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Original Article

Synthesis and Biological Evaluation of Novel 5,5-Diphenylimidazolidine Derivatives with Anticonvulsant Activity

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ABSTRACT

Background: A heterocyclic hydrocarbon having a 5, 5-diphenylimidazolidine heterocyclic ring that possesses distinctive fundamental structural characteristics. It is a fused ring of aromatic di-benzene and imidazolidine. The flexible heterocyclic molecules in 5, 5-diphenylimidazolidine that have two nitrogen atoms. The biological activity of the 5, 5-diphenylimidazolidine ring and its derivatives is significant and encouraging. We produce a variety of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid and its derivatives in this investigation. In literature survey and molecular docking; it was confirmed that 5, 5-diphenylimidazolidine-2,4-dione gives anticonvulsant effects. The pharmacological samples were examined for their ability to prevent convulsions using the strychnine-induced convulsion method. **Materials and Methods:** Benzoin; Benzil; Urea; Glacial Acetic Acid; 4-amino benzoic acid; Con. HNO_3; Formic Acid; 2- Nitro Aniline; 4- Nitro Aniline; Aniline; Acetyl Chloride; Formic Acid; 4- amino Phenol are used for the synthesis.IR, NMR and MS are used for interpretation. **Results:** Our research led us to the conclusion that a variety of compounds have strong anticonvulsant properties. The compound 4-(2-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW5)- (scheme II A); 4-(3-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW6)- (scheme II A); 4-(2,5-dichloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW7) (scheme II A) and 4-(N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW3) (scheme II A) gives strong anti-convulsant effects against phenytoin drug. **Conclusion:** The title compounds and its derivatives were examined for their ability to treat convulsions. Studies of the relationship between structure and activity revealed that compounds containing 5, 5-diphenylimidazolidine derivatives that have an electron-withdrawing group have higher activity than those that have an electron-donating group.

Keywords: 5, 5-diphenylimidazolidine, Benzil, Urea, 4-amino benzoic acid, 2-Nitro Aniline, 4-Nitro Aniline, Aniline, Strychnine, Anti Convulsant Activity, Phenytoin.

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INTRODUCTION

Anticonvulsant medication development has been one of the most visible research areas in recent years. Almost 86 years have passed since Putnam discovered that phenytoin, also known as Dilantin, is the medicine of choice for the treatment of generalised tonic-clonic seizures (also known as grand mal epilepsy) and focal motor seizures.[1] The IUPAC designation for phenytoin, often known as Dilantin, is 5,5-diphenyl imidazolidine-2,4-dione. Although the scientist Biltz synthesised phenytoin (I) in 1908, its anti-epileptic effect was not recognised until 1938 by Putnam.[2] Phenytoin was not synthesised again until the 1920s, and it was classified as a "inactive" compound.[3] Their analogues are important molecules with varying biological and therapeutic activity. Among the most popular are the Biltz synthesis, the Read synthesis, and the Bucherer-Bergs synthesis.[4] The N3-alkylation of 5,5-diphenylimidazolidine-2,4-dione is a general procedure used to change the core scaffold and thus the characteristics of the resultant materials. The structure of 5, 5-diphenylimidazolidine-2,4-dione heterocyclic nucleus was given in Figure 1.

Many phenytoin (I) compounds have been synthesised and claimed to have a variety of pharmacological actions, including anticonvulsants.[5] The interaction and blockage of brain Na+ channels by hydantoin derivatives mediates their anticonvulsant activity.[6] The therapeutic properties of phenytoin are so diverse that

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they include anticancer and antibacterial activity,[7] 5,5-Diphenyl-imidazolidine2,4-dione (I) and its derivatives are well suited for use as medications due to their long shelf life, however easy breakdown in the body is preferred.[8] Despite its chemical and thermal stability, it can be hydrolyzed more easily in biological systems in the presence of hydantoinase enzymes.[9] This indicates that this compound can easily undergo nucleophilic substitution reactions, and so mono-alkylated at the imide position N3-H is a widely used procedure to alter the core scaffold and thus the characteristics of the resultant materials.[10] Water-soluble prodrug of 5,5-diphenyl-imidazolidine-2,4-dione were also discovered by adding suitable side chains to the imidic group N3-H.[11] The current study describes numerous enhancements and an evaluation of a new reliable strategy for manufacturing derivatives of 5,5-diphenyl imidazolidine-2,4-dione (I) as a building block via acylation, halogenation, reduction, and nucleophilic substitution reactions.[12]

The synthetic and pharmaceutical interest in imidazolidine-2,4-diones, or hydantoins, has not waned over the last decade, giving rise to over 3000 articles and patents in chemical and medicinal chemistry.[13] The synthesis of these five-membered heterocycles has been the subject of several reviews. This report provides an update on the advancement of hydantoin chemistry and references publications from 2004 to May 2016. It is organised differently than the last report from 2004: hydantoins are categorised according to the substitution pattern on the main backbone, and the synthetic procedures for each family of compounds are highlighted.[14] This method is extremely useful not only for synthetic chemists, but also for a broader audience in the field of medicinal chemistry, where target-oriented syntheses are required.

The following assumptions regarding the synthesised compounds were used to establish the structural activity connection. In this study, imidazolidine derivatives comprising 5,5-diphenyl imidazolidine-2,4-dione were synthesised and their anti-epileptic effects were investigated.[15] It is worth noting that the imidazolidine moiety shown strong effectiveness against both anti-epileptic activities.[16] The 4-substituted phenyl ring functions as a lipophilic domain, while the NH in the imidazolidine ring functions as a hydrogen bonding domain. As a result, the imidazolidine ring may be regarded as essential pharmacophoric criteria for anti-epileptic activities.[17] The biological activity of the 5,5-diphenyl imidazolidine-2,4-dione rings was examined, and the structure-activity correlations of modifying the substitution pattern surrounding that compound were discussed. This emphasises that the compounds' hydrophobic and lipophilic regions are responsible for their powerful anticonvulsant action. Furthermore, the effect of electron donating groups on the substituted benzene with imidazolidine moiety was investigated. The SAR analysis discovered that substances with anti-epileptic properties such as 4-(2-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW5)- (scheme II A); 4-(3-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW6)- (scheme II A); 4-(2,5-dichloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW7) (scheme II A) and 4-(N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW3). The activity of imidazolidin-2,4-dione-containing compounds was dramatically increased. These findings suggest that the substitution of the NO_2 group connected to 5,5-diphenyl imidazolidine-2,4-dione derivatives leads to an increase in anti-epileptic activity.

MATERIALS AND METHODS

Materials

4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine -1-yl) carbonyl] benzene sulfonic acid and its derivatives was prepared by using 5,5-diphenylimidazolidine-2,4-dione, 2-hydroxy-5-sulfobenzoic acid, Dichloromethane, 2-nitro aniline, 4-nitro aniline, aniline, acetyl chloride, formic acid etc. Analytical grade chemicals were used throughout. Some chemicals are available at colleges; however, all were obtained from Modern Chemicals in Nashik.

Methods

By using a traditional approach, all diphenyl imidazolidine derivatives were created. By using the open tube capillary method, melting points were measured and determined. The chemicals' purity was examined using Thin Layer Chromatography (TLC) techniques and by IR spectra. It was shown in Schemes I A and II B illustrate the synthesis pathway for 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid and its derivatives.

Synthetic procedures

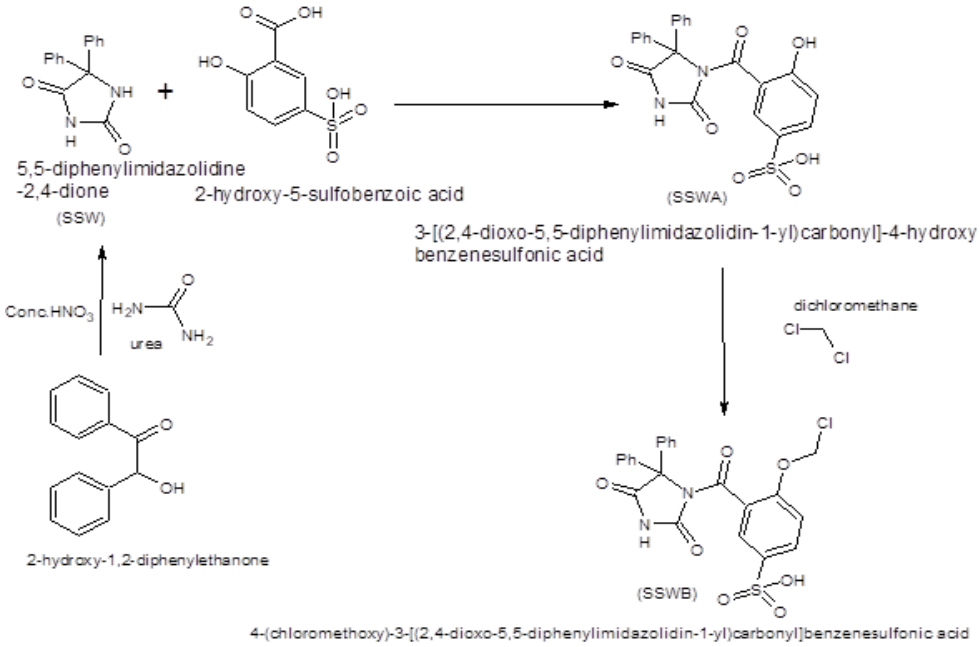
Synthesis of 5,5-diphenylimidazolidine -2,4-dione (SSW)- (scheme I A)

Take 5.3 g of 2-hydroxy-1,2-diphenylethanone in 100 mL RBF, then add 3.0 g of urea in that RBF, then add 15 mL 30% aq. NaOH (sodium hydroxide). Lastly add 75 mL of C_2H_5OH(ethanol).

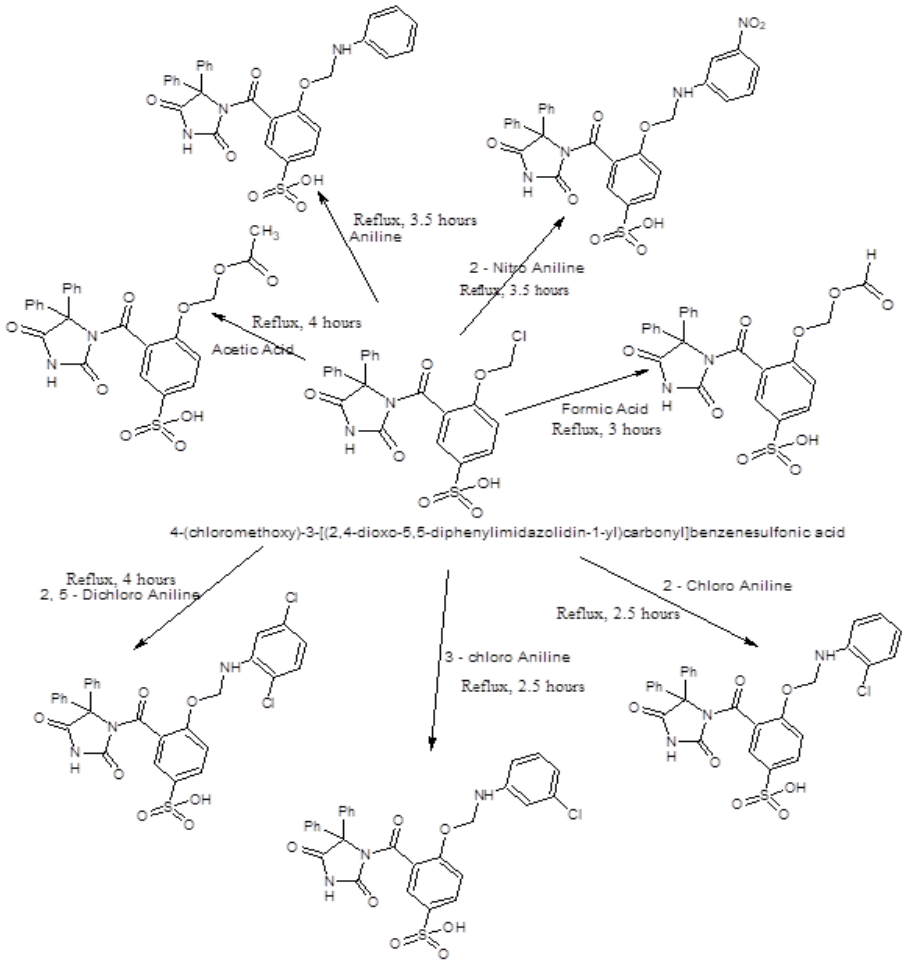
5,5-diphenylimidazolidine-2,4-dione

Figure 1: 5, 5-diphenylimidazolidine-2,4-dione heterocyclic nucleus.

Experimental Work



Scheme I A: Synthesis of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid.



Scheme II B: Synthesis of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (SSWB) (SSW1-SSW7).

Using a heating mantle and a reflux condenser, boil the mixture for at least 2 hr. to a comfortable temperature Mix thoroughly after adding the reaction mixture product to 125 mL of water. Permit to stand for 10 min. In order to eliminate an insoluble by-product, filter under suction pump next. Render the product filtrate with strongly acidic acid with concentrated HCl. Cool in Ice water and immediately filter off ppt.

Synthesis of 3-[(2,4-dioxo-5,5-diphenylimidazolidin-1-yl) carbonyl]-4-hydroxy benzene sulfonic acid (SSWA)- (scheme I A)

Take 1 g of 5,5-diphenylimidazolidine -2,4-dione into the round bottom flask, add 5 mL of 2-hydroxy-5-sulfobenzoic acid into the RBF of 100 mL. Heat the reaction mixture at about 80-100°C for 4 hr, using a heating mantle and a reflux condenser, boil the mixture for at least 2 hr. to a comfortable temperature Mix thoroughly after adding the reaction mixture product to 125 mL of water. Permit to stand for 10 min. In order to eliminate an insoluble by-product, filter under suction pump next, it gives 3-[(2,4-dioxo-5,5-diphenylimidazolidin-1-yl) carbonyl]-4-hydroxy benzene sulfonic acid. Record Melting point, Theoretical yield, Practical yield and % of Practical yield.

Synthesis of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB)- (scheme I A)

Take 1 g of 3-[(2,4-dioxo-5,5-diphenylimidazolidin-1-yl) carbonyl]-4-hydroxy benzene sulfonic acid into the round bottom flask, add 5 mL dichloromethane in a flask with a circular bottom. Reflux the reaction mixture at about 80-100°Cfor 3 hr. Cool the reaction mixture by adding 5 ml of crushed ice water. Filter the reaction mixture and collect the product, it gives 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid. Record Melting point, Theoretical yield, Practical yield and % of Practical yield.

4-(phenoxymethyl formate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW1)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of formic acid in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 3 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(2-phenoxymethyl formate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(2-phenoxymethyl acetate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW2)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of acetic acid in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 4 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(2-phenoxymethyl acetate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(N-(phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW3)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of Aniline in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 3.5 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(2-nitro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW4)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of 2-Nitro Aniline in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 3.5 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(2-nitro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(2-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW5)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of 2-chloro Aniline in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 2.5 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min.

re-crystallize the product using ethanol after filtering it to produce 4-(2-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(3-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW6)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine -1-yl) carbonyl] benzene sulfonic acid, 10 mL of 3-chloro Aniline in a flask with a circular bottom.; the reaction mixture heat under reflux condition for 2.5 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(3-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

4-(2,5-dichloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: ((SSW7)- (scheme II A)

Take 2 g of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid, 10 mL of 2,5-dichloro Aniline in a flask with a circular bottom. The reaction mixture heat under reflux condition for 4 hr; After the reaction is complete, remove the RBF from the hot water bath and let the reaction mixture cool before adding 50 mL of ice cold water. Let the reaction mixture stand for 10 min. re-crystallize the product using ethanol after filtering it to produce 4-(2,5-dichloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid.

RESULTS

Characterization

Physical Data like % yield, Molecular weight and Melting Point etc. of various derivatives of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (SSWB) (SSW1 – SSW7) are given in Table 1.

Spectral Data

Synthesis of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB)- (scheme I A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1671.98 C=C Stretch (Aromatic), 1085.74 C-C Stretch (Aromatic), 1294.0 C-N Stretch (Aromatic), 3247.54 N-H Stretch (Aromatic), 1718.26 C=O Stretch (Aryl ketone), 1341.54 S=O Stretch (sulfonic acid), 693.28 C-Cl Stretch (Aliphatic),1998.25 C-H bend (Aromatic); 1H NMR (400 MHz, DMSO): δ 11.5 Ar N-H (s, 1H), δ 8.7-7.1 Ar C-H (m, 15H), δ 6.3 CH_2 Group (s, 2H), δ 6.5 CH_2 Group (s, 2H), δ 5.1 O-H (s, 1H); Mol.Wt: 500.91.

4-(2-phenoxyethyl formate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW1)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1679.69 C=C Stretch (Aromatic), 1232.29 C-C Stretch (Aromatic), 2804.96 C-N Stretch (Aromatic), 3267.79 N-H Stretch (Aromatic), 1718.26 C=O Stretch (Aryl ketone), 1349.28 S=O Stretch (sulfonic acid), 1957.39 C-H bend (Aromatic); 1H NMR (400 MHz, DMSO): δ 10.6 N-H (s, 1H), δ 8.6-7.1 Ar C-H (m, 19H), δ 6.3 CH_2 Group (s, 2H), δ 6.7 CH_2 (s, 2H), δ 5.1 O-H (s, 1H); Mol.Wt: 510.47

4-(2-phenoxyethyl acetate)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW2)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1655.26 C=C Stretch (Aromatic), 1232.29 C-C Stretch (Aromatic), 2828.10 C-N Stretch (Aromatic), 3229.22 N-H Stretch (Aromatic), 1742.26 C=O Stretch (Aryl ketone), 1949.68 S=O Stretch (sulfonic acid), 1H NMR (400 MHz, DMSO): δ 10.1 Ar N-H (s, 1H), δ 7.8-6.6 Ar C-H (m, 16 H), δ 6.0 CH_2 Group (d, 4H), δ 5.5 C-OH (s, 1H), 3.1 CH_3 Group (s, 3H), Mol.Wt: 524.50.

Table 1: Physical Data of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (SSWB) (SSW1-SSW7).

Sl. No.	Compounds	Colors of compounds	Molecular formula	Melting point	%yields	Molecular weight
1	SSW1	Yellow	$C_{24}H_{18}N_2O_9S$	310°C	95%	510.47
2	SSW2	Brown	$C_{25}H_{20}N_2O_9S$	320°C	90%	524.50
3	SSW3	Brown	$C_{29}H_{23}N_3O_7S$	305°C	82%	557.57
4	SSW4	White	$C_{29}H_{22}N_4O_9S$	278°C	79%	602.57
5	SSW5	White	$C_{29}H_{22}ClN_3O_7S$	317°C	75%	592.02
6	SSW6	White	$C_{29}H_{22}ClN_3O_7S$	323°C	68%	592.02
7	SSW7	Light green	$C_{29}H_{21}Cl_2N_3O_7S$	293°C	80%	626.46

Physical Data like % yield, Molecular weight and Melting Point etc. of various derivatives of 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (SSWB) (-SSW7) are given in Table 1.

4-(N-(2-phenoxyethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW3)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1620.29 C=C Stretch (Aromatic), 1047.15 C-C Stretch (Aromatic), 2835.81 C-N Stretch (Aromatic), 3401.82 N-H Stretch (Aromatic), 1728.87 C=O Stretch (Aryl ketone), 2003.68 S=O Stretch (sulfonic acid); ^{1}H NMR (400 MHz, DMSO): δ 12.3 N-H (s, 1H), δ 8.5-7.0 Ar C-H (m, 15H), δ 6.3 CH_2 Group (s, 4H), δ 5.4 C-OH (s, 1H); Mol. Wt: 557.57.

4-(2-nitro-N-(2-phenoxyethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW4)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}: 1671.98 C=C Stretch (Aromatic), 1132.01 C-C Stretch (Aromatic), 1266.86 C-N Stretch (Aromatic), 3321.78 N-H Stretch (Aromatic), 1720.10 C=O Stretch (Aryl ketone), 1995.96 S=O Stretch (sulfonic acid); ^{1}H NMR (400 MHz, DMSO): δ 12.0 N-H (s, 1H), δ 8.7-7.1 Ar C-H (m, 15H), δ 6.1 CH_2 Group (s, 4H), δ 5.4 C-OH (s, 1H); Mol. Wt: 602.57.

4-(2-chloro-N-(2-phenoxyethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW5)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1610.27 C=C Stretch (Aromatic), 1085.73 C-C Stretch (Aromatic), 1278.57 C-N Stretch (Aromatic), 3306.36 N-H Stretch (Aromatic), 1717.55 C=O Stretch (Aryl ketone), 2026.86 S=O Stretch (sulfonic acid), 908.30 C-Cl (Aliphatic); 1H NMR (400 MHz, DMSO): δ 11.5 Ar N-H (s, 1H), δ 8.717-7.158 Ar C-H (m, 19H), δ 6.0 CH_2 Group (s, 4H), δ 5.1 C-OH (s, 1H); Mol.Wt: 592.02.

4-(3-chloro-N-(2-phenoxyethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW6)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}:1610.27 C=C Stretch (Aromatic), 1087.11 C-C Stretch (Aromatic), 1363.43 C-N Stretch (Aromatic), 3105.81 N-H Stretch (Aromatic), 1726.95 C=O Stretch (Aryl ketone), 2003.38 S=O Stretch (sulfonic acid), 916.22 C-Cl (Aliphatic); 1H NMR (400 MHz, DMSO): δ δ 10.6 N-H (s, 1H), δ 8.5-7.1 Ar C-H (m, 18H), δ 6.1 CH_2 Group (d, 4H), δ 5.4 C-OH (s, 1H); Mol.Wt: 592.02.

4-(2,5-dichloro-N-(2-phenoxyethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid: (SSW7)- (scheme II A)

FTIR Analysis or FTIR Spectroscopy (KBr) ν cm^{-1}: 1602.56 C=C Stretch (Aromatic), 1032.01 C-C Stretch (Aromatic), 1363.43 C-N Stretch (Aromatic), 3105.80 N-H Stretch (Aromatic), 1726.26 C=O Stretch (Aryl ketone), 1995.96 S=O Stretch (sulfonic acid), 901.55 C-Cl (Aliphatic); ^{1}H NMR (400 MHz, DMSO): δ δ 10.1 N-H (s, 1H), δ 8.7-7.1 Ar C-H (m, 15H), δ 6.3 CH_2 Group (d, 4H), δ 5.1 C-OH (s, 1H); Mol.Wt: 626.46.

Biological evaluation

Anticonvulsant activity

There are numerous 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (SSWB) (SSW1-SSW7) are effective against tonic-clonic (grand mal) generalized seizures.[13] Strychnine can be purchased on the market as a crystalline powder that is white, odorless, and bitter. Strychnine was administered intravenously (direct injection into a vein), orally (eaten by mouth, breathed in), or combined with a solution. A small amount of strychnine, a potent poison, is all that is required to cause convulsions.

Strychnine Induced Convulsion Method

Six groups of Wistar Rats will be divided. Each group has 6 animals (n=6) and receives treatment for 10 days. The 1st group will be given distilled water as a control treatment, and the 2nd group will be given the normal medication. It uses 100mg/kg of phenytoin. The 3rd group will receive a lower dose of novel substituted 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (a), the 4th group will receive a New inserted in the midway dosage 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (b), and the 5th group will receive an increased dosage of new substituted 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (c). For the next 30 min, each animal will be examined individually for convulsive behaviour. We employed 36 Wistar rats with body weights ranging from 150 to 250 gm in this procedure. Wistar rats were divided into six groups in this Strychnine Induced Convulsion Method: Group 1 is Vehicle control; Group 2 is Negative control (Strychnine 85mg/kg); Group 3 is Standard (Phenytoin 100 mg/kg); and Group 4 is Novel substituted 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) (SSW1-SSW7) derivatives (a) Lower dose; Group 5 is Novel substituted 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) (SSW1-SSW7)derivatives (b) Middle dose; Group 6 is Novel substituted 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) (SSW1-SSW7) derivatives (c) Higher dose. The grouping of Anticonvulsant Activity testing of the Wistar rats were shown in Tables 2 and 3.

DISCUSSION

Anticonvulsant action was observed in hydantoin derivatives. An exhaustive literature search revealed that no such hydantoin derivatives in the suggested scheme had previously been described. The compounds were made by reacting substituted anilines with urea in the presence of hydrochloric acid and glacial acid in dry ethanol. Hot water was used to separate the phenyl urea and diphenyl urea mixture. Diphenyl urea remains undissolved while phenyl urea dissolves in hot water. The crystallized substituted Phenyl urea derivatives were collected, filtered, and dried in an oven. The Novel substituted syntheses 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) Derivatives from (SSW1-SSW7) were produced in accordance with scheme II B. It was prepared by 1 g of 3-[(2,4-dioxo-5,5-diphenylimidazolidin-1-yl) carbonyl]-4-hydroxy benzene sulfonic acid into the round bottom flask, add 5 mL dichloromethane into the RBF of 100 mL. Reflux the reaction mixture at about 80-100°C for 3 hr. Cool the reaction mixture by adding 5 mL of crushed ice water. Filter the reaction mixture and collect the product, it gives 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid. 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenyl imidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) was reacts with various reagents to produce various products. A typical model of strychnine-induced convulsion was used to screen the newly synthesised 4-(chloroethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) derivatives for anticonvulsant activity. At lower dose levels (30 mg/kg) and higher dose levels (200 mg/kg), compound (SSW1-SSW7) containing halogen aromatic group derivative shown greater protection against induced seizures. At higher dose levels (30 mg/kg), compound (SSW1 - SSW7) containing aliphatic group derivative shown decreased protection against produced seizures. A drug called phenytoin is used to control and treat epilepsy, complex partial seizures, generalised tonic-clonic seizures, and status epilepticus. It belongs to the medication class of anticonvulsants.

According to the results obtained in the Strychnine Induced Convulsion Method, at least 75% of protection (three mice protected out of four tested) was demonstrated for compounds like 4-(2-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW5)- (scheme II A); 4-(3-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW6)- (scheme II A) containing chlorine halogen group in their structure (2-C1-Aniline)-SSW5 and (3-C1--Aniline)-SSW6 (Table 3). Notably, 4-(2,5-dichloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW7) (scheme II A) and 4-(N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW3) (scheme II A) derivatives provided maximal (100%) protection. Other substances showed weak (25%) at a dose of 100 mg/kg. An equally important, well-established, and commonly used preclinical seizure model in the discovery which is effective in human focal epilepsy. Therefore, in the next step of the pharmacological characterization, all final compounds obtained were studied in this seizure model.

As a result, compounds 4-(2,5-dichloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW7) (scheme II A) and 4-(N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW3) (scheme II A) displayed a potent anticonvulsant efficacy providing more than 75% protection, whereas 4-(2-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW5)- (scheme II A); 4-(3-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW6)- (scheme II A) protected at least 75% of protection (three mice protected out of four tested animals). The compounds with the best anticonvulsant and safety profile were given a more thorough pharmacological characterisation, which revealed their effectiveness in the strychnine-induced convulsion method. It should be emphasised that one of the most crucial screening models for the discovery and characterization of new drugs with potential efficacy in pharmacoresistant epilepsy is the strychnine-induced convulsion method. In conclusion, the *in vivo* data collected allowed for the identification of compounds like SSW7, SSW5, and SSW6 as strong and broad-spectrum anticonvulsants for upcoming preclinical research (particularly after oral administration). It should be noted that the primary chemical modification used in the current experiments enabled the production of water-soluble salts that were close mimics of the hybrid anticonvulsants previously reported. The results of

Table 2: Strychnine Induced Convulsion Method by using Wistar Rats.

No of Groups	No. of Rats
Vehicle Control (Water)	6
Negative Control (Strychnine 85mg/kg)	6
Standard (Phenytoin 100mg/kg)	6
4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (a) Lower dose	6
4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (b) Middle dose	6
4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid Derivatives (c) Higher dose	6
Total	36

Table 3: Anticonvulsant Activity result of Synthesized 4-(chloromethoxy)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] benzene sulfonic acid (SSWB) derivatives.

Compounds	Doses (mg/kg)	Onset of Convulsions (sec)	Duration of Convulsions (sec)	Avg. % Protection	Recovery/Death
SSWB	50	93	148	67.52%	Recovery
	100	104	52		
	200	122	26		
SSW1	50	84	119	62.63%	Recovery
	100	98	90		
	200	114	46		
SSW2	50	86	183	64.16%	Recovery
	100	100	103		
	200	127	41		
SSW3	50	82	139	100%	Recovery
	100	91	89		
	200	107	53		
SSW4	50	81	119	75.63%	Recovery
	100	90	80		
	200	106	66		
SSW5	50	63	163	76.38%	Recovery
	100	79	101		
	200	96	63		
SSW6	50	58	142	79.10%	Recovery
	100	70	99		
	200	88	73		
SSW7	50	69	150	100%	Recovery
	100	78	91		
	200	96	52		
Std. Phenytoin	100	119	11	100%	Recovery

Anticonvulsant Activity testing of the prepared compounds were shown in Table 3.

CONCLUSION

According to the proposed scheme, new hydantoin compounds were synthesized with high percentage yields. Different physical, analytical, and spectral data (^{1}H NMR and FT-IR) validated and characterized the structures, yielding positive results. Because hydantoin compounds have strong anticonvulsant properties, it was determined to test them for anticonvulsant pharmacological action. On the Wistar Rat, all of the compounds demonstrated anticonvulsant action. In the Central Instrumentation Facility, FTIR, NMR spectroscopy, and MS were used to confirm the structures of synthesized chemicals Pune University; Savitribai Phule; and Pune. Wistar rats weighing 150-200 g were used to test the biological effects of anti-convulsant. In this study, derivatives demonstrated more potent anticonvulsant effects against various convulsion kinds. It was discovered that some of the synthesized chemicals have strong anti-convulsant properties. When compared to other 5,5-diphenylimidazolidine-2,4-dione derivatives, synthetic molecules were more active. Hence, the compound 4-(2-chloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW5)- (scheme II A); 4-(3-chloro-N-(2-phenoxymethyl) aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW6)- (scheme II A); 4-(2,5-dichloro-N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW7) (scheme II A) and 4-(N-(2-phenoxymethyl)aniline)-3-[2,4-dioxo-5,5-diphenylimidazolidine-1-yl) carbonyl] sulfonic acid (SSW3) (scheme II A) gives strong anti convulsant effects against phenytoin drug.

Furthermore, compounds demonstrated anticonvulsant activity in a Strychnine-induced convulsion animal. 5,5-diphenylimidazolidine is frequently used in the synthesis of several chemical compounds because it is simply made in high

yields by condensation of various substituted aliphatic/aromatic amines in a hot medium. Because it has such a wide range of chemical and medicinal uses, 5,5-diphenylimidazolidine is abundant in both heterocyclic and non-heterocyclic compounds and complexes. The purpose of this work is to describe rationalised knowledge of 5,5-diphenylimidazolidine derivatives with anticancer, anti-TB, antibacterial, anticonvulsant, antioxidant, anti-inflammatory, antidiabetic, and anti-HIV activity. It is possible to propose hybridization with various pharmacophores, prodrugs, and metal complexes to build an alluring framework for cutting-edge, secure, efficient, and economical treatment approaches. Through structural alterations on 5,5-diphenylimidazolidine scaffolds, which can be used to develop potentially active agents in future studies, the versatile nucleus 5,5-diphenylimidazolidine must serve as a future therapeutic lead for developing various biological agents in the field of medicinal chemistry. Finally, we developed a straightforward method that produces competitively high yields of 5,5-diphenylimidazolidine base derivatives employing mild reaction conditions and phenytoin. The current approach is suitable for producing 5,5-diphenylimidazolidine bases derivatives on a large scale because to its operational simplicity, high efficiency, lack of side product formation, simple workup procedure, and quick reaction time.

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CONFLICT OF INTEREST

The authors declare 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.

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