International Journal of Education and Science Research Review
E-ISSN 2348-6457
Volume-10, Issue-1 Jan-Feb-2023 P-ISSN 2349-1817
www.ijesrr.org Email- editor@ijesrr.org

SYNTHESIS OF PYRIMIDINE DERIVATIVES AND ITS BIOLOGICAL ACTIVITY

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ABSTRACT

There has been a significant amount of interest in the synthesis of novel pyrimidine derivatives due to the varied biological effects that they possess, such as antibacterial, anticancer, and antiviral properties. The synthesis of a series of pyrimidine derivatives under moderate circumstances is described in this article. The synthesis was carried out using a three-component cyclocondensation technique that included aromatic aldehydes, ethyl acetoacetate, and urea. Characterisation of the substances that were created was accomplished by the use of a number of spectroscopic techniques, such as infrared and pulsed mass spectrometry. With the use of these approaches, it was determined that the items were both pure and structurally sound. In order to determine the extent to which the pyrimidine derivatives were able to limit the development of a wide variety of bacteria, including Escherichia coli, Bacillus subtilis, Pseudomonas aeruginosa, and Staphylococcus aureus, we conducted biological tests on these compounds. With a particular emphasis on Streptococcus aureus and Pseudomonas aeruginosa, the data demonstrated a zone of inhibition of three millimetres in diameter and moderate antibacterial activity. On the basis of these findings, the pyrimidine derivatives that were synthesised have the potential to serve as useful starting points for the development of new antibacterial treatments. Additionally, the compounds have the ability to be fine-tuned in order to boost their biological activity. This might potentially lead to new options for research into the creation of medications that are based on pyrimidines.

Keywords- *5-Bromo-2, 4-dichloropyrimidine, MES, Rotorod, Anticonvulsant, Antioxidant, biological evaluation, IR spectroscopy, PMR spectroscopy, antimicrobial agents, Streptococcus aureus, Pseudomonas aeruginosa*

INTRODUCTION

When people speak about epilepsy, they are often referring to a group of widespread long-term neurological illnesses in which synchronised neuronal activity in the brain generates recurrent convulsions that are not induced by any external stimulus. The discovery of novel drugs, particularly ones that are effective against

complex partial seizures, continues to be a prominent focus of study in the field of antiepileptic medication development. The following medications are included in this category: vigabatrin, lamotrigine, gabapentin, tiagabine, felbamate, topiramate, fosphenytoin, and levetiracetam have recently been introduced to the market. An article that discusses unique structural entities that possess anticonvulsant effects has just been published in a review. There is a growing body of research that links oxidative stress to the genesis of human disorders. This has sparked the interest of medical experts in the possible therapeutic applications of antioxidants during the last several years. When it comes to understanding how biological systems deal with the processes of transamination and racemization, the imine group, which is a hallmark of Schiff bases, plays a crucial role.

An immense amount of practical use of fused pyrimidines continues to attract a large amount of research, primarily due to the fact that they exhibit a wide variety of biological activities. When one examines the published descriptions of the chemistry of systems that include the pyrimidine ring fused to heterocycles such as purines, quinazolines, pyridopyrimidines, triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, furopyrimidines, and pyralopyrimidines, it becomes very evident that this is the case. Particularly noteworthy among the many heterocyclic compounds that have uses in the fields of medicine and biology are triazolopyrimidines. As a consequence of this, there is a significant amount of interest in the development of methodologies that are both versatile and relevant to a wide range of situations for the synthesis of triazolopyrimidines. Existing methods for the preparation of triazolopyrimidines include the use of either hydrazine or heterocyclic hydrazone precursors. Several chemical firms in the pharmaceutical and agricultural industries depend on pyrimidines and the derivatives of these compounds. There are a number of pyrimidine derivatives that have been shown to possess antibacterial, antiviral, anticancer, anti-inflammatory, and antitumor effects. In the course of this work, a wide variety of new pyrimidine analogues, including 3, 4, 5, 6(a-d), and 7(a-d), have been synthesised, and the potential biological effects of these compounds have been determined.

OBJECTIVES

The purpose of this research was to evaluate the antioxidant and anticonvulsant properties of pyrimidine analogues 3, 4, 5, 6(a-d), and 7(a-d) that were synthesised in liquid form.

MATERIALS AND METHODS

CHEMISTRY

The range of melting temperatures was determined with the use of the Veego Melting Point VMP III equipment. VarioMICRO superuser V1.3.2 Elementar was used in order to meticulously record the analysis of the components. KBr discs were used in order to acquire the spectra, which were then recorded by means of an infrared spectrophotometer known as the FT-IR Jasco 4100. The 1H nuclear magnetic resonance (NMR) spectra were recorded at 400/300 MHz using a Bruker DRX-500 spectrometer. A mixture of d6-DMSO and CDCl3 was used as the solvent, while TMS was utilised as the internal standard. The LC-MSD-TrapXCT apparatus was used in order to get the mass spectra of the individuals being examined. All of our solvents and chemicals were purchased from Sigma Aldrich Chemicals Pvt Ltd. throughout our business.

- **Synthesis of 1-(5-bromo-2-chloropyrimidin-4-yl)hydrazine (2)**

Using an ice bath, the 5-bromo-2,4-dichloropyrimidine (1) solution in methanol was brought down to a temperature of 0-5 degrees Celsius. In terms of concentration, the solvent had a value of 0.01 mol. Following the addition of 0.01 mol of trietheylamine to the cold reaction mixture, 0.012 mol of hydrazine hydrate was progressively added while the temperature was maintained between 5 and 10 degrees Celsius. The reaction mass was allowed to agitate for a period of one hour while it was kept at room temperature. Compound 2, which is a solid that has a light yellow colour, was obtained by filtering the solid, rinsing it with cold water, and then drying it. The output was 82%. This is the 1H nuclear magnetic resonance (NMR) spectrum that was produced by using DMSO-d6 at a frequency of 400 MHz: δ = 8.06 (s, 1H, NH), 7.85 (s, 1H, py-H), and 4.34 (s, 2H, NH2).

- **Synthesis of 8-bromo-5-chloro-3-methyl[1,2,4]triazolo[4,3-c]pyrimidine (3)**

The second compound (0.01 mol) and ten millilitres of acetic anhydride were reflux-heated for four hours. Reduced pressure was used to concentrate the reaction mixture. The resulting solid was subjected to filtration, water washing, drying, and crystallisation from methanol to produce compound 3, also known as the white solid. Results: 71%. pressure: 190–194 °C. The following chemical shifts were observed in the FT-IR spectrum (KBr, cm−1): 2937 (C-H), 1635 (CN), 1463 (CC), 1372 (C-N), 722 (C-Cl), 422 (C-Br). The 1H NMR spectrum showed a peak at 8.40 cm-1 (s, 1H, Py-H) and 2.48 cm-1 (s, 3H OCH3) in DMSO-d6, at 400 MHz. 13C mass-to-z ratio: 248.2. C, 29.12; H, 1.63; N, 22.64 are the percentages calculated analytically for C6H4BrClN4. Discovered: 29.0 C, 1.58 H, and 22.54 N.

- **Synthesis of 8-bromo-5-chloro-[1,2,4]triazolo[4,3-c]pyrimidine-3-amine (4)**

In order to dissolve Compound 2 (0.01 mol), ten millilitres of dioxane were used. Following this, five millilitres of Na2CO3 (0.02 mol) in water were added to the solution. To maintain a reaction temperature

that was lower than 10 degrees Celsius, 5 millilitres of dioxane (0.2 mol) was added to the mixture while it was still being kept in an ice bath. This was done while stirring the mixture for two hours. In order to produce compound 4, also known as the brown solid, the solvent was first extracted from the ethanol solution, and then the solution was crystallised at reduced pressure. 36% is the productivity rate. 206–208 degrees Celsius in pressure? The chemical shifts that were determined by Fourier transform infrared spectroscopy (FT-IR) in KBr, cm⁞1 are as follows: 2937 (C-H), 1635 (CN), 1463 (CC), 1375 (C-N), 722 (C-Cl), and 522 (C-Br). The 1H nuclear magnetic resonance (Microsoft DMSO-d6, 400 MHz) δ values are 8.47 (s, 1H, Py-H) and 6.64 (s, 2H, -NH2). 239.42 m/z using mass spectrometry (ESI). According to the analytical calculations, the percentages for C5H3BrClN5 are as follows: C, 24.17; H, 1.22; and N, 28.19. C, 24.29; H, 1.32; and N, 28.30 were found to be the elements.

- **Synthesis of 5-bromo-2-chloro-4-(3,5-dimethyl-1H-pyrazol-1-yl)-pyrimidine (5)**

After adding one millilitre of acetylacetone to a solution of compound 2 (0.01 mol) in fifty millilitres of methanol, the mixture was well mixed. The production of compound 5, which is the brown solid, was accomplished by first allowing the reaction mixture to reflux for a period of five hours, then filtering off the solid, drying it, and then crystallising it from ethanol. The results are 71%. The melting point is between 214 and 215 degrees Celsius. The FT-IR bands that were found in KBr at a wavelength of cm−1 were as follows: 2940 (C-H), 1655 (CN), 1510 (CC), 728 (C-Cl), and 530 and 530, respectively. DMSO-d6 was used to record 1H nuclear magnetic resonance spectra at a frequency of 400 MHz. The peak intensities were discovered to be 8.67 (seconds, 1H, Py-H), 6.10 (seconds, 1H), 2.30 (seconds, 3H, OCH3), and 2.16 (seconds, 3H, OCH3). The mass-to-charge ratio is 288.50 MS (ESI). The following are the results of the analytical calculations for C9H8BrClN4 (in percent): C = 37.59, H = 2.80, and N. It was found that C: 37.79, H: 2.86, and N: 19.40 were all present.

- **General procedures for the synthesis 8-bromo-5-chloro-3-aryl-[1,2,4]triazolo[4,3-c]pyrimidine 6(a–d)**

Following the addition of 0.01 mol of Compound 2 and 0.012 mol of substituted benzoic acid to 5 ml of POCl3, the mixture was heated to reflux for a period of six hours following the temperature. After being concentrated at a lower pressure, the mass of the reaction was kept at a lower temperature in ice. The solid that was produced was extracted from the methanol solvent by the processes of filtration, washing with water, drying, and crystallisation until it was eventually eliminated.

- **8-Bromo-5-chloro-3-(4-ethylphenyl)[1,2,4]triazolo[4,3-c]pyrimidine (6a)**

The product obtained from compound 2 (0.01 mol) and 4-ethyl benzoic acid (0.01 mol). White solid. Yield: 83%. M.p.: 102–104 °C. FT-IR (KBr, cm−1): 2937 (C–H), 1645 (CN), 1453 (CC), 1375 (C–N), 720 (C–Cl), 522 (C–Br). 1H NMR (CDCl3, 300 MHz) δ: 7.85 (s, 1H, Py-H), 7.63 (d, 2H, J = 8.13 Hz, Ar-H), 7.35 (d, 2H, J = 8.34 Hz, Ar-H), 2.73-2.68 (m, 2H, CH2), 0.99 (t, 3H, J = 7.50 Hz, OCH3). MS (ESI) m/z: 338.2. Anal. Calcd. for C13H10BrClN4 (in %): C, 46.25; H, 2.99; N, 16.60. Found: C, 46.15; H, 2.79; N, 16.67.

- **8-Bromo-5-chloro-3-(4-methoxyphenyl)[1,2,4]triazolo[4,3-c]pyrimidine (6b)**

Chemical 2 and 4-methoxy benzoic acid work together to produce a molecule with a molecular weight of 0.01 when they are combined. A hue that is solid off-white. The results are 79%. There is a temperature range of 165 to 168 K. Through the use of Fourier transform infrared spectroscopy (KBr, cm−1), the following parameters were determined: 2940 (C-H), 1639 (C=N), 1460 (C=C), 1371 (C-N), 726 (C-Cl), and 520 (C-Br). The following 1H nuclear magnetic resonance (NMR) spectra were obtained using CDCl3 at a frequency of 300 MHz: 7.88 (s, 1H, Py-H), 7.71 (d, 2H, J = 6.40 Hz, Ar-H), 7.54 (d, 2H, J = 6.21 Hz, Ar-H), and 3.90 (s, 3H, OCH3). In terms of mass-to-z resolution (MS), the ESI has a value of 340.0. The results of the analytical calculation for C12H8BrClN4O (in percent) are as follows: 42.44 degrees Celsius, 2.37 hydrogen atoms, and 16.50 newtons. A total of 42.58, 2.32, and 16.50 were obtained as the results.

- **8-Bromo-5-chloro-3-(4-flurophenyl)[1,2,4]triazolo[4,3-c]pyrimidine (6c)**

Upon completion of the reaction between chemical 2 and 4-fluro benzoic acid (0.01 mol), this is the final product. A distinct, light brown colour. The success rate is 76%. 167–169 degrees Celsius. Pressure. The FT-IR (KBr, cm−1) technique was used to identify the compounds 2937 (C-H), 1630 (C=N), 1450 (C=C), 1378 (C-N), 710 (C-Cl), and 510 (C-Br). 1H nuclear magnetic resonance spectra: 7.88 (s, 1H, Py-H), 7.70 (dd, 2H, J = 2.60, 7.62 Hz, Ar-H), and 7.63 (dd, 2H, J = 2.44, 10.08 Hz, Ar-H). m/z measures 329.2 in MS (ESI). Analytical calculations for C11H5BrClFN4 (in %): C=40.34, H=1.54, and N= 17.11. C = 40.30, H = 1.51, and N = 17.01 were the values that were found to be significant discovery.

- **8-Bromo-5-chloro-3-(4-methylphenyl)[1,2,4]triazolo[4,3-c]pyrimidine (6d)**

In the process of combining chemical 2 with 4-methyl benzoic acid, we get a product that has a molecular weight of 0.01. A colour that is completely white. 82% is the result. temperature range: 197–199 degrees Celsius). There are a total of 2937 bands (C-H), 1635 bands (C=N), 1463 bands (C=C), 1375 bands (C-N), 722 bands (C-Cl), and 522 bands (C-Br) in the FT-IR spectrum (KBr, cm−1). The following 1H nuclear magnetic resonance (NMR) spectra were obtained using CDCl3 at a frequency of 300 MHz: 7.84 (s, 1H, Py-H), 7.61 (dd, 2H, J = 2.50, 7.60 Hz, Ar-H), 7.32 (dd, 2H, J = 2.45, 9.60 Hz, Ar-H), and 2.18 (s, 3H,

CH3). 324.1 is the mass-to-z ratio in the MS (ESI) system. It was determined by analytical calculations that the percentages for C12H8BrClN4 are as follows: C = 46.54, H = 1.49, and N = 17.31. C = 46.45, H = 1.55, and N = 17.11 are the found values.

- **General procedures for the synthesis aryl-(5-bromo-2-chloro-pyrimidine-4-yl) hydrazone 7(a–d)**

Compound 2 was dissolved in ethanol, and then aryl aldehyde was added to the solutions. To get the combination down to room temperature, it was allowed to reflux in a water bath for one hour before being allowed to cool down. Through the processes of filtering, washing with ethanol, and drying, compound 7(a-d) was successfully extracted from the crystalline solid that was produced.

- **3-Methoxybenzaldehyde-(5-bromo-2-chloropyrimidin-4-yl)hydrazone (7a)**

0.01 mol is the product that is obtained after the reaction between (2) and 3-methoxybenzaldehyde (0.012 mol) is completed. Mast temperature: 150–154 degrees Celsius; yield: 85 percent; white solid. The FT-IR (KBr, cm−1) spectrum reveals the following chemical elements: 2930 (C–H), 1482 (C=N), 3447 (NH), 1375 (C–N), and 720 (C–Cl). The 1H nuclear magnetic resonance (NMR) spectra obtained from DMSO-d6 at a frequency of 400 MHz include the following values: 11.21 (s, 1H, NH), 8.52 (s, 1H, Py-H), 8.47 (s, 1H, CH), 7.40 (t, 1H, J = 7.84 Hz, Ar-H), 7.31 (d, 1H, J = 7.64 Hz, Ar-H), 7.25 (s, 1H, Ar-H), 7.06 (d, 1H, J = 7.61 Hz, Ar-H), and 3.81 (s, 3H, OCH3). There is a mass-to-z ratio of 342.7 for the MS (ESI). C=42.19, H=2.95, and N=16.40 are the result of the analytical calculations for C12H10BrClN4O (in percent). It was found that C=42.23, H=2.75, and N=16.47 were all correct.

- **2,4-Dimethoxybenzaldehyde-(5-bromo-2-chloropyrimidin-4-yl)hydrazone (7b)**

The end product of reacting (2) with 0.012 mol of the later solvent and 0.001 mol of 2,4-dimethoxybenzaldehyde is the final product. The colour is a solid yellow, The yield is 88% when the temperature is between 171 and 174 degrees Celsius. In the FT-IR spectrum, there are a total of 2937 bands (C-H), 1490 bands (C=N), 3491 bands (NH), 1370 bands (C-N), and 726 bands (C-Cl) (KBr, cm−1). The following 1H nuclear magnetic resonance (NMR) spectra were acquired using DMSO-d6 at a frequency of 400 MHz: 11.74 (s, 1H, NH), 8.29 (s, 1H, Py-H), 8.26 (s, 1H, CH), 7.20 (d, 1H, J = 7.42 Hz, Ar-H), and 7.03 (d, 1H, J = 7.15 Hz, Ar-H). in MS (ESI), the chemical shift (m/z) found is 373.1. According to the analytical calculations, the percentages for C13H12BrClN4O2 are as follows: C, 42.02; H, 3.25; and N, 15.08. The values C = 42.22, H = 3.35, and N = 15.28 have been found.

- **2,6-Diflurobenzaldehyde-(5-bromo-2-chloropyrimidin-4-yl)hydrazone (7c)**

The product obtained from (2) (0.01 mol) and 2,6-diflurobenzaldehyde (0.012 mol). White solid, Yield: 92%, M.p.: 140–142 °C. FT-IR (KBr, cm−1): 2928 (C–H), 1488 (C=N), 3349 (NH), 1375 (C–N), 720 (C–Cl). 1H NMR (DMSO-d6, 400 MHz) δ: 11.31 (s, 1H, NH), 8.74 (s, 1H, Py-H), 8.49 (s, 1H, CH), 7.51-7.50 (m, 2H, Ar-H), 7.20 (t, 1H, J = 6.60 Hz, Ar-H). MS (ESI) m/z: 350.0. Anal. Calcd. for C11H6BrClF2N4 (in %): C, 38.01; H, 1.74; N, 16.12. Found: C, 38.21; H, 1.64; N, 16.32.

- **3,4-Dichlorobenzaldehyde-(5-bromo-2-chloropyrimidin-4-yl)hydrazone (7d)**

Molecular compound (3) is the end product of the reaction between molecules (2) and 3-chlorobenzaldehyde (0.02 mol). This material has a solid brown hue, a melting point that ranges between 156 and 158 degrees Celsius, and an 85 percent production rate. According to the Fourier transform infrared spectroscopy (KBr, cm−1), the values that were found were as follows: 2947 (C-H), 1660 (C=N), 3439 (NH), 1370 (C-N), and 716 (C-Cl). The following proton states are shown in the 1H NMR spectrum in DMSO-d6 at a frequency of 400 MHz: 11.38 (s, 1H, NH), 8.51 (s, 1H, Py-H), 8.48 (s, 1H, CH), 7.91 (d, 1H, J = 8.20 Hz, Ar-H), 7.87 (d, 1H, J = 8.10 Hz, Ar-H), and 7.72 (s, 1H, Ar-H). By using mass spectrometry (ESI), the mass-to-z-coordinate ratio is 381.56. The percentages that are derived analytically for C11H6BrCl3N4 are as follows: C, 34.73; H, 1.59; and N, 14.73. C: 34.53, H: 1.65, and N: 14.93 were found to be the values.

ANTICONVULSANT ACTIVITY

- **Animals**

Male Wistar rats weighing between 190 and 220 grammes were procured from the National Institute of Nutrition in Hyderabad. For the first week, the animals were kept in cages that were kept isolated from one another so that they could get used to the environment in the laboratory. They had full access to both food and water while they were there. We followed all of the protocols set forth by the CPCSEA (Committee for the Control and Supervision of Experiments on Animals) when we conducted these experiments. The Institutional Animal Ethics Committee of the G. Pulla Reddy College of Pharmacy in Hyderabad, India, reviewed the study and provided its approval for it to proceed.

- **Maximal electroshock seizure model (MES)**

The maximum electroshock seizure paradigm was used to assess the anticonvulsant impact of the substances on male Wistar rats. An electroshock of 150 milliamperes for 0.2 seconds was administered to

rats using a convulsiometer in combination with ear clip electrodes. This was done in order to induce seizures in the rats. Oral administration of a solution containing the test chemicals, which were dissolved in 1% sodium carboxymethyl cellulose, was performed thirty minutes before to the maximal electroshock seizure test. The dose of the solution was one hundred milligrammes per kilogramme. For a period of two minutes, the animals were observed with great caution. In comparison to the control group, we recorded and calculated the percentage of children who were able to manage their seizures. Phenytoin, administered at a dose of 100 milligrammes per kilogramme, was the usual medication that was used.

Neurotoxicity screening

In order to establish the appropriate level of motor impairment in mice, the rotorod test was used. The rotorod test was used in order to ascertain the acute neurological toxicity that was present in the mice. At a pace of ten rotations per minute, the rotorod rotates, and the mice have been instructed to stay on it during the whole process. In terms of diameter, the rod measured 3.2 centimetres. At a dose of one hundred milligrammes per kilogramme, the test compounds were administered to animals that had been trained. An indication of neurotoxicity was present in each of the three trials when the animal experienced a loss of equilibrium on the rod for a period of at least one minute. For the sake of reference, the medication phenytoin was used.

- **Statistical analysis**

A one-way analysis of variance (ANOVA) and a Dunnett test were used to compare the groups in this investigation.

ANTIOXIDANT ACTIVITY

In order to study the synthesised compounds' capacity to scavenge free radicals in a laboratory environment, we used the 1, 1-diphenyl-2-picrylhydrazyl (DPPH) assay. One hundred to two hundred milligrammes per millilitre of methanol was used to dilute the stock solution of the medication to a variety of concentrations. One millilitre of a DPPH methanol solution with a weight-to-volume ratio of 0.003% was combined with two millilitres of the synthesised compounds in a methanolic solution. Following a vigorous shaking of the mixture, it was allowed to rest for a period of thirty minutes. The absorbance at 517 nm was measured in order to ascertain the percentage of scavenging activity that was present. Ascorbic acid was considered to be the most effective medicine. For the purpose of determining the inhibitory ratio (I%) of the compounds that were assessed, the absorbance of the sample (a) and the absorbance of the control (c) were used.

RESULT AND DISSCUION

- **Spectral studies**

The synthesis of hydrazinopyrimidine (1) was accomplished by following the technique that was outlined."14" In the presence of methanol, the reaction between 5-bromo-2,4- dichloropyrimidine and hydrazine hydrate results in the formation of hydrazino-pyrimidine (2). The eight-bromo-5-chloro-3-methyl[1,2,4]triazolo[4,3-c]pyrimidine (3) was produced by the reaction of hydrazino-pyrimidine with acetic anhydride under reflux conditions, as described in method 15. In accordance with the instructions provided in Procedure 16, the chemical 8-bromo-5-chloro-1,2,4-triazolo[4,3-c]pyrimidine-3-amine was created by reacting chemical 2 with Cyanogen Bromide in the presence of Na2CO3. (4). In order to get 5-bromo-2- chloro-4-(3,5-dimethyl-1H-Pyrazol-1-yl)pyrimidine (5), Compound 2 was put through the reaction that was detailed in Procedure 14 with Acetylacetone. It was possible to get 8-bromo-5-chloro-3-aryl-1,2,4-triazolo [4,3-c]pyrimidine 6(a-d) by the reaction of hydrazino-pyrimidine 2 with substituted benzoic acid. The reaction between 2-Hydrazinopyrimidine and substituted benzaldehyde resulted in the formation of 7-aryl-(5-bromo-2-chloropyrimidine-4-yl)hydrazone. It was determined that two novel pyrimidine derivatives, 6(aed) and 7(aed), could be synthesised by using the information shown in Figure 1. Each of the compounds that were synthesised has its chemical formula listed in Table 1, which may be found here.

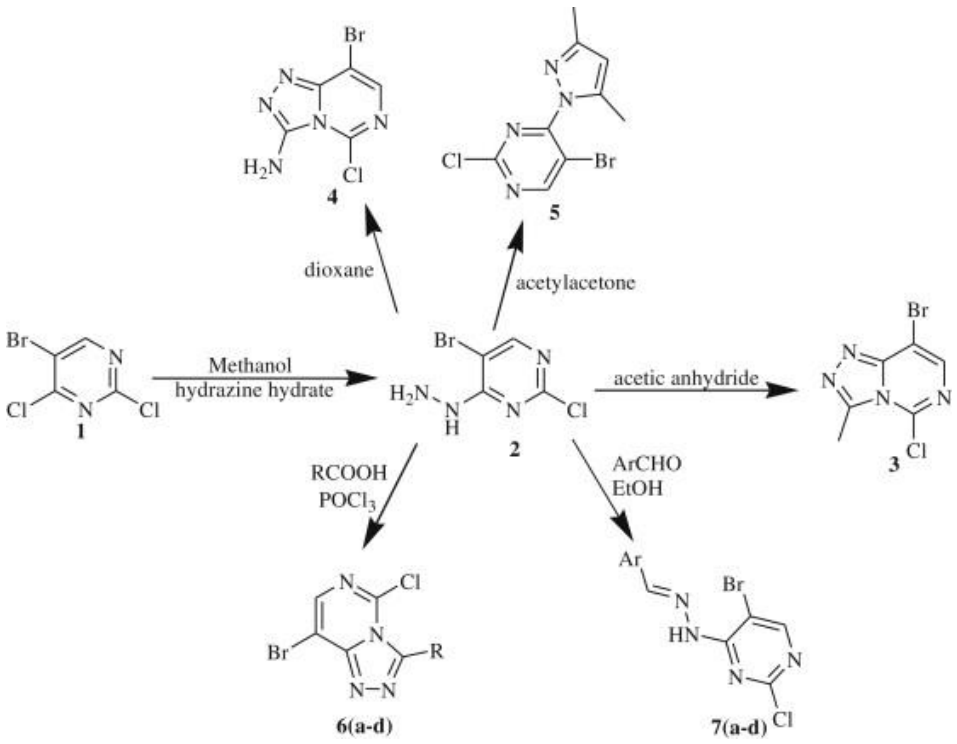
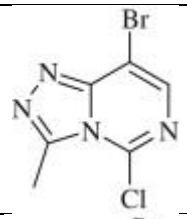
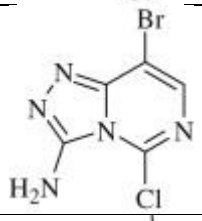
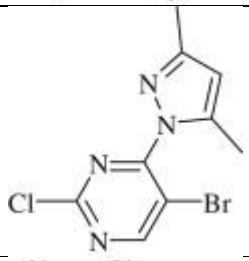
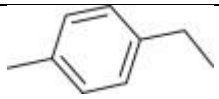
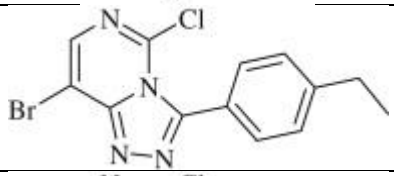
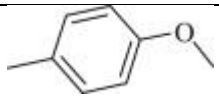
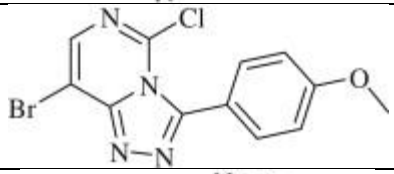
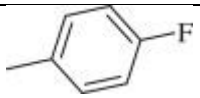
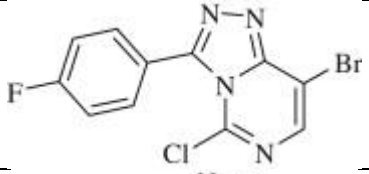
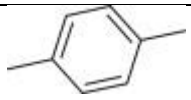
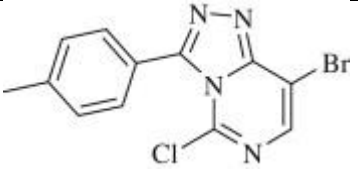
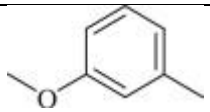
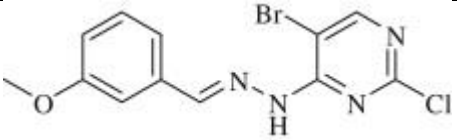
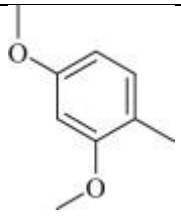
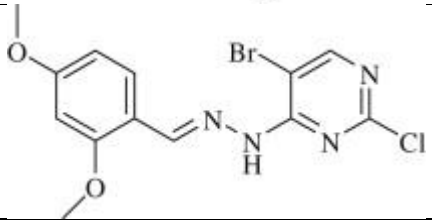
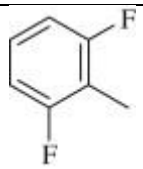
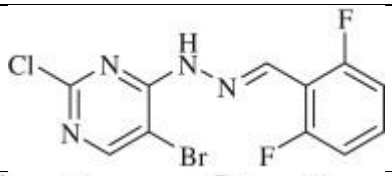
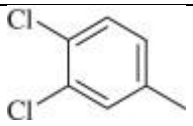
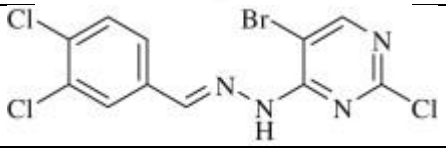


Fig 1. Synthetic route of pyrimidine analogs.

Table 1 e Chemical structure of pyrimidine derivatives 6(aed) and 7(aed)

Compound	R/Ar	Structure
3	-	
4	-	
5	-	
6a		
6b		
6c		
6d		
7a		
7b		

7c		
7d		

This approach is particularly appealing and convenient for the synthesis of a wide variety of pyrimidines because it makes use of starting materials that are easily accessible and because the techniques for synthesis are straightforward. The recording of the elemental analyses, 1 H NMR, FT-IR, and mass spectra of the products after they were formed was a confirmation of their formation. Both 6c and 7c exhibited a single in the area of d, with the pyrimidine ring accounting for 7.88 and the CH group accounting for 8.49 in their respective 1 H NMR spectra. A molecular ion peak was seen in the mass spectrum of 7c at a mass-to-charge ratio of 350.0, which is consistent with the molecular formula, which is C11H6BrClF2N4. The findings from the elemental analyses demonstrated a satisfactory level of agreement between the values that were found via experimentation and the values that were estimated theoretically, with a margin of agreement of ±0.4%.

- **In vivo anticonvulsant activity**

Researchers in the area of antiepileptic drugs have spent decades examining the effects of various stimulants on single acute seizures in rodents such as mice and rats in an attempt to uncover new compounds with anticonvulsant capabilities. These treatments are intended to treat epileptic seizures. There is at least one MES model in which anticonvulsant effect has been shown by every antiepileptic medicine that is currently available.a 17 For the purpose of this study, we evaluated the anticonvulsant efficacy of the synthesised compounds by using the MES model at a dose of one hundred milligrammes per kilogramme. There is a summary of the results in Table 2. Both compound 6c and compound 7c had a protective effect against seizures brought on by MES that was equivalent to the protective effect shown with phenytoin, which is considered to be the gold standard. In terms of protectiveness, compounds 3, 4, 5, 6a, 6b, 6d, 7a, 7b, and 7d did not differ substantially from the control group. However, they did have some effects, although those that were not very significant. At a dose of one hundred milligrammes per kilogramme, the rotorod method was used to evaluate the neurotoxicity of each and every drug. Every single one of the compounds, with the exception of compounds 3, 4, and 5, did not demonstrate any neurotoxicity. According to Table 3, these compounds were 25% more harmful than the average after being

administered orally for a period of two hours for therapy. While compounds 3, 4, 5, 6(aed), and 7(aed) all exhibited activity ranging from 27.11 to 72.57 percent relative to phenytoin, which completely inhibited the electro-convulsometer-produced convulsions, compound 7c, which contains electron withdrawing groups, demonstrated exceptional anticonvulsant activity. Compound 7c was found to be the most effective anticonvulsant.

Table: 2 Effect of compounds in the maximal electroshock seizure test.

Treatment	E/F	% Protection
3	7.01	27.11
4	6.13	32.41
5	6.53	37.10
6a	5.49	42.61
6b	6.53	44.76
6c	2.07	71.14
6d	6.25	41.31
7a	2.98	45.40
7b	2.21	51.26
7c	1.81	72.57
7d	2.14	54.41
Standard	1.98	75.88
Control (Vehicle)	8.21	-

E/F = Extension/Flexion [Decrease in ratio of extension phase (in seconds)/flexion phase (in seconds)]. % Protection = control.

Table: 3 Neurotoxicity screening of the compounds

Compound	Neurotoxicity Screening			
	0.5 h	1 h	2 h	4 h
3	0/4	0/4	1/4	1/4
4	0/4	0/4	1/4	1/4
5	0/4	0/4	1/4	1/4
6a	0/4	0/4	0/4	0/4
6b	0/4	0/4	0/4	0/4
6c	0/4	0/4	0/4	0/4
6d	0/4	0/4	0/4	0/4
7a	0/4	0/4	0/4	0/4
7b	0/4	0/4	0/4	0/4
7c	0/4	0/4	0/4	0/4
7d	0/4	0/4	0/4	0/4
Standard	0/4	0/4	0/4	0/4

- **Antioxidant activity**

In order to carry out the spectrophotometric in vitro DPPH radical scavenging experiment, ascorbic acid was used as a positive control. Table 4 displays the findings of the DPPH radical scavenging activity

percentages calculated for the experiment. The chemical 6b demonstrated percentage scavenging effects of 32.2%, 43.4%, and 54.8%, respectively, when it was present at concentrations of 100, 150, and 200 mg/ml. When compound 7b is present at concentrations of 100, 150, and 200 mg/ml, the percentage of inhibition is 51.1, 60.8, and 68.1, respectively. Ascorbic acid showed a scavenging effectiveness of 98.2% when it was administered at a dose of 200 mg/ml. The inhibition of 7c was 52.0%, 61.7%, and 69.2%, respectively, when the concentration was 200 mg/ml. All of the medications, with the exception of 6b, 7b, and 7c, demonstrated a somewhat lower level of inhibition. It was shown that the electron-donating methoxy group in compounds 6b, 7b, and 7c exhibited a greater level of antioxidant activity compared to the other compounds in the series.

Table: 4 e DPPH radical scavenging activity of the tested compounds.

Compound	Scavenging Effect (%) of Pyrimidine Derivatives at Different Concentrations		
	100 µg/ml	150 µg/ml	200 µg/ml
3	10.2	18.3	26.5
4	12.2	18.8	27.1
5	12.6	19.5	28.0
6a	21.3	31.8	38.3
6b	32.2	43.4	54.8
6c	22.0	32.1	39.0
6d	23.1	33.0	41.1
7a	35.2	46.3	52.1
7b	51.1	60.8	68.1
7c	52.0	61.7	69.2
7d	37.1	47.8	53.8
Ascorbic acid	73.0	85.3	98.2

CONCULSION

A number of new pyrimidine analogues, including 3, 4, 5, 6(aed), and 7(aed), were effectively synthesised, characterised using a variety of spectrum studies, and evaluated for their ability to inhibit seizures. Several different pyrimidine derivatives, particularly those that included electron withdrawing groups, were shown to have powerful anticonvulsant properties. In comparison to the other compounds that were synthesised, the anticonvulsant effects of 6c and 7c were particularly noteworthy. It was shown that the electron-donating methoxy group in compounds 6b, 7b, and 7c exhibited a greater level of antioxidant activity compared to the other compounds in the series.

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