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Design, synthesis and anticonvulsant potential of (*E*)-3-(5-(substituted aminomethyl)-1,3,4-thiadiazol-2-yl)-2-substituted styrylquinazolin-4-(3H)-one

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ABSTRACT

Objective: The prime objective of the paper was to design and synthesize new derivatives of (*E*)-3-(5-(substitutedaminomethyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one and evaluated for their anticonvulsant potential.

Material and methods: Various derivatives of (*E*)-3-(5-(substitutedaminomethyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one derivatives has been synthesized by reacting 2-substituted benzoxazin-4-one with (*E*)-2-(4-Substituedstyryl)-4H-benzo[d][1,3]oxazin-4-one. All synthesized compounds have been characterized by the IR, NMR and mass spectral analysis. Proposed compounds have been evaluated for anticonvulsant potential by subcutaneous pentylenetetrazole (scPTZ) and maximal electroshock seizure (MES) model and compared with the reference drug phenytoin &carbamazepine.

Result and discussion: The subcutaneous pentylenetetrazoles (scPTZ) model denotes that compounds SB-6, SB-12, SB-14 and SB-18 were found most active at anticonvulsant screening when compared with phenytoin and carbamazepine (standard drug).The most active compound of the series was SB-1, SB-4, SB-6, SB-9, SB-12, SB-14, SB-14 and SB-18. In most of the Cl and nitro group phenyl ring in position of the 1,3,4-thiadiazoles nucleus and Cl on phenyl ring of 4(3H)-quinazolinone has shown the potent activity.

Keywords: quinazolinone, anticonvulsant, maximal electroshock seizure, phenytoin, carbamazepine

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INTRODUCTION

Quinazoline is an organic compound with the formula $C_8H_6N_2$. It is an aromatic heterocycles with a bi-cyclic structure consisting of two fused six-member aromatic rings, a benzene ring and pyrimidine ring. Quinazoline is a compound made up of two fused six-member aromatic rings, a benzene ring and a pyrimidine ring. Quinazoline is a fused bi-cyclic compound earlier known as benzo-1,3-diazine was first prepared in the laboratory by Gabriell. Depending upon the position of the keto or oxo group, these compounds may be classified into three types including 4(3H)-quinazolinone, 2(1H)quinazolinone and 2,4 (1H,3H)-quinazolinedione, of the three quinazolinone structures 4(3H)-quinazolinone are most prevalent, either as intermediates or as natural products in many proposed bio synthetic pathways.

Epilepsy is a central nervous system (CNS) malfunction that leads either to generalized hyperactivity involving essentially all parts of the brain or hyperactivity of only a portion of the brain. It has been estimated that adequate control of seizures could not be obtained in up to 20% of the patients with epilepsy using first generation of antiepileptic drugs (phenobarbital, phenytoin, carbamazepine, sodium valproate and diazepam. The convulsions of approximately 25% of epileptics are adequately controlled by current clinically available drugs. Current drug therapy is accompanied by numerous side effects including drowsiness, ataxia, gastrointestinal disturbances, gingival hyperplasia, hirsutism and megaloblastic anemia[1]. The past decade has witnessed a continuous interest in the development of anticonvulsant drugs.

Quinazolinone is a potent hypnotic agent and other 4(3H)-Quinazolinone and its derivatives have been reported to exhibits analgesic, anesthetic, antibacterial[2], anticancer, anticonvulsant, antihypertensive, anti-inflammatory & antioxidant[3], diuretic, muscle relaxant, sedative, anti-hepatitis-A virus[4] and tranquilizer properties. The 4(3H)-quinazoline and its derivatives have been reported to exhibit anticonvulsant, antimicrobial, sedative, tranquilizer, analgesic, anesthetic, anticancer, antihypertensive, anti-inflammatory, diuretic and muscle relaxant properties[5-15]. 2-Methyl-3-o-tolyl-4(3H)-quinazolinone (Methaqualone) is the most frequently prescribed quinazolinone derivative as a safe sedative-hypnotic and anticonvulsant drug.

Literature survey revealed that the presence of substituted aromatic ring at 3rd position and methyl/phenyl group at 2nd position of 4(3H)-quinazolinone are necessary requirement for the central nervous system (CNS) depression and anticonvulsant activity. This hypothesis encourages us to build the modification of quinazolinone at 2nd and 3rdposition. The objective of the papers was to design, synthesize and evaluation of synthesized compounds for anticonvulsant potential.

EXPERIMENTAL

Material and method

2-chloroacetyl chloride, thiosemicarbazide, formaldehyde was purchased from Sigma Aldrich, New Delhi. Substituted anilines (4-chloro, 4-fluro aniline, 4-nitro aniline, 4-methyl aniline, 4-methoxy aniline, 4-ethyl aniline, 4-ethoxy aniline) were purchased from Hi-Media. Acetic anhydride, di-methyl formamide, glacial acetic acid substituted and benzaldehyde (4-Chloro, 4-nitro, 4-CH_3 and 4-OCH_3) was purchased from CDH (Chemical Drug House), New Delhi, India. The chemical used for experimental work were synthetic grade. The melting points of the synthesized compounds were determined in open glass capillaries. IR spectra were recorded on ALPHA (Bruker) FTIR Spectrometer. Elemental analysis was performed and found values were within 0.4% of theoretical values. 13C NMR spectra were recorded on Bruker Avance 400 spectrophotometer at 400 MHz, 5mm multi-nuclear inverse probe head, low and high-temperature facility and HRMAS accessory. Mass Spectra were recorded using Mass Spectrometers Jeol SX-102 (FAB) by ESI.

Chemistry

The synthesis of (*E*)-3-(5-(substitutedaminomethyl)-1,3,4-thiadiazol-2-yl)-2-styryl quina zolin-4(3H)-one is accompanied in **Figure 1** and present synthesis comprises of three steps. These are -

1. **Scheme 1**

Synthesis of 1,3,4-thiadiazole

Step 1: Synthesis of 5-(chloromethyl)-1,3,4-thiadiazol-2-amine

Step 2: Synthesis of 5-(substituted-amino methyl)-1,3,4-thiadiazol-2-amine

2. **Scheme 2**

Synthesis of titled compounds

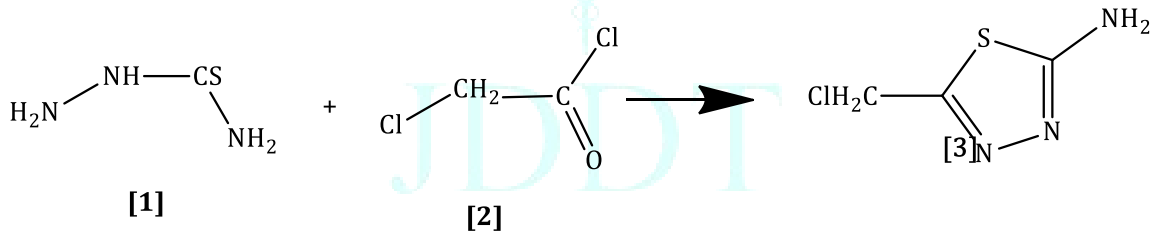
Step 1: Synthesis of 2-substituted-benzoxazin-4-one

Step 2: Synthesis of (E)-2-(4-Substituedstyryl)-4H-benzo[d][1,3]oxazin-4-one

Step 3: Synthesis of (E)-3-(5-(substitutedaminomethyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one

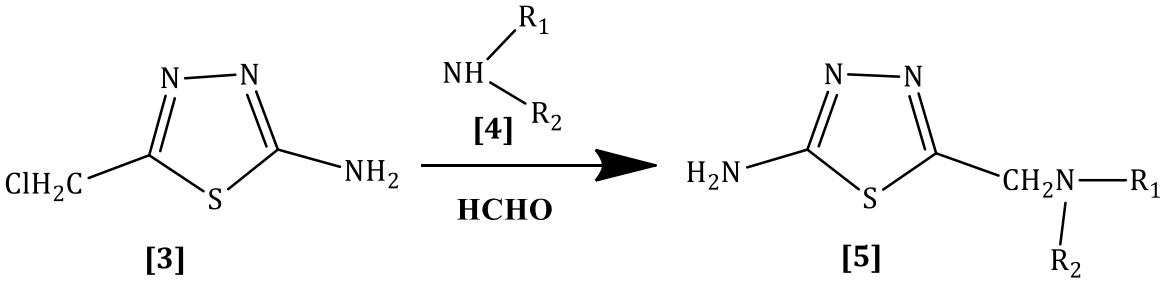
A. General method for the synthesis of 1,3,4-thiadiazole:

Step 1: Synthesis of 5-(chloromethyl)-1,3,4-thiadiazol-2-amine[16]



Substituted amino thiadiazole [3] was prepared by the conventional method by following procedure: In this reaction 2-chloroacetyl chloride [2] (0.1 mol) and thiosemicarbazide [1] (0.1 mol) was mixed thoroughly. The reaction mixture was heated under reflux in the presence of conc. H_2SO_4. The reaction was cooled to room temperature and neutralized with ammonia solution. The solid was filtered and washed with water followed by few drops of ether. The product was recrystallized from ethanol and characterized by 1H NMR, mass and UV-spectral analysis.

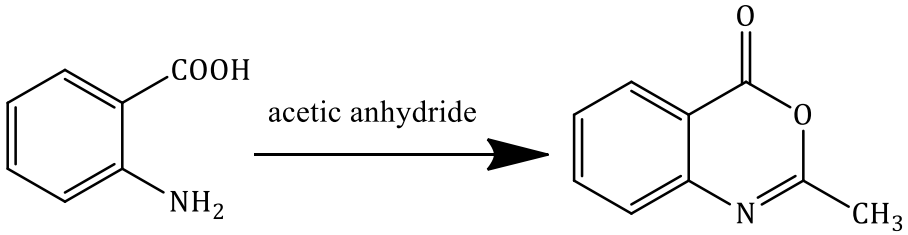
Step 2: Synthesis of 5-(substituted-amino methyl)-1,3,4-thiadiazol-2-amine[17]



5-(chloromethyl)-1,3,4-thiadiazol-2-amine [3] (0.1 mol) was taken in round bottom flask and formaldehyde was dissolved in methanol (3.0 ml) was added drop wise with continuous stirring. The resulting mixture was stirred during half an hour to complete the mixing. To this reaction mixture methanolic solution of p-chloro aniline/ p-fluoro aniline/p-nitro aniline/p-methyl aniline/p-methoxy aniline/p-ethyl aniline/p-ethoxy aniline (0.1 mol) [4] was added drop wise with stirring in about half an hour for temperature at 30°C and refluxed for 2h at 65-75°C . It was allowed to cool and poured in cold water. The solid was obtained, filtered off and washed thoroughly with hot water and air dried. Obtained compound [5], was characterized by IR, NMR and were found consistent with an expected structure. TLC has been performed each and every steps to confirm the completion of the reaction.

Synthesis of Titled Compounds

Step 1: Synthesis of 2-methyl-4H-benzo[d][1,3]oxazin-4-one[18]

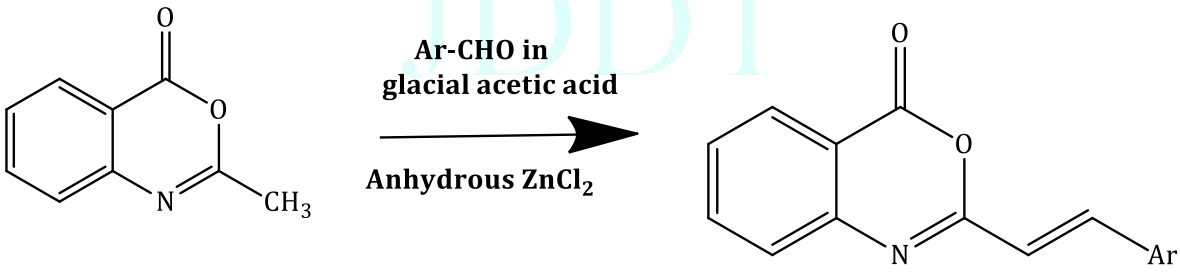


[6] **[7]**

Anthranilic acid [6] (0.01 M) was dissolved in acetic anhydride and refluxed under anhydrous condition for 4h. Excess of acetic anhydride was then distilled off under reduced pressure to get solid mass of N-acetyl anthranilic acid. Then N-acetyl anthranilic acid was further reflux with acetic anhydride, under anhydrous condition for 4 hr. Excess of acetic anhydride was then distilled off under reduced pressure to get solid mass of 2-methyl benzoxazin-4-one [7]. The products were dried and recrystallized from petroleum ether. Reaction was monitored by the TLC for the completion of the reaction.

Note: Purification of anthranilic acid: The anthranilic acid, used for the synthesis was purified by following procedure. The crude anthranilic acid (100 g) was dissolved in hot distilled water (500 ml) and activated charcoal (2g) was added to it with constant stirring. It was refluxed for 20-30 min and filtered hot. On cooling the crystals of anthranilic acid separated out which was filtered and dried. (Percent yield: 60%, melting point: 144-145^{0}C).

Step 2: Synthesis of (E)-2-(4-Substituedstyryl)-4H-benzo[d][1,3]oxazin-4-one[19]

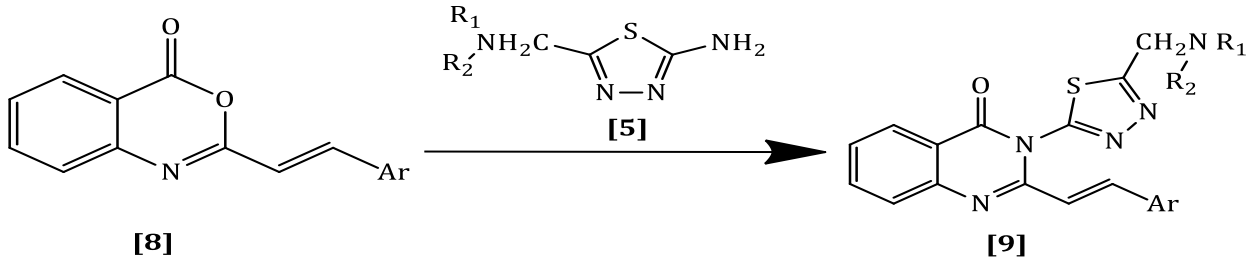


[7] **[8]**

A 2-methyl-4H-benzo[d][1,3]oxazin-4-one [7] (0.1 M), respective substituted aldehyde (0.2 M) and anhydrous zinc chloride (0.1 g) was refluxed at 130-140^{0}C for 2h. After cooling, the reaction mixture was treated with cold water to dissolve zinc chloride. The residue left after filtration was washed with cold ethanol. Purification of the synthesized compounds [8] was done by dissolving the compounds in minimum quantity of dimethyl formamide (DMF) and then adding the solution to distilled water.

The above method gave very low yield therefore some modification has carried to get high yield and purity of the product. Equimolar amount of 2-methyl-3-(substituted 1,3,4-thiodiazole-2-yl)-4(3H)-quinazolinone [7] (0.2M) and respective substituted aldehyde (0.2 M)were taken in glacial acetic acid (10 ml) and refluxed for 12 hr (Raffa *et al.,* 2004). After cooling, product [8] was separated out, which was filtered off. The purification of the product was done by using DMF and the melting points determined. This synthesis was monitored by the TLC to confirm the completion of the reaction.

Step 3: Synthesis of (E)-3-(5-(substitutedaminomethyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one



Equimolar quantity of compound [8] (0.01 M) was taken in round bottom flask and obtained compound [5], and dissolved in glacial acetic acid and refluxed for 4h. After cooling, it was poured into crushed ice and kept overnight in the refrigerator. The solid product [9] which was separated out, filtered, washed thoroughly with cold distilled water, dried and recrystallized from hot ethanol. Synthesis was monitored by the TLC for the completion of the reaction.

Characterization

The synthesized compounds were subjected to qualitative tests for nitrogen, sulphur and halogen wherever desired. Quantitative analysis for nitrogen and sulphur was done by Elemental Vario EL III Carlo Erba 1108. IR spectra were recorded on Perkin Elmer Spectrum RXI IR spectrophotometer in KBr pellets. NMR spectra were recorded on C13 Advance Bruker DRX 300 MHz spectrometer. Mass spectra were recorded on JeolSx 102/DA-6000 mass spectrometer using fast moving bombardment (FAB) technique. Solubility of the synthesized compound was checked in different solvent at room temperature (18-300°C). The purity of the synthesized compound was confirmed by thin layer chromatography (TLC) using silica gel G in various solvent systems like Hexane/ethanol(95%)/Chloroform/ benzene, visualization was done using iodine vapors in a iodine chamber or in 30% sulphuric acid. List of all synthesized compounds was tabulated in Table. 1. Physical properties of the synthesized title compounds shown in Table 2.

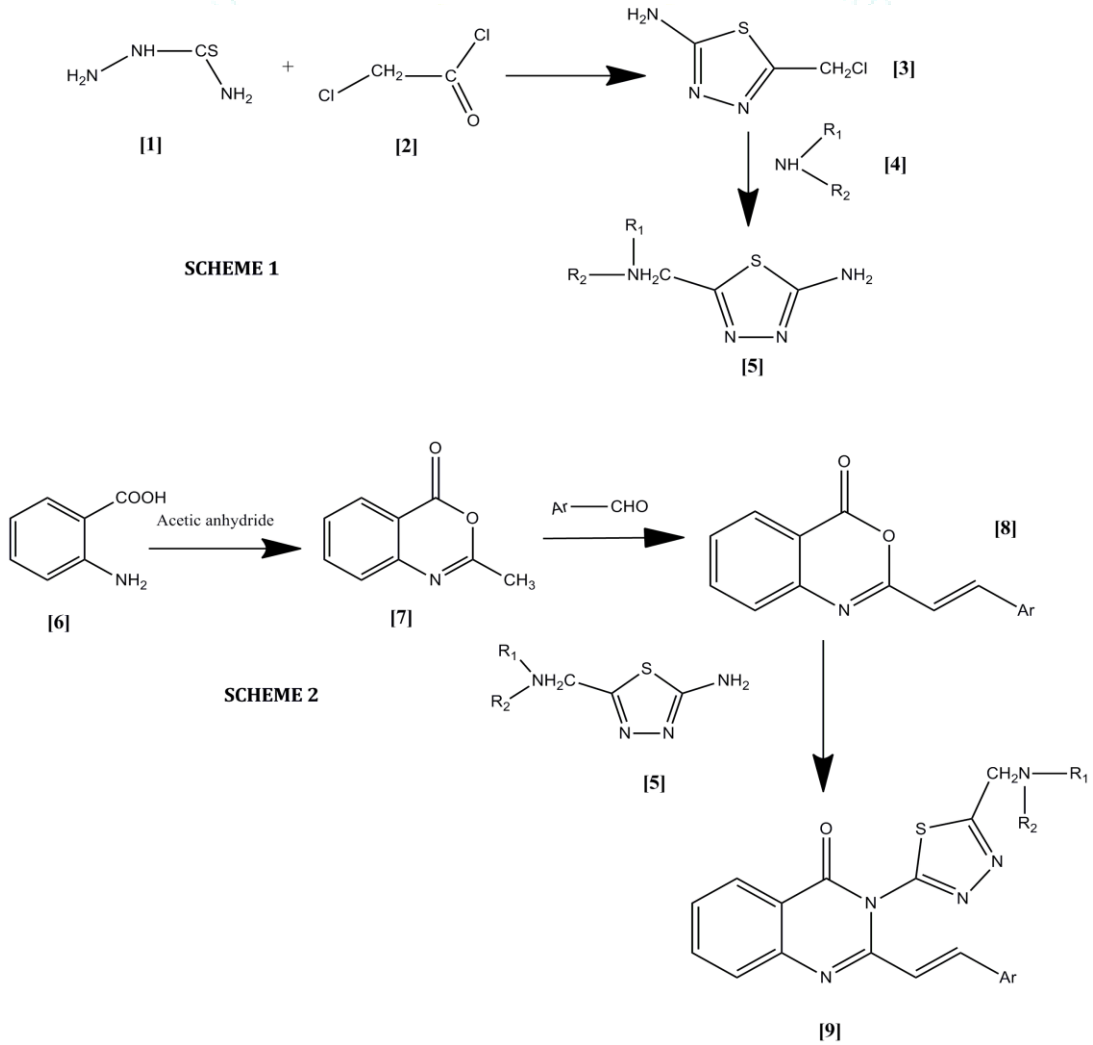


Figure 1: Synthesis scheme of compounds

SB-1: *(E)*-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-styryl quinazolin-4(3H)-one

Molecular formula**:** $C_{25}H_{18}ClN_5OS$; Molecular weight: 471.96. IR (cm^{-1}): 3020(C-H str.); 760 (C-H def.) 1700 (C=O str.); 1174 (C_6H_5); 1516C=Cstr.; 2856 (C-H str.); 3120 (C-H str.); 1461 (C-H str.); 1580 (C-C str.); 1614 (C=C str.); 1326 (C-N str.) 1555 (C=N str.); 760 (C-S str.); 620 (C-Cl str.). 13C NMR(DMSO-d6, δ ppm): 113.3 C11; 126.7 (C8, 4-quinazolinone ring); 128.5 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 145.5 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.9 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6, 4-quinazolinone ring); 128.6 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 129.6 (phenyl ring attached to 1,3,4 thiadiazole ring; 126.6 (C5, 4-quinazolinone ring; 133.4 (C7, 4-quinazolinone ring); 135.2 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.1 (C12, styryl group attached to 4-quinazolinone ring); 147.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.8 (C10, 4-quinazolinone ring; 158.9 (C2, 4-quinazolinone ring); 160.6 (C4, 4-quinazolinone ring). FAB Mass (m/z): 472 (Quassi-molecular ion peak).

SB-2: *(E)*-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-styryl quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{18}BrN_5OS$; Molecular weight: 516.41; TLC (Rf value): 0.72 IR (cm-1): 3120 (C-H str.); 775 (C-H def); 1737 (C=O str.); 1598 (C=C str.); 2975 (C-H str.); 3020 (C-H str.); 1378(C-H def.); 1458 (C-C str.); 1610(C=C str.); 1269(C-N str.); 733 (C-S str.); 520 (C-Br str.); 13C NMR (ppm): 113.3(C11; styryl group attached to 4-quinazolinone ring; 126.7 (C8, 4-quinazolinone ring); 128.5 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring) 114.9 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.9 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6, 4-quinazolinone ring); 115.1 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring) 132.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.6 (C5, 4-quinazolinone ring); 133.4 (C7, 4-quinazolinone ring); 135.2 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.1 (C12, styryl group attached to 4-quinazolinone ring); 148.3 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.8 (C10, 4-quinazolinone ring); 158.9 (C2, 4-quinazolinone ring); 160.6 (C4, 4-quinazolinone ring). FAB Mass (m/z): 516 (Quassi-molecular ion peak).

SB-3: *(E)*-3-(5-(((4-nitrophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one

Molecular formula: $C_{25}H_{18}N_6O_3S$; Molecular weight: 482.51; TLC (Rf value): 0.67. IR (cm-1): 3261 (C-H str.); 812 (C-H def); 1700 (C=O str.); 1174 (-C6H5); 1540 (N=O str.); 1320 (N-O str.); 1593 (C=C str.); 1076 (-C_6H_5); 2856 (C-H str.); 3057 (C-H str.); 1382 (C-H def); 1442 (C-C str.); 1620 (C=C str.); 1274 (C-Nstr.); 740 (C-S str.) 13C NMR (ppm): 113.5 (C11; styryl group attached to 4-quinazolinone ring); 126.9 (C8, 4-quinazolinone ring); 128.1 (C14 & C18 phenyl substituted styryl group attached to 4-quinazolinone ring); 114.4 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.9 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6, 4-quinazolinone ring); 136.3 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring) 127.5 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.3 (C5, 4-quinazolinone ring); 133.6 (C7, 4-quinazolinone ring) 135.1 (C13 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 138.6 (C12, styryl group attached to 4-quinazolinone ring); 155.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.3 (C10, 4-quinazolinone ring); 158.7 (C2, 4-quinazolinone ring); 160.9 (C4, 4-quinazolinone ring; FAB Mass (m/z): 482 (Quassi-molecular ion peak).

SB-4: *(E)*-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}Cl_2N_5OS$; Molecular weight: 506.41; TLC (Rf value): 0.61; IR (cm-1): 3055 (C-H str.); 810 (C-H def (oop)); 1739 (C)=O str.); 1596 (C=C str.); 2833 (C-H str.); 3001 (C-H str.); 1373 (C-H def.); 1438 (C-C str.); 1642 (C=C str.); 1334 (C-N str.); 1542 (C=N str.); 759 (C-S str.); 650 (C-Cl str.); 13C NMR (ppm): 113.2 (C11, styryl group attached to 4-quinazolinone ring); 126.4 (C8, 4-quinazolinone ring); 129.3 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.9 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring; 133.7 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.7 (C6, 4-quinazolinone ring); 126.1 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 129.6 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.4 (C5, 4-quinazolinone ring); 133.8 (C7, 4-quinazolinone ring); 135.3 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.5 (C12, styryl group attached to 4-quinazolinone ring); 147.4 (phenyl ring attached to 1,3,4 thiadiazole ring; 120.1 (C10, 4-quinazolinone ring); 158.4 (C2, 4-quinazolinone ring) 160.6 (C4, 4-quinazolinone ring). FAB Mass (m/z): 506 (Quassi-molecular ion peak).

SB-5: *(E)*-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}BrClN_5OS$; Molecular weight: 550.86; TLC (Rf value): 0.61; IR (cm-1): 3211 (C-H str.); 774 (C-H def (oop); 1701 (C=O str.); 1596 (C=C str.); 2896 (C-H str.); 3060(C-H str.); 1447(C-H def.); 1470 (C-C str.); 1637 (C=C str.); 1316 (C-N str.); 1530 (C=N str.); 719 (C-S str.); 650 (C-Cl str.); 570 (C-Br str.); 13C NMR (ppm): 113.2 (C11, styryl group attached to 4-quinazolinone ring); 126.4 (C8, 4-quinazolinone ring); 129.0 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.5 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 133.5 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.7 (C6, 4-quinazolinone ring; 115.1 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 132.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.4 (C5, 4-quinazolinone ring); 133.8 (C7, 4-quinazolinone ring); 135.3 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.5 (C12, styryl group attached to 4-quinazolinone ring); 148.3 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.1 (C10, 4-quinazolinone ring;158.4 (C2, 4-quinazolinone ring ; 160.6 (C4, 4-quinazolinone ring). FAB Mass (m/z): 551 (Quassi-molecular ion peak)

SB-6: *(E)*-3-(5-(((4-nitrophenylamino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chloro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}ClN_6O_3S$; Molecular weight: 516.96; TLC (Rf value): 0.61; IR (cm-1): 3074 (C-H str.); 718 (C-H def (oop);1734 (C=O str.); 1580 (N=O str.); 1350 (N-O str.); 1596 (C=C str.); 1542 (C-Cl str.); 2944 (C-H str.); 3020 (C-H str.); 1380 (C-H def); 1456 (C-C str.); 1634 (C=C str.);

1239 (C-N str.); 658 (C-S str.). 13C NMR (ppm): 113.2 (C11, styryl group attached to 4-quinazolinone ring); 126.4 (C8, 4-quinazolinone ring): 128.4 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.9 (C9, & C12, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 133.5 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 129.1 (C6, 4-quinazolinone ring);136.3 (C15, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 129.6 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.3 (C5, 4-quinazolinone ring); 133.4 (C7, 4-quinazolinone ring);135.1 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.2 (C12, styryl group attached to 4-quinazolinone ring); 155.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.2 (C10, 4-quinazolinone ring); 158.6 (C2, 4-quinazolinone ring);160.3 (C4, 4-quinazolinone ring). FAB Mass (m/z): 517 (Quassi-molecular ion peak).

SB-7: *(E)*-3-(5-(((4-fluorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chloro styryl)quinazolin-4 (3H)-one

Molecular formula: $C_{25}H_{17}ClFN_5OS$; Molecular weight: 489.95; TLC (Rf value): 0.61; IR (cm-1): 3125 (C-H str.); 808 (C-H def (oop); 1700 (C=O str.); 1590 (C=C str.); 533 (C-Cl str.); 2933 (C-H str.); 3050 (C-H str.); 1450 (C-H def); 1570 (C-C str.); 1630 (C=C str.); 1348 (C-N str.); 1560 (C=N str.); 575 (C-S str.); 1210 (C-Br str.); 1320 (C-F str.); 13C NMR (ppm): 113.3 (C11, styryl group attached to 4-quinazolinone ring); 126.2 (C8, 4-quinazolinone ring); 128.5 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 118.9 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.8 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.9 (C6, 4-quinazolinone ring); 155.2 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 116.3 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.3 (C5, 4-quinazolinone ring); 133.7 (C7, 4-quinazolinone ring); 135.2 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.5 (C12, styryl group attached to 4-quinazolinone ring); 144.9 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.5 (C10, 4-quinazolinone ring); 158.2 (C2, 4-quinazolinone ring); 160.1 (C4, 4-quinazolinone ring); FAB Mass (m/z): 489 (Quassi-molecular ion peak).

SB-8: *(E)*-3-(5-(((4-methylphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chloro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}ClN_5OS$; Molecular weight: 485.99; TLC (Rf value): 0.61; IR (cm-1): 3092 C-H str. Aromatic ring; 758 C-H def (oop); 1708 C=O str; 1578 (C=C str.); 1096 (C-Cl str.); 2841 (C-H str.); 3008 (C-H str.); 1442 (C-H def); 1466 (C-C str.); 1608 (C=C str.); 1278 (C-N str.); 1505 (C=N str.); 620 (C-S str.); 720 (C-Cl str.); 13C NMR (ppm); 113.3 (C11, styryl group attached to 4-quinazolinone ring); 126.2 (C8, 4-quinazolinone ring); 128.4 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 113.7 (C9, & C13, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.5 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.7 (C6, 4-quinazolinone ring); 129.6 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 129.8 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.2 (C5, 4-quinazolinone ring); 133.7 (C7, 4-quinazolinone ring); 135.2 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.5 (C12, styryl group attached to 4-quinazolinone ring); 146.4 (phenyl ring attached to 1,3,4 thiadiazole ring; 120.1 (C10, 4-quinazolinone ring); 158.3 (C2, 4-quinazolinone ring; 160.2 (C4, 4-quinazolinone ring); 21.3 (CH_3, phenyl ring). FAB Mass (m/z): 486 (Quassi-molecular ion peak).

SB-9: *(E)*-3-(5-(((4-ethylphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chloro styryl)quinazolin-4(3H)-one

Molecular formula: $C_{27}H_{22}ClN_5OS$; Molecular weight: 500.01; TLC (Rf value): 0.61; IR (KBr, cm-1): 3159 (C-H str.); 761 (C-H def (oop)); 1701(C=O str.); 1562 (C=C str.); 2907 (C-H str.); 3010 (C-H str.); 1375 (C-H def); 1439 (C-C str.); 1693 (C=C str.); 1316 (C-N str.); 761 (C-S str.); 650 (C-Cl str.); 13C NMR (ppm): 113.3 (C11, styryl group attached to 4-quinazolinone ring); 126.2(C8, 4-quinazolinone ring); 128.4 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 113.4 (C9 & C13, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.1 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.4 (C6, 4-quinazolinone ring); 136.7 (C15, C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 128.5 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.2 (C5, 4-quinazolinone ring); 133.5 (C7, 4-quinazolinone ring); 135.5 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.7 (C12, styryl group attached to 4-quinazolinone ring); 146.5 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.2 (C10,4-quinazolinone ring; 158.3 (C2, 4-quinazolinone ring); 160.6 (C4, 4-quinazolinone ring); 28.2 CH_2 (phenyl ring attached to 1,3,4-thiadiazole ring); 14.5 (CH_3 phenyl ring attached to 1,3,4-thiadiazole ring). FAB Mass (m/z): 500 (Quassi-molecular ion peak).

SB-10: *(E)*-3-(5-(((4-methoxyphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl)quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}ClN_5O_2S$; Molecular weight: 501.99; TLC (Rf value): 0.61; IR (KBr, cm-1): 3157 (C-H str.); 819 (C-H def (oop); 1703 (C=O str.); 1080 (C-O-C str.); 1559 (C=C str.); 2909 (C-H str.); 3050 (C-H str.); 1417 (C-H def); 1450 (C-C str.); 1609 (C=C str.); 1252 (C-N str.); 1519 (C=N str.); 615 (C-S str.); 650 (C-Cl str.) 13C NMR (ppm): 113.1 (C11, styryl group attached to 4-quinazolinone ring); 126.2 (C8, 4-quinazolinone ring); 128.3 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 113.3 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 127.6 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6, 4-quinazolinone ring); 151.7 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring; 115.1 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.5 (C5, 4-quinazolinone ring; 133.4 (C7, 4-quinazolinone ring); 135.7 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.8 (C12, styryl group attached to 4-quinazolinone ring); 141.6 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.3 (C10, 4-quinazolinone ring); 158.6 (C2, 4-quinazolinone ring); 160.8 (C4, 4-quinazolinone ring; 55.8 (OCH_3, phenyl ring attached to 1,3,4-thiadiazole ring). FAB Mass (m/z): 501 (Quassi-molecular ion peak).

SB-11: *(E)*-3-(5-(((4-ethoxyphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chloro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{27}H_{22}ClN_5O_2S$; Molecular weight: 516.01; TLC (Rf value): 0.61; IR (KBr, cm^{-1}): 3159 (C-H str); 822 (C-H def (oop); 1692(C=O str.); 1210 (C-O-C str.); 1562 (C=C str.); 2907 (C-H str.); 3031 (C-H str.); 1438 (C-H def); 1450 (C-C str.); 1650 (C=C str.); 1313 (C-N str.); 1520

(C=N str.); 670 (C-S str.); 720 (C-Cl str.); 13 CNMR (ppm): 113.1 (C11 due to styryl group attached to 4-quinazolinone ring); 126.3 (C8 4-quinazolinone ring); 128.4 (C14 & C18 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 112.9 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring; 127.3 (C16 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 127.5 (C6 due to 4-quinazolinone ring); 150.4 (C15 and C17 phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 115.2 (C & C due to phenyl ring attached to 1,3,4 thiadiazole ring);126.1 (C5 due to 4-quinazolinone ring); 133.3 (C7 due to 4-quinazolinone ring); 135.3 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.6 (C12 due to styryl group attached to 4-quinazolinone ring); 140.9 (C due to phenyl ring attached to 1,3,4 thiadiazole ring); 120.1 (C10 due to 4-quinazolinone ring); 158.2 (C2 due to 4-quinazolinone ring); 160.5 (C4 due to 4-quinazolinone ring); 58.4 (CH_2 phenyl ring attached to 1,3,4-thiadiazole ring); 14.8 (CH_3 phenyl ring attached to 1,3,4-thiadiazole ring). FAB Mass (m/z): 516 Quassi-molecular ion peak.

SB-12: *(E)*-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}ClN_6O_3S$; Molecular weight: 516.96; TLC (Rf value): 0.61; IR (KBr, cm-1): 3160 (C-H str.); 760 (C-H def (oop); 1693(C=O str.); 1590(C=C str.); 2902 (C-H str.); 3020 C-H str.); 1373 (C-H def); 1437 (C-C str.); 1580 (N=O str.); 1370 (N-O str.); 1610 (C=C str.); 1316 (C-N str.) 1568 (C=N str.); 667 (C-S str.); 499 (C-Cl str.). 13C NMR (ppm): 113.1 (C11, styryl group attached to 4-quinazolinone ring); 126.3 (C8 due to 4-quinazolinone ring); 129.0 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.9 (C9, C & C due to 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 147.1 (C16 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6 due to 4-quinazolinone ring); 123.8 (C15 and C17, C due to phenyl substituted styryl group attached to 4-quinazolinone ring &phenyl ring attached to 1,3,4-thiadiazole ring); 129.6 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.1 (C5 due to 4-quinazolinone ring); 133.7 (C7 due to 4-quinazolinone ring); 141.3 (C13 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 138.2 (C12 due to styryl group attached to 4-quinazolinone ring); 147.4 (phenyl ring attached to 1,3,4 thiadiazole ring);120.8 (C10 due to 4-quinazolinone ring); 158.2 (C2, 4-quinazolinone ring); 160.3 (C4, 4-quinazolinone ring). FAB Mass (m/z): 517 Quassi-molecular ion peak.

SB-13: (E)-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}BrN_6O_3S$; Molecular weight: 561.41; TLC (Rf value): 0.61; IR (KBr, cm-1): 3162.6 (C-H str.); 824.6 (C-H def (oop)); 1695.3 (C=O str.); 1570 (C=C str.); 2914 (C-H str.); 3080 (C-H str.); 1580 (N=0 str.); 1370 (N-O str.); 1368 (C-H def); 1437 (C-C str.); 1610 (C=C str.); 1254 (C-N str.); 1530 (C=N str.); 618 (C-S str.); 560 (C-Cl str.) 13C NMR (ppm): 113.3 (C11, styryl group attached to 4-quinazolinone ring); 126.2 (C8, 4-quinazolinone ring); 129.2 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.5(C9 & C13, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 147.3 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.1 (C6, 4-quinazolinone ring); 115.1 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 132.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.3 (C5, 4-quinazolinone ring); 133.5 (C7, 4-quinazolinone ring); 141.1 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.4 (C12, styryl group attached to 4-quinazolinone ring); 148.3 (C due to phenyl ring attached to 1,3,4 thiadiazole ring; 120.3 (C10, 4-quinazolinone ring); 158.4 (C2, 4-quinazolinone ring); 160.1 (C4, 4-quinazolinone ring). FAB Mass (m/z): 561 (Quassi-molecular ion peak).

SB-14: *(E)*-3-(5-(((4-nitrophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitro styryl)quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}N_7O_5S$; Molecular weight: 527.51; TLC (Rf value): 0.61; IR (KBr, cm-1): 3148 (C-H str.); 824 (C-H def (oop); 1708 (C=O str.); 1556 (C=C str.); 1560 (N=0 str.); 1320 (N-O str.); 2893.2 (C-H str.); 3029(C-H str.); 1436 (C-H def); 1420 (C-C str.); 1600 (C=C str.); 1311 (C-N str.); 1520 (C=N str.); 633 (C-S str.). 13C NMR (ppm): 113.1 (C11, styryl group attached to 4-quinazolinone ring); 126.3 (C8, 4-quinazolinone ring); 129.2 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.4 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 147.4 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6, 4-quinazolinone ring); 136.3 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 127.5 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.3 (C5, 4-quinazolinone ring); 133.7(C7, 4-quinazolinone ring); 141.1 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.3 (C12, styryl group attached to 4-quinazolinone ring); 155.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.5 (C10, 4-quinazolinone ring); 158.4 (C2, 4-quinazolinone ring); 160.2 (C4, 4-quinazolinone ring. FAB Mass (m/z): 527 (Quassi-molecular ion peak).

SB-15: *(E)*-3-(5-(((4-fluorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitro styryl) quinazolin-4(3H)-one

Molecular formula: $C_{25}H_{17}FN_6O_3S$; Molecular weight: 500.50; TLC (Rf value): 0.61; IR (KBr, cm-1): 3161 (C-H str.); 820 (C-H def (oop); 1692 (C=O str); 1564 (C=Cstr.);1580(N=0 str.); 1370(N-O str.); 2903 (C-H str.) 3032 (C-H str.); 1376(C-H def); 1438(C-C str.); 1610 (C=C str.); 1315 (C-N str.); 1530 (C=N str.); 608 (C-S str.); 1320 (C-F str.).13C NMR (ppm): 113.3 (C11, styryl group attached to 4-quinazolinone ring 126.5 (C8, 4-quinazolinone ring); 129.0 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 118.9 (C9 & C13, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 147.1 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.1 (C6, 4-quinazolinone ring); 123.4 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring. 116.3 (phenyl ring attached to 1,3,4 thiadiazole ring; 126.3 (C5, 4-quinazolinone ring); 133.8 (C7, 4-quinazolinone ring; 141.1 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.6 (C12, styryl group attached to 4-quinazolinone ring); 144.9 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.4 (C10, 4-quinazolinone ring); 158.3 (C2, 4-quinazolinone ring); 160.1 (C4, 4-quinazolinone ring). FAB Mass (m/z): 500 (Quassi-molecular ion peak).

SB-16: (E)-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methyl styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}ClN_5OS$; Molecular weight: 485.99; TLC (Rf value): 0.61; IR (KBr, cm-1): 3117.3 (C-H str.); 752.8 C-H def (oop); 1689.5 (C=O str.); 1594 (C=C str.); 2917 (C-H str.); 3020 (C-H str.); 1448.3 (C-H def); 1610(C=C str.); 1311(C-N str.); 1519(C=N str.); 645 (C-S str.); 464.4 (C-Cl str.). 13C NMR (ppm) 113.4 (C11, styryl group attached to 4-

quinazolinone ring); 127.3 (C8, 4-quinazolinone ring); 128.5 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.4 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 137.6 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.1 (C6, 4-quinazolinone ring); 128.9 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 129.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.5 (C5, 4-quinazolinone ring); 133.4 (C7, 4-quinazolinone ring); 132.2 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.4 (C12, styryl group attached to 4-quinazolinone ring); 147.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.3 (C10, 4-quinazolinone ring); 158.1 (C2, 4-quinazolinone ring); 160.7 (C4, 4-quinazolinone ring); 21.3 (CH3; phenyl substituted styryl group attached to 4-quinazolinone ring). FAB Mass (m/z): 486 Quassi-molecular ion peak.

SB-17: *(E)*-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methyl styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}BrN_5OS$; Molecular weight: 530.44; TLC (Rf value)0.61; IR (KBr, cm-1): 3163.3 (C-H str.); 822 (C-H def (oop); 1691 (C=O str.); 1568.1 (C=C str.); 2911 (C-H str.); 3032 (C-H str.); 1374.6 (C-H def); 1438.2 (C-C str); 1600 (C=C str.); 1313.7 (C-N str.); 1520 (C=N str.); 670 (C-S str.); 502.5 (C-Br str.). 13C NMR (ppm): 113.3 (C11, styryl group attached to 4-quinazolinone ring); 127.5 (C8, 4-quinazolinone ring); 128.3 (C14 & C18, phenyl substituted styryl group attached to 4-quinazolinone ring); 114.5 (C9 & C13, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 137.5 (C16, phenyl substituted styryl group attached to 4-quinazolinone ring); 127.6 (C6, 4-quinazolinone ring); 118.7 (C15 and C17, phenyl substituted styryl group attached to 4-quinazolinone ring &enyl ring attached to 1,3,4-thiadiazole ring); 132.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.2 (C5, 4-quinazolinone ring); 133.1 (C7, 4-quinazolinone ring); 132.1 (C13, phenyl substituted styryl group attached to 4-quinazolinone ring); 138.2 (C12, styryl group attached to 4-quinazolinone ring); 148.5 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.1 (C10, 4-quinazolinone ring); 158.7 (C2, 4-quinazolinone ring; 160.2 (C4, 4-quinazolinone ring); 21.1 (CH3 phenyl substituted styryl group attached to 4-quinazolinone ring). FAB Mass (m/z):530 Quassi-molecular ion peak (M+H)+

SB-18: *(E)*-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxy styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}ClN_5O_2S$; Molecular weight: 501.99; TLC (Rf value): 0.61; IR (KBr, cm-1): 3166.3 (C-H str.); 826.4(C-H def (oop); 1690.1 (C=O str.); 1579 (C=C str.); 2918 (C-H str.); 3020 (C-H str.); 1369.7(C-H def); 1439.1 (C-C str.); 1610 (C=C str.); 1325 (C-N str.); 1540(C=N str.); 666 (C-S str.); 495.6 (C-Cl str.). 13C NMR (ppm): 113.3 (C11 due to styryl group attached to 4-quinazolinone ring); 127.1 C8 due to 4-quinazolinone ring); 130 (C14 & C18 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 114.9 (C9, 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring; 159 (C16 due to phenyl substituted styryl group attached to 4-qinazolinone ring); 127.4 (C6, 4-quinazolinone ring); 114 (C15, C17 phenyl substituted styryl group attached to 4-quinazolinone ring &enyl ring attached to 1,3,4-thiadiazole ring); 129.6 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.2 (C5 due to 4-quinazolinone ring); 133.5 (C7 due to 4-quinazolinone ring); 127.5(C13 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 138.3 (C12 due to styryl group attached to 4-quinazolinone ring); 147.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.1(C10, 4-quinazolinone ring); 158.3 (C2 due to 4-quinazolinone ring); 160.4 (C4 due to 4-quinazolinone ring); 21.3 (OCH3); phenyl substituted styryl group attached to 4-quinazolinone ring. FAB Mass (m/z): 502 (Quassi-molecular ion peak).

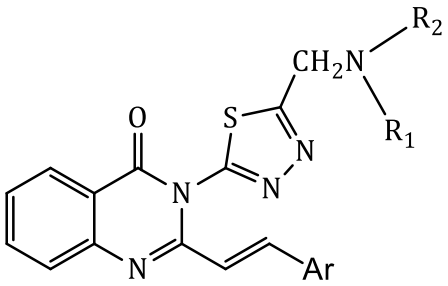
SB-19: (E)-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxy styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}BrN_5O_2S$; Molecular weight: 546.44; TLC (Rf value): 0.61; IR (KBr, cm-1): 3163 C-H str; 824 (C-H def (oop); 1695 (C=O str.); 1565 (C=C str.); 2909 (C-H str.); 3050 (C-H str.); 1368 (C-H def); 1440(C-C str.); 1600(C=C str.); 1322 (C-N str.); 1520 (C=N str.); 619(C-S str.); 720 (C-Br str.). 13C NMR (ppm) 113.3 (C11 due to styryl group attached to 4-quinazolinone ring) 127.5 C8 due to 4-quinazolinone ring); 130.3 (C14 & C18 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 114.5 (C9, C & C due to 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 159.6 (C16 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 127.3 (C6 due to 4-quinazolinone ring); 115.1 (C15 and C17, C due to phenyl substituted styryl group attached to 4-quinazolinone ring &phenyl ring attached to 1,3,4-thiadiazole ring); 132.4 (phenyl ring attached to 1,3,4 thiadiazole ring); 126.6 (C5 due to 4-quinazolinone ring); 133.1(C7 due to 4-quinazolinone ring); 127.6 (C13 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 138.7 (C12 due to styryl group attached to 4-quinazolinone ring); 148.3(phenyl ring attached to 1,3,4 thiadiazole ring); 120.3 (C10 due to 4-quinazolinone ring); 158 (C2 due to 4-quinazolinone ring); 160.7 (C4 due to 4-quinazolinone ring); 55.8OCH3; phenyl substituted styryl group attached to 4-quinazolinone ring); FAB Mass (m/z): 546 (Quassi-molecular ion peak).

SB-20: *(E)*-3-(5-(((4-fluorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxy styryl) quinazolin-4(3H)-one

Molecular formula: $C_{26}H_{20}FN_5O_2S$; Molecular weight: 485.33; IR (KBr, cm-1): 3147 (C-H str.); 823 (C-H def) (oop); 1706 (C=O str.); 1500 (C=C str.); 2807(C-H str.); 3020 (C-H str.); 1377(C-H def); 1434 (C-C str.); 1600`(C=C str.); 1311(C-N str.); 1558 (C=N str.); 681 (C-S str.); 710 (C-Br str.); 13C NMR (ppm): 113.3 (C11 due to styryl group attached to 4-quinazolinone ring); 127.3 (C8 due to 4-quinazolinone ring); 130.1 (C14 & C18 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 118.9(C9, C & C due to 4-quinazolinone ring & phenyl ring attached to 1,3,4 thiadiazole ring); 159.8 (C16 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 127.1 (C6 due to 4-quinazolinone ring); 114.2 (C15 and C17due to phenyl substituted styryl group attached to 4-quinazolinone ring & phenyl ring attached to 1,3,4-thiadiazole ring); 116.3 (phenyl ring thiadiazole ring); 126.2 (C5 due to 4-quinazolinone ring); 133.5 (C7 due to 4-quinazolinone ring); 127.3(C13 due to phenyl substituted styryl group attached to 4-quinazolinone ring); 138.3 (C12 due to styryl group attached to 4-quinazolinone ring); 144.9 (phenyl ring attached to 1,3,4 thiadiazole ring); 120.1 (C10 due to 4-quinazolinone ring); 158.4 (C2 due to 4-quinazolinone ring); 160.2 (C4 due to 4-quinazolinone ring); 55.5 (OCH3; phenyl substituted styryl group attached to 4-quinazolinone ring). FAB Mass (m/z): 485 (Quassi-molecular ion peak).

Table 1: List of synthesized compounds



Code	Chemical name	Ar	R_1	R_2
SB-1	(E)-3-(5-(((4-chlorophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one	$-C_6H_5$	$-C_6H_5Cl$	H
SB-2	(E)-3-(5-(((4-bromophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one	$-C_6H_5$	$-C6H_5Br$	H
SB-3	(E)-3-(5-(((4-nitrophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-styrylquinazolin-4(3H)-one	$-C_6H_5$	$-C_6H_5NO_2$	H
SB-4	(E)-3-(5-(((4-chlorophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5Cl$	H
SB-5	(E)-3-(5-(((4-bromophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5Br$	H
SB-6	(E)-3-(5-(((4-nitrophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl)quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5NO_2$	H
SB-7	(E)-3-(5-(((4-fluorophenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5F$	H
SB-8	(E)-3-(5-(((4-methylphenyl) amino) methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5CH_3$	H
SB-9	(E)-3-(5-(((4-ethylphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl)quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5C_2H_5$	H
SB-10	(E)-3-(5-(((4-methoxyphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5OCH_3$	H
SB-11	(E)-3-(5-(((4-ethoxyphenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-chlorostyryl) quinazolin-4(3H)-one	$-C_6H_5Cl$	$-C_6H_5OC_2H_5$	H
SB-12	(E)-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitrostyryl) quinazolin-4(3H)-one	$-C_6H_5NO_2$	$-C_6H_5Cl$	H
SB-13	(E)-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitrostyryl) quinazolin-4(3H)-one	$-C_6H_5NO_2$	$-C_6H_5Br$	H
SB-14	(E)-3-(5-(((4-nitrophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitrostyryl)quinazolin-4(3H)-one	$-C_6H_5NO_2$	$-C_6H_5NO_2$	H
SB-15	(E)-3-(5-(((4-fluorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-nitrostyryl) quinazolin-4(3H)-one	$-C_6H_5NO_2$	$-C_6H_5F$	H
SB-16	(E)-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methylstyryl) quinazolin-4(3H)-one	$-C_6H_5CH_3$	$-C_6H_5Cl$	H
SB-17	(E)-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methylstyryl) quinazolin-4(3H)-one	$-C_6H_5CH_3$	$-C_6H_5Br$	H
SB-18	(E)-3-(5-(((4-chlorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxystyryl) quinazolin-4(3H)-one	$-C_6H_5OCH_3$	$-C_6H_5Cl$	H
SB-19	(E)-3-(5-(((4-bromophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxystyryl) quinazolin-4(3H)-one	$-C_6H_5OCH_3$	$-C_6H_5Br$	H
SB-20	(E)-3-(5-(((4-fluorophenyl)amino)methyl)-1,3,4-thiadiazol-2-yl)-2-(4-methoxystyryl) quinazolin-4(3H)-one	$-C_6H_5OCH_3$	$-C_6H_5F$	H

Pharmacological evaluation:

Animals:

Albino mice of either sex (20-30 g) were used as experimental animals for anticonvulsant. Animals were kept in wire-mesh cages in a restricted-access room for one week before the experiments. Twelve days wash period was allowed prior to start of next study. The animals were fed with standard lab pellets and purified water. Prior to the ad libitum experiments animals were fasted for 12 h. All the test compounds were suspended in 0.5% w/v methyl cellulose. In each of the experiment a control group was made which received the vehicle (0.5% w/v methyl cellulose). All the experiments were carried out according to protocols approved by the Institutional Animal Ethical Committee, Baba Loknath Institute of Pharmacy Sciences and Research Centre, Sagar (Committee registration number CPCSEA/April/2018/01 and Letter reference number is Animal ethical committee BLIPS/IAEC/2018/01 dated 19/04/2018).

Table 2: Physico chemical properties of the synthesized compounds

S. No.	Code	Percent Yield	Melting point (°C)	Mol. Formula	Mol. Weight
1.	SB-1	62	248-250	$C_{25}H_{18}ClN_5OS$	471.96
2.	SB-2	75	278-280	$C_{25}H_{18}BrN_5OS$	516.41
3.	SB-3	68	282-284	$C_{25}H_{18}N_6O_3S$	482.51
4.	SB-4	69	246-248	$C_{25}H_{17}Cl_2N_5OS$	506.41
5.	SB-5	64	262-264	$C_{25}H_{17}BrClN_5OS$	550.86
6.	SB-6	66	289-291	$C_{25}H_{17}ClN_6O_3S$	516.96
7.	SB-7	68	>300*	$C_{25}H_{17}ClFN_5OS$	489.95
8.	SB-8	78	244-245	$C_{26}H_{20}ClN_5OS$	485.99
9.	SB-9	64	212-214	$C_{27}H_{22}ClN_5OS$	500.01
10.	SB-10	63	243-245	$C_{26}H_{20}ClN_5O_2S$	501.99
11.	SB-11	57	>300*	$C_{27}H_{22}ClN_5O_2S$	516.01
12.	SB-12	66	276-278	$C_{25}H_{17}ClN_6O_3S$	516.96
13.	SB-13	76	215-217	$C_{25}H_{17}BrN_6O_3S$	561.41
14.	SB-14	63	282-284	$C_{25}H_{17}N_7O_5S$	527.51
15.	SB-15	68	>300*	$C_{25}H_{17}FN_6O_3S$	500.50
16.	SB-16	71	286-288	$C_{26}H_{20}ClN_5OS$	485.99
17.	SB-17	64	289-291	$C_{26}H_{20}BrN_5OS$	530.44
18.	SB-18	58	297-299	$C_{26}H_{20}ClN_5O_2S$	501.99
19.	SB-19	45	244-245	$C_{26}H_{20}BrN_5O_2S$	546.44
20.	SB-20	60	272-274	$C_{26}H_{20}FN_5O_2S$	485.33

* Melting point at their decomposition.

Pharmacological evaluation of Synthesized compounds

Anticonvulsant evaluation of(E)-3-(5-(substituted aminomethyl)-1,3,4-thiadiazol-2-yl)-2-styryl quinazolin-4(3H)-one was done by the anticonvulsant drug development (ADD) program protocol. The profile of anticonvulsant activity was established after injection by the i.p. MES pattern test[20]. Subcutaneous pentylentetrazol (sc-PTZ)[21] and subcutaneous pentylenetetrazole (scPTZ) seizure threshold test. Minimal motor impairment was measured by the roto-rod (neurotoxicity, NT) test using doses of 30, 100 and 300 mg/kg at two different time intervals[22].

Study protocol

Healthy young swiss albino mice weighing between 20-30 gm were used. Before the administration of the test samples, standard and control, the mice were first tested by giving current of 50 mA for 0.2 seconds using electro convulsometer. Those animals which showed characteristic course of convulsions were selected for experiment. The selected animals were divided into three groups of six animals each. After 1 hour of administration of the standard drug (phenytoin) and the test samples the electric shock was induced. The different phases of convulsions i.e. tonic flexion, tonic extensor, clonic convulsion, stupor and recovery time or death were observed. The time (seconds) spent by the animals in each phase was recorded. The percentage protection provided by the standard and test samples was calculated. The scPTZ test was performed by administering PTZ dissolved in 0.9% NaCl solution in posterior midline of the animals. A minimal time of 30 min consequent to administration of PTZ was used for seizure detection. Protection was referred to as the failure to observe an episode of clonic convulsions of least 5s duration during this time period.

Anticonvulsant screening

Initially all the compounds were administered i.p. in a volume of 0.01 ml/gm body weight for mice at doses of 30, 100, 300 mg/kg to one to six animals. Activity was established using the MES, scPTZ tests and these data are presented in table 3.

Neurotoxicity screening

Minimal motor impairment was measured in mice by the roto-rod test. The mice were trained to stay on an accelerating roto-rod thatrotates at six revolutions per minute. The rod diameter was 3.2cm. Neurotoxicity was indicated by the inability of the animal to maintain equilibrium on the rod for at least 1 min in each of the three trials. The data was presented in table 3.

RESULTS AND DISCUSSION

Spectral analysis

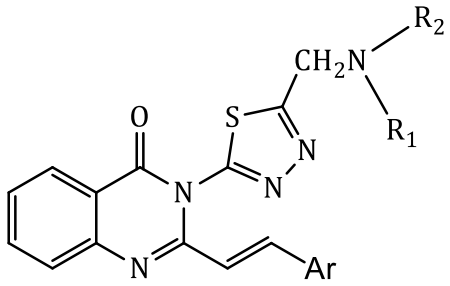
The structures of the synthesized compounds (SB-1 to SB-20) were characterized by IR, 13C NMR spectra, and mass spectroscopy. The infrared spectra of the synthesized compounds showed characteristic absorption band between 1680-1700 cm^{-1} due to C=O str (quinazolinone ring); between 1600-1650 cm^{-1} due to C=C str. (vinyl group); between 1520-1560 cm^{-1} due to C=N str. (1,3,4-thiadiazole and quinazolinone ring), between 1210 to 1250 due to C-N str of quinazolinone ring; between 550-780 cm^{-1} due to C-S str. (1,3,4-thiadiazole ring); 1090 cm^{-1} due to Ar-Cl str. and between 400-500 cm^{-1} due to aryl C-Cl in chloro containing compounds. In 13C-NMR spectra of the synthesized compounds C-2 and C-4 of quinazolinone were observed between 160-165 and 167—168 (δ, ppm) respectively, C-11 and (C-5, C-6, C-7, C-8, C-9, C-10, C-12, C-13, C-14 & C18, C16, C15 & C17, C16) of quinazolinone were observed between 112-115 and 122.1-147.8 (δ, ppm) respectively. Methoxy and methyl carbons were observed at 55.4 and 21 ppm. In addition peaks at δ 77.0 ppm for $CDCl_3$ (solvent) and at δ 39.0 ppm for DMSO-d6 (solvent) were also observed in respective cases. Elemental analysis of all synthesized compound were within the ±0.4% of the theoretical values. Generation of dense sooty flame and formation of oily layer after nitration of the compounds confirmed the presence of aromatic ring in all the synthesized compounds. In the FAB mass spectra two prominent peaks were observed.

Anticonvulsant activity

These synthesized compounds were screened for anticonvulsant activity. Anticonvulsant activity was

evaluated by maximal electroshock (MES), subcutaneous pentylene tetrazole (scPTZ) and neurotoxicity screens respectively. Initial anticonvulsant activity and neurotoxicity data for the quinazolinone analogs are reported in table 3, along with the literature data on phenytoin, carbamazepine (Flaherty *et al*., 1996; Dimmock *et al*., 1996). Only Nine compounds as shown below showed protection against MES convulsion at dose levels as mentioned against their names. Compounds SB-1, SB-6, SB-9, SB-12, SB-16 has shown the effect thirty minutes after administration of 30mg/kg of the drug (Table 3). In the ScPTZ model, only 8 compounds i.e. SB-3, SB-5, SB-8, SB-9, SB-10, SB-13, SB-17 and SB-18 showed protection of the convulsions but that too at the dose level of 300 mg/kg. Out of these compounds showing protection two compounds i.e. SB-10 and SB-19 failed to protect the convulsion after 4 hrs of administration of the drugs. Anticonvulsant effect (MES Test and scPTZ Test) of the synthesized compounds (SB-1 to SB-20) was depicted in Table 3.

Table 3: Anticonvulsant effect of the synthesized compounds (SB-1 to SB-20)



S. No.	Code No.	Ar	R_1	R_2	Minimum Active Dose (mg/kg)[a]				Neurotoxicity Dose (mg/kg)[b]	
					MES Test		scPTZ Test			
					0.5h	4h	0.5h	4h	0.5h	4h
1	SB-1	$-C_6H_5$	$-C_6H_5Cl$	H	30	-	-	-	-	-
2	SB-2	$-C_6H_5$	$-C6H_5Br$	H	-	-	-	-	-	-
3	SB-3	$-C_6H_5$	$-C_6H_5NO_2$	H	-	100	-	-	-	-
4	SB-4	$-C_6H_5Cl$	$-C_6H_5Cl$	H	100	100	-	-	-	-
5	SB-5	$-C_6H_5Cl$	$-C_6H_5Br$	H	-	100	-	-	-	-
6	SB-6	$-C_6H_5Cl$	$-C_6H_5NO_2$	H	30	100	-	-	-	-
7	SB-7	$-C_6H_5Cl$	$-C_6H_5F$	H	-	300	100	-	100	-
8	SB-8	$-C_6H_5Cl$	$-C_6H_5CH_3$	H	-	100	-	100	-	100
9	SB-9	$-C_6H_5Cl$	$-C_6H_5C_2H_5$	H	30	-	-	-	-	-
10	SB-10	$-C_6H_5Cl$	$-C_6H_5OCH_3$	H	100	300	-	300	-	-
11	SB-11	$-C_6H_5Cl$	$C_6H_5OC_2H_5$	H	-	300	-	-	-	-
12	SB-12	$-C_6H_5NO_2$	$-C_6H_5Cl$	H	30	100	-	-	-	-
13	SB-13	$-C_6H_5NO_2$	$-C_6H_5Br$	H	-	-	100	-	100	-
14	SB-14	$-C_6H_5NO_2$	$-C_6H_5NO_2$	H	-	-	-	300	-	-
15	SB-15	$-C_6H_5NO_2$	$-C_6H_5F$	H	-	100	300	-	300	-
16	SB-16	$-C_6H_5CH_3$	$-C_6H_5Cl$	H	30	300	-	-	-	-
17	SB-17	$-C_6H_5CH_3$	$-C_6H_5Br$	H	-	-	-	-	-	-
18	SB-18	$-C_6H_5OCH_3$	$-C_6H_5Cl$	H	-	-	-	-	-	-
19	SB-19	$-C_6H_5OCH_3$	$-C_6H_5Br$	H	100	-	100	-	-	-
20	SB-20	$-C_6H_5OCH_3$	$-C_6H_5F$	H	-	-	300	-	300	-
Phenytoin					30	30	-	-	100	100
Carbamazepine					30	100	100	300	100	300

[a]Dose in mg/kg at which bioactivity was observe in majority of the animals. The (-) sign indicates absence of protection of convulsion at the maximum dose administered i.e. 300 mg/kg. [b]Dose in mg/kg at which neurotoxicity was observed in majority of the animal the (-) sign indicate absence neurotoxicity at the maximum dose administered i.e. 300 mg/kg.

In the earlier reports it was highlighted that the presence of electron richatom/group attached at the para position of the aryl ring showed increased potency in the MES screen. All the synthesized compounds were active in MES screen for a long duration of time (after 4 h). SB-6, SB-12, SB-14 and SB-18 showed broad spectrum of anticonvulsant activity which is advantageous as compared to phenytoin. For broad spectrum the compounds should have electronegative substitution at least at either at R/Ar. Above mentioned compounds may be employed in both clonic-tonic (p) seizures and absence seizures (g). The most active compound of the series SB-1, SB-4, SB-6, SB-9, SB-12, SB-14, SB-14 and SB-18 (30 mg/kg i.p.; MES screen) contains un-substituted R/Ar site which is very unique feature of the present study. Almost all, except SB-1, have chloro group substitution on either position i.e R/Ar. In most of the cases Cl, and nitro group phenyl ring in position of the 1,3,4-thiadiazoles nucleus and Cl on phenyl ring of 4(3H)-quinazolinone has shown the potent activity. Maximum compounds did not produce protection against either type of method, the reason may be quick metabolism of the compounds due to presence of carbonyl group or breakdown of chain at 2 position. In nutshell lipophilicity type of substitution, is sensitive towards metabolism, size of the molecule and concept of affinity and activity play major role

in determining the anticonvulsant property of the synthesized molecules.

Neurotoxicity study

Except 05 compounds, all other compounds showed no neurotoxicity at a maximum dose level of 300mg/kg. Compounds SB-7, SB-8, and SB-13 only showed the neurotoxicity at 100 mg/kg. Rest of the compounds SB-15 and SB-20 i.e. showed neurotoxicity at 300 mg/kg dose level. About 89% compounds showed no neurotoxicity at a maximum dose level of 300mg/kg, which shows that they are non-toxic and safe used up to maximum dose levels. All the compounds were safe, nontoxic and no lethality was observed at the above mentioned dose levels.

CONCLUSION

This study concluded that these synthesized compounds have potential anticonvulsant activity and other pharmacological activity also prompted. Generally compounds possessing higher log p value showed higher decrease in locomotor activity. Bulkier compounds are more lipophilic and can cross blood brain barrier to exert their effect on CNS. Present study explored that substitution of 4(3H)-quinazolinone at second and third H position of 4(3H)-quinazolinone leads to the development of new chemical entities with potent sedative-hypnotic as compared to anticonvulsant activity.

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CONFLICTS OF INTEREST

The author declares no conflicts of interest

REFERENCES

1. Serban G, Stanasel O, Serban E, Bota S. 2-Amino-1,3,4-thiadiazole as a potential scaffold for promising antimicrobial agents. Drug Design Development and Therapy 2018; 12:1545-1566.
2. Rivas FM, Stables JP, Murphree L, Edwankar RV, Edwankar CR, Huang S, Jain HD, Zhou H, Majumder S, Sankar S, Roth BL, Ramerstorfer J, Furtmüller R, Sieghart W, Cook JM. Antiseizure activity of novel gamma-aminobutyric acid (A) receptor subtype-selective benzodiazepine analogues in mice and rat models. Journal of Medicinal Chemistry 2009; 52(7):1795-8.
3. Raja AS, Pandeya SN, PandaJ SS, Stables P. Synthesis and anticonvulsant evaluation of semicarbazones of acetophenone mannich bases. Pharmaceutical Chemistry Journal, 2007; 41(6):302–307.
4. Pester RJ, Cereghino JJ, Gladding GD, Hessie BJ, Kupferberg HJ, Seoville B, White B. Antiepileptic Drug Development Program. Cleveland Clinic Journal of Medicine 1984; 51: 293-305.
5. Narayana BN, Bhushan B, Madhavan V. Synthesis and Biological activity of some Novel 1,3,4-Thiadiazole derivatives. International Journal of ChemTech Research 2012; 4(1):74-78
6. Mohamed M. Abdel-Daim, Khaled Abo-EL-Sooud, LotfiAleya, Simona G. Bungău, Agnieszka Najda and Rohit Saluja. Alleviation of Drugs and Chemicals Toxicity: Biomedical Value of Antioxidants. Oxidative Medicine and Cellular Longevity. 2018;12;135-140
7. Mishra P, Jatav V, Kashaw SK. Some Novel 2-Methyl-3-(1′,3′,4′-thiadiazoyl)-4-(3H) quinazolinone with Anticonvulsant and CNS Depressant Activity. Chemical Information 2007; 38(34).
8. Mandhane SN, Aavula K, Rajamannar T. Timed pentylenetetrazol infusion test: a comparative analysis with s.c.PTZ and MES models of anticonvulsant screening in mice. Seizure. 2007; 16(7):636-44.
9. Kumar A, Kashaw V, Irchhiaya R, Kashaw SK, Shukla SK. Synthesis and biological screening of some novel 2-amino-5-aryl-1,3,4-oxadiazole analogues. Medicinal Chemistry Research 2010; 19:S46-S46.
10. Kashaw SK, Kashaw V, Mishra P, Jain NK. Design, synthesis and potential CNS activity of some novel 1-(4-substituted-phenyl)-3-(4-oxo-2-propyl-4Hquinazolin-3-yl)-urea. Arkivoc 2008; 14:17-26.
11. Kashaw SK, Kashaw V, Mishra P, Jain NK, Stables JP. Synthesis, anticonvulsant and CNS depressant activity of some new bioactive 1-(4-substituted-phenyl)-3-(4-oxo-2-phenyl/ethyl-4H-quinazolin-3-yl)-urea. European Journal of Medicinal Chemistry 2009; 44(11):4335-43.
12. Kashaw SK, Kashaw V, Mishra P, Jain NK, Stables JP. Design, synthesis, and potential CNS activity of some new bioactive 1-(4-substituted-phenyl)-3-(4-oxo-2-methyl-4H-quinazolin-3-yl)-urea. Medicinal Chemistry Research 2011; 20(6):738-45.
13. Kashaw SK, Gupta V, Kashaw V, P. Mishra, Stables JP, N.K. Jain. Medicinal Chemistry Research 2010; 19:250- 261.
14. Jatav V, Mishra P, Kashaw S, Stables JP. Synthesis and CNS depressant activity of some novel 3-[5-substituted 1, 3, 4-thiadiazole-2-yl]-2-styryl quinazoline-4 (3H)-ones. European Journal of Medicinal Chemistry 2008; 43(1):135-41.
15. Jatav V, Mishra P, Kashaw S, Stables JP. CNS depressant and anticonvulsant activities of some novel 3-[5-substituted 1, 3, 4-thiadiazole-2-yl]-2-styryl quinazoline-4 (3H)-ones. European Journal of Medicinal Chemistry 2008; 43(9):1945-54.
16. Jatav V, Kashaw S, Mishra P. Synthesis, antibacterial and antifungal activity of some novel 3-[5-(4-substituted phenyl) 1, 3, 4-thiadiazole-2-yl]-2-styryl quinazoline-4 (3H)-ones. Medicinal Chemistry Research 2008; 17(2-7):169-81.
17. Jatav V, Jain SK, Kashaw SK, Mishra P. Synthesis and anti-microbial activity of novel 2-Methyl-3-(1'3'4'-Thiadiazoyl)-4-(3h) Quinazolinones. Indian Journal of Pharmaceutical Sciences 2006; 68(3):360-363.
18. Gatadi S, Lakshmi TV, Nanduri S. 4(3H)-Quinazolinone derivatives: Promising antibacterial drug leads. European Journal of Medicinal Chemistry 2019; 170:157-172.
19. Chaudhari PS, Chitlange SS, Nanda RK. Synthesis and Biological Evaluation of Novel 2-(4-acetyl-3-methyl- 5-(arylamino) thiophen-2-yl)-3-arylquinazolin-4(3H)-one derivatives as potential anti-inflammatory and antioxidant agents. Medicinal Chemistry 2018; 17(2):102-114.
20. Al-Salahi R, Anouar EH, Marzouk M, Abuelizz HA. Anti-HAV evaluation and molecular docking of newly synthesized 3-benzyl(phenethyl)benzo[g]quinazolines. Bioorganic Medicinal Chemistry Letter 2019; 12: 134-139.
21. Akerbladh L, Chow SY, Odell LR, Larhed M. Synthesis of 4*H*-Benzo[*e*][*1,3*]oxazin-4-ones by carbonylation Cyclization Domino Reaction of *ortho*-Halo phenols and Cyanamide. Chemistry Open. 2017; 6(5):620-628.
22. Aggarwal N, Mishra P. Synthesis and evaluation of 4-substituted semicarbazones of levulinic acid for anticonvulsant activity. J Zhejiang University Science B, 2005; 6(7): 617-21.