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SYNTHESIS, CHARACTERIZATION, MOLECULAR DOCKING, AND ANTICONVULSANT ACTIVITY OF SOME NEW BENZOXAZOLE DERIVATIVES

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ABSTRACT
A new series of analogues of N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-2-(piperazin-1-yl) acetamides was synthesised and characterised using melting point determination, elemental analysis, and spectral techniques (FTIR, ^{1}H NMR, and MS). The anticonvulsant activity of selected analogues was evaluated using the maximal electroshock-induced convulsion model in albino mice. Test compounds were administered intraperitoneally at a dose of 50 mg/kg body weight, and acute neurotoxicity was assessed with the rotarod apparatus. Among the tested analogues, some exhibited superior potency, showing statistically significant activity compared with the reference drug, phenytoin. Additionally, these compounds showed favourable molecular docking scores against the target protein.
Keywords: Benzoxazole, Synthesis, Docking Studies, Anticonvulsant, Human Health, Maximal Electroshock.
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INTRODUCTION

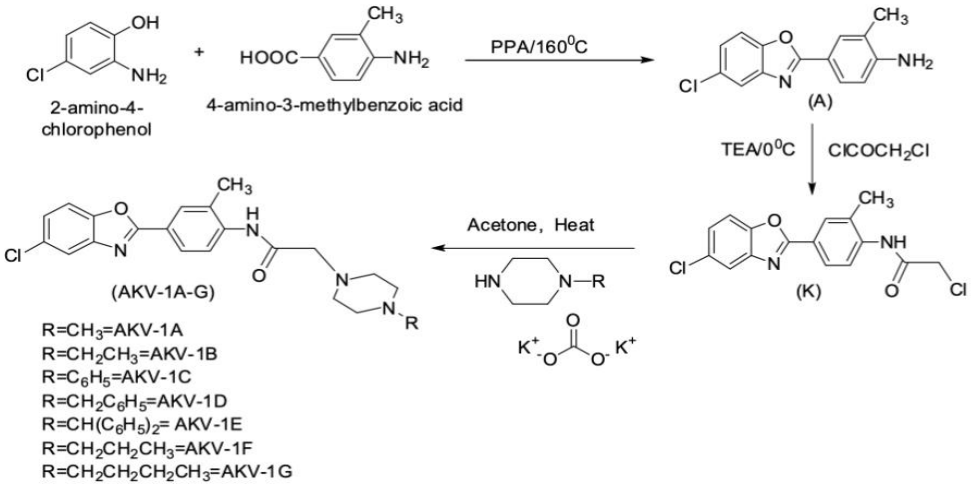
Epilepsy is a chronic neurological disorder characterised by recurrent, unprovoked seizures, affecting approximately 50 million people worldwide. Despite the availability of various antiepileptic drugs (AEDs), many patients continue to experience inadequate seizure control or adverse side effects, highlighting the urgent need for novel therapeutic agents with improved efficacy and safety profiles. Benzoxazole is a privileged nitrogen-containing heterocyclic scaffold with considerable anticonvulsant potential.[1] Advances in understanding the cellular and molecular mechanisms underlying neuronal hyperexcitability have enabled the identification of novel therapeutic targets, leading to the development of clinically available antiepileptic drugs such as zonisamide, gabapentin, diazepam, vigabatrin, phenobarbital, lamotrigine, phenytoin, tiagabine, felbamate, and nitrazepam.[2] The benzoxazole moiety, which combines features of both benzene and oxazole rings, can interact with a variety of biological targets, making it an attractive core for developing central nervous system (CNS) active agents.[3-5] Building on previous research efforts, this study aims to identify novel synthetic anticonvulsant lead compounds. Guided by these considerations, a new series of benzoxazole analogues was designed. Herein, the synthesis of N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-2-(piperazin-1-yl) acetamides (AKV-1A-1G) is reported. Such structural modifications are expected to enhance anticonvulsant potency while producing compounds with a favourable therapeutic index (TI). Additionally, in silico molecular docking studies of the synthesised compounds were conducted using AutoDock Vina against the target protein (PDB ID: 3PO7).

EXPERIMENTAL

Material and Methods

All reagents and solvents used in this study were of analytical grade and obtained from commercial suppliers without any further purification. The progress of the reactions was monitored by thin-layer chromatography (TLC) on silica gel plates (Merck, 60 F254), and the spots were visualised under iodine

vapours. The final benzoxazole derivatives were purified by either recrystallisation or column chromatography using silica gel (60-120 mesh) as the stationary phase and suitable solvent systems based on the polarity of the compound.[6] Melting points of the synthesised compounds were determined using the open capillary method and are reported without correction. Infrared (IR) spectra were recorded on a PerkinElmer FTIR spectrometer using KBr pellets. Proton nuclear magnetic resonance (^{1}H NMR) spectra were acquired on a Bruker 300 MHz spectrometer, with $CDCl_3$ as the solvent and tetramethyl silane (TMS) serving as the internal standard. Mass spectra were obtained using a Direct Analysis in Real Time (DART) mass spectrometer to confirm the molecular weights and structural integrity of the synthesised derivatives.[7,8]



Scheme-1: Synthesis of N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-2-(piperazin-1-yl) acetamides (AKV-1A-G)

General Procedure

Synthesis of Benzoxazole Derivatives

The benzoxazole core was synthesised through the cyclisation of o-aminophenol with substituted benzoic acids using polyphosphoric acid (PPA) as a dehydrating agent under reflux conditions. Following cyclisation, acylation, and substitution reactions were performed to introduce various side chains. These modifications were achieved by reacting the benzoxazole intermediates with appropriate acid chlorides or alkyl halides in the presence of a base such as triethylamine or potassium carbonate (K_2CO_3) to facilitate nucleophilic substitution. The resulting compounds were purified using recrystallisation or column chromatography and characterised by spectroscopic methods as described above.[9,10]

Synthesis of Seven Benzoxazole Derivatives (AKV-1A-G)

4-(benzo[d]oxazol-2-yl) Aniline (A)

Intermediate (A) was synthesised using the known procedure, as shown in Scheme-1.[11]

N-(4-(benzo[d]oxazol-2-yl) phenyl)-2-chloroacetamide. (K)

To a stirred, ice-cold solution of (A) (0.012 mol) in tetrahydrofuran (50 mL), triethylamine (0.132 mol, 1.90 mL) was added dropwise under stirring. Subsequently, a solution of chloroacetyl chloride (1.056 mL, 0.014 mol) in tetrahydrofuran (15 mL) was added slowly to the reaction mixture over a period while maintaining continuous stirring and low temperature. After the addition was complete, the reaction mixture was warmed to room temperature and stirred for a further 1 hour. The solvent was then evaporated under reduced pressure using a rotary evaporator. The crude residue was washed thoroughly with water to remove inorganic impurities and dried in a vacuum oven. The crude product was purified by recrystallisation from ethanol, yielding the pure compound.[12] Whitish grey solid, yield: 86%, m.p = 164.5–166.3°C, FTIR - (ATR, cm^{-1}): 3365.17 (N-H), 2935.45 (C-H), 1682.03 (C=O), 846. ^{1}H-N M R (300-MHz, CDCl3 δ) 4.334 (2 H, s, CH_2), (2H, m, benzoxazole Ar-H.), 7.547–7.578 (2H, m, benzoxazole Ar-H,), 7.746–7.775 (2 H, d, phenyl Ar- H,), 8.225–8.256 (2 H, d, Ar- H.), 9.368 (1 H, s, NH.). ESI-MS

m/*z* for C_{16} H_{12} Cl_2N_2 O_2: 334.03, found; M+1 335.06, M+3 336.14. Anal. Calcd (Found) %: C,57.33 (57.38); H, 3.61(3.63); N, 8.36 (8.34).

N-(4-(benzo[d]oxazol-2-yl) phenyl)-2-(piperazin-1-yl) acetamides (AKV-1A-G)

A mixture of 2-chloro-*N*-(2-substituted-4-(5-substituted-benzoxazol-2-yl) phenyl) acetamide (0.001 mol), potassium carbonate (0.138 g,0.001 mol), and a 1-substituted piperazine (0.0015 mol) was refluxed in 50 mL of acetone for seven hours. Upon completion of the reaction, acetone was removed under reduced pressure. The resulting residue was mixed with 20 mL of water and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried and concentrated to obtain the crude product, which was subsequently recrystallised from ethanol to afford the pure compound.[13]

Spectral Data

N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-2-(4-methylpiperazin-1-yl) acetamide. (AKV-1A).

Whitish grey solid, yield: 86 %, m.p. = 181-182 °C, FTIR (ATR, cm-1): 3397.25 (NH), 2921.17 (C-H), 1614.63 (C=O). ^{1}HNMR (300 MHz, $CDCl_3$): δ = 2.349 (3 H, s, CH_3), 2.445 (3H, s, CH_3), 2.619 (4 H, s, pip.), 2.764 (4H, s, pip.), 3.282 (2 H, s,-CO-CH_2-), 7.316-7.372 (2H, m, benzoxazole Ar-H), 7.555-7.586 (2H, m, benzoxazole Ar-H), 7.759-7.778 (3H, d, Ar-H), 9.266 (1 H, s, N H). M S: (E S I+) m/z 399.2, M+1 400.2, M+3 401.2. Elemental analysis. Found, %: C, 63.22; H, 5.82; N, 14.03. C_{20} H_{22} N_4 O_2. Calculated, %: C, 63.23, H, 5.81, N, 14.05.

N-(4-(5, -chlorobenzo[d]oxazol -2-yl)-2-methylphenyl)-2-(4-ethylpiperazin-1-yl)- acetamide. (AKV-1B)

Whitish grey solid, yield: 87 %, M.P. = 173-175 °C, FTIR (ATR, cm^{-1}): 3372.60 (N-H), 2919.14 (C-H), 1613.04 (C=O). ^{1}H-N M R (300, M Hz, $CDCl_3$): δ = 2.349 (3H, s, CH_3), 2.859(3H s, CH_3), 2.543 (4 H, s, pip.), 2.692 (4 H, s, pip.), 3.186 (2H, s,-CO-CH_2-),7.334-7.378 (2 H, m, benzoxazole Ar - H), 7.551-7.608 (1H, m, benzoxazole Ar - H), 7.748-7.777 (3 H, t, Ar - H), 8.227-8.256 (1 H, d, A r- H), 9.370 (1 H, s, N H). MS: (E S I+) m/z 413.3, M+1 414.3, M+3 415.3. Elemental-analysis. Found, %: C, 63.96; H, 6.09; N, 13.55. C_{20} H_{22} N_4 O_2. Calculated, %: C, 63.99, H, 6.10, N, 13.57.

N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-2-(4-phenylpiperazin-1-yl) acetamide. (AKV-1C)

Greyish white solid, yield: 82 %, m.p. = 181-183 °C, FTIR (ATR, cm^{-1}): 3373.97 (N-H), 2920.24 (C-H), 1614.71 (C = O). ^{1}HNMR (300, M Hz, $CDCl_3$): δ = 2.272 (3 H, s, CH_3),2.463 (4 H, s, pip.), 2.614 (4 H, s, pip), 3.178 (2 H, s,-CO-CH_2-), 7.313-7.371 (3 H, m, benzoxazole Ar - H), 7.557-7.584 (2 H, m, benzoxazole Ar - H), 7.748-7.772 (3 H, t, Ar - H), 7.923-7.952 (3 H, d, Ar - H), 9.496 (1 H, s, N H). M S: (E S I+) m/z 461.4, M+1 462.4, M+3 463.2. Elemental-analysis. Found, %: C, 67.73; H, 5.45; N, 12.13. C_{20} H_{22} N_4 O_2. Calculated, %: C, 67.75, H, 5.47, N, 12.15.

2-(4-benzhydrylpiperazin-1-yl)-N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)acetamide. (AKV-1D)

Whitish brown solid, yield: 88 %, m.p. = 132-134 °C, FTIR (ATR, cm^{-1}): 3373.31 (N- H), 2921.14 (C-H), 1616.44 (C = O). ^{1}H-NM R (300, M Hz, $CDCl_3$): δ = 2.353 (3 H, s, CH_3),2.524 (4 H, s, pip.), 2.638 (4H, s, pip.), 3.215 (2 H, s,-$COCH_2$), 3.562 (2 H, s, -CH_2-), 7.314-7.378 (2 H, m, benzoxazole A r- H), 7.556-7.586 (2 H, m, benzoxazole Ar - H), 7.747-7.773 (4 H, t, Ar - H), 8.232-8.245 (3 H, d, Ar - H), 9.353 (1 H, s, N H). MS: (E S I+) m/z 475.4, M+1 476.4, M+3 477.4. Elemental-analysis. Found, %: C, 71.90; H, 5.65; N, 10.18. C_{20} H_{22} N_4 O_2. Calculated, %: C, 71.92, H, 5.67, N, 10.17.

2-(4-benzhydryl-piperazin-1-yl)-N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methylphenyl)-acetamide. (AKV-1E)

Whitish grey solid, yield: 84 %, m.p. = 162-164 °C, F T I R (A T R, cm^{-1}): 3429.20 (N - H), 2921.86 (C - H), 1622.52 (C = O). 1 H-N M R (300, M Hz, $CDCl_3$): δ = 2.339 (3 H, s, CH_3),2.548 (4 H, s, pip.), 2.689 (4 H, s, pip.), 3.186 (2 H, s,-CO-CH_2-), 7.334-7.361 (3 H, m, benzoxazole Ar - H), 7.549-7.595 (2 H, m, benzoxazole Ar - H), 7.750-7.776 (8 H, d, Ar - H), 8.116-8.138 (3 H, d, Ar - H), 9.265 (1 H, s, N H). MS:

(E S I+) m/z 552.1, M+1 553.1, M+3 554.1. Elemental-analysis. Found, %: C, 71.90; H, 5.68; N, 10.19. C_{20} H_{22} N_4 O_2. Calculated, %: C, 71.92, H, 5.67, N, 10.17.

N-(4-(5-chloro-benzo[d]oxazol-2-yl)-2-methylphenyl)-2-(4-propylpiperazin-1-yl)-acetamide. (AKV-1F)

Whitish grey solid, yield: 86 %, m.p. = 183-185 °C, FTIR (ATR, cm^{-1}): 3373.97 (N - H), 2920.24 (C-H), 1614.71 (C= O). ^{1}H-N M R (300, M Hz, $CDCl_3$): δ = 0.845 (3 H, s, CH_3),1.354-1.383 (2H, s, CH_2),2.213 (2 H, s, CH_2),2.444 (3 H, s, CH_3),2.617 (4 H, s, pip.), 2.765 (4 H, s, pip), 3.283 (2 H, s,-CO-CH_2-), 7.315-7.373 (2 H, benzoxazole Ar - H), 7.554-7.585 (1 H, m, benzoxazole Ar - H), 7.758-7.779 (3 H, t, Ar - H), 9.496 (1 H, s, N H). M S: (ESI+) m/z 427.22, M+1 428.22, M+2 429.27, M+3 430.24. Elemental-analysis. Found, %: C, 64.68; H, 6.36; N, 13.11. C_{20} H_{22} N_4 O_2. Calculated, %: C, 64.70, H, 6.37, N, 13.12.

2-(4-butylpiperazin-1-yl)-N-(4-(5-chlorobenzo[d]oxazol-2-yl)-2-methyl-phenyl)- acetamide. (AKV-1G)

Whitish grey solid, yield: 78 %, m.p. = 131-133 °C, F T I R (A T R, cm^{-1}): 3373.31 (N-H), 2921.14 (C-H), 1616.44 (C =O). ^{1}H-N M R (300, M Hz, $CDCl_3$): δ = 0.838-0.880 (3 H, m, CH_3),1.254 (2 H, m, CH_2),2.348 (3 H, s, CH_3),2.479-2.539 (4 H, s, pip.), 2.690 (4 H, s, pip.), 3.184 (2 H, s,-$COCH_2$-), 3.562 (2 H, s, -CH_2-), 7.330-7.358 (2 H, m, benzoxazole Ar - H), 7.561-7.588 (1 H, m, benzoxazole Ar - H), 7.753-7.770 (2 H, d, Ar - H), 8.232-8.249 (2 H, d, Ar - H), 9.366 (1 H, s, N H). M S: (E S I+) m/z 441.32, M+1 442.32, M+2 443.43, M+3 444.37. Elemental analysis. Found, %: C, 65.36; H, 6.65; N, 12.71. C_{20} H_{22} N_4 O_2. Calculated, %: C, 65.37, H, 6.63, N, 12.71.

Molecular Docking Study

To gain insight into the binding interactions between the synthesised benzoxazole derivatives and the target receptor, molecular docking studies were performed using Auto Dock Vina 1.5.7. The three-dimensional crystal structure of the receptor protein, identified by PDB ID: 3PO7, was retrieved from the Protein Data Bank (PDB). Before docking, the protein structure was pre-processed by removing all crystallographic water molecules, adding polar hydrogen atoms, and assigning appropriate atomic charges. Energy minimisation and structure optimisation were carried out using the default parameters to ensure accurate and reliable docking results.[14,15] Docking simulations revealed that several synthesised benzoxazole derivatives exhibited strong binding affinities toward the active site of the receptor protein. The calculated binding energy values ranged from -7.9 to -9.8 kcal/mol, suggesting favourable and stable ligand–receptor interactions (Table 1). The docking poses demonstrated that key interactions included hydrogen bonding with critical amino acid residues such as LeuA492 and ArgB484, as well as π–π stacking interactions with aromatic side chains within the binding pocket. Additionally, hydrophobic contacts contributed to the stabilisation of the ligand–protein complexes. These interactions are indicative of a high degree of complementarity between the active site and the synthesised ligands, supporting their potential as effective modulators of the receptor's activity.[16]

Notably, compound 3e exhibited the highest binding affinity among the tested derivatives, with a docking score of –9.8 kcal/mol. The docking analysis revealed that 3e formed two hydrogen bonds with the side chains of LeuA492, and a significant π–π stacking interaction with TyrA112. These specific interactions are aligned with known structural features critical for receptor modulation, suggesting that compound 3e may effectively influence channel activity. The strength and nature of these interactions further support the potential of 3e as a promising lead compound for antiepileptic drug development.[17]

The docking results showed a strong correlation with the observed in vivo anticonvulsant activity, reinforcing the hypothesis that the receptor protein channel serves as a likely molecular target for the synthesised benzoxazole derivatives. Compounds exhibiting higher binding affinities, such as 3e, also demonstrated enhanced anticonvulsant effects in animal models, indicating that effective receptor binding contributes to their pharmacological activity. The detailed docking poses and ligand–receptor interaction maps provide valuable structural insights that can guide future lead optimisation and structure-based drug design efforts aimed at improving potency and selectivity.[18]

Animal Ethics

Albino mice weighing between 25-30 grams, of either sex, were used in the study. Before experimentation, the animals were acclimatised for seven days. They were housed under controlled environmental conditions of 27 ± 1°C with a 12-hour light/dark cycle. Each mouse was kept individually in polyacrylic cages containing sterile rice husk bedding. All animals were provided a standard pellet diet and had free access to clean drinking water. The experimental procedures were reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of the Faculty of Pharmacy, Integral University, Lucknow, operating under the guidelines of the Committee for Control and Supervision of Experiments on Animals (CPCSEA). The ethics approval number is IU/IAEC/2025/21, dated February 10, 2025.

Table-1: Docking Scores and Key Interactions of Benzoxazole Derivatives with MAO, PDBID: 3PO7

Compound	Binding Energy (kcal/mol)	Key Interactions	Residues Involved
AKV-1A	–7.9	H-bond, π–π stack	PROB:177, ARGA:36, TYRA:393, LEUA:250, ASPB:239, GLUB:248
AKV-1B	–8.1	H-bond, hydrophobic	PHEA:103, TRPA:119, THRA:196, ARGA:120, ASPA:123, ARGA:127, ILEA:477, LYSA:190, HISA:431
AKV-1C	–9.4	H-bond, π–π stack	ILEA:477, ASPA:123, THRA:479, GLUA:483, PHEA:103, PROA:105
AKV-1D	–9.6	2 H-bonds, π–π stack	ARGB:484, THRB:479, ARGB:120, ASNB:116, TRPB:119, PHEB:103, GLUB:483, PROB:105
AKV-1E	–9.8	π–π stack	LEUA:492, LEUA113PRAA:109, TYRA:112
AKV-1F	–9.4	H-bonds, π–π stack	VALA:106, TYRA:112, PHEA:103, TRPA:119, ARGA:120, ILEA:477, GLYA:193
AKV-1G	–9.2	π–π stack, amide π stack	ASNA:116, ARGA:120, GLUA:483, ARGA:120, GLYA:193, PROA:476, ILEA:477
Zonisamide	-6.6	H-bonds, π–π stack	PHEB:103, GLUB:483, ASNB:116, TYRB:112

Anticonvulsant Activity

Maximal Electroshock Method (MES)

The experimental protocol was adapted from the method described.[19] Albino mice (25–30 g, either sex) were fasted overnight with free access to water. The animals were randomly divided into eight groups (n = 6 per group) and treated intraperitoneally as follows: control group with PEG-200 (1 mL/100 g), standard group with diazepam (20 mg/kg), and test groups with compounds AKV-1A–AKV-1G (20 mg/kg each, dissolved in PEG-200). Thirty minutes post-treatment, all animals were subjected to electroshock stimulation (45 mA, 0.2 s) to induce convulsions. The duration of increased extensor muscle tone was recorded, along with any complete abolition or reduction of hindlimb extension. The sequential durations (in seconds) of the following seizure phases were also measured:[19]

i. **Tonic flexion:** characterised by forelimb contraction and generalised muscle rigidity;
ii. **Tonic extension:** marked by extension of both forelimbs and hindlimbs;
iii. **Clonus:** a phase of rhythmic relaxation following tonic extension;
iv. **Stupor:** a period of unconsciousness preceding recovery.

Rotarod Test for Acute Neurotoxicity

The acute neurotoxicity of the synthesised compounds was evaluated using a rotarod apparatus equipped with a rod of 3.2 cm diameter, rotating at a constant speed of 6 rpm. Animals were pre-trained to maintain balance on the rotating rod before testing. Following training, the test compounds were administered at doses of 30, 100, and 200 mg/kg body weight. Neurotoxicity was assessed by observing each animal's ability to remain on the rod for at least 1 minute during three consecutive trials. Failure to maintain balance for the required duration in any trial was recorded as an indication of neurotoxic effects.[20]

RESULTS AND DISCUSSION

In the present investigation, seven benzoxazole derivatives were synthesised. The intermediates required for the preparation of these derivatives were obtained following previously reported procedures. The final derivatives (AKV-1A–AKV-1G) were synthesised via condensation reactions. Thin-layer chromatography (TLC) analysis of each compound, using n-hexane: acetonitrile (4:6) as the mobile phase, yielded a single, well-defined spot without tailing, confirming their purity. All synthesised analogues were further characterised by their physical, spectral, and analytical data.

Docking Study

All seven synthesised benzoxazole derivatives show a better docking score than the reference drug against the protein 6PO7 (Table-2).

Table-2: Docking Score of Synthesised Derivatives and Standard Zonisamide

Name of Compound	Docking Score, (kcal/mol)
Standard (Zonisamide)	-6.6
AKV-1A	-7.9
AKV-1B	-8.1
AKV-1C	-9.4
AKV-1D	-9.6
AKV-1E	-9.8
AKV-1F	-9.3
AKV-1G	-9.2

Anticonvulsant Activity

The anticonvulsant activity of the six synthesised compounds (AKV-1A–AKV-1G) and the standard drug was evaluated using the maximal electroshock (MES) method. The test compounds demonstrated anticonvulsant activity at doses ranging from 50–100 mg/kg. Compared to the standard drug phenytoin (5 mg/kg), the analogues exhibited 20–80% of its activity. Overall, all tested analogues showed improved potency (Table-3).

Table-3: Anticonvulsant Activity by Maximal Electroshock Method

Compound	Dose. (mg/kg)	% Protection (HLTE Abolition)	Mean Recovery Time (s)	Remarks
AKV-1A	30	20%	58 ± 5	Mild activity
AKV-1A	100	40%	45 ± 4	Moderate
AKV-1B	30	30%	50 ± 3	Moderate
AKV-1B	100	50%	38 ± 4	Good
AKV-1C	30	50%	36 ± 2	Significant
AKV-1C	100	70%	28 ± 3	Strong effect
AKV-1D	30	60%	30 ± 3	Strong effect
AKV-1D	100	80%	22 ± 2	Very strong activity
AKV-1E	30	10%	65 ± 6	Weak
AKV-1E	100	30%	50 ± 4	Mild
AKV-1F	30	60%	30 ± 3	Strong effect
AKV-1F	100	80%	22 ± 2	Very strong activity
AKV-1G	30	10%	65 ± 6	Weak
AKV-1G	100	30%	50 ± 4	Mild
Phenytoin (Std)	25	100%	18 ± 1	Standard reference
Control	—	0%	70 ± 5	No protection

CONCLUSION

In this study, a series of newly synthesised benzoxazole derivatives was successfully constructed, and their structures were confirmed through spectral and analytical techniques. These synthesised derivatives were evaluated for anticonvulsant activity, revealing significant pharmacological effects across all seven

benzoxazole derivatives (AKV-1A-1G), indicating promising potential as anticonvulsant agents. These findings suggest that future investigations may elucidate the precise mechanism underlying the anticonvulsant action of these synthesised derivatives. Additionally, further exploration of the benzoxazole scaffold is planned, focusing on modifying ring substitutions to enhance anticonvulsant efficacy.

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CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest related to this study.

AUTHOR CONTRIBUTIONS

The present work is related to *SDG-15: Life on Land*. All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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