

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

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ABSTRACT

Epilepsy is a prevalent neurological disorder characterized by recurrent seizures resulting from abnormal neuronal excitability. The indole nucleus represents an important pharmacophore in medicinal chemistry due to its diverse biological activities and potential CNS effects. The present study was designed to synthesize and evaluate novel substituted 2-phenyl indole derivatives as potential antiepileptic agents.

A series of substituted 2-phenyl indole derivatives were designed based on structural modification of the indole scaffold. The target compounds were synthesized through appropriate synthetic routes and characterized using physicochemical and spectroscopic techniques including FT-IR, ^1H NMR, and mass spectrometry. The synthesized compounds were evaluated for anticonvulsant activity using experimental seizure models. Molecular docking and ADME studies were performed to investigate possible target interactions and pharmacokinetic properties.

The synthesized derivatives demonstrated variable anticonvulsant potential depending on the nature and position of substituents present on the phenyl and indole rings. Structure–activity relationship studies indicated that electron-donating and electron-withdrawing substitutions significantly influenced biological activity. Selected compounds exhibited promising anticonvulsant activity and favorable drug-like properties, suggesting that substituted 2-phenyl indole derivatives may serve as potential lead molecules for further development of antiepileptic agents.

KEYWORDS: Indole derivatives, 2-Phenyl indole, Antiepileptic activity, Anticonvulsant, Medicinal chemistry, Molecular docking, ADME

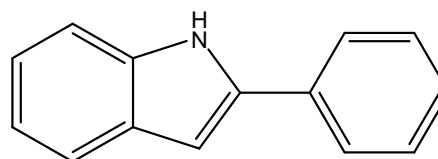
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INTRODUCTION

Epilepsy is a neurological disorder characterized by recurrent seizures due to excessive and uncontrolled neuronal discharge. It affects millions of people worldwide and remains a major therapeutic challenge. Currently available antiepileptic drugs such as phenytoin, carbamazepine, valproate, and levetiracetam provide symptomatic relief but are associated with toxicity, drug interactions, and resistance in some patients. The discovery of novel chemical entities with improved efficacy and safety profiles remains a major goal in CNS drug development. Heterocyclic compounds, particularly indole derivatives, have attracted considerable attention because of their structural similarity to biologically active molecules and their ability to interact with multiple biological targets. The indole nucleus is present in several pharmacologically active molecules and has demonstrated anticonvulsant, neuroprotective, anti-inflammatory, and antioxidant properties. Substitution at the 2-position of indole with phenyl groups provides additional structural flexibility and may enhance receptor binding, lipophilicity, and CNS penetration. Previous studies have reported substituted 2-phenyl indole derivatives showing anticonvulsant activity in experimental models.

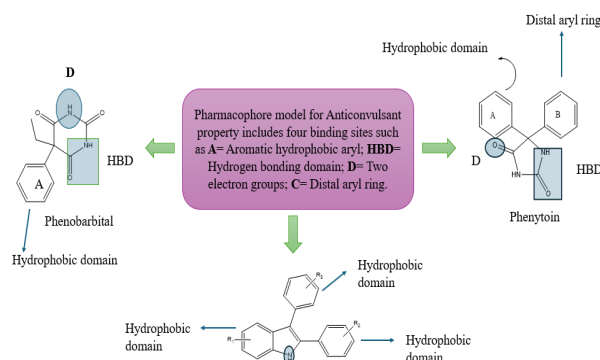
Therefore, the present study focuses on the design, synthesis, characterization, and biological evaluation of novel substituted 2-phenyl indole derivatives as potential antiepileptic agents. The chemical compound 2-phenylindole has the molecular formula $\text{C}_{15}\text{H}_{11}\text{N}$. It is an organic heterocyclic molecule with an attached phenyl group and an indole ring structure. Because of its special qualities and wide range of uses, this

chemical has garnered a lot of attention in the fields of organic synthesis, medicinal chemistry, and material science [1]. Numerous techniques, including the Fischer indole synthesis, N-alkylation of indole, and cyclisation of aryl hydrazones, can be used to create 2-phenylindole. The compound has a melting point of about $175\text{--}177^\circ\text{C}$ and is a crystalline solid. It dissolves readily in organic solvents such as ethanol, CCl_4 , and dichloromethane [2]



The pharmacophoric model for antiepileptic drugs has four binding sites:

1. Aryl hydrophobic site
2. Hydrogen bonding domain
3. An electron donor group
4. Distal aryl ring



DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

2. MATERIALS AND METHODS

2.1 Chemical and Reagents

All the chemicals, reagents, and solvents were procured through commercial suppliers from Central Drug House (CDH), BLD Pharma tech, Avantor Performance Materials India Ltd., etc., Jupiter Reagents Pvt. Ltd., Fisher Scientific Pvt. Ltd., Tokyo Chemical Industry Chemicals (TCI), and Spectrochem used them without purification.

2.2 Instrumentation

The glassware used in the laboratory consisted of heat- and chemical-resistant class I borosilicate glass, sourced from Borosil and ASGI Glassware. Using a Bruker FT-IR ALPHA-T (Eco-ATR) spectrophotometer (Bruker, Tech. Pvt. Ltd., USA), infrared (IR) spectra were captured. The results were displayed in cm^{-1} . A Bruker FT-NMR operating at 400 MHz was used to obtain ^1H -NMR spectra. Tetramethylsilane was used as the internal standard (0 ppm for ^1H NMR), and chemical shifts were reported in ppm (δ value). A Waters UPLC-TQD Mass spectrometer (Waters Corporation, USA) was used to acquire mass spectra using APCI-MS or LC-ESI methods. This setup ensures accurate and reliable characterization of synthesized compounds in the laboratory, facilitating detailed analysis of their chemical properties.

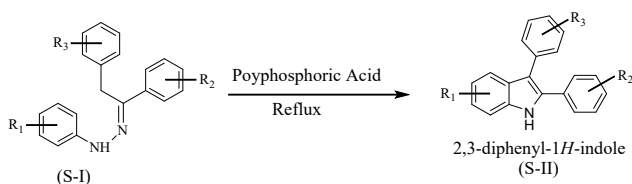
2.3 Synthesis

Step-I: Synthesis of intermediate S-I

A combination of 2.0g (0.0102mol) of benzyl phenyl ketone and 1.8g (0.0167mol) of phenyl hydrazine with 6.0ml of ethanol and 2-3 drops of glacial acetic acid will be warmed. The cold reaction combination will be filtered and washed with dil. HCl followed by about 12ml of cool rectified spirit.

Step-II: Synthesis for the different derivatives (S-II A to S-II F)

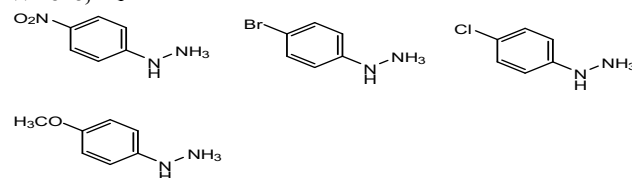
2.8g of the crude intermediate S-I will be added into 12.85g of Polyphosphoric acid and maintained at 100-120°C for 10 minutes. 32.14 ml of cold water will be added and stirred well to complete solution of the polyphosphoric acid and the solution will be filtered and washed with water. The crude solid will be refluxed with 21.42ml of rectified spirit; a little decolorizing charcoal will be added, filtered and washed with 40ml of hot rectified spirit to get S-II. TLC was monitoring the completion of the reaction [3,4].



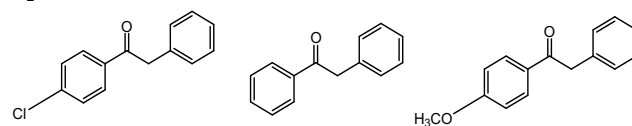
A mixture of 2.0g (0.016mol) of 1-(4-chlorophenyl)-phenylethan-1-one and 1.8g (0.0167mol) of 4'-Nitro phenyl hydrazine/4-Bromophenyl hydrazine/ 4'-Chlorophenyl hydrazine/(4-methoxyphenyl) hydrazine/4'-nitrophenyl hydrazine with 6.0ml of ethanol and 2-3 drops of glacial acetic acid will be warmed. The cold reaction

combination will be filtered and washed with dil. HCl followed by about 12ml of cool rectified spirit. To get pure intermediate S-I, recrystallization with ethanol will be carried out. 2g of the Intermediate S-I will be added into 12.85g of polyphosphoric acid and maintained at 100-120 °C for 10 minutes. 32.14ml of cold water will be added and stirred well to complete solution of the polyphosphoric acid and the solution will be filtered and washed with water. To get indole derivative S-II A, the crude solid will be heated with 21.42 ml of rectified spirit and refluxed with it. A little amount of decolorizing charcoal will then be added. An n-hexane: ethyl acetate solvent solution (9:1) was used by TLC to monitor reaction completion.

Where, $R_1 =$



$R_2 =$



2.4 Physicochemical Characterization

The synthesized derivatives (S-II A to S-II F) were characterized by various physicochemical methods such as solubility profile and physical state, colour, melting range, and R_f values as shown in the Table.1

2.5 Spectral Characterization

The synthesized derivatives (S-II A to S-II F) were characterized through different spectral methods such as Mass Spectrometry, IR, and ^1H - NMR, using standard procedure, the value was interpreted as corresponding peak/signals.

2.6 Computational Studies

2.6.1 Docking

The docking study was based on binding affinity and binding mode of synthesize derivatives (S-II A to S-II F) against thebiological targets. The molecular docking between ligands and two different proteins such as reduced human cytosolic branched-chain aminotransferase (VGSCs, PDB ID: [2COJ](#)) was performed using Auto Dock 4.2 software. The protein was retrieved from the RCSB protein data bank (<https://www.rcsb.org/>) in PDB format, and heteroatoms and water molecules are removed from the Swiss PDB viewer and Biovia drug discovery studios. The 2D interaction complex of the target protein and ligand is obtained from visualizing in Biovia drug discovery studio software.

2.6.2 In-Silico Pharmacokinetic Prediction

Prediction of the pharmacokinetic profiles like Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) of synthesize derivatives were carried out by computational tools i.e., Swiss-ADME and pkCSM. These tools provide insights into the compound's bioavailability, toxicity, and overall suitability for further development as

3 Biological Activity

3.1 Animals and Their Housing Condition

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

Swiss Albino Mice (weighing 25-30g) of either gender were collected from Animal House of Hygia Institute of Pharmaceutical Education and Research, Lucknow, for use in experiment. This study was conducted approval from Institutional Animal Ethics Committee (HIPPER/IAEC/157/06/2024). The animals were housing under controlled environmental conditions, maintaining 50% humidity and temperature at $25\pm 2^{\circ}\text{C}$, with 12- hour light/dark cycle. They allowed to acclimate for 7 days in standard polypropylene cages and were given with a pellet feed and water ad libitum. The bedding in the cages was changed every other day throughout the study to ensure cleanliness and comfort.

3.2 Antiepileptic Activity

Every animal will be split up into eight groups (n=5). Group I's vehicle will be a CMC suspension (10 mL/kg) p.o. Phenytoin (25 mg/kg) intraperitoneally will be administered as standard to Group II. Test medications (30 mg/kg) will be given to the remaining six groups. Using an ear electrode, each animal will get an electric shock (50 Hz) for 0.02 seconds following 60 minutes of treatment. The length of each stage of the epileptic attack—tonic flexion, tonic extensor, tonic-clonic, stupor, recovery, or death—will be noted following the electric current. Extensor phase decrease will be regarded as the primary metric for the medication's antiepileptic effect [43].

Table 1: Grouping of Animals

S.No.	Group	Treatment	Route	No. of Animals
1.	Disease control	Vehicle (CMC) (10ml/kg) + Maximal Electroshock Method	Oral	5
2.	Standard (Phenytoin)	Phenytoin (25mg/kg) + Maximal Electroshock Method	i.p	5
3.	Test group I	Test drug (0.5mL of 0.5%w/v + S-II A 30mg/kg) + Maximal Electroshock Method	Oral	5
4.	Test group II	Test drug (0.5mL of 0.5%w/v + S-II B 30mg/kg) + Maximal Electroshock Method	Oral	5
5.	Test group III	Test drug (0.5mL of 0.5%w/v + S-II C + 30mg/kg)	Oral	5

		+ Maximal Electroshock Method		
6.	Test group IV	Test drug (0.5mL of 0.5%w/v + S-II D 30mg/kg) + Maximal Electroshock Method	Oral	5
7.	Test group V	Test drug (0.5mL of 0.5%w/v + S-II E 30mg/kg) + Maximal Electroshock Method	Oral	5
8.	Test group VI	Test drug (0.5mL of 0.5%w/v + S-II F 30mg/kg) + Maximal Electroshock Method	Oral	5

4. RESULTS AND DISCUSSION

The synthesis of the intermediate and the target derivatives (S-II A to S-II F) was carried out according to the synthetic route illustrated in Scheme 1. Intermediate S-I ((E)-1-(1,2-diphenylethylidene)-2-phenylhydrazine) was synthesized by the acid-catalyzed condensation reaction between substituted phenylhydrazine and substituted benzyl phenyl ketone in ethanol using glacial acetic acid as a catalyst. The reaction proceeds through nucleophilic addition followed by dehydration, resulting in the formation of the corresponding hydrazone intermediate (S-I). The synthesized intermediate (S-I) was confirmed by thin-layer chromatography (TLC) and mass spectrometric analysis. The progress of the reaction was monitored using TLC on pre-coated silica gel plates with *n*-hexane acetate (7:3, v/v) as the mobile phase. The *R_f* value of intermediate S-I was found to be 0.64, while its mass spectrum exhibited a base peak at *m/z* 237, confirming the successful formation of the intermediate. The second step of the synthetic pathway involves the cyclization of the hydrazone intermediate (S-I) into the corresponding substituted indole derivative (S-II) through the Fischer indole synthesis. Polyphosphoric acid (PPA) was employed as both a strong acidic catalyst and a dehydrating agent, while reflux conditions provided sufficient thermal energy to facilitate the cyclization process. Initially, the imine nitrogen (C=N) of the hydrazone intermediate is protonated by polyphosphoric acid, increasing the electrophilic character of the azomethine carbon. The protonated hydrazone subsequently undergoes tautomerization to generate the corresponding **enehydrazine intermediate**, which is the key reactive species in the Fischer indole synthesis.

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

Table 2: Characterization Of compounds (S-II A- S-II F)

The enehydrazine intermediate undergoes intramolecular electrophilic aromatic substitution, in which the aromatic ring attacks the electrophilic carbon to form a new carbon-carbon bond, resulting in the formation of a cyclic intermediate. Subsequent proton transfer, nitrogen-nitrogen bond cleavage, and aromatization yield the thermodynamically stable substituted 1H-indole derivative (S-II A to S-II F). Polyphosphoric acid acts as both an acid catalyst and a dehydrating agent, promoting cyclization and facilitating reaction completion. After completion, the reaction mixture is poured into cold water to precipitate the product, which is purified by filtration and recrystallization. The progress of the reaction is monitored by thin-layer chromatography (TLC), where the disappearance of the hydrazone spot and the appearance of a new product spot confirm successful cyclization.

Structural characterization of the synthesized derivatives was performed using Fourier-transform infrared (FT-IR) spectroscopy, proton nuclear magnetic resonance (¹H NMR) spectroscopy, and mass spectrometry. The combined spectral data provided comprehensive evidence for the presence of the expected functional groups, proton environments, molecular weight, and overall structural integrity of the synthesized compounds, thereby confirming their identity and purity. The intermediates were characterized primarily by their physicochemical properties, including melting point and R_f value, together with mass spectrometric analysis to verify their successful synthesis before further synthetic transformation. The FT-IR spectrum of the synthesized indole derivative exhibited characteristic absorption bands corresponding to the proposed molecular structure. A broad absorption band at 3392.16 cm⁻¹ was assigned to the N-H stretching vibration of the indole nucleus. The bands observed at 3012.81 cm⁻¹ and 2923.57–2850.54 cm⁻¹ corresponded to aromatic and aliphatic C-H stretching vibrations, respectively. The absorption bands at 1598.83 cm⁻¹ and 1512.81 cm⁻¹ were attributed to aromatic C=C stretching vibrations, while the bands at 1264.02–1023.99 cm⁻¹ were assigned to C-O-C-N stretching vibrations. The peaks at 808.88 cm⁻¹ and 755.05 cm⁻¹ corresponded to out-of-plane C-H bending vibrations of substituted aromatic rings. Overall, the FT-IR spectral data confirmed the presence of the characteristic

functional groups and supported the successful synthesis of the target indole derivative.

The ¹H NMR spectrum of the synthesized indole derivative showed a characteristic broad singlet at δ 11.3 ppm, corresponding to the N-H proton of the indole nucleus. Multiple signals observed between δ 7.20 and 8.00 ppm were assigned to the aromatic protons of the indole and substituted phenyl rings. The observed chemical shift values were in agreement with the proposed molecular structure, confirming the successful synthesis of the target indole derivative. The combined FT-IR, ¹H NMR, and mass spectral data confirmed the molecular structures of the synthesized derivatives. The observed molecular ion peaks ([M]⁺ or [M+1]⁺), fragmentation patterns, and chemical shift values were consistent with the proposed structures. All analyses were performed under appropriate quality control conditions to ensure

the accuracy and reliability of the results.

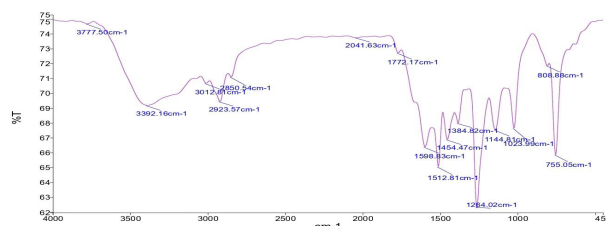
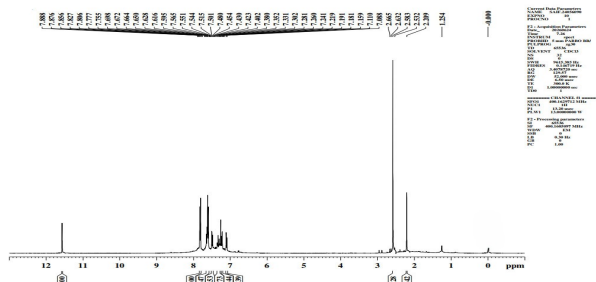


Table 3: IR Characterization of Derivatives S-II A

S.No.	Functional Group	IR Reported (cm ⁻¹)	IR Observed (cm ⁻¹)
1.	C-H Stretching	2950-2850	2923.57
2.	N-H (Amine) Stretching	3550-3250	3392.16
3.	NO ₂ Asymmetric stretch	1690-1640	1598.83
4.	NO ₂ Symmetric stretch	1300-1000	1264.02
5.	C=C Stretching	1600-1400	1512.81
6.	C-Cl Stretch	850-650	808.88



DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

¹H NMR Spectrum of Derivative S-II A

[(MHz 400, CDCl₃): δ 7.15 (d, 2H, aromatic); 7.28 (d, 2H, aromatic); 7.43 (s, 1H, aromatic); 7.45 (s, 1H, aromatic); 7.59 (d, 2H, aromatic); 7.61 (d, 2H, aromatic); 7.85 (s, 1H, aromatic); 7.88 (s, 1H, aromatic); 11.46 (s, 1H, 2-indole)

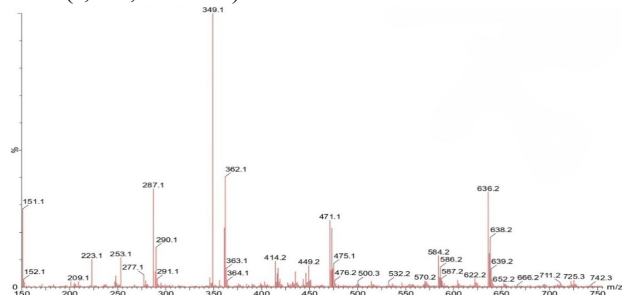
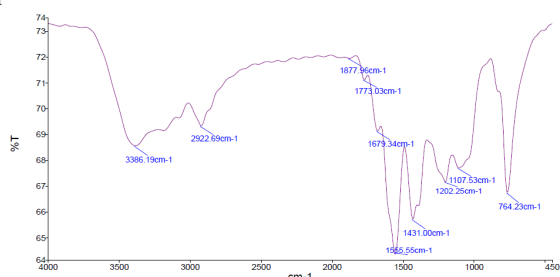


Figure 1: Mass Spectrum of Derivative S-II A

Observed molecular ion [M]⁺ peak; MS-ESI(m/z): 349.1 (100%)

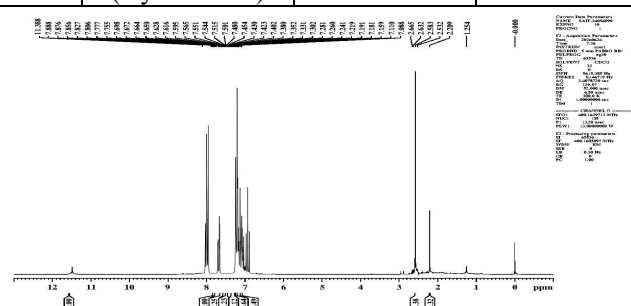
Spectral Characterization of Derivative S-II C



IR Spectrum of Derivative S-II C

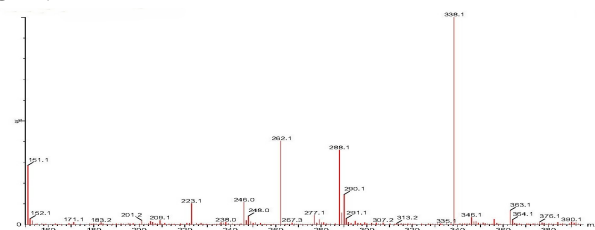
Table 4: IR Characterization of Derivatives S-II C

S.No.	Functional Group	IR Reported (cm ⁻¹)	IR Observed (cm ⁻¹)
1.	C-H Stretching	2950-2850	2920.03
2.	N-H (Amine) Stretching	3550-3250	3381.07
3.	C=N(Imine) Stretching	1690-1640	1673.87
4.	C-Cl Stretch (para-Cl phenyl)	850-650	816.88
5.	C=C Stretching	1600-1400	1529.94
6.	C-Cl Stretch (aryl chloride)	770-530	764.23



¹H NMR Spectrum of Derivative S-II C

[(MHz 400, CDCl₃): δ 7.21 (s, 1H, aromatic); 7.30 (s, 1H, aromatic); 7.48 (s, 1H, aromatic); 7.50 (s, 1H, aromatic); 7.51 (d, 2H, aromatic); 7.54 (d, 2H, aromatic); 7.55 (s, 1H, aromatic); 7.69 (d, 2H, aromatic); 7.77 (d, 2H, aromatic); 11.46 (s, 1H, 2-indole)

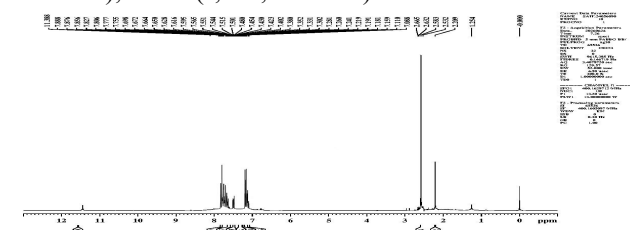


Mass Spectrum of Derivative S-II C

Observed molecular ion [M]⁺ peak; MS-ESI(m/z): 338.1(95%)

¹H NMR Spectrum of Derivative S-II D

[(MHz 400, CDCl₃): δ 7.21 (s, 1H, aromatic); 7.30 (s, 1H, aromatic); 7.48 (s, 1H, aromatic); 7.50 (s, 1H, aromatic); 7.51 (d, 2H, aromatic); 7.54 (d, 2H, aromatic); 7.55 (s, 1H, aromatic); 7.69 (d, 2H, aromatic); 7.77 (d, 2H, aromatic); 11.46 (s, 1H, 2-indole)



Spectral Characterization of Derivative S-II E

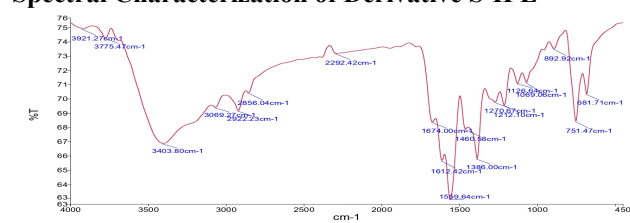
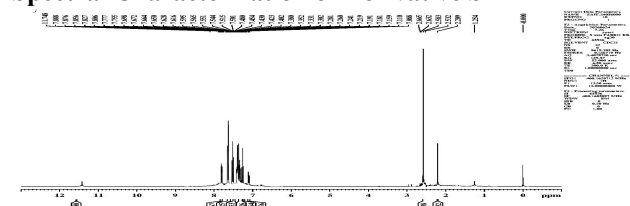


Table 5: IR Characterization of Derivatives S-II E

S.No.	Functional Group	IR Reported (cm ⁻¹)	IR Observed (cm ⁻¹)
1.	C-H Stretching	2950-2850	2922.23
2.	N-H (Amine) Stretching	3550-3250	3403.80
3.	Ar-O-C Stretch (methoxy)	1690-1255	1270.67
4.	C-O-C Symmetric Stretch	1300-1000	1069.06
5.	C=C Stretching	1600-1400	1612.42
6.	O-CH ₃ C-H Stretch (x2 methoxy)	2860-2800	2856.04

Spectral Characterization of Derivative S-II F



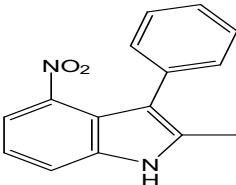
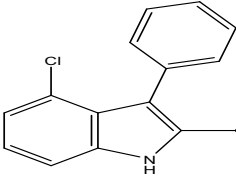
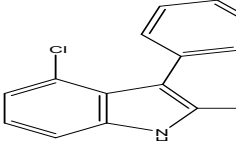
¹H NMR Spectrum of Derivative S-II F

[(MHz 400, CDCl₃): δ 7.21 (s, 1H, aromatic); 7.30 (s, 1H, aromatic); 7.48 (s, 1H, aromatic); 7.50 (s, 1H, aromatic); 7.51 (d, 2H, aromatic); 7.54 (d, 2H, aromatic); 7.55 (s, 1H, aromatic); 7.69 (d, 2H, aromatic); 7.77 (d, 2H, aromatic); 11.74 (s, 1H, 2-indole)

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

Visualization of Docked S-II A to S-II F molecules on 2COJ

Table- 6: Docking studies of S-II A to S-II F molecule on protein 2COJ

Compound	Structure	Docking score Kcal/mol	Hydrogen bonding	Hydrophobic interaction and Pi-Pi Stacking	No. of H Bond
S-II A		-7.3	ARG-B:292	LEU-B:115, PRO-B:287, VAL-B:289, ARG-B:119, ARG-B:122, CYS-B:221	1
S-II B		-8.4	ALA-B:334	VAL-B:336, PHE-B:199, CYS-B:335, VAL-B:202, CYS-B:338, PHE-B:194	1
S-II C		-8.4	ALA-B:334	ASN-B:200, CYS-B:338, PHE-B:194, VAL-B:202, CYS-B:335, PHE-B:199	1

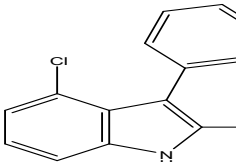
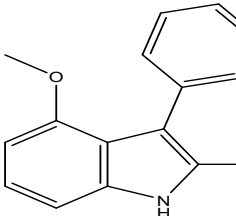
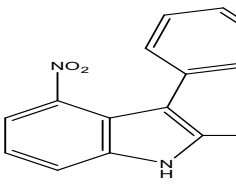
				VAL-B:336	
S-II D		-7.7	NA	CYS-B:335, PRO-B:192, VAL-B:336, SER-B:157, TYR-B:374, PHE-B:101, GLN-B:373	0
S-II E		-7.0	CYS-B:221	ARG-B:122, PRO-B:287, LEU-B:115, ARG-B:292, ARG-B:119	1
S-II F		-8.0	ALA-B:334	CYS-B:335, VAL-B:336, SER-B:157, PHE-B:199, CYS-B:338	1

Table-7: 2D and 3D interaction of S-II A to S-II F molecule on protein 2COJ.

Compound	3D interaction	2D interaction
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DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

S-II A		
S-II B		
S-II C		
S-II D		
S-II E		
S-II F		

Table 8: ADMET Prediction Using pk CSM

Parameter	S-II A	S-II B	S-II C	S-II D	S-II E	S-II F	Phen ytoin
Molec ular Proper ties							
Mol. Weigh t	348.07	348.24	337.04	333.09	329.14	314.11	252.273
Log P	6.0635	6.2644	6.8087	6.1639	5.5191	5.4101	1.7696
No. of Rotabl e Bonds	3	2	2	3	4	3	2
HBA	2	0	0	1	2	2	2
HBD	1	1	1	1	1	1	2
Surfac e Area	148.393	137.304	144.043	145.218	146.393	138.089	110.000
Lipins ki Rule							
Absor ption							
Water Solubi lity	-3.814	-7.072	-4.073	-4.119	-4.146	-6.782	-3.448

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIPILEPTIC ACTIVITY

Intestinal Absorption	92.171	95.486	92.462	94.303	96.266	96.273	95.761
Distribution							
VDss (human)	-0.568	-0.606	-0.242	-0.34	-0.396	-0.963	-0.009
BBB Permeability	-0.318	1.221	-0.242	0.64	0.176	-0.264	0.162
Excretion							
Total Clearance	0.474	0.339	0.297	0.341	0.419	0.254	0.253
Renal OCT2 Substrate	No	No	No	No	No	No	No

5. BIOLOGICAL ACTIVITY

5.1 Evaluation of Anticonvulsant Activity Using the MES Model

The anticonvulsant activity of the synthesized derivatives (S-II A–S-II F) was evaluated using the maximal electroshock seizure (MES) model in mice. The MES model was employed as an experimental method for assessing the ability of the synthesized compounds to reduce electrically induced seizure activity. The duration of the extensor phase was considered an important parameter for comparing the anticonvulsant effects of the different treatment groups. Group I received 1% CMC (10 mL/kg) and served as the disease/vehicle-control group. Group II received phenytoin (25 mg/kg) as the standard drug. Groups III–VIII received the synthesized derivatives S-II A–S-II F at a dose of 30 mg/kg. The synthesized derivatives were administered orally 30 minutes before application of the electroshock stimulus. Five animals were included in each group (n = 5).

The disease-control group showed an extensor-phase duration of 14.60 ± 1.11 sec. Administration of phenytoin markedly reduced the extensor duration to 2.60 ± 0.49 sec, demonstrating the anticonvulsant effect of the standard treatment. Among the synthesized derivatives, S-II A showed the greatest reduction in the extensor phase, with a

mean duration of 5.00 ± 0.95 sec. S-II E and S-II F showed extensor durations of 5.80 ± 0.77 sec and 6.60 ± 0.45 sec, respectively. S-II B, S-II C and S-II D produced extensor durations of 10.20 ± 0.58 , 11.20 ± 0.89 and 12.20 ± 0.86 sec, respectively. Thus, based on the extensor-phase duration, the synthesized derivatives showed the following comparative order of activity: S-II A > S-II E > S-II F > S-II B > S-II C > S-II D. This ranking is based specifically on the reduction of the extensor phase, with a shorter duration indicating greater suppression of the tonic extensor response.

When compared with the disease-control group, the approximate reductions in extensor-phase duration were 65.75% for S-II A, 60.27% for S-II E, 54.79% for S-II F, 30.14% for S-II B, 23.29% for S-II C and 16.44% for S-II D. Phenytoin produced an approximately 82.19% reduction compared with the disease-control group.

All animals in the supplied dataset were reported to recover after the seizure episode, and no mortality was recorded.

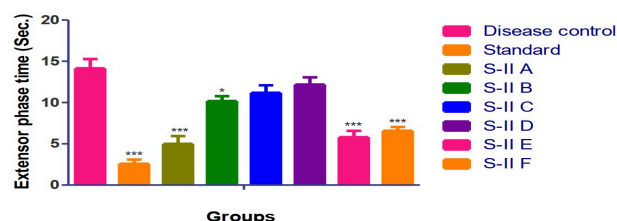


Figure 2: Antiepileptic Activity of Synthesized Derivatives (S-II A to S-II F)

5.2 Evaluation of Anticonvulsant Activity (MES Model)

This study used the maximal electroshock seizure (MES) method to evaluate anticonvulsant activity of the synthesized derivatives (S-II A to S-II F). Mice were given a transauricular electroshock of 50 Hz for 0.2 seconds by corneal electrodes, and the incidence and duration of the extensor phase of the seizures were recorded. The animals were grouped according to the treatment schedule:

Group I: Disease Control (1% CMC, 10 mL/kg)

Group II: Standard (Phenytoin 25 mg/kg)

Table 9: Antiepileptic Activity of Synthesized Derivatives (S-II A to S-II F)

DESIGN SYNTHESIS AND EVALUATION OF NOVEL SUBSTITUTED 2-PHENYLE INDOLE DERIVATIVES AS ANTIEPILEPTIC ACTIVITY

Groups III to VIII: Synthesized Derivatives (S-II A to S-II F, 30 mg/kg)

The synthesized derivatives (S-II A to S-II F) were given orally to the test animals (n=5) 30 minutes before electroshock was applied at dose of 30 mg/kg. Both the duration of tonic hind leg extension and the mortality from convulsions were assessed in order to determine the impact of the chemicals on seizure severity. Following the MES seizures, each animal was observed separately for two hours. A 24-hour observation period was then conducted to determine mortality.

6. SUMMARY & CONCLUSION

The study indicated that the synthesized derivatives (S-II A to S-II F), especially when combined with other heterocyclic rings, could act as promising lead compounds

for developing potent antiepileptic drugs. Efficacy of the newly synthesized derivatives was evaluated through their ability to reduce seizures at various time intervals, utilizing the (MES) method in swiss albino mice. Results revealed significant differences in the effectiveness of these compounds compared to standard antiepileptic drug Phenytoin. This suggests that the new derivatives not only demonstrate substantial antiepileptic activity but also possess the potential to offer a valuable alternative or adjunct in the treatment of seizures. The findings warrant further exploration and optimization of these compounds to enhance their therapeutic profiles.

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