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Research Article

# Synthesis, *In-vivo* Estimation of Novel 3-(6-Substituted Benzthiazole-2-yl/Oxadiazole-2-yl)-2-Substituted 4-Quinazolinones

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ABSTRACT

Even with all of the new and old therapies available, seizure management is infamously difficult. Scientists will continue to search for novel drugs with high selectivity and low central nervous system side effects in the hopes of finding the newest and most effective treatment. This work designates the synthesis of several 4-quinazolinones substituted with oxadiazoles and benzothiazoles through condensation of 2-substituted-4H-benzo(1,3)-oxazin-4-ones with substituted-oxadiazole and 6-substituted-benzothiazol-2-amine. The title compounds were confirmed through IR, $^{1}$H-NMR, and $^{13}$C-NMR analyses. The compounds were evaluated for anticonvulsant activity. Compounds A3, A4, A9, A5, A10 possess good potential. They reduced the extent of the tonic phase up to 1.3 to 1.1 seconds and stupor up to 100 to 51 seconds with the absence of the straub phase when compared to the control group.

## Introduction

Nearly 1 to 2% of the population suffers from epilepsy, the most common neurological illness worldwide.[1,2] Even though there are traditional AEDs available and a number of new anticonvulsants are being developed, epilepsy treatments are still insufficient since resistance develops after a protracted period of medication exposure. Antiepileptic drugs (AEDs) used are currently connected with adverse effects, dose-dependent toxicity, and long-lasting toxicity that affect almost every organ system. All AEDs now on the market are anticipated to have deleterious effects on behavior and cognition.[3] The use of polypharmacy in the treatment with an unclear history raises the possibility of adverse reactions and drug interactions. As a result, demand for safer, novel drugs with fewer side effects to treat epilepsy is always increasing.[4] It has been revealed that a number of oxadiazoles, thiadiazole, azetidinone, and thiazolidinone congeners may have antipsychotic, antidepressant, and anticonvulsant properties.[5] The methyl and benzodioxadiazole moieties improve the anticonvulsant effectiveness of benzyl-substituted entities with reduced seizure prevention.[6] 4-thiazolidinone is a new inhibitor of the bacterial enzyme Mur B, which is involved in the synthesis of peptidoglycan. Additionally, a number of N1-[4-(4-methoxybenzoylamino) benzoyl] compounds have anticonvulsant, antibacterial, and antifungal qualities. Methylene hydrazines with -N-2 substituting groups are also reported.[7] The biological activity of a few of the quinazolinone derivatives linked to an oxadiazole thioether was developed and assessed against phytopathogenic bacteria.[8] Studies of quinazolinone's structure-activity relationship (SAR) showed that the ring systems' positions two, six, and eight are important for various pharmacological actions. Furthermore, it has been proposed that activity may

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be raised by including additional heterocyclic moieties at position 3.[9] Under microwave irradiation, a new thiazole-dicarbonitrile derivative was synthesized using combination chemistry. This adaptable molecular platform can be used to synthesize a wide range of bioactive derivatives. A group of four Ser/Thr kinases selected for their significance in various regulatory processes, including Alzheimer's disease (AD), was used to assess the kinase inhibition of the final drugs. Thiazole-substituted quinazoline skeleton represents a possible source for the synthesis of new bioactive compounds in light of the findings of this first screening.[10] Several attempts have been made to develop quinazolinone compounds with good pharmacological activity.[11-13]

As the punishing adverse effects of available drugs make cure difficult, there is a considerable desire for new anticonvulsants. Antiepileptic medicines are currently only used to treat lower ictal epileptiform episodes. Thus, in medicinal chemistry, quinazolinone is regarded as the favored structure. It is one of the noteworthy heterocycle groupings with diverse biological characteristics. In continuation of our efforts[14-16] to develop new antiepileptic compounds, In this work, we propose to synthesize the coupling of quinazolinones conjugated with heterocycles, namely 1,3,4-oxadiazole and Aminobenzthiazole moieties, in order to achieve enhanced anticonvulsant action and generate lead compounds.

## Materials and Methods

Reagents of LR grade were utilized after being suitably dried and purified. Melting points are uncorrected. The yield of the compounds is stated after the in parenthesis. The solvent system used for TLC is chloroform: Ethyl acetate (30:70) if not specified separately. After being exposed to iodine vapors, the produced TLC plates were checked for colored spots. Here, individual characterization represents the $R_f$ values of purified substances. Single spot TLC was used to establish the compounds' purity using different solvent systems. All synthetic compounds' IR spectra were captured using a JASCO FTIR 4000 spectrophotometer with KBr as a diluent. The values are expressed in $cm^{-1}$. The Bruker Advance (400 MHz) was used to confirm the NMR ($\delta$ ppm) in DMSO-$d_6$ (PLATE 35-50). Mass analyses were done using a Varian Inc. 410 Prostar.

### Procedure for Synthesis

#### *Synthesis of 2-substituted-4H-benzoxazinone*

2-aminobenzoic acid (0.01 mol) was dissolved in sufficient pyridine. It was stirred continuously for 30 minutes on a magnetic stirrer at room temperature after the addition of aryl chloride (0.02 mol) isolated in the cold. Benzene: Methanol (9:1) was used as to check the product's purity by TLC (Scheme 1).

#### *Synthesis of 5-substituted-1, 3, 4-oxadiazole-2-amine*

The substituted semicarbazone (0.01 mol) and sodium acetate (0.02 mol) was measured and taken in an iodine flask and continuously stirred in sufficient glacial acetic acid. Bromine (0.7 mL) in glacial acetic acid (5 mL) was slowly added to the above solution, stirred, and continued for at least 1 hour, then isolated in cold (Scheme 2).

#### *Synthesis of 6-substitutedbenzothiazol-2-amine*

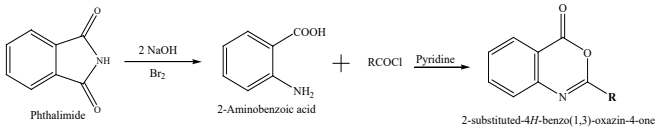
Substituted aniline and potassium thiocyanate (1:4 mixture) was prepared in 40 mL of glacial acetic acid (mixture 1). Cooled in the ice bath. A solution of bromine in glacial acetic acid (3 mL bromine in acetic acid up to 20 mL) was added to it. Stirred for 2 hours at ambient temperature and kept overnight at room temperature. The next day, water to the quenched mixture the slurry thus formed was heated a steam bath for 20 minutes and filtered hot. Cooled and neutralized with ammonia. Collected the precipitate formed (Scheme 3).

#### *Synthesis of 3-(5-(4-substitutedphenyl)-1,3,4-oxadiazol-2-yl-2-substitutedphenyquinazolin -4(3H)-one*

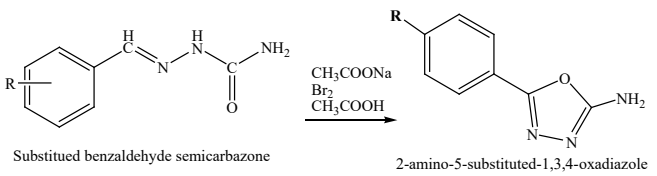
An equimolar combination of 2-amino-5-substituted-1,3,4-oxadiazole and a benzoxazole derivative in glacial acetic acid was refluxed over a water bath for 4 hours, isolated in the cold (Scheme 4).

#### *Synthesis of 3-(6-substituted benzothiazol-2-yl)-2-substitutedquinazolin-4[3H]-one*

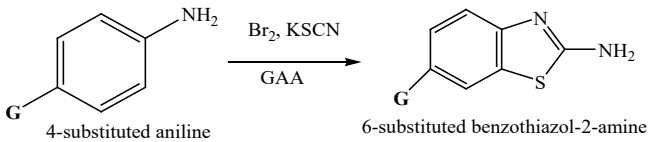
A blend of 6-substitutedbenzothiazol-2-amine and Benzoxazone (1 mmol each) derivative was allowed to



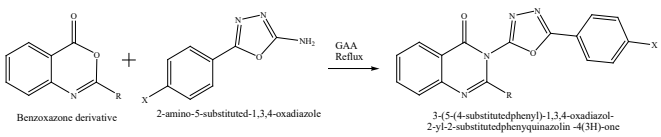

**Scheme 1:** R: Phenyl (B1); 4-chlorophenyl (B2)




**Scheme 2:** R: -Cl (O1); -$NO_2$ (O2), -OH (O3),




**Scheme 3:** G: -Cl (AB1); -$NO_2$ (AB2)




**Scheme 4:** A1-A4, A7, A9

reflux on water bath in glacial acetic acid (5 hours.), isolated in the cold (Scheme 5).

## Pharmacological Evaluation

### *Acute toxicity studies*

To determine $LD_{50}$ the OECD recommendations (425) were followed. For a duration of 14 days, every animal was monitored daily for the first 30 minutes following dosage, then every 4 hours on occasion, and for any indicators of toxicity and mortality.

### *Anticonvulsant activity*

The capability of the compounds to shield mice from convulsions caused by electroshock was used to measure their anticonvulsant activity. A shock was applied to the ear pinna electrodes. It is sufficient to induce typical tonic clinic convulsions with characteristic phases. Six male Swiss albino mice weighing between 22 and 30 g were used in each group. The anticonvulsant action of phenytoin at a dosage of 25 mg/kg was used as a reference. Compound solution or suspension in tween 80 was administered 30 minutes before to the application of electroshock. The protocol for the study was approved vide no. MET-IOP-IAEC/2019-20/02

# Results

## B1

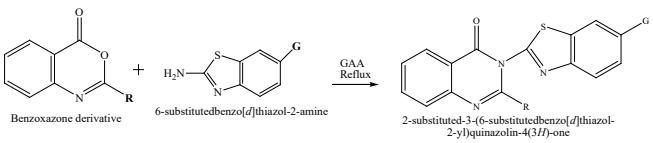
$C_{14}H_9NO_2$, Mol. wt: 223, MP (°C): 121–123, %yield: 75.01, Rf: 0.76, IR $\nu_{max}$: 3069 (C-H), 1741 (C=O), 1641 (-C=N), 1573 (Ar-C=C), 1062 (C-O). $^1$H-NMR: 7.2914–7.5329 (*m*, 4H, Ar), 7.6635–8.1479 (*m*, 5H). $^{13}$C-NMR: 122.2–135.3 (*m,*12C, Ar-C carbon), 156.1 (*s,* Imine), 159.5 (*s,* carbonyl). MS (m/z): 223.13.

## B2

$C_{14}H_8ClNO_2$, Mol wt.: 257, MP (°C): 190–192, %yield: 76.25, Rf: 0.80, IR $\nu_{max}$: 3071(C-H), 1739(carbonyl), 1631 (Imine), 1566 (Ar-), 1060 (C-O). $^1$H-NMR: 7.3321–7.5623(*m*, 4H, Ar), 7.7759–8.0799 (*m*, 4H, Ar). $^{13}$C-NMR: 127.4–136.6 (*m,* 12C, Ar-C carbon), 156.1 (*s,* 1C, C=N carbon), 160.1 (*s,* 1C, C=O carbon). MS (m/z): 256.13.

## O1

$C_8H_6ClN_3O$, Mol wt.: 195, MP (°C): 170–172, %yield: 80.14, Rf: 0.75, IR $\nu_{max}$ : 3307 (N-H Str), 3060 (C-H), 1662 (-C=N), 1547 (Ar-C=C), 1103 (C-O). $^1$H-NMR: 4.0191(*s*, 2H, Amino proton), 7.2971–7.6789 (*m*, 4H, Ar). $^{13}$C-NMR: 49.7(*s*, 1C, C-$NH_2$) 128.9–134.7 (*m,* 6C, Ar-C carbon), 164.1(*s,* 1C, O-C=N carbon). MS (m/z): 194.11.




**Scheme 5:** G: -$NO_2$ (A8); G: -$NO_2$, R: 4-chlorophenyl (A10)

## O2

$C_8H_6N_4O_3$, Mol wt.: 206, MP (°C): 189–191, %yield: 85.21, Rf: 0.74, IR $\nu_{max}$: 3294 (N-H Str), 3098 (Ar-Alkane), 1601 (Imine), 1511 (Ar-alkene), 1048 (C-O). $^1$H-NMR: 3.4761 (*s*, 2H, Amino proton), 7.7148–8.2140 (*m*, 4H, Ar). $^{13}$C-NMR: 54.6 (*s*, 1C, C-$NH_2$), 121.4–148.4 (*m,* 6C, Ar-C carbon), 164.5 (*s,* 1C, O-C=N carbon). MS (m/z): 205.07.

## O3

$C_8H_7N_3O_2$, Mol wt.: 177, MP (°C): 162–164, % yield: 81.70, Rf: 0.74, IR $\nu_{max}$: 3299 (N-H Str), 2999 (C-H), 1616 (-C=N), 1547 (Ar-C=C), 998 (C-O). $^1$H-NMR : 4.2411 (*s*, 2H, Amino proton), 5.0121 (*s*, 1H, Hydroxy proton) 6.7814–7.3247 (*m*, 4H, Ar). $^{13}$C-NMR: 98.1 (*s*, 1C, C-$NH_2$), 116.4–158.5 (*m,* 6C, Ar-C carbon), 172.9 (*s,* 1C, O-C=N carbon). MS (m/z): 176.01.

## AB1

$C_7H_5ClN_2S$, Mol wt.: 184, MP(°C): 197–199, %yield: 85, Rf: 0.81, IR $\nu_{max}$ : 3199 (N-H Str), 3029 (C-H), 1611 (-C=N), 1571 (Ar-C=C). $^1$H-NMR : 3.5471 (*s*, 2H, Amino proton), 7.5624–8.1775 (*m*, 3H, Ar). $^{13}$C-NMR: 121.3–144.9 (*m,* 6C, Ar-C carbon), 166.4 (*s*, 1C, C-$NH_2$). MS (m/z): 183.09.

## AB2

$C_7H_5N_3O_2S$, Mol wt.: 195, MP (°C): 190–192, %yield: 90, Rf: 0.79, IR $\nu_{max}$ : 3246 (N-H Str), 2998 (C-H), 1611 (-C=N), 1571 (Ar-C=C). $^1$H-NMR : 4.0014 (*s*, 2H, Amino proton), 8.4801–9.0105 (*m*, 3H, Ar). $^{13}$C-NMR : 117.8–150.1 (*m,* 6C, Ar-C carbon), 160.3 (*s*, 1C, C-$NH_2$). MS (m/z): 194.24.

### *3-(5-(p-chlorophenyl)-oxadiazol-2-yl)-2-phenyl-4-quinazolinone (A1)*

$C_{22}H_{13}ClN_4O_2$, Mol wt.: 400, MP(°C): 144–146, %yield: 89.46, Rf: 0.74, IR $\nu_{max}$: 2957(C-H), 1727 (-C=O), 1544(Ar-C=C), 1343(C-N), 1179(-C-O), 693(-C-Cl). $^1$H-NMR: 7.4127–7.6784, 7.7771–7.8614, 8.0124, 8.2586. $^{13}$C-NMR: 119.8-132.9(*m,* 17C, Ar-C carbon), 148.5, 158.1, 160.2, 165.7, 171.2. MS (m/z): 399.80.

### *2-(p-chlorophenyl)-3-(5-(p-chlorophenyl)-oxadiazol-2-yl)-4-quinazolinone (A2)*

$C_{22}H_{12}Cl_2N_4O_2$, Mol wt.: 435, MP (°C): 186-188, %yield: 79.68, Rf: 0.80, IR $\nu_{max}$ : 3009( C-H), 1724 (-C=O), 1538 (Ar-C=C), 1321 (C-N), 1178 (-C-O), 690(-C-Cl). $^1$H-NMR: 7.2983–7.4001, 7.5021–7.7584, 7.9668, 8.1125. $^{13}$C-NMR: 119.7-132.6(*m,* 17C, Ar-C carbon), 144.6 (*s*, 1C, C-Cl), 159.3, 161.2, 167.2, 172.3. MS (m/z): 434.01.

### *3-(5-(p-hydroxyphenyl)-oxadiazol-2-yl)-2-phenyl-4-quinazolinone (A3)*

$C_{22}H_{14}N_4O_3$, Mol wt.: 382, MP(°C): 172-174, % yield: 82.22, Rf: 0.64, IR $\nu_{max}$: 3109, 2997, 1730, 1554, 1301, 1100, 701. $^1$H-NMR: 4.9638, 6.7452–7.0160, 7.1883-7.3983, 7.2953–7.9984. $^{13}$C-NMR: 116.6–140.1, 153.26, 159.3, 161.2, 164.5, 175.2. MS (m/z): 381.11.

### *2-(p-chlorophenyl)-3-(5-(p-hydroxyphenyl)-oxadiazol-2-yl)-4-quinazolinone (A4)*

$C_{22}H_{13}ClN_4O_3$, Mol wt.: 416, MP (°C): 180–182, %yield: 74.84, Rf: 0.78, IR $\nu_{max}$: 3119(Ar-OH), 3010(C-H), 1714 (-C=O), 1566 (Ar-C=C), 1299(C-N), 1090 (-C-O), 703 (-C-Cl). $^1$H-NMR: 5.1038(*s*, 1H, Hydroxy proton) 6.9758–7.3320 (*m*, 8H, Ar), 7.5652–8.1944(*m*, 4H, Ar). $^{13}$C-NMR: 109–133.3(*m,* 17C, Ar-C carbon), 158.2(*s*, 1C, C-OH), 162.2(*s*, 1C, C-Phenyl), 163.7(*s*, 1C, C=O), 167.9(*s*, 1C, C-$C_{oxadiazole}$), 170.7(*s*, 1C, N-$C_{oxadiazole}$). MS (m/z): 415.06.

### *3-(6-chlorobenzo[d]thiazol-2-yl)-2-phenyl-4-quinazolinone (A5)*

$C_{21}H_{12}ClN_3OS$, Mol wt.: 389, MP (°C): 192–194, %yield: 76.16, Rf: 0.62, IR $\nu_{max}$ : 3012 (C-H), 1728 (-C=O), 1534 (Ar-C=C), 1338 (C-N), 1158 (-C-O). $^1$H-NMR: 7.2935-7.4837 (*m*, 4H, Ar), 7.5233–7.9748 (*m*, 5H, Ar), 8.0265 (*s*, 1H, Ar), 8.1374-8.2935 (*q*, 2H, Ar). $^{13}$C-NMR: 125.2–151.3 (*m,* 18C, Ar-C carbon), 160.1 (*s*, 1C, C=O), 160.9 (*1*, 1C, N=C), 164.6 (*s*, 1C, C-Phenyl) MS (m/z): 388.04.

### *3-(6-chlorobenzo[d]thiazol-2-yl)-2-(p-chlorophenyl)-4-quinazolinone (A6)*

$C_{21}H_{11}Cl_2N_3OS$, Mol wt.: 424, MP (°C): 202–204, %yield: 68.52, Rf: 0.70, IR $\nu_{max}$ : 2971 (C-H), 1732 (-C=O), 1542 (Ar-C=C), 1346 (C-N), 1162 (-C-O). $^1$H-NMR : 7.3012–7.5124 (*m*, 4H, Ar), 7.6145–8.0001 (*m*, 4H, Ar), 8.1015 (*s*, 1H, Ar), 8.1426–8.4251 (*q*, 2H, Ar)/ $^{13}$C-NMR: 122.4–149.8 (*m,* 18C, Ar-C carbon), 157.2 (*s*, 1C, C=O), 161.7 (*1*, 1C, N=C), 164.6 (*s*, 1C, C-Phenyl). MS (m/z): 423.11.

### *3-(5-(p-nitrophenyl)-oxadiazol-2-yl)-2-phenyl-4-quinazolinone (A7)*

$C_{22}H_{13}N_5O_4$, Mol wt.: 411, MP (°C): 164-166, %yield: 73.35, Rf: 0.77, IR $\nu_{max}$: 2999(C-H), 1722 (-C=O), 1544 (Ar-C=C), 1351 (C-N), 1172 (-C-O). $^1$H-NMR: 7.2160–7.5628 (*m*, 4H, Ar), 7.6278–7.8956, 7.9951–8.2541. $^{13}$C-NMR ($\delta$ ppm): 121.6-148.4, 164.2, 167.7, 171.2, 173.2. MS (m/z): 410.37.

### A8

$C_{21}H_{12}N_4O_3S$, Mol wt.: 400, MP (°C): 158–160, %yield: 64.28, Rf: 0.68, IR $\nu_{max}$: 2988, 1734, 1540, 1322, 1150. $^1$H-NMR: 7.2204–7.6225, 8.4179–9.0562. $^{13}$C-NMR: 120.1–152.8, 155.2, 160.4, 166.6. MS (m/z): 399.24.

### *2-(p-chlorophenyl)-3-(5-(p-nitrophenyl)-oxadiazol-2-yl)-4-quinazolinone (A9):*

$C_{22}H_{12}ClN_5O_4$, Mol wt.: 445, MP (°C): 188–190, %yield: 78.46, Rf: 0.74, IR $\nu_{max}$ : 2987 (C-H), 1726 (-C=O), 1538 (Ar-C=C), 1346 (C-N), 1154 (-C-O). $^1$H-NMR: 7.3142–7.5678,

**Table 1:** Observation of characteristic phases

| *S. No.* | *Code* | *Dose (mg/kg)* | *Interval (seconds)* | | |
|---|---|---|---|---|---|
| | | | *Tonic* | *Straub tail* | *Stupor* |
| 1 | Control | 54 mA (0.2 sec) | 5 ± 0.000 | Present | 186 ± 0.8367 |
| 2 | Phenytoin | 25 | 2.6 ± 0.5477 | -- | 42 ± 2.074 |
| 3 | A1 | 110 | 1.8 ± 0.7456 | Absent | 113 ± 1.643 |
| | | 150 | 1.4 ± 0.2388** | Absent | 81.2 ± 1.304** |
| 4 | A2 | 110 | 2.1 ± 0.5482 | Absent | 133 ± 2.074 |
| | | 150 | 2.0 ± 0.4472 | Absent | 124 ± 1.384 |
| 5 | A3 | 110 | 1.4 ± 0.2388** | Absent | 115 ± 1.235* |
| | | 150 | 1.2 ± 0.4140** | Absent | 80 ± 0.564** |
| 6 | A4 | 110 | 1.6 ± 0.1267* | Absent | 84 ± 2.550** |
| | | 150 | 1.2 ± 0.2344** | Absent | 51.2 ± 0.837 |
| 7 | A5 | 110 | 1.3 ± 0.1145* | Absent | 135 ± 0.236* |
| | | 150 | 1.1 ± 0.1325** | Absent | 100 ± 0.146* |
| 8 | A6 | 110 | 1.6 ± 0.2477* | Absent | 183 ± 1.000* |
| | | 150 | 1.4 ± 0.2302* | Absent | 147 ± 3.000** |
| 9 | A7 | 110 | 1.9 ± 0.2617* | Absent | 104 ± 1.155* |
| | | 150 | 1.7 ± 0.2491* | Absent | 91.2 ± 0.716* |
| 10 | A8 | 110 | 1.8 ± 0.1627* | -- | 108 ± 0.135* |
| | | 150 | 1.6 ± 0.3790* | -- | 99.3 ± 0.306* |
| 11 | A9 | 110 | 1.5 ± 0.1532* | Absent | 101.2 ± 0.225* |
| | | 150 | 1.2 ± 0.2230* | Absent | 69.1 ± 1.112 |
| 12 | A10 | 110 | 1.7 ± 0.2721* | Absent | 111.2 ± 1.53* |
| | | 150 | 1.3 ± 0.1002* | Absent | 84.0 ± 1.41** |

N = 6, in each group; *$p$ < 0.05; **$p$ < 0.01; One Way ANOVA followed by Dunnett's test.



7.6714–8.1143. $^{13}$C-NMR: 122.4–150.1, 160.0, 164.6, 166.3, 170.2. MS (m/z): 444.06.

### A10

$C_{21}H_{11}N_4O_3S$, Mol wt.: 434, MP (°C): 182–184, %yield: 69.94, Rf: 0.76, IR $\nu_{max}$ : 3003 (C-H), 1731 (-C=O), 1533 (Ar-C=C), 1340 (C-N), 1162 (-C-O). $^1$H-NMR: 7.3023–7.9124(*m*, 8H, Ar), 8.2991–9.0415 (*m*, 3H, Ar). $^{13}$C-NMR: 129.5–154.6, 156.5, 163.2, 167.0. MS (m/z): 433.19.

### Anticonvulsant Activity Study

The median lethal dose was 1090.05 mg/kg. The decline in characteristic tonic phase, absence of straub tail phases and death or recovery of animals were observed (Table 1).

## Discussion

The infrared spectra of 2-aminobenzoic acid revealed the characteristic IR ranges ($cm^{-1}$) of $NH_2$ str at 3500 to 3100, carbonyl stretch at 1725 to 1700 and O-H stretch at 3400 to 2400. The infrared ranges are 1350 to 1000 for C-N aromatic vibrations, 785 to 540 $cm^{-1}$ for carbon-chlorine stretch, 1300 to 1000 for carbon-oxygen stretch, and 1600 and 1725 to 1705 for C=C aromatic and C=O str vibrations, which are indicative of the substituted oxadiazole-containing 4(3H)-quinozolinones. The characteristic infrared spectra of 4(3H)-quinazolinones containing benzothiazole derivatives revealed the presence of C-H str of aromatic H at 750 to 700, carbon-oxygen stretch and carbon-carbon double bond stretch of aromatic near 1300 to 1000 and 1600, C-N aromatic vibrations near 1350 to 1000, and carbonyl stretch near 1725 to 1705. The NMR spectra of benzothiazole and substituted oxadiazole derivatives condensed with 4-quinozolinones revealed the presence of aromatic hydrohens at approximately 7δ and the C-H multiplet close to 8 δ. $^{13}$C-NMR spectrum of the final derivatives of 4-quinazolinones showed the carbon of quinazolinone found to be near 148, the carbon of oxadiazole was near 171 δ, the carbon of carbonyl was near 160 δ, the carbon of phenyl was near 158 δ, and the carbon of quinazolinone was near 148. The carbon attached to chlorine was detected near 133 δ, and aromatic carbons were found within 119 to 130 δ. In the mass spectra of the final derivatives, every molecular ion peak matched its corresponding molecular weight.

A54 mA current was applied for two seconds using ear pinna electrodes to cause a tonic-clonic convulsion with a discernible stupor and straub tail phase. The tonic phase lasted 5 s and the stupor phase lasted 184 s in the control group. By giving the necessary dose, the nonappearance of the straub tail, the reduction in the length of phases, and the animals' revival were examined and contrasted with the control. All animals were recovered after the treatment. Compared to the control group, it was discovered that tonic phase was shortened to 1.1 s at 150 mg/kg and stupor phase to 51s.

## Conclusion

The current study effectively produced 3-(6-substituted benzthiazole-2-yl/oxadiazole-2-yl)-2-substituted-4-quinaozlinones, which were analyzed using spectral techniques. The compounds' anticonvulsant potential was evaluated using the maximal electroshock-induced seizures technique. The compounds listed below demonstrated remarkable promise in lessening and preventing convulsions in mice. Compounds A3, A4, A9, A5, A10 exhibit strong anticonvulsant potential as evidenced by shorter tonic phase durations (1.3–1.1 seconds) and stupor phase durations (100–51 seconds) without a straub phase in comparison to the control group.

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## References

1. Sirven JI. Epilepsy: A Spectrum Disorder. Cold Spring Harbor perspectives in medicine. 2015; 5(9): a022848. Available from: https://doi.org/10.1101/cshperspect.a022848.
2. D'Antuono M, Köhling R, Ricalzone S, Gotman J, Biagini G, Avoli M. Antiepileptic drugs abolish ictal but not interictal epileptiform discharges in vitro. Epilepsia. 2010; 51(3):423-31. Available from: https://doi.org/10.1111/j.1528-1167.2009.02273.x
3. *Nain S, Sharma A, Singh HO, Paliwal S.* Recent Advances in use of Semicarbazones as Anticonvulsant Agents: A Review. Journal of Biomedical and Therapeutic Sciences. 2015; 2(1): 1-7.
4. Maruthamuthu R, Christina D, Bharathi R. The chemistry and biological significance of imidazole, benzimidazole, benzoxazole, tetrazole and quinazolinone nucleus. Journal of Chemical and Pharmaceutical Research. 2016; 8(5): 505-526.
5. Kaur H, Kumar S, Vishwakarma P, Sharma M, Saxena KK, Kumar A. ChemInform Abstract: Synthesis and Antipsychotic and Anticonvulsant Activity of Some New Substituted Oxa/Thiadiazolylazetidinonyl/Thiazolidinonylcarbazoles. European Journal of medicinal Chemistry. 2010; 45:2777-2783. Available from: https://doi.org/10.1016/j.ejmech.2010.02.060.
6. Abuelizz HA, Dib RE, Marzouk M, Anouar E-H, A. Maklad Y, N. Attia H, Al-Salahi R. Molecular Docking and Anticonvulsant Activity of Newly Synthesized Quinazoline Derivatives. *Molecules*. 2017; 22(7):1094. Available from: https://doi.org/10.3390/molecules22071094
7. Küçükgüzel SG, Oruç EE, Rollas S, Sahin F, Ozbek A. Synthesis, characterisation and biological activity of novel 4-thiazolidinones, 1,3,4-oxadiazoles and some related compounds. European Journal of Medicinal Chemistry. 2002;37(3):197-206. Available from: https://doi.org/10.1016/s0223-5234(01)01326-5.
8. Wang X, Hu H, Zhao X, Chen M, Zhang T, Geng C, Mei Y, Lu A, Yang C. Novel quinazolin-4(3H)-one derivatives containing a 1,3,4-oxadiazole thioether moiety as potential bactericides and fungicides: Design, synthesis, characterization and 3D-QSAR analysis. Journal of Saudi Chemical Society. 2016; 23(8): 1144-1156. Available from: https://doi.org/10.1016/j.jscs.2019.07.006.
9. Alsibaee AM, Al-Yousef HM, Al-Salem HS. Quinazolinones, the Winning Horse in Drug Discovery. Molecules. 2023;28(3):978. Available from: https://doi.org/10.3390/molecules28030978.
10. Foucourt A, Hédou D, Dubouilh-Benard C, Désiré L, Casagrande A-S, Leblond B, Loäec N, Meijer L, Besson T. Design and Synthesis of Thiazolo[5,4-*f*]quinazolines as DYRK1A Inhibitors, Part I. *Molecules.* 2014; 19(10):15546-15571. Avaibale form https://doi.org/10.3390/molecules191015546

11. Lanting X, Yongwen J, Dawei M. Synthesis of 3-Substituted and 2,3-Disubstituted Quinazolinones via Cu-Catalyzed Aryl Amidation. Organic Letters. 2012; 14(4): 1150–1153. Available from: https://doi.org/10.1021/ol300084v
12. Lin H, Haoquan L, Jianbin C, Xiao-Feng W. Recent advances in 4(3*H*)-quinazolinone syntheses. RSC Advances. 2014;4(24):12065-12077. Available from: https://doi.org/10.1039/C4RA00351A
13. Mahmoud MR, El-Shahawi MM, Abu El-Azm FSM. Synthesis of novel quinazolinone and fused quinazolinones. European Journal of Chemistry. 2011; 2(3):404-409. Available from: https://doi.org/10.5155/eurjchem.2.3.404-409.267.
14. Rishipathak DD, Patil KV, Wajpeyi PS, Daryani MJ. Design and molecular docking studies of some 1,3,4-thiadiazole derivatives. International Journal of Pharmaceutical Sciences and Research. 2016; 7(12): 5044-51. Available from: https://doi.org/10.13040/IJPSR.0975-8232.7(12).5044-51
15. Rishipathak DD, Karanjikar C, Udavant PB. Microwave Assisted Synthesis and Evaluation of Anticonvulsant Activity of Some 3-(3-(Substituted benzylidine)amino)phenyl-2-phenylquinazolin-4(3H)-ones. Asian Journal of Chemistry. 2023;35(1): 95–98. Available from: https://doi.org/10.14233/ajchem.2023.26877
16. Rishipathak DD, Vaidya S, Ghodke SS. Synthesis and Evaluation of Anticonvulsant Activity of Some 5,5-Disubstituted-N3-[(2-aryl thiazolidine-4-one-3-yl)amino]hydantoins. Asian Journal of Chemistry. 2023;35(3):591-597. Available from: https://doi.org/10.14233/ajchem.2023.27282

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