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Original Article

Synthesis, Characterization and Attenuation of Strychnine-Induced Epilepsy on 3-(3-Aminophenyl)-1-[3-(2-Hydroxyphenyl)-3-Oxopropanoyl]-5,5-Diphenylimidazolidine-2,4-Dione Derivatives on Experimental Rats

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ABSTRACT

Background: It was a heterocyclic hydrocarbon whose molecular structure has some fundamental structural features. In this study, we synthesise eleven different imidazolidine-2,4-dione derivatives that have convulsive properties. Seizures can be divided into two categories: partial and generalised. While partial seizures occur when electrical activity spikes in only one area of the brain, generalised seizures involve aberrant electrical activity on both sides of the patient's brain. **Materials and Methods:** 2-chloromethyl benzene; 1-phenyl methanone; 4-oxo-4-phenoxybutanoic acid; 1-phenyl ethanone; phenol acetate; 4-aminophenol; oxalic acid etc., were used for the synthesis. Every chemical was of the analytical variety. Add 1 g of phenytoin to the flask with a round bottom. To the 100 mL RBF, add 1 mL of glacial acetic acid and 3 amino phenols. Refluxing the reaction mixture, heat it for 2 hr at a temperature between 80 and 100ºC. Add 10 mL of crushed ice to the reaction mixture to cool it down. Pour in more ice-cold water. Gather the product after filtering the reaction mixture. **Results:** overall compounds had strong anti-convulsive properties against epilepsy. (BJ)-(scheme 1B); (BG)-(Scheme 1B): (BE)-(scheme 1B); (BN)-(scheme 1B); (BM)- (scheme 1B) had strong anti-convulsive properties against epilepsy**.** **Conclusion:** Research examining the relationship between structural activity and activity has shown that compounds containing imidazolidine derivatives with an electron-withdrawing group exhibited higher levels of activity compared to those with an electron-donating group.

Keywords: 5, 5-diphenylimidazolidine, Benzil Urea, 2- amino benzoic acid 2-Nitro Aniline4-Nitro Aniline Aniline, Strychnin Anti-convulsion activity.

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INTRODUCTION

The nucleus of imidazolidine was found in 1954. It has an imidazolidine ring and dibenzene bonded together. The medication phenytoin and its structure are similar.[1] Because 5, 5-diphenylimidazolidine has so many pharmacological uses, it has an essential heterocyclic nucleus (refer to Figure 1).[2] These days, 5, 5-diphenylimidazolidine is the preferred moiety due to its many pharmacological characteristics.

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Although there are over forty different anti-epileptic medications on the Indian market,[3] barely thirty percent of individuals with uncontrollable seizures have found relief.[4] Thus, a lot of research is being done on antiepileptic compounds these days. Its primary goal is to investigate novel anticonvulsant medications.[5] Based on the kind of seizure, *in vivo* screening assays were used to identify these compounds.[6] Seizures are defined as aberrant electrical activity in the brain and are characterised by the physical alterations in a patient's behaviour that take place during therapy.[7] When a patient experiences a seizure, there is an issue with disorganised brain activity. Generally speaking, an excess of patient brain cells becoming activated at the same moment causes a seizure. Seizures can be divided into two categories: partial and generalised.[8] While partial seizures occur when electrical activity spikes in only one area of the brain, generalised seizures involve aberrant electrical activity on both sides of the patient's brain.[9] There are several causes of seizures, including elevated blood sugar or salt levels, brain damage after a stroke, or issues related to head trauma.[10] Patients may occasionally have brain tumours from birth. Alzheimer's disease, elevated fevers, illicit drug usage and alcohol or drug withdrawal are some conditions that might result in seizures.[11]

MATERIALS AND METHODS

Materials

2-chloromethyl benzene; 1-phenyl methanone; 4-oxo-4-phenoxybutanoic acid; 1-phenyl ethanone; phenol acetate; 4-aminophenol; oxalic acid etc., were used for the synthesis. Every chemical was of the analytical variety. All of the chemicals were bought from Modern Chemicals in Nashik, while others are offered by the college.

Methods

The standard approach was utilised to synthesise all 5, 5-diphenylimidazolidine derivatives. Through the use of thin layer chromatography techniques, the compounds' purity was examined (TLC). KBr pellets were used to produce IR spectra using the Perkin Elmer Spectrum FTIR instrument, 1H-NMR spectra. The synthetic routes for (BD) derivatives were shown in Scheme 1A and Scheme 1B.

Experimental Work

Chemistry: (Scheme IA)

(Scheme IB)

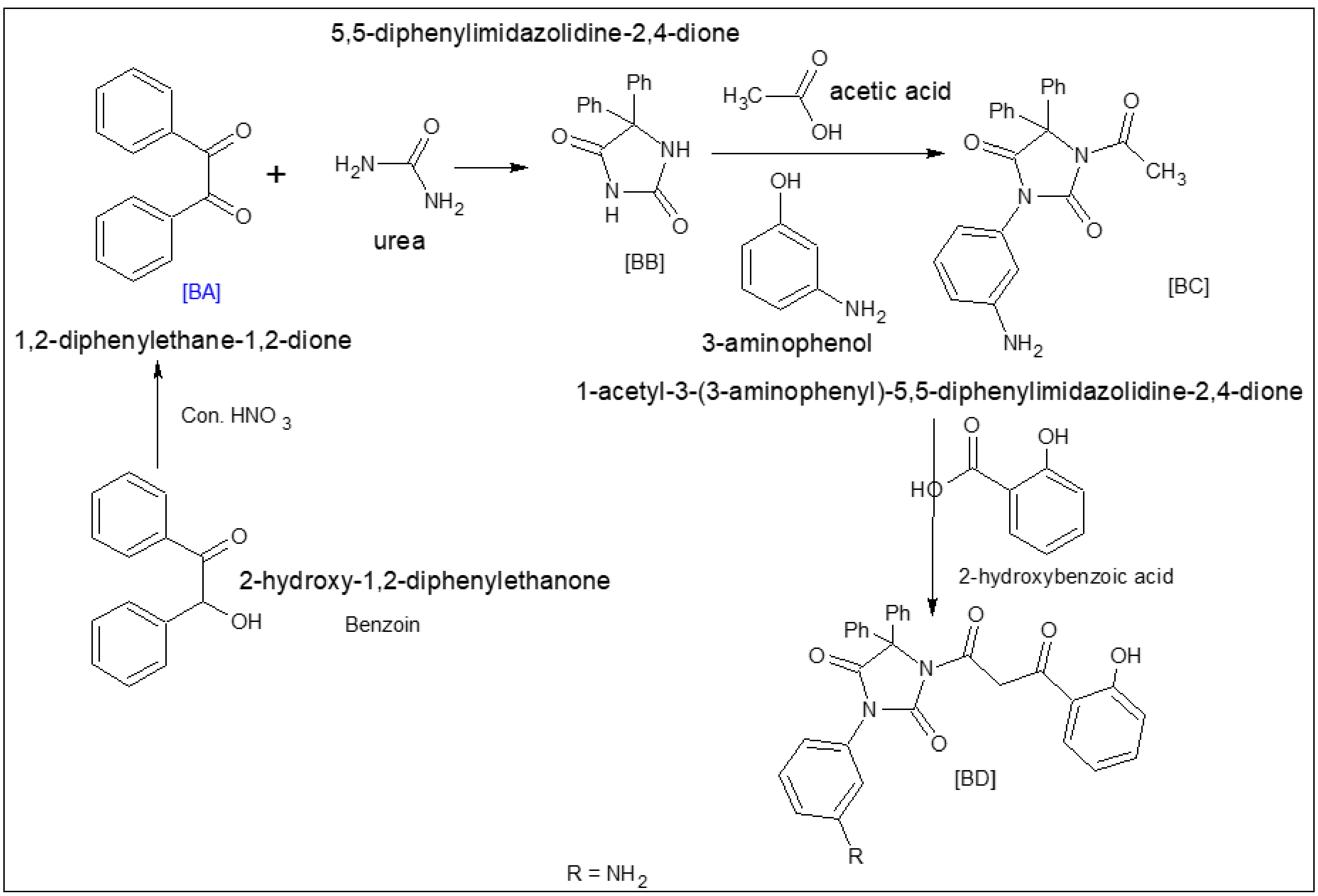
Procedure

Synthesis of Benzil (BA)-(scheme 1A)

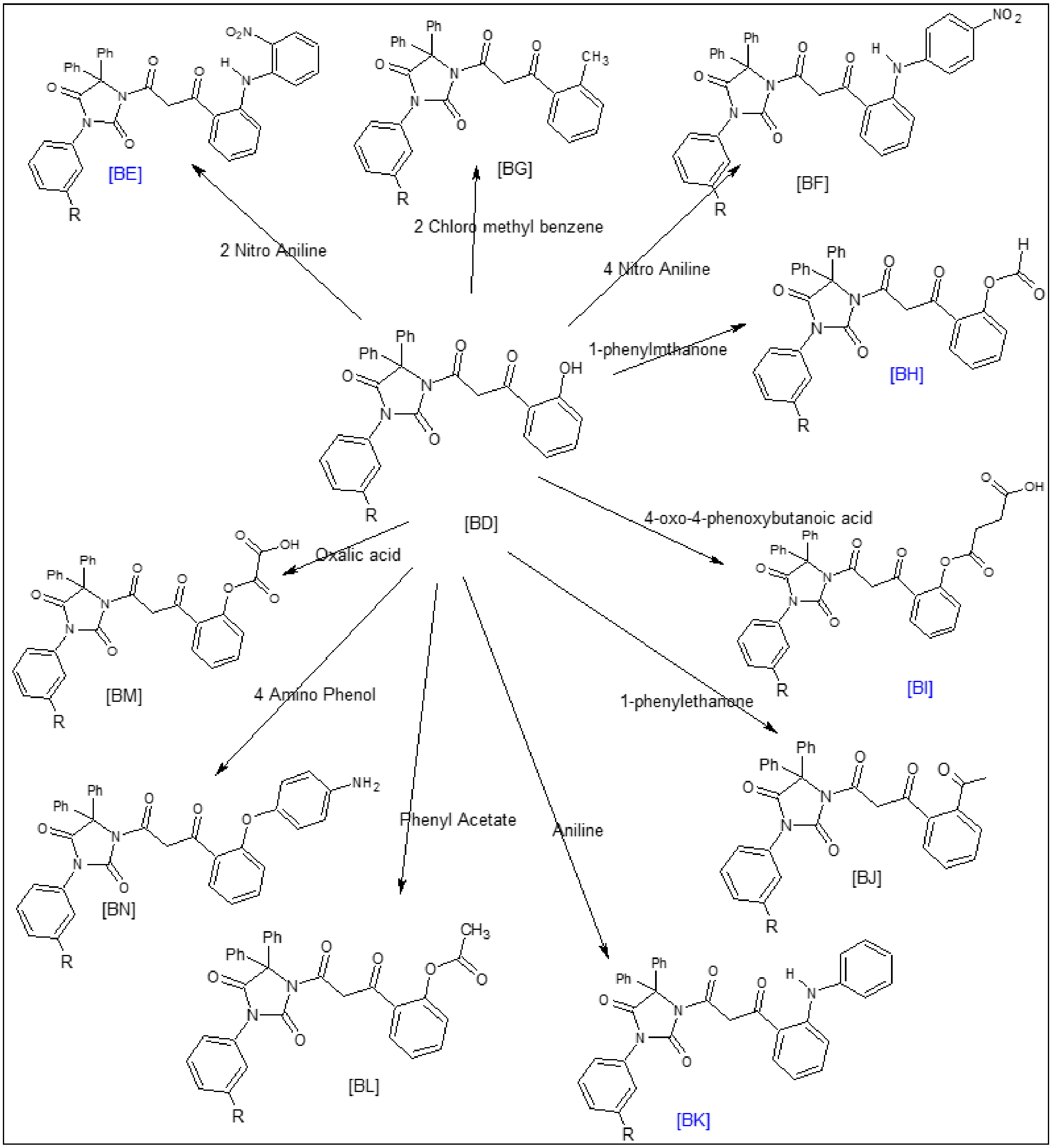
4 g of 2-hydroxy-1,2-diphenylethanone and 14 mL of concentrated HNO_3 is heated in an RBF over a hot water bath for 11 min. Following the reaction, add 75 mL of water to the mixture, allow it to cool, recrystallize it using 10 mL of ethanol. To attain the cloud point, add water dropwise once the substance has dissolved. Permit the product to re-solidify. After the material has re-crystallized and allow it to dry.

Synthesis of 5,5-diphenylimidazolidine-2,4-dione (BB)-(scheme 1A)

Pour 100 mL of RBF with 5.3 g of benzoyl. 3.0 g of urea was added to that RBF. Next, add 15 mL of 30% aq. Sodium hydroxide, or



Scheme 1A: Synthesis of 3-(3-aminophenyl)-1-[3-(2-hydroxyphenyl)-3-oxopropanoyl]]-5,5-diphenylimidazolidine-2,4-dione (BD).



Scheme 1B: Synthesis of 3-(3-aminophenyl)-1-[3-(2-hydroxyphenyl)-3-oxopropanoyl]]-5,5-diphenylimidazolidine-2,4-dione (BE-BN).

NaOH Add 75 mL of C_2H_5OH (ethanol) last. Connect the reflux condenser and then use the heating mantle to boil under reflux for at least 2 hr. Bring the temperature down. After 10 min of standing, filter using a suction pump to get rid of any insoluble by product. Use concentrated HCl to render the product filtrate with very acidic acid. After cooling in ice water, remove PPT right away.

Synthesis of 1-acetyl-3-(3-aminophenyl)-5,5-diphenylimidazolidine-2,4-dione (BC)-(scheme 1A)

Add 1 g of phenytoin to the flask with a round bottom. To the 100 mL RBF, add 1 mL of glacial acetic acid and 3 amino phenols. Refluxing the reaction mixture, heat it for 2 hr at a temperature between 80 and 100°C. Add 10 mL of crushed ice to the reaction mixture to cool it down. Pour in more ice-cold water. Gather the product after filtering the reaction mixture.

Synthesis of 3-(3-aminophenyl)-1-[3-(2-hydroxyphenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine -2,4-dione (BD)-(scheme 1A)

Put 2 g of (BC)-(scheme 1A) with 100 mL RBF, add 50 mL ethanol and 1 g 2-hydroxy benzoic acid. For two and a half hour, reflux the reaction mixture between 80 and 100°C. Crushed ice water (5 mL) is added to cool the reaction mixture. Gather the product after filtering the reaction mixture.

Synthesis of 1-[3-(*N*-Phenyl-2-nitroaniline)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenyl imidazolidine-2,4-dione(BE)-(scheme 1B)

Put 2 g of BD (scheme 1A) in a flask with a round bottom, 25 mL of ethanol and 2 mL of nitro aniline, the reaction mixture is heated for an hour while experiencing reflux. To obtain the product, filter it and then recrystallize it using ethanol.

Synthesis of 1-[3-(*N*-Phenyl-4-nitroaniline)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BF)-(scheme 1B)

Put 1 g of BD (scheme 1A) in a flask with a round bottom, to which 25 mL of ethanol and 1 mL of 4-nitro aniline are added. After heating the reaction cool. To get the product, filter the reaction mixture and then dry it and recrystallize it using ethanol.

Synthesis of 1-[3-(*N*-phenylformamide)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BG)-(scheme 1B)

Put 2 g of BD (Scheme 1A) in a flask with a round bottom, reflux the reaction mixture after adding 30 mL of ethanol (used as a solvent) and 5 mL of 2-chloromethyl benzene. After heating the reaction cool. To get the product, filter the reaction mixture and then dry it and recrystallize it using ethanol.

Synthesis of 1-[3-(2-oxyphenyl)amino]benzoic acid)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BH)-(scheme 1B)

Put 2 g of BD (scheme 1A) in a flask with a round bottom in 30 mL of ethanol with 2 g of 1-phenyl methanone. Give it a good shake. For 1 hr, heat the reaction mixture cool to room temperature after an hour. Let it stand for 5 min. To obtain the product, filter it, then dry it and recrystallize it using ethanol.

Synthesis of 1-[3-(2-aminophenyl)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BI)-(scheme 1B)

Put 2 g of 3 BD (scheme 1A) in a flask with a round bottom and include 30 mL of ethanol and 2 mL of 4-oxo-4-phenoxybutanoic acid. For 1 hr, heat the reaction mixture to allow it to cool when the reaction is finished. After the result has been filtered, dried and recrystallized with ethanol.

Synthesis of 1-[3-(2-phenyl acetate)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BJ)-(scheme 1B)

Put 2 g of BD (Scheme 1A) in a flask with a round bottom and add 2 mL of 1-phenyl ethanone. Heat the reaction mixture under reflux conditions for 30 min at a constant 50 degrees. Set the RBF aside for a few minutes when the response is finished. Incorporate ice water into the blend. To get the product, filter, dry and then recrystallize.

Synthesis of 1-[3-(oxo(phenyl-amino)acetic acid)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BK)-(scheme-1B)

Put 2 g of BD (scheme 1A) in a flask with a round bottom, together with 30 mL of ethanol, 2 g of aniline. For 1 hr, the reaction mixture is heated. After the result has been filtered, dried and recrystallized with ethanol

Synthesis of 1-[3-(*N*-phenyl benzene)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BL)-(scheme 1B)

Put 2 g of 3 BD (scheme 1A) in a flask with a round bottom and include 30 mL of ethanol and 2 g of phenol acetate. For one and a half hours, heat the mixture to allow it to cool when the reaction is finished. After filtering, dry the item combined it with ethanol to form a crystal to produce.

Synthesis of 2-(2-(3-(2,4-dioxo-5,5-diphenylimidazolidin-1-yl) -(3-aminophenyl)--3-oxopropanoyl)phenoxy)-2-oxoacetic acid (BM)- (scheme 1B)

Put 2 g of BD (scheme 1A) in a flask with a round bottom together with 30 mL of ethanol, 2 g of oxalic acid. For 1 hr, the reaction mixture is heated, when the reaction is finished. After the product has been filtered, dried and recrystallized with ethanol.

Synthesisof1-(3-(2-(4-aminophenoxy) phenyl) -(3-aminophenyl)-3-oxopropanoyl)-5,5-diphenylimidazolidine-2,4-dione (BN)-(scheme 1B)

Put 2 g of BD (scheme 1A) in a flask with a round bottom and combine with 30 mL of ethanol and 2 g of 4-aminophenol. For one and a half hours, heat the mixture then cool when the reaction is finished. After filtering, dry the item. Using ethanol recrystallized it to produce a product.

RESULTS

Spectral Data

Synthesis of 1-[3-(2-phenyl acetate)-(3-aminophenyl)--3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BJ)-(scheme 1B)

FTIR (KBr) ν cm^{-1}: 1957.39 C=C Stretch (Aromatic), 1186.01 C-C Stretch (Aromatic), 1341.88 C-N Stretch (Aromatic), 3275.55 N-H Stretch (Aromatic), 1712.26 C=O Stretch (Aryl ketone) 728.13 O-H (Bend); 1H NMR (400 MHz, DMSO): δ 12.17 Ar N-H (s, 1H), δ 8.721-7.158 Ar C-H (m, 19H), δ 3.3 CH_3 Group (s, 3H), 5.2 O-H Group (s,1H).

Synthesis of 1-[3-(*N*-phenylformamide)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BG)-(scheme 1B)

FTIR (KBr) ν cm^{-1}: 1949.68 C=C Stretch (Aromatic), 1020.16 C-C Stretch (Aromatic), 1340.18 C-N Stretch (Aromatic), 3275.5 N-H Stretch (Aromatic), 1715.98 C=O Stretch (Aryl ketone), 700.99 O-H (Bend), 1409.71 S=O Stretch, 1183.11 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 11.506 Ar N-H (s, 1H), δ 5.1 O-H (s, 1H), δ 8.717-7.158 Ar C-H (m, 20H), δ 4.348 CH_2 Group (s, 2H), δ 3.3 CH_3 Group (s, 3H).

Synthesis of 1-[3-(*N*-Phenyl-2-nitroaniline)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenyl imidazolidine-2,4-dione(BE)-(scheme 1B)

FTIR (KBr) ν cm^{-1}: 1953.54 C=C Stretch (Aromatic),1068.59 C-C Stretch (Aromatic), 1266.75 C-N Stretch (Aromatic), 3267.49 N-H Stretch (Aromatic), 1710.69 C=O Stretch (Aryl ketone), 778.13 O-H (Bend), 1402.0 S=O Stretch, 1173.11 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 12.075 Ar N-H (s, 1H), δ 8.471-6.949 Ar C-H (m, 20H), δ 5.4 O-H (s, 1H).

Synthesis of 1-[3-(oxo(phenyl-amino)acetic acid)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BK)-(scheme-1B)

FTIR (KBr) ν cm^{-1}: 1934.25 C=C Stretch (Aromatic), 1124.3 C-C Stretch (Aromatic),3238.7 N-H Stretch (Aromatic), 1714.55 C=O (Aryl Ketone), 886.13 O-H (Bend), 1433.12 S=O Stretch, 1128.1 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 10.695 Ar N-H (s, 1H), δ 8.464-7.927 Ar C-H (m, 19H), δ 5.0 O-H (s, 1H).

Synthesis of 1-[3-(2-oxyphenyl)amino]benzoic acid)-(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BH)-(scheme 1B)

FTIR (KBr) ν cm^{-1}: 1880.26 C=C Stretch (Aromatic), 3298.64 N-H Stretch (Aromatic), 1714.27 C=O Stretch (Aryl ketone), 887.09 O-H (Bend), 1428.32 S=O Stretch, 1147.44 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 12.955 Ar N-H (s, 1H), δ 8.266-7.483 Ar C-H (m, 19H), δ 5.334 O-H (s, 1H).

Synthesis of 1-[3-(*N*-Phenyl-4-nitroaniline) -(3-aminophenyl)-3-oxopropanoyl]-5,5-diphenylimidazolidine-2,4-dione(BF)-(scheme 1B)

FTIR (KBr) ν cm^{-1}: 1872.54 C=C Stretch (Aromatic), 1139.72 C-C Stretch (Aromatic), 1270.86 C-N Stretch (Aromatic), 3306.36 N-H Stretch (Aromatic), 1718.38 C=O Stretch (Aryl ketone), 908.30 O-H (Bend), 1140.14 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 13.088 Ar N-H (s, 1H), δ 7.893-7.236 Ar C-H (m, 18H), δ 5.589 O-H (s, 1H).

Synthesisof1-(3-(2-(4-aminophenoxy) phenyl) -(3-aminophenyl)--3-oxopropanoyl)-5,5-diphenylimidazolidine-2,4-dione (BN)- (scheme 1B)

FTIR (KBr) ν cm^{-1}:1886.60 C=C Stretch (Aromatic), 1138.90 C-C Stretch (Aromatic), 1319.60 C-N Stretch (Aromatic), 3398.4 N-H Stretch (Aromatic), 1718.60 C=O (Aryl ketone), 1319.60 C-O Stretch (Aromatic), 948.57 O-H (Bend), 1129.34 O-H Stretch sulfonic acid;; 1H NMR (400 MHz, DMSO): δ 12.955 Ar N-H (s, 1H), δ 8.266-7.483 Ar C-H (m, 19H), δ 5.33 O-H (s, 1H).

Synthesis of 2-(2-(3-(2,4-dioxo-5,5-diphenylimidazolidin-1-yl)-(3-aminophenyl)--3-oxopropanoyl)phenoxy)-2-oxoacetic acid (BM)- (scheme 1B)

FTIR (KBr) ν cm^{-1}: 1951.54.06 C=C Stretch (Aromatic),1065.59 C-C Stretch (Aromatic), 1261.75 C-N Stretch (Aromatic), 3260.49 N-H Stretch (Aromatic), 1710.69 C=O Stretch (Aryl ketone), 1735.31 C=O Stretch (Ester), 779.13 O-H (Bend), 1401.0 S=O Stretch, 1171.11 O-H sulfonic acid; 1H NMR (400 MHz, DMSO): δ 11.075 Ar N-H (s, 1H), δ 8.471-6.949 Ar C-H (m, 19H), δ 5.1 O-H (s, 1H).

Biological evaluation

The anti-convulsant properties of newly synthesised 5,5-diphenylimidazolidin-1-yl derivatives were examined. Eleven compounds in total three step products and eight

5,5-diphenylimidazolidin-1-yl derivatives were assessed for biological screening. The anticonvulsant action is briefly described in the section that follows.

Anticonvulsant activity (Strychnine Induced Convulsion Method)

Several 5,5-diphenylimidazolidin-1-yl derivatives are useful in treating tonic-clonic (grand mal) seizures, which are characterised by widespread seizures.[12] Because strychnine is such a potent toxin, a minimal dose is required to cause convulsions. Using an intravenous Strychnine paradigm, the synthetic compounds' anticonvulsant efficacy was assessed by screening them against Strychnine.[13] The fundamental idea behind the anti-convulsant test is to compare the produced molecules to the reference drug, phenytoin. Comparing the duration of convulsions, the start of action in seconds (sec.), the percentage of protection (%protection) and other factors should be done to draw a conclusion.[14] This sc Strychnine model uses strychnine as a negative control. In order to choose the dose for the standard and negative control, the S.K. Kulkarni practical book was used. The Wistar Rats will be divided into six groups. Each group consists of six animals ($n = 6$) who receive therapy for 10 days.[15] The first group will get distilled water as the control vehicle, while the second group will receive the traditional medication. Phenytoin 100 mg/kg is used in it. On the 10th day, 60 min preceding the previous dosage, 85 mg/kg of strychnine was administered into each group to cause convulsions in the rats.[16] The results of the anticonvulsant activity tests of the generated compounds were shown in Table 1 and Figure 2.

Table 1: Strychnine Induced Convulsion Method by using Wistar Rats.

No. of Groups	No. of Rats
Vehicle Control (Water)	6
Negative Control (Strychnine 85 mg/kg).	6
Standard (Phenytoin 100 mg/kg).	6
5,5-diphenylimidazolidin-1-yl derivative (a) Lower dose.	6
5,5-diphenylimidazolidin-1-yl derivative (b) Middle dose.	6
5,5-diphenylimidazolidin-1-yl derivative (c) Higher dose.	6
Total	36

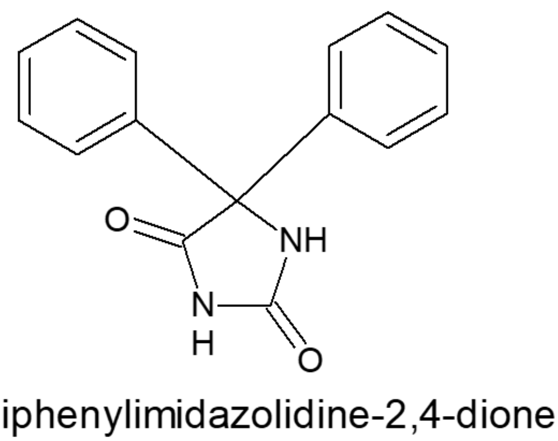


Figure 1: 5, 5-diphenylimidazolidine heterocyclic nucleus.

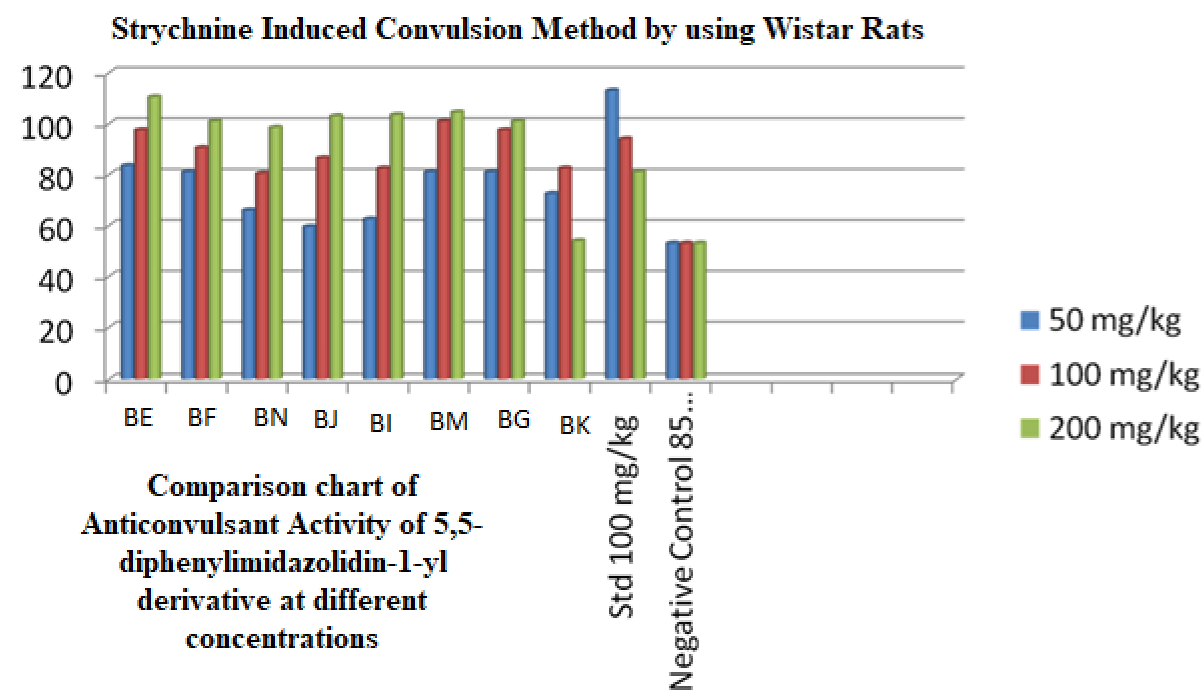


Figure 2: Comparison chart of Anticonvulsant Activity of 5,5-diphenylimidazolidin-1-yl derivative at different concentrations.

Table 2: Anti-convulsant result of 5,5-diphenylimidazolidin-1-yl derivatives at different concentrations.

Compounds	Doses (mg/kg)	Onset of Convulsions (sec)	Duration of Convulsions (sec)	Avg. % Protection	Recovery/Death
BE	50	83.5	139	76.35%	Recovery
	100	975	89		
	200	110.5	53		
BN	50	81	119	75.63%	Recovery
	100	90.5	80		
	200	101	66		
BG	50	66	163	66.38%	Recovery
	100	80.5	101		
	200	98.5	63		
BH	50	59.5	142	59.10%	Recovery
	100	86.5	99		
	200	103	73		
BI	50	62.5	150	66.10%	Recovery
	100	82.5	91		
	200	103.5	52		
BJ	50	81	148	71.56%	Recovery
	100	101	84		
	200	104.5	50		
BK	50	81	165	67.50%	Recovery
	100	97.5	89		
	200	101	39		
BL	50	72.5	172	62.88%	Recovery
	100	82.5	105		
	200	54	38		
BM	50	83.5	139	76.35%	Recovery
	100	975	89		
	200	110.5	53		
BN	50	81	119	75.63%	Recovery
	100	90.5	80		
	200	101	66		
Std. Phenytoin 100 mg/kg	100	119	11	100	Recovery

DISCUSSION

The technique 1B was followed in the synthesis of Novel Substituted 5,5-diphenylimidazolidin-1-yl derivatives from BE to BN. Additionally, the response mixture was mixed for the duration indicated in the table below at room temperature. After that, the strong product was cleaned with distilled water and dried to produce smooth goods in excellent yields, ranging from BE to BN. Table 2 presents a comparative chart, which shows the convulsion activity of novel substituted 5,5-diphenylimidazolidin-1-yl derivatives at varying concentrations. The methods include low, middle and high doses, with the aim of minimising seizure spread. The typical medication was phenytoin 100 mg/kg. For the following 30 min, each animal will be watched separately to see if it exhibits convulsions. Table 2 summarises the anti-convulsant results of the named compounds (BE to BN). Compounds BN and BJ demonstrated protection at a maximal dose level of 200 mg/Kg and for the following 30 min; each animal will be monitored separately for convulsion behaviour. At the highest dose level (100 mg/kg), compound BN and BJ showed protection and over the following 30 min, each animal will be watched separately for convulsion behaviour. At lower dosage levels (50 mg/kg), compounds BN and BJ containing aromatic groups demonstrated reduced protection against convulsions that were generated. Table 2 displayed the anti-convulsant test findings for the produced compounds. The anti-convulsant properties of recently synthesised compounds were investigated using the Strychnine Induced Convulsion Method. Oral administration at a dosage of 100 mg/kg was used to test each chemical. Table 2 displays the study's findings. It's noteworthy to note that every chemical in the current series exhibited some degree of anti-convulsion properties. The data suggest that all of the BN and BJ had stronger anti-convulsant effects than the ones that matched them. In comparison to their 5,5-diphenylimidazolidin-1-yl derivatives, nitro aniline derivatives showed reduced percentage suppression of convulsion but superior efficacy overall. The most active compounds were found to be BM, BG and BE, which have amino groups at the ortho, meta and para positions on the phenyl ring. These compounds were investigated at three different dosage levels (200 mg/kg orally). Of the newly synthesised compounds, compound BI demonstrated the most powerful and dose-dependent anti-convulsant action. The efficacy of novel substituted 5,5-diphenylimidazolidin-1-yl derivatives to prevent seizure spread at different concentrations, such as low, middle and high doses, is demonstrated by a comparison chart see Figure 2 and Table 2. For the following 30 min, each animal will be watched separately for convulsive behaviour. Table 2 summarises the anticonvulsant results of compounds named BE to BN. Compounds BM and BG demonstrated protection at a maximal dosage level of 200 mg/kg and for the following 30 min, each animal will be monitored separately for convulsive behaviour. Compounds BF and BE showed protection at the highest dose level (100 mg/kg) and for the following 30 min, each animal will be watched separately for convulsive behaviour. At lower dosage levels (50 mg/kg), compounds BF and BE containing aromatic groups demonstrated weaker protection against provoked seizures. Table 2 and Figure 2 display the findings of the produced compounds' anticonvulsant activity testing.

CONCLUSION

The 5,5-diphenylimidazolidin-1-yl reported in this work, in conclusion, has remarkable drug-like properties, low neurotoxicity and strong anticonvulsive activity, all of which suggest their potential for use in the development of new anticonvulsant medications. More action was discovered when synthesised compounds were compared to other phenytoin at 100 mg/kg. Finally, it was demonstrated that a range of 5,5-diphenylimidazolidin-1-yl derivatives (BE to BN) and their more hydrophobic counterparts (BE to BN) were effective anticonvulsants *in vivo*. More than half of the chemicals in the BE to BN family showed anticonvulsant efficacy in models of induced seizures.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

FTIR: Fourier transform infrared spectroscopy; **NMR spectroscopy:** Nuclear magnetic spectroscopy; **MS:** Mass spectroscopy; **KBr:** Potassium Bromide; **% yield:** Percentage yields; **M.P:** Melting point; **mg/kg:** Milligram/ kilograms; **sec:** seconds**; δ:** Chemical shift; Mol. **Wt:** Molecular Weight; **gm:** Gram.

REFERENCES

1. French JA, Staley BA. AED treatment through different ages: as our brains change, should our drug choices also? Epilepsy Curr. 2012; 12(1); Suppl 3: 22-3.
2. Anger T, Madge DJ, Mulla M, Riddall D. Medicinal chemistry of neuronal voltage-gated sodium channel blockers. J Med Chem. 2001;44(2):115-37. doi: 10.1021/jm000155h , PMID 11170622.
3. Ragavendran JV, Sriram D, Kotapati S, Stables J, Yogeeswari P. Newer GABA derivatives for the treatment of epilepsy including febrile seizures: A bioisosteric approach. Eur J Med Chem. 2008;43(12):2650-5. doi: 10.1016/j.ejmech.2008.01.036, PMID 18403060.
4. Wu T, Ido K, Ohgoh M, Hanada T. Mode of seizure inhibition by sodium channel blockers, an SV2A ligand and an AMPA receptor antagonist in a rat amygdala kindling model. Epilepsy Res. 2019;154:42-9. doi: 10.1016/j.eplepsyres.2019.03.011 , PMID 31035244.
5. Alexander MS, Scott KR, Harkless J, Butcher RJ, Jackson-Ayotunde PL. Enaminones 11. An Examination of Some Ethyl Ester enaminone Derivatives as anticonvulsant agents. Bioorg Med Chem. 2013;21(11):3272-9. doi: 10.1016/j.bmc.2013.03.036, PMID 23602623.
6. Heinbockel T, Wang ZJ, Jackson-Ayotunde PL. Allosteric modulation of GABAA receptors by an anilino enaminone in an olfactory center of the mouse Brain. Pharmaceuticals (Basel). 2014;7(12):1069-90. doi: 10.3390/ph7121069, PMID 25525715.
7. Wang ZJ, Sun L, Jackson PL, Scott KR, Heinbockel T. A Substituted anilino enaminone acts as a novel positive allosteric modulator of GABAA Re-ceptors in the Mouse Brain. J Pharmacol Exp Ther. 2011;336(3):916-24. doi: 10.1124/jpet.110.173740, PMID 21163867.
8. Jackson PL, Hanson CD, Farrell AK, Butcher RJ, Stables JP, Eddington ND, *et al.* Enaminones 12. An explanation of anticonvulsant activity and toxicity per Linus Pauling's clathrate hypothesis. Eur J Med Chem. 2012;51:42-51. doi: 10.1016/j.ejmech.2012.02.003, PMID 22417639.
9. Anderson AJ, Nicholson JM, Bakare O, Butcher RJ, Wilson TL, Scott KR. Enaminones 9. Further studies on the anticonvulsant activity and potential Type IV phosphodiesterase inhibitory activity of substituted vinylic benzamides. Bioorg Med Chem. 2006;14(4):997-1006. doi: 10.1016/j.bmc.2005.09.023, PMID 16219468.
10. Jackson PL, Scott KR, Southerland WM, Fang YY. Enaminones 8: CoMFA and CoMSIA studies on some anticonvulsant enaminones. Bioorg Med Chem. 2009;17(1):133-40. doi: 10.1016/j.bmc.2008.11.014, PMID 19059784.
11. Edafiogho IO, Kombian SB, Ananthalakshmi KV, Salama NN, Eddington ND, Wilson TL, *et al.* Enaminones: Exploring additional therapeutic activities. J Pharm Sci. 2007;96(10):2509-31. doi: 10.1002/jps.20967, PMID 17621683.
12. Amaye IJ, Heinbockel T, Woods J, Wang Z, Martin-Caraballo M. 6 Hz Active Anticonvulsant Fluorinated N-Benzamide Enaminones and Their Inhibitory Neuronal Activity. Int J Environ Res Public Health. 2018;15(8):1784: 6Hz. doi: 10.3390/ijerph15081784, PMID 30127263.
13. Sula A, Booker J, Ng LC, Naylor CE, DeCaen PG, Wallace BA, *et al.* The complete structure of an activated open sodium channel. Nat Communi Cations. 2012;8(1):14205.

14. Wang ZJ, Sun L, Jackson PL, Scott KR, Heinbockel T. A Substituted anilino enaminone Acts as a Novel Positive allosteric Modulator of GABAA Re-ceptors in the Mouse Brain. J Pharmacol Exp Ther. 2011;2011(3):916-24.
15. Jackson PL, Hanson CD, Farrell AK, Butcher RJ, Stables JP, Eddington ND, *et al.* Enaminones 12. An explanation of anticonvulsant activity and toxicity per Linus Pauling's clathrate hypothesis. Eur J Med Chem. 2012;51:42-51. doi: 10.1016/j.ejmech.2012.02.003, PMID 22417639.
16. Anderson AJ, Nicholson JM, Bakare O, Butcher RJ, Wilson TL, Scott KR, *et al.* Further Studies on the Anticonvulsant Activity and Po tential Type IV phosphodiesterase Inhibitory Activity of Substituted Vinylic benzamides. Bioorg Med Chem. 2006;2006(4):997-1006.

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