[11], antiprion agents[12]. Since quinoline moiety exerts anti-inflammatory and analgesic activities[13], and it has been noticed that introduction of additional heterocyclic rings to the quinoline core tends to exert profound influence in increasing the activity[14,15]. Previous reports demonstrated that the efficacy and rapidity of the quinoline constructions by new metal-catalized coupling cyclizations or acid catalyzed cycloaddition of appropriate precursors may compete with classical synthesis of quinoline derivatives[16]. In view of these observations and as a part of an ongoing research program on development of newer anti-inflammatory and analgesic agents, the synthesis and pharmacological activities of a series of novel thiazolidinones scaffolds fused with the quinoline derivatives are reported herein.

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RESULTS AND DISCUSSION

Chemistry

The desired thiazolidinones substituted quinoline derivatives were prepared in multisteps summarized in **Scheme 1**. In the first step, acetanilide (**1**) was allowed to react with Vilsmeier-Haack reagent (DMF + $POCl_3$) to form 2-chloroquinoline-3-carbaldehyde (**2**) with 80% yield. The Vilsmeier-haack reagent was prepared by adding $POCl_3$ dropwise to DMF at 0-5 °C and allowed to stir. The ^1H NMR spectra of compound (**2)** indicated the presence of an aldehyde proton at ä 10.21 ppm. The compound (**2)** was further treated with p-toluenesulphonic acid (PTSA) and sodium azide (NaN_3) to yield tetrazolo[1,5-1] quinoline-4-carbaldehyde **(3)** with 64% yield. The ^1H NMR spectrum of compound (**3)** indicated the presence of singlet peak at ä 10.43 ppm due to an aldehyde proton. The nucleophilic reaction between formyl group and amino group of various substituted amine **(4a-g)** gave corresponding Schiff base intermediates **(5a-g)**. Final thiazolidinones analogues **(6a-g)** were obtained from Schiff base intermediates **(5a-g)** by thir reaction with thioglycolic acid and solvent DMF in presence of catalytic amount of aluminium chloride. IR spectra of all final thiazolidinones analogues **(6a-g)** showed a strong, characteristic band in the region 756-773 cm^{-1} due to the C-S stretching vibration. The ^1H NMR spectra of products (**6a–g)** show a doublet at ä 3.12–3.66 due to the CH-S of thiazolidinone ring and a singlet at ä 5.36–5.96, indicating the presence of CH-N at thiazolidinone ring which confirm the conversion of substrates into the expected products. All the other aromatic and aliphatic protons were observed at expected regions. In the mass spectra of all compounds (**6a-g**), the $[M+1]^+$ peak was observed**.** All compounds gave satisfactory elemental analysis.

BIOLOGICALACTIVITY

Anti-inflammatory activity

Anti-inflammatory activities of the synthesized compounds (**6a-g**) were evaluated by Carrageenan induced rat paw edema model. In this model measurement was done to assess the ability of the test compound to reduce local edema induced in the rat paw by injection of an irritant agent i.e. carrageenan[17]. The results are summarized in **Table-1**. Among all the compounds **6f**, **6d**, **6e** and **6b** showed very good anti-inflammatory activity at 4th hr.

The animals were randomly divided into groups of nine. Group I served as control which received only 0.5 % carboxymethyl cellulose (CMC) solution. Group II served as the standard and received diclofenac (20 mg/kg; *p.o.*). Half hr after the administration of the test compounds (20 mg /kg; *p.o.*) and the standard drugs, 0.1 ml of carrageenan solution (0.1 % in sterile 0.9 % NaCl solution) was injected subcutaneously into the sub-plantar region of the right hind paw of each rat. Digital plethysmometer was utilized to measure the paw volume by saline displacement shown on the screen at 0, 1, 2, 3, and 4 hr after carrageenan injection. The edema volume in the control group (*V*c) and edema volume in the test compound treated groups (*V*t) was measured and the percentage inhibition of edema was calculated using the formula (20):

Anti-inflammatory activity (% inhibition) = 100 (*V*c–*V*t/*V*c)

where *V*c is the paw volume of the control group and *V*t is the paw volume of the test group.

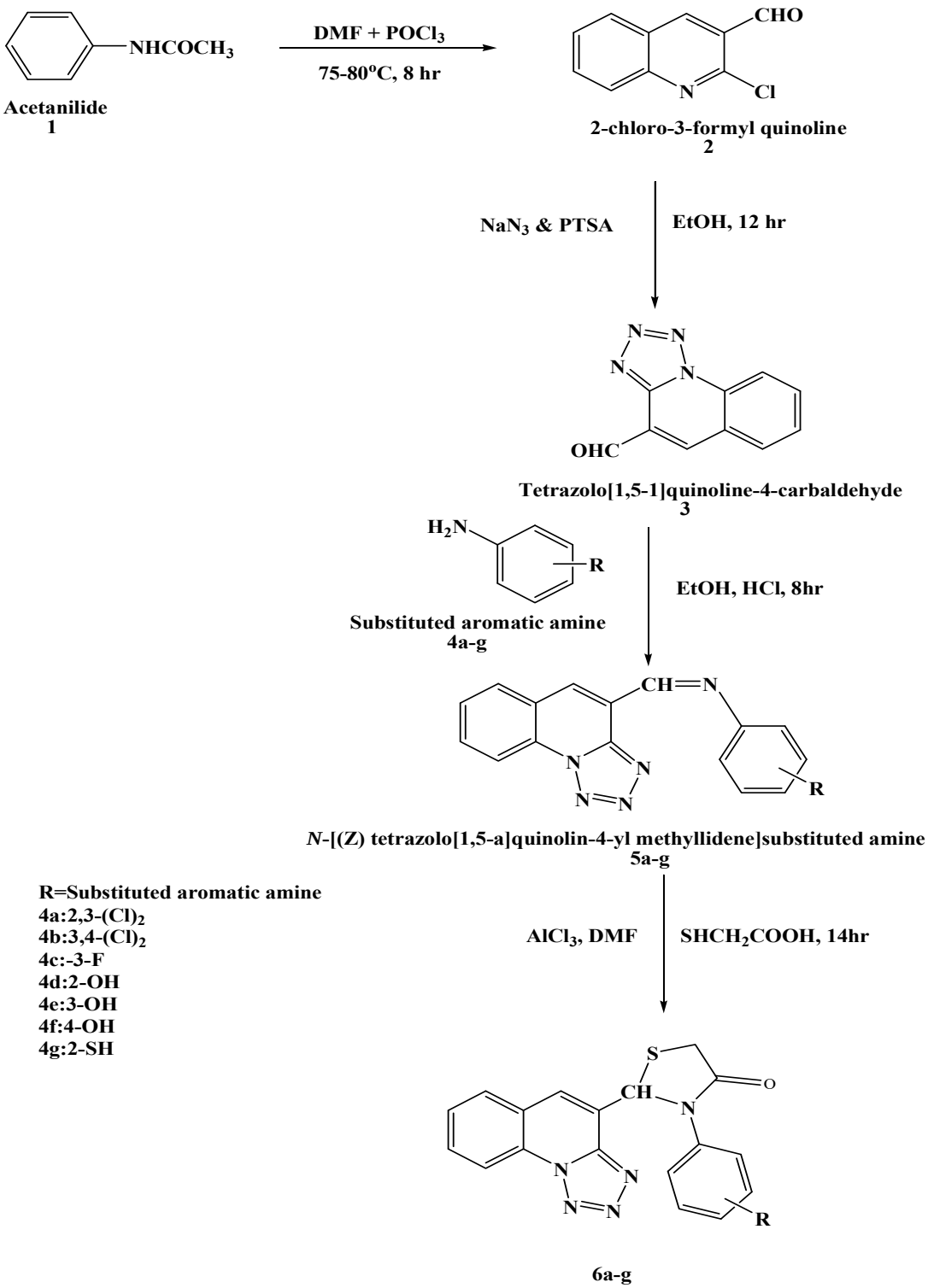
The % inhibition of control (distilled water + carrageenan) was considered as 0 % inhibition. The compounds treated groups were calculated accordingly. The data was analysed by simple arithmetic mean and standard error compare to the control. Data of the test drug were analyzed using two way ANOVA (Graph pad prism software) followed by Dunnett's test.

Analgesic activity

Analgesic activity of the synthesized compounds was evaluated by Eddy's hot plate method. Analgesic activity obtained for the test compounds were compared with control group. Data are expressed as Mean reaction time ± S.E.M. analyzed by One-way ANOVA followed by Dunnett test. Pentazocine at the dose of 10 mg/kg exhibited significant analgesic activity ($p < 0.01$) at all time intervals as compared to the control group. Compounds **6f, 6d, 6e** and **6b** at 20 mg/kg exhibited significant analgesic activity at all time intervals as compared to control group. Almost all the derivatives showed good analgesic activity at 2 hr interval as shown in Table 2.

Eddy's hot plate method

Eddy's hot plate method was utilized to evaluate the analgesic activity of the compounds using Swiss albino mice. Animals were divided into nine different groups. Animals were kept deprived of food 12 hr prior to drug administration till the experiment gets completed. The animals were weighed and numbered appropriately. Hot plate was maintained at 55°C. The animals were placed on the hot plate and basal reaction time was recorded by observing licking or jumping. Standard group received pentazocine (0.1 ml; 10 mg/kg) intra-peritoneally. Synthesized compounds were administered orally to the test groups (0.1 ml, 20 mg/kg). Analgesic activity of synthesized compounds was evaluated at equimolar doses. The basal reaction time was recorded at 30, 60, 90 and 120 min following administration of the standard or the test compound. Fifteen seconds cut off period was



SCHEME-1

observed to prevent tissue damage in animals. Among the derivatives, compounds **6f** & **6d** showed most promising results. This may be due to the available OH group present in **6f** & **6d**. In the current research work it was shown that substitution of hydoxy group on the benzene ring increases the potential of compound.

Table-1 Anti-inflammatory activity of compounds 6a-g in carrageenan-induced rat paw model

Groups	Paw oedema Volume (mm)							
	0 hr	% inhibition	**1 hr**	**% inhibition**	**2 hr**	**% inhibition**	**4 hr**	**% inhibition**
Control	1.11 ± 0.23		1.34 ± 0.43		1.56 ± 0.34		1.83 ± 0.09	
Std.	**1.03 ± 0.26**	**7.20**	**0.64 ± 0.03**	**52.23*** **	**0.66 ± 0.03**	**57.69*** **	**0.72 ± 0.06**	**60.65*** **
6a	1.07 ± 0.53	3.60	1.05 ± 0.29	21.64	0.92 ± 0.16	41.02**	0.93 ± 0.02	49.18***
6b	1.09 ± 0.41	1.80	1.02 ± 0.87	23.88	0.89 ± 0.48	42.94**	0.91 ± 0.04	49.27***
6c	1.05 ± 0.73	5.40	1.15 ± 0.43	14.17	1.22 ± 0.29	21.79	1.48 ± 0.66	19.12
6d	**1.05 ± 0.32**	**5.40**	**0.89 ± 0.08**	**33.58***	**0.81 ± 0.07**	**48.07*** **	**0.85 ± 0.02**	**53.55*** **
6e	**1.04 ± 0.67**	**6.30**	**0.93 ± 0.04**	**30.59***	**0.8 ± 0.04**	**47.43*** **	**0.88 ± 0.03**	**51.91*** **
6f	**1.04 ± 0.52**	**6.30**	**0.82 ± 0.08**	**38.80****	**0.74 ± 0.12**	**52.56*** **	**0.84 ± 0.23**	**54.09*** **
6g	1.09 ± 0.32	1.80	1.26 ± 0.69	5.97	1.24 ± 0.23	20.51	1.38 ± 0.27	24.59

Data are expressed as Mean ± SEM for paw edema volume. Statistical analysis was performed using two way ANOVA followed by Dunnett's test. ***P<0.001 vs control (carrageenan); **P<0.05 vs control (carrageenan); *P<0.01 vs control (carrageenan).

Table -2 Analgesic activity data of compounds using Eddy's hot plate method

Compound	Basal Reaction time (sec) before treatment (Mean ± SEM)	Basal reaction time (sec) after treatment (Mean ± SEM) **15 min**	**30 min**	**60 min**	**120 min**
Control	3.72 ± 0.1121	3.20 ± 0.7265	3.42 ± 0.7865	3.19 ± 0.3498	3.66 ± 0.4532
Std.	3.52 ± 0.2342	11.56 ± 06721***	13.06 ± 0.4392***	14.66 ± 0.5567***	13.16 ± 0.2132***
6a	3.12 ± 0.2318	7.47 ± 0.1542**	8.44 ± 0.2232***	9.78 ± 0.5423***	7.34 ± 0.6482**
6b	3.08 ± 0.1275	7.66 ± 0.2876***	8.98 ± 0.5793***	9.98 ± 0.5231***	8.66 ± 0.8332***
6c	2.98 ± 0.7652	6.71 ± 0.4213**	8.98 ± 0.1292***	9.89 ± 0.5634 ***	8.23 ± 0.5462***
6d	**3.16 ± 0.5324**	**9.21 ± 0.6553****	**9.88 ± 0.3356*****	**10.86 ± 0.4162*****	**10.13 ± 0.6532*****
6e	**3.28 ± 0.1982**	**8.55 ± 0.2742*****	**9.52 ± 0.5463*****	**10.88 ± 0.3421*****	**9.32 ± 0.3762*****
6f	**3.40 ± 0.1239**	**9.88 ± 0.2341*****	**10.22 ± 0.3241*****	**11.32 ± 0.5423*****	**10.22 ± 0.2341*****
6g	2.27 ± 0.2713	7.22 ± 0.3269**	7.66 ± 0.5673**	6.45 ± 0.4298*	4.66 ± 0.5583^{ns}

Data are expressed as Mean reaction time ± SEM. Statistical analysis was performed using two way ANOVA followed by Dunnett's test. ***P<0.001 vs control; **P<0.05 vs control; *P<0.01 vs control

EXPERIMENTAL

The melting points were determined in open capillary tubes and was uncorrected. The purity of all the synthesized compounds were checked by TLC on precoated silica gel-G aluminum sheets (Type 60 GF_{254}, Merck) and the spots were detected by exposure to iodine vapors. The infrared (FT-IR) spectra were recorded on 470-Shimadzu infrared spectrophotometer using the KBr disc prepared by pressed pellet technique and $V_{max}$is expressed in cm^{-1}. NMR spectra were measured in DMSO-d_6 as solvent at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR) on a BRUKER AVANCE-300 spectrometer using tetramethylsilane (TMS) as an internal standard. Chemical shifts (ä) are given in parts per million (ppm) and coupling constants (*J*) are given in Hertz (Hz). Spin multiplicities are given as s (singlet), d (doublet), dd (double doublet) and m (multiplet). Mass spectra were obtained on Shimadzu 2010A LC-MS spectrometer. Elemental analysis was carried on Elemental Vario EL III

Carlo Erba 1108 and the values were within ±0.04% of the theoretical values. All the solvents were distilled and dried with usual desiccant.

Synthesis of 2-chloro-3-formyl quinoline (2)

Phosphorus oxychloride ($POCl_3$) (13.77g, 0.09 mol) was added dropwise to anhydrous dimethyl formamide (DMF) (2.19g, 0.03 mol) at 0-5 ºC asd the mixture was stirred for 5 min. Acetanilide (1.35g, 0.01 mol) **(1)** was added to above mixture and refluxed for 8 hr at 75-80 ºC. The reaction mixture was first cooled and then poured into crushed ice with stirring; a pale yellow precipitate of 2-chloro-3-formyl quinoline (**2**) was appeared immediately. The precipitate was filtered, washed with water and recrystallized from ethyl acetate to give compound **(2)**[18-20]. Yield 80%; eluent-*n*-hexane/ethyl acetate 70:30 v/v, $R_{f=}$ 0.73; Light yellow crystal; mp 142-144°C; 1H NMR: ä 6.99 (s, 1H, Ar-H), 7.28 (s, 1H, Ar-H), 7.83 (s, 1H, Ar-H), 8.06 (s, 1H, Ar-H), 8.30 (s, 1H, Ar-H), 10.21 (s, 1H, -CHO).

Synthesis of tetrazolo[1,5-1] quinoline-4-carbaldehyde (3)

A solution of compound **(2)** (0.01 mol) and absolute ethanol (50 ml) were added in sodium azide (0.015 mol) and p-toluenesulphonic acid (0.01 mol) and the reaction mixture was refluxed for 12 hr. The reaction mixture was poured onto crushed ice under continuous stirring, brown coloured precipitate of **(3)** was appeared, filtered, washed with water and dried compound was recrystallized from acetone[21]. Yield 64 %; eluent-*n*-hexane/ethyl acetate 70:30 v/v, $R_{f=}$ 0.63; brown colour crystal; mp 137-138°C; 1H NMR: ä 4.67 (s, 1H, Ar-H), 5.08 (s, 1H, Ar-H), 6.48-6.73 (s, 2H, Ar-H), 8.06 (s, 1H, Ar-H), 10.43 (s, 1H, -CHO).

General procedure for the synthesis of *N*-[(Z)tetrazolo[1,5-*a*]quinoline-4-ylmethyllidene] substituted amine (5a-g)

Tetrazolo[1,5-1]quinoline-4-carbaldehyde (**3**) (0.01 mol) and substituted aromatic amine **(4a-g)** (0.01 mol) were added to ethanol (50 ml) with catalytic amount of conc. HCl (2 ml) and the mixture was refluxed for 8 hr. The reaction mixture was poured onto crushed ice, precipitate was formed and filtered, then washed with water and (**5a-g)** were recrystallized from ethanol.

3-(3-substituted)-2-(tetrazolo[1,5-*a*]quinolin-4-yl)thiazolidin-4-one (6a-I):General procedure A mixture of *N*-[(Z) tetrazolo [1,5-*a*]quinoline-4-yl methyllidene]substituted amine (**5a-g)** (0.01 mol) and catalytic amount of aluminium chloride (0.05 gm) in benzene was taken in Dean Stark apparatus and to it thioglycolic acid (1.40 ml, 0.02 mol) in DMF was added slowly. The resulting mixture was refluxed for 14 hr. The benzene was distilled off to give the solid mixture. This was then treated with an excess of 10% w/v sodium bicarbonate solution to remove excess of thioglycolic acid. The solid product thus obtained was filtered, washed with water and recrystallized from ethanol to give compound (**6a-g).**

3-(2,3-dichlorophenyl)-2-(tetrazolo[1,5-*a*]quinolin-4-yl)thiazolidin-4-one (6a) Yield: 74%; $R_{f=}$ 0.62; brown crystal; mp 261-262 °C; FTIR (KBr, $\acute{\imath}$ cm^{-1}): 3058 (Ar C-H), 1727 (C=O), 1598 (C-N), 767 (C-S), 728 (C-Cl); ^{1}H NMR (300 MHz, DMSO-d_6): 3.41 (d, 2H, CH-S, *J* = 7.6 Hz), 5.96 (s, 1H, CH-N), 6.74-7.13 (m, 4H, Ar-H), 7.29 (dd, 2H, Ar-H, *J* = 8.4 Hz, 2.4 Hz), 7.56 (dd, 2H, Ar-H, *J* = 8.4 Hz, 2.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 33.6, 60.5, 121.9, 125.7, 126.7, 127.7, 128.2, 128.3, 128.7, 128.9, 130.2, 131.1, 133.7, 134.7, 141.5, 143.2, 152.6, 171.2; EIMS (m/z): 416.28 $[M]^+$, 417.29 $[M+1]^+$; Anal. Calcd.for $C_{18}H_{11}Cl_2N_5OS$: C, 51.93; H, 2.66; N, 16.82. Found: C, 51.91; H, 2.64; N, 16.84 %

3-(3,4-dichlorophenyl)-2-(tetrazolo[1,5-*a*]quinolin-4-yl)thiazolidin-4-one (6b) Yield 69%; eluent-benzene: ethyl acetate: ethanol 60:20:20 v/v, $R_{f=}$ 0.66; brown crystal; mp 267-268 °C; FTIR (KBr, $\acute{\imath}$ cm^{-1}): 3051 (Ar C-H), 1735 (C=O), 1589 (C-N), 762 (C-S), 1037 (C-Cl); ^{1}H NMR (300 MHz, DMSO-d_6): 3.12 (d, 2H, CH-S, *J* = 7.4 Hz), 5.36 (s, 1H, CH-N), 6.84-7.34 (m, 4H, Ar-H), 7.88 (dd, 2H, Ar-H, *J* = 7.4 Hz, 1.6 Hz), 8.16 (dd, 2H, Ar-H, *J* = 8.2 Hz, 2.2 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): ä 33.9, 59.2, 121.2, 125.1, 126.2, 126.5, 128.1, 128.3, 128.6, 128.2, 130.8, 131.3, 133.7, 134.7, 140.5, 142.2, 153.6, 171.7; EIMS (m/z): 416.28 $[M]^+$, 417.30 $[M+1]^+$ Anal. Calcd.for $C_{18}H_{11}Cl_2N_5OS$: C, 51.93; H, 2.66; N, 16.82. Found: C, 51.92; H, 2.65; N, 16.83 %

3-(3-fluorophenyl)-2-(tetrazolo[1,5-*a*]quinolin-4-yl)thiazolidin-4-one (6c) Yield 58%; $R_{f=}$ 0.74; white solid; mp 167-168 °C; FTIR (KBr, $\acute{\imath}$ cm^{-1}): 3065 (Ar C-H), 1743 (C=O), 1602 (C-N), 1232 (C-F), 763 (C-S); ^{1}H NMR (300 MHz, DMSO-d_6): 3.66 (d, 2H, CH-S, *J* = 7.8 Hz), 5.92 (s, 1H, CH-N), 6.56-7.02 (m, 5H, Ar-H), 7.92 (dd, 2H, Ar-H, *J* = 8.2 Hz, 1.6 Hz), 8.06 (dd, 2H, Ar-H, *J* = 8.4 Hz, 1.8 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 34.8, 66.3, 122.8, 125.6, 126.2, 127.3, 128.1, 128.6, 129.1, 130.2, 131.4, 132.4, 133.8, 134.5, 141.4, 143, 152.5, 171.2; EIMS (m/z): 365.38 $[M]^+$, 366.31 $[M+1]^+$; Anal. Calcd.for $C_{18}H_{12}FN_5OS$: C, 59.17; H, 3.31; N, 19.17. Found: C, 59.19; H, 3.33; N, 19.18 %

3-(2-hydroxyphenyl)-2-(tetrazolo[1,5-*a*]quinolin-4-yl)thiazolidin-4-one (6d) Yield 71%; $R_{f=}$ 0.77; white solid ;mp 211-212 °C; FTIR (KBr, $\acute{\imath}$ cm^{-1}): 3366 (Ar -OH), 3061 (Ar C-H), 1739 (C=O), 1597 (C-N), 769 (C-S); ^{1}H NMR (300 MHz, DMSO-d_6): 3.37 (d, 2H, CH-S, *J* = 7.4 Hz), 5.04 (s, 1H, O-H, D_2O exchangeable), 5.55 (s, 1H, CH-N), 6.98-7.13 (m, 5H, Ar-H), 7.39 (dd, 2H, Ar-H, *J*= 8.6 Hz, 2.6 Hz,), 7.78

(dd, 2H, Ar-H, *J* = 7.4 Hz, 2.6 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 31.2, 61.4, 121.2, 124.8, 126.3, 127.7, 128.1, 129.3, 130.2, 132.7, 134.3, 134.8, 141.5, 143.4, 155.3, 172.2; EIMS (m/z): 363.39 $[M]^+$, 364.41 $[M+1]^+$; Anal. Calcd. for $C_{18}H_{13}N_5O_2S$: C, 59.49; H, 3.61; N, 19.27; Found: C, 59.51; H, 3.60; N, 19.29 %

3-(3-hydroxyphenyl)-2-(tetrazolo[1,5-a]quinolin-4-yl)thiazolidin-4-one (6e) Yield 71%; R_f= 0.70; white solid ; mp 218-219 °C; FTIR (KBr, $\tilde{\nu}$, cm^{-1}): 3342 (Ar -OH), 3063 (Ar C-H), 1749 (C=O), 1616 (C-N), 7 (dd, 2H, Ar-H, *J* = 8.4, 2.4 Hz), 7.98 (dd, 2H, Ar-H, *J* = 8.4 Hz, 2.8 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 31.8, 60.4, 121.8, 125.8, 126.9, 127.7, 128.2, 129.8, 130.3, 131.3, 132.4, 134.5, 134.7, 141.6, 143.5, 152.2, 155.5, 173.3; EIMS (m/z): 363.39 $[M]^+$, 364.40 $[M+1]^+$; Anal. Calcd.for $C_{18}H_{13}N_5O_2S$: C, 59.49; H, 3.61; N, 19.27 Found: C, 59.48; H, 3.59; N, 19.26 %

3-(4-hydroxyphenyl)-2-(tetrazolo[1,5-a]quinolin-4-yl)thiazolidin-4-one (6f) Yield 77%; R_f= 0.68; white solid ; mp 222-223 °C; FTIR (KBr, $\tilde{\nu}$, cm^{-1}): 3320 (Ar -OH), 3135 (Ar C-H), 1749 (C=O), 1607 (C-N), 756 (C-S); ^{1}H NMR (300 MHz, DMSO-d_6): 3.32 (d, 2H, CH-S, *J* = 8.4 Hz), 5.12 (s, 1H, O-H, D_2O exchangeable), 5.82 (s, 1H, CH-N), 6.48-7.32 (m, 5H, Ar-H), 7.89 (dd, 2H, Ar-H, *J* = 8.2 Hz, 2.2 Hz), 8.02 (dd, 2H, Ar-H, *J* = 8.2 Hz, 2.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 32.6, 60.3, 121.8, 123.2, 125.6, 126.9, 127.7, 128.5, 129.9, 130.3, 131.2, 134.6, 134.9, 141.2, 143.4, 152.8, 154.5, 172.7; EIMS (m/z): 363.39 $[M]^+$, 364.42 $[M+1]^+$; Anal. Calcd. for $C_{18}H_{13}N_5O_2S$: C, 59.49; H, 3.61; N, 19.27; Found: C, 59.50; H, 3.59; N, 19.30 %

3-(2-mercaptophenyl)-2-(tetrazolo[1,5-a]quinolin-4-yl)thiazolidin-4-one (6g) Yield 66%; R_f= 0.57; yellow solid; mp 246-247 °C; FTIR (KBr, $\tilde{\nu}$, cm^{-1}): 3051 (Ar C-H), 2552 (S-H), 1721 (C=O), 1598 (C-N), 773 (C-S); ^{1}H NMR (300 MHz, DMSO-d_6): 3.11 (s, 1H, H-S, D_2O exchangeable), 3.62 (d, 2H, CH-S, *J* = 7.8), 5.66 (s, 1H, CH-N), 6.84-7.34 (m, 5H, Ar-H), 7.82 (dd, 2H, Ar-H, *J* = 8.2 Hz, 2.2 Hz,), 8.04 (dd, 2H, Ar-H, *J* = 8.2 Hz, 2.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): 32.8, 58.2, 121.8, 123.2, 125.9, 126.2, 127.4, 128.6, 129.3, 130.3, 131.4, 133.5, 134.5, 141.4, 143.8, 152.5, 154.3, 177.2; EIMS (m/z): 379.46 $[M]^+$, 380.47 $[M+1]^+$; Anal. Calcd.for $C_{18}H_{13}N_5OS_2$: C, 56.97; H, 3.45; N, 18.46. Found: C, 56.95; H, 3.43; N, 18.44%

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