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Design, Synthesis and Anticonvulsant Activity of 1, 2, 4-Triazole Derivatives

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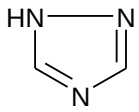
Abstracts-A series of novel 1,2,4-triazole derivatives (NJ-01 to NJ-12) were synthesized and evaluated for their antimicrobial and anticonvulsant potential. Structural confirmation of synthesized compounds was achieved using IR, ^1H NMR, and mass spectroscopic techniques. Anticonvulsant activity was evaluated using the maximal electroshock (MES) model in albino rats. Among all compounds, NJ-01, NJ-05, and NJ-09 exhibited significant biological activity in both models.NJ-05 and NJ-09 were identified as lead candidates due to their dual pharmacological activity and favorable properties.

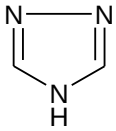
Keywords:- Triazole Derivatives ,Benzoic Acid, Anticonvulsant activity , MES, biological activity

Introduction :- Disease caused by bacteria, virus, fungi and other parasites and major caused of death,Disability, social and economical disruption for million of people.[1] Infection deasese raise awrensee of our global vulnerabilit the need for strong health care system and potentially broad abd borderless impactof disease.[2] According to world heath statics 2008 report published by world helath organisation (WHO), The induction will be one of the most serious problem in 2030.[3] Thus developementof novel antimicrobial drug still in demand.

Five member aromatic ring with three atom are called 1,2,4 Triazole is also pyrodiazole.



1H-1,2,4-triazole



4H-1,2,4-triazole

S-Triazole or 1, 2, 4-Triazole

Thus Copound carring Triazole compounds gained importance in medicinal and pharmacetyical field due to a broad range of buiological activity. such as antifungal[4] , anticonvulsant[5], antitubercular[6], antiinflamatory[7] and antimicribial[8] activity.

Although many drugs are available, no drugs has fullfilled all the expectation in term of toxicity, resistance and cost factores. Thera are two types of approches to get new drugs for microbial infection treatments.

A. Synthesis of analogues, modifiaction of exicting compounds for improving microbial infection treatment.

B. Searching novel structure,which pathogen organism never seen before fore the treatment of bacterail and fungus infection.

Various 1, 2, 4-triazole derivatives were synthesized by reacting aromatic acid esters with hydrazine hydrate followed by reaction with alcoholic potassium hydroxide and carbon disulphide. The obtained potassium dithiocarbazinates were cyclized with hydrazine to yield 1, 2, 4-triazole. And further reacted with chloro acetyl chloride and then with amines to give title compound.

All the synthesized compounds were recrystallized and their purity was checked by performing thin layer chromatography. The structure of the compounds was confirmed on the basis of IR, NMR &^{1}H NMR spectral data.

Material And Methodology:-

Melting points was determining by open capillary method and are uncorrected. The IR spectra (in KBr pellets) were recorded on IR spectrophotometer. ^{1}HNMR spectra were recorded (DMSO-d6) on MHz spectrophotometer in $CDCl_3$ using TMS as an internal standard. Chemical shift (δ) are expressed in part per million (ppm). Chemical shift values are given in d scales. Mass spectra were recorded by mass spectrophotometer by using electron ionization detector. The progress of reaction was monitored by thin layer chromatography using plate coated silica gel G of 0.25 mm thickness. Eluents used were hexane and ethyl acetate (6:4) as a solvent system and iodine vapors was used as a detecting agent. Spot were visualized through iodine chamber. Solubility of newly synthesized triazole derivative was determined in various organic solvents at room temperature. The reaction pathway summarized in figure 01.

Syntheses of compounds were carried out as per following scheme

Step-I: Synthesis of esters of aromatic acid

A mixture of substituted benzoic acid (0.3 mol), 130 mL of absolute alcohol and 3.3 mL of conc. H_2SO_4 was refluxed for 2 h on water bath. After completion of reaction, excess of ethanol was distilled off and content was transferred into separating funnel containing 310 mL distilled water. Carbon-tetrachloride (20 mL) was added, aqueous layer and ester layer were separated. Ester layer (lower layer) was taken in another separating funnel and shaked it with a strong solution of sodium bicarbonate until all free acid was removed and no further evolution of carbon dioxide occur. Washed once with water and dried by pouring into a small conical flask containing 7.5g magnesium sulphate. Cork the flask, shacked for 2 minutes then carbon tetrachloride was distilled off under reduced pressure. The resulting colourless liquid was collected and the completion of reaction was checked by TLC using hexane and ethyl acetate (6:4) and iodine vapour as a detecting reagent.

Step-II: Synthesis of hydrazide of synthesized ester

Produced aromatic esters (0.1 mol) and 80 % hydrazine hydrate (0.1 mol) was refluxed on a water bath for 15 min. enough absolute ethanol was added to obtain a clear solution. Again contents were refluxed for 2 h. Excess alcohol was evaporated and solution was cool down. The solid obtained was separated and recrystallised from ethanol to get the needle shaped crystals.

Step-III: Synthesis of potassium dithiocarbazinate

Substituted aromatic hydrazides (0.02 mol), KOH (0.012 mol) and CS_2 (0.015 mol) in absolute ethanol (350 mL) were stirred for 10 h. After the completion of reaction ether (200 mL) was added. The obtained precipitate was filtered, washed and dried. The synthesized dithiocarbazinate was used for the next step without further purification.

Step-IV: Synthesis of 5-aryl-4-amino-3-mercapto-1,2,4-triazole

Substituted produced dithocarbazinate (0.1 mol), hydrazine hydrate (0.3 mol) and water (30 mL) was refluxed for 3 h, H_2S was evolved during the reaction and clear solution resulted, enough cold water was added and cooled to 5^0c. Acidified the cooled solution with dil. HCl. Obtained precipitate was filtered, washed and recrystallized from 95% ethanol.

Step-V: Synthesis of 5-aryl-4-(chloroacetylamino)-3-mercapto-1,2,4- triazole:

In a two necked flask fitted with reflux condenser containing 100 mL benzene and obtained compound and separating funnel contained chloro acetyl chloride in 30 mL benzene. The mixture was refluxed and chloro acetyl chloride was added in small portions. After addition of chloro acetyl chloride, solution was again refluxed for 5-6 h, cooled and contents were poured on crushed ice. The obtained precipitate was filtered, washed and recrystallized from absolute ethanol.

Step-VI: Synthesis of amino derivative of 5-aryl-4-(chloroacetylamino) -3-mercapto-1,2,4- triazole:

Synthesized substituted 5-aryl-4-(chloroacetylamino)-3-mercapto-1, 2, 4- triazole (0.03 mol), respective amines (0.03 mol) and 75 mL benzene was taken in round bottom flask. The contents were refluxed for 5-6 h and cooled. Filtered the precipitate and washed with distilled water several times to remove traces of hydrochloride. Product obtained was recrystallized from appropriate solvent.

Characterization of synthesized compounds:-

01. 2-(Dimethylamino)-N-(3-mercapto-5-phenyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-01)

IR (KBr,cm^{-1}):3310 (N-H stretching),3116.0 (aromatic C-H stereching), 2962.6 (C-H streching of methyl group), 2928.8 & 2858.7 (C-H streching of methylene group),2584.5 (S-H streching),1660.6 (C=O streching),1614.8(C=N streching),1580.0 (C=C streching), 760.8 (C-H out of plane bending), 670.0 (C-S streching)

MS(m/s): M^+ Calculated – 277

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.2-7.6(m, 5H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.3(s, 6H, -CH_3)

02. 2-(Diethyl amino)-N-(3-mercapto-5-phenyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-02)

IR (KBr,cm^{-1}):3349.1 (N-H stretching),3116.0 (aromatic C-H stereching),2968.0 (C-H streching of methyl group), 2928.8 & 2848.9 (C-H streching of methylene group),2556.4 (S-H streching),1579.9 (C=N streching), 1664.0 (C=O streching),1579.9 (C=C streching), 786.7 (C-H out of plane bending), 661.5,623.1 (C-S streching)

MS(m/s): M^+ Calculated – 305

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.2-7.6(m, 5H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.5(q, 6H, -CH_3), 1.2(t,2H,CH_2)

03. 2-(Dipropyl amino)-N-(3-mercapto-5-phenyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-03)

IR (KBr,cm^{-1}):3355.1 (N-H stretching),3116.2 (aromatic C-H stereching),2968.0 (C-H streching of methyl group), 2928.8 & 2848.9 (C-H streching of methylene group),2556.4 (S-H streching),1416.1 (C=N streching),1662.0 (C=O streching),1579.9 (C=C streching), 823.0 (C-H out of plane bending), 661.5,623.1 (C-S streching)

MS(m/s): M^+ Calculated – 333

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.2-7.6(m, 5H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.9(t,2H,-CH_2), 1.7 (m,5H,-CH_2CH_3),1.1 (t,2H,-CH_2)

04.2-(Diisopropyl amino)-N-(3-mercapto-5-phenyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-04)

IR (KBr,cm^{-1}):3325.5 (N-H stretching),3102.5,3095.5 (aromatic C-H stereching),2580.1 (S-H streching),1662.7 (C=O streching), 1429.3 (C=N streching), 1575.6 (C=C streching),1380.8,1365.5 (C-H bendin due to isoprpyl group),819.1 (C-H out of plane bending), 684.0, 630.1 (C-S streching)

MS(m/s): M^+ Calculated – 333

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.2-7.6(m, 5H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.3(s, 6H, -CH_3),1.1(d,1H,-CH)

05. 2-(Dimethyl amino)-N-(3-mercapto-5-p-tolyl-4*H*-1, 2, 4-triazol-4-yl)-acetamide (NJ-05)

IR (KBr,cm^{-1}):3226.6 (N-H stretching),3106.0 (aromatic C-H stereching),2958.0 (C-H streching of methyl group), 2928.8 & 2848.9 (C-H streching of methylene group),2564.4 (S-H streching),1662.6 (C=O streching),1611.4 (C=N streching), 787.8 (C-H out of plane bending). **MS(m/s):** M^+ Calculated – 291

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.0-7.2(m, 4H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.3(s, 6H, -CH_3),2.1 (s,3H,CH_3)

06. 2-(Diethyl amino)-N-(3-mercapto-5-p-tolyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-06)

IR (KBr,cm^{-1}):3266.6 (N-H stretching),3106.0 (aromatic C-H stereching),2958.0 (C-H streching of methyl group), 2928.8 & 2848.9 (C-H streching of methylene group),2556.4 (S-H streching),1662.6 (C=O streching),1573.8 (C=C streching), 684.9,631.3 (C-S streching)

MS(m/s): M^+ Calculated – 319

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.2-7.6(m, 5H, -C_6H_5), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH),2.5 (q,3H,-CH_3,) 1.1 (t, 2H, -CH_2).

07. 2-(Dipropyl amino)-N-(3-mercapto-5-p-tolyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-07)

IR (KBr,cm^{-1}):3325.1 (N-H stretching),3116.2 (aromatic C-H stereching),2968.0 (C-H streching of methyl group), 2928.8 & 2848.9 (C-H streching of methylene group),2556.4 (S-H streching),1626.6 (C=O streching),1579.9 (C=C streching), 1416.1 (C=N streching), 823.0 (C-H out of plane bending), 661.5,623.1 (C-S streching)

MS(m/s): M^+ Calculated – 347

^{1}H-NMR (400 MHz,DMSO-d_6) δ 8.0(s, 1H, -NH), 7.0-7.2(m, 4H, -C_6H_4), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH),2.9 (t,3H,-CH_2),2.3 (s,3H,-CH_3),1.7 (m,5H,-CH_2CH_3), 1.1 (t, 2H, -CH_2).

08. 2-(Diisopropyl amino)-N-(3-mercapto-5-p-tolyl-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-08)

IR (KBr,cm^{-1}):3292.5 (N-H stretching),3102.5,3045.5 (aromatic C-H stereching), 2582.0 (S-H streching),1429.3 (C=N streching),1575.6 (C=C streching),1662.7(C=O streching), 1380.8,1365.5 (C-H bending due to isopropyl group), 921.6 (C-H bending, rocking), 819.1 (C-H out of plane bending), 674.0,630.1 (C-S streching)

MS(m/s): M^+ Calculated – 247

^{1}H-NMR (400 MHz,DMSO-d$_6$) δ 8.0(s, 1H, -NH), 7.0-7.2(m, 4H, -C_6H_4), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.9(m, 6H, -CH_3), 2.3 (s, 3H, -CH_3), 1.1(d, 1H, -CH).

09.2-(Dimethylamino)-N-(3-mercapto-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-09)

IR (KBr,cm^{-1}):3310 (N-H stretching), 2952.6 (C-H streching of methyl group), 2928.8 & 2858.7 (C-H streching of methylene group),2584.5 (S-H streching),1660.6 (C=O streching), 1614.8 (C=N streching),1585.0 (C=C streching), 773.4 (C-H out of plane bending), 614.5 (C-Sstreching)

MS(m/s): M^+ Calculated – 307

^{1}H-NMR (400 MHz,DMSO-d$_6$) δ 8.0(s, 1H, -NH), 6.7-6.9 (m, 4H, -C_6H_4), 3.7(s, 3H, -OCH_2), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.3(s, 5H, -CH_3)

10.2-(Diethylamino)-N-(3-mercapto-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-4-yl)-acetamide (NJ-10)

IR (KBr,cm^{-1}):3319.1 (N-H stretching),3116.2 (aromatic C-H stereching),2958.0 (C-H streching of methyl group), 2925.8 & 2848.9 (C-H streching of methylene group),2566.4 (S-H streching),1644.6 (C=O streching),1579.9 (C=C streching), 786.7 (C-H out of plane bending), 671.5,623.1 (C-Sstreching)

MS(m/s): M^+ Calculated – 335

^{1}H-NMR (400 MHz,DMSO-d$_6$) δ 8.0(s, 1H, -NH), 6.7-6.9 (m, 4H, -C_6H_4), 3.7(s, 2H, -OCH_3), 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.5(q, 3H, -CH_3), 1.1(s, 3H, -CH_3),

11.2-(Dipropylamino)-N-(3-mercapto-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-4-yl)acetamide (NJ-11)

IR (KBr,cm^{-1}):3310.9 (N-H stretching),3116.9,3032.1 (aromatic C-H stereching),2928.7 (C-H streching of methylene group),2562.8.5 (S-H streching),1660.0 (C=O streching),1562.9 (C=C streching), 1313.6 (C=N streching), 822.6 (C-H out of plane bending), 670.0,615.0 (C-S streching)

MS(m/s): M^+ Calculated – 363

^{1}H-NMR (400 MHz,DMSO-d$_6$) δ 8.0(s, 1H, -NH), 6.7-6.9(m, 4H, -C_6H_4),3.7(s, 3H, -OCH_3) 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.9(s, 2H, -CH_2), 1.7(m, 5H, -CH_2CH_3),1.1(t, 2H, -CH_2).

12.2-(Diisopropylamino)-N-(3-mercapto-5-(4-methoxyphenyl)-4*H*-1,2,4-triazol-4-yl)acetamide (NJ-12)

IR (KBr,cm^{-1}):3310 (N-H stretching),3116.9,3032.1 (aromatic C-H stereching), 2928.7 & 2851.3(C-H streching of methylene group),2562.8 (S-H streching),1660.0 (C=O streching),1562.9 (C=C streching), 1520.0 (C=N streching),1384.7,1373.7 (C-H Bending due to isopropyl group), 922.6 (C-H bending,rocking) 822.6 (C-H out of plane bending), 670.9,615.0 (C-S streching)

MS(m/s): M^+ Calculated – 363

^{1}H-NMR (400 MHz,DMSO-d$_6$) δ 8.0(s, 1H, -NH), 6.7-6.9(m, 4H, -C_6H_4),3.7(s, 3H, -OCH_3) 3.25(s, 2H, -CH_2), 3.1(s, 1H, -SH), 2.9(m, 6H, -CH_3), 1.1(d, 1H, -CH).

Anticonvulsant Activity Study:

Anticonvulsant activity was determined by Maximal Electro Shock (MES) induced method. Albino rats of either sex weighing 150-200 g were divided into different group for different synthesized compound, control and standard. The animals of all groups were treated with 100 mg/kg, 150mg/kg in suitable solvent by i.p. route. Except control group which received only solvent. Standard group received (Phenytoin) 25 mg/kg body weight by i.p. route. The effect of drug was observed after 30 min and 4h of the drug treatment.

Seizures were produced in rats by 'Techno' convulsometer by delivering a current of 150 mA through the corneal electrodes for a period of 0.2 seconds. The animal was placed on the table and its head was fixed. The electrodes were dipped in normal saline and placed gently on the cornea. The shock was delivered by putting on the switch of the instrument. The animals were observed for the following parameters.

(a) Tonic phases - Flexor phase - Extensor phase

(b) Clonic phase (intermediate jerking of the limbs).

(c) Stupor (unconsciousness).

(d) Recovery/Death.

Time for each phase was noted by stop watch. Drug treated animals, were observed for presence or absence of extensor and flexor component of tonic phase during seizures.

Result and discussion:-

All the Physiochemical properties such as their Melting point determination, TLC (determination of R_F value) and percentage yield data of compounds summarized in **Table No.01**.

Anticonvulsant screening of synthesized compounds NJ1, NJ5 and NJ9 showed seizure protection at both 100 and 150 mg/kg dose after 30 min and 4 h showing quick onset of action. The synthesized compound NJ2, NJ6 and NJ10 were somewhat less active than NJ1, NJ5 and NJ9 reveals that their high concentration is required to cross blood brain barrier. Remaining compound (NJ3, NJ7, NJ11, NJ4, NJ8, and NJ12) was inactive as shown in **Table No.02 to Table No. 05**

Comparison of anticonvulsant activity:

1. Effect of substituents on benzene ring

NJ05>NJ01>NJ09

From present study it was found that methyl substituted ring was most active and unsubstituted ring was least active. Methoxy substituted compound was intermittent in activity. Study revealed that electron releasing\donating group generally exhibiting activity.

2. Effect of chain length

NJ01>NJ02>NJ03>NJ04>NJ05>NJ06>NJ07>NJ08>NJ09>NJ10>NJ11>NJ12

Study revealed that as chain length of compounds is increased from methyl to propyl or isopropyl, the activity of compounds decreases. It may be due to steric hindrance. Electron donating group of benzene ring exhibited better anticonvulsant activity as compared to unsubstitution.

The study establishes that:

- Compounds with optimal **lipophilicity, electronic properties, and minimal steric hindrance** exhibit superior biological performance.
- This correlation can be effectively used for **future drug design and optimization of triazole derivatives**.

- **In-vivo anticonvulsant activity** (inverse extensor phase → higher value = better activity)
- The anticonvulsant activity of the synthesized 1,2,4-triazole derivatives was evaluated using the maximal electroshock (MES) model at two dose levels (100 mg/kg and 150 mg/kg) and at different time intervals (30 min and 4 h). The results are presented in Tables 02–05.
- At a dose of 100 mg/kg, several compounds exhibited varying degrees of protection against MES-induced seizures. Compounds NJ-01, NJ-05, and NJ-09 showed significant anticonvulsant activity, as indicated by a reduction in the duration of the extensor phase, which is a key parameter in MES

screening. These compounds also demonstrated shorter clonic and stupor phases compared to the control group, suggesting effective seizure suppression.

- Compounds NJ-02, NJ-06, and NJ-10 displayed moderate activity, whereas NJ-03, NJ-04, NJ-07, NJ-08, NJ-11, and NJ-12 showed comparatively weaker effects. The control group exhibited prolonged seizure phases, confirming the severity of induced convulsions, while the standard drug (phenytoin) significantly reduced all seizure parameters, validating the experimental model.
- At the higher dose of 150 mg/kg, an overall improvement in anticonvulsant activity was observed. Compounds NJ-01, NJ-05, and NJ-09 again demonstrated superior activity with further reduction in extensor, clonic, and stupor phases. This indicates a dose-dependent enhancement of anticonvulsant effect.
- Time-dependent observations (30 min vs. 4 h) revealed that the active compounds maintained their efficacy over time, suggesting a sustained duration of action. In contrast, less active compounds showed minimal changes over time, indicating weaker pharmacological potential.
- Structure–activity relationship (SAR) analysis suggests that electron-donating substituents such as methyl and methoxy groups on the aromatic ring enhance anticonvulsant activity. Additionally, compounds with shorter alkyl chains (dimethyl derivatives) exhibited better activity compared to those with longer chains (propyl and isopropyl), likely due to reduced steric hindrance and improved penetration across the blood–brain barrier.
- Overall, compounds NJ-05 and NJ-09 emerged as the most promising candidates, showing consistent and significant anticonvulsant activity across different doses and time intervals.

Conclusion: - In the present study, a series of novel 1,2,4-triazole derivatives (NJ-01 to NJ-12) were successfully designed, synthesized, and characterized using IR, ^1H NMR, and mass spectroscopic techniques. The spectral data confirmed the proposed chemical structures of all synthesized compounds.

The anticonvulsant activity of the synthesized compounds was evaluated using the maximal electroshock (MES) model in albino rats. Among the tested compounds, NJ-01, NJ-05, and NJ-09 demonstrated significant anticonvulsant activity, while NJ-02, NJ-06, NJ-07, NJ-10, and NJ-11 showed moderate activity. The remaining compounds exhibited low or negligible effects.

Structure–activity relationship (SAR) analysis revealed that the presence of electron-donating substituents on the aromatic ring enhances anticonvulsant activity. Additionally, shorter alkyl chain substitutions were found to be more favorable, whereas increased chain length likely reduced activity due to steric hindrance and decreased ability to cross the blood–brain barrier. The graph represents the anticonvulsant activity of synthesized 1,2,4-triazole derivatives (NJ-01 to NJ-12) evaluated using the maximal electroshock (MES) model.

The **X-axis** shows the different synthesized compounds (NJ-01 to NJ-12), while the **Y-axis** represents the duration of the **extensor phase (in seconds)**, which is a critical parameter for assessing anticonvulsant activity.

Four different lines are plotted in the graph, corresponding to:

- 100 mg/kg dose after 30 minutes
- 100 mg/kg dose after 4 hours
- 150 mg/kg dose after 30 minutes
- 150 mg/kg dose after 4 hours

A **decrease in extensor phase duration indicates better anticonvulsant activity**. From the graph, compounds **NJ-05, NJ-01, and NJ-09** show significantly lower extensor phase durations across all conditions, indicating superior anticonvulsant potential. In contrast, compounds such as **NJ-08 and NJ-12** exhibit higher extensor phase durations, suggesting lower activity.

Additionally, the graph demonstrates a **dose-dependent trend**, where compounds generally show improved anticonvulsant activity at the higher dose (150 mg/kg). The activity is also relatively sustained over time, as observed at both 30 minutes and 4 hours.

Overall, the results indicate that 1,2,4-triazole derivatives represent a promising class of compounds for the development of new anticonvulsant agents. Compounds NJ-05 and NJ-09, in particular, emerged as potential lead candidates due to their superior biological activity. Further studies, including detailed pharmacological evaluation and toxicity profiling, are recommended to optimize these molecules for clinical applications.

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Table 01: Physical parameters of triazole derivatives synthesized compounds

S. No.	R	R_1& R_2	Mol. Form.	Rf Value	Mol.Wt.	%Yield	M.P. (°C)
NJ-1	H	Methyl	$C_{12}H_{15}O_1N_5S_1$	0.56	277	56	170-172
NJ-2	H	Ethyl	$C_{14}H_{19}O_1N_5S_1$	0.63	305	63	153-155
NJ-3	H	Propyl	$C_{16}H_{23}O_1N_5S_1$	0.45	333	46	174-176
NJ-4	H	Isopropyl	$C_{16}H_{23}O_1N_5S_1$	0.66	333	52	108-110
NJ-5	CH_3	Methyl	$C_{13}H_{18}O_1N_5S_1$	0.48	291	48	158-160
NJ-6	CH_3	Ethyl	$C_{15}H_{22}O_1N_5S_1$	0.52	319	42	128-130
NJ-7	CH_3	Propyl	$C_{17}H_{26}O_1N_5S_1$	0.74	347	54	184-186
NJ-8	CH_3	Isopropyl	$C_{17}H_{26}O_1N_5S_1$	0.61	347	46	202-204
NJ-9	OCH_3	Methyl	$C_{13}H_{18}O_2N_5S_1$	0.59	307	55	212-214
NJ-10	OCH_3	Ethyl	$C_{15}H_{22}O_2N_5S_1$	0.60	335	49	166-168
NJ-11	OCH_3	Propyl	$C_{17}H_{26}O_2N_5S_1$	0.68	363	61	196-198
NJ-12	OCH_3	Isopropyl	$C_{17}H_{26}O_2N_5S_1$	0.78	363	58	182-184

Table 02: Effect of Synthesized Compounds on Maximal Electro Shock Convulsion in albino rats 100mg/kg dose after 4 h

Code No.	Time(sec) in various phase of convulsion				
	Flexion (mean±SE)	Extensor (mean±SE)	Clonic (mean±SE)	Stupor (mean±SE)	Recovery /Death
NJ1	0.3±0.04	5.7±0.4	1.6±0.2	97±0.7	Recovery
NJ2	1.2±0.25	6.7±0.47	2.8±0.2	102±0.47	Recovery
NJ3	2.5±0.34	10.7±0.47	6.4±0.3	120±0.64	Recovery
NJ4	3.7±0.47	11.9±0.4	6.1±0.3	125±0.6	Recovery
NJ5	-	5.2±0.2	1.0±0.2	93±0.47	Recovery
NJ6	1.2±0.3	6.4±0.7	2.7±0.2	98±0.6	Recovery
NJ7	2.6.± 0.3	11.1±0.4	6.4±0.3	131±0.6	Recovery
NJ8	3.6±0.3	13.2±0.3	6.8±0.4	128±0.6	Recovery
NJ9	0.7±0.2	6.1±0.4	1.9±0.2	101±0.7	Recovery
NJ10	1.4±0.2	6.8±0.2	3.0±0.2	108±0.7	Recovery
NJ11	2.9± 0.2	12.6±0.4	5.9±0.4	123±0.5	Recovery
NJ12	3.8±0.2	12.8±0.4	7.2±0.3	126±0.2	Recovery
C	4.0±0.3	13.8±0.5	7.8±0.3	133±0.4	Recovery
Sd	-	4±0.7	0.8±0.3	86±1.8	Recovery

* C: control

* Sd: standard (phenytoin)

* - : no activit

Table 03: Effect of Synthesized Compounds on Maximal Electro Shock Convulsion in albino rats (at 100mg/kg dose after 4 h)

Code No.	Time(sec) in various phase of convulsion				
	Flexion (mean±SE)	Extensor (mean±SE)	Clonic (mean±SE)	Stupor (mean±SE)	Recovery /Death
NJ1	1.1±0.2	6.2±0.6	2.0±0.3	102±0.6	Recovery
NJ2	1.8±0.2	7.0±0.7	3.8±0.3	112±0.6	Recovery
NJ3	2.8±0.3	11.3±0.7	7.0±0.3	129±0.6	Recovery
NJ4	3.9±0.4	11.9±0.7	6.1±0.6	125±0.6	Recovery
NJ5	0.8±0.2	5.8±0.6	1.6±0.3	98±0.4	Recovery
NJ6	1.5±0.2	6.5±0.7	3.1±0.3	106±0.7	Recovery
NJ7	2.7±0.3	11.3±0.7	6.8±0.6	132±0.6	Recovery
NJ8	3.6±0.4	13.2±0.7	6.8±0.6	133±0.5	Recovery
NJ9	1.7±0.2	7.1±0.6	3.4±0.3	111±0.6	Recovery
NJ10	2.1±0.3	7.3±0.6	3.6±0.4	117±0.6	Recovery
NJ11	2.9±0.3	12.8±0.7	6.2±0.6	125±0.7	Recovery
NJ12	3.8±0.4	12.9±0.7	7.2±0.6	126±0.7	Recovery
C	4.0±0.3	13.8±0.5	7.8±0.3	133±0.4	Recovery
Sd	-	4±0.7	0.8±0.3	86±1.8	Recovery

* C: control
* Sd: standard (phenytoin)
* - : no activity

Table 04: Effect of Synthesized Compounds on Maximal Electro Shock Convulsion in albino rats. (At 150 mg/kg dose after 30 min)

Code No.	Time (sec) in various phase of convulsion				
	Flexion (mean±SE)	Extensor (mean±SE)	Clonic (mean±SE)	Stupor (mean±SE)	Recovery /Death
NJ1	-	5.6±0.5	1.5±0.3	92±0.4	Recovery
NJ2	1.2±0.2	6.4±0.5	2.7±0.3	100±0.2	Recovery
NJ3	2.1.± 0.2	9.8±0.7	5.9±0.3	113±0.2	Recovery
NJ4	3.9±0.2	11.9±0.5	6.1±0.2	125±0.2	Recovery
NJ5	-	5.0±0.5	1.0±0.3	91±0.3	Recovery
NJ6	1.2±0.2	6.3±0.7	2.2±0.2	98±0.2	Recovery
NJ7	1.9.± 0.2	9.1±0.6	5.4±0.3	105±0.4	Recovery
NJ8	3.6±0.4	13.2±0.5	6.8±0.3	128±0.2	Recovery
NJ9	0.6±0.2	5.8±0.5	1.6±0.4	98±0.2	Recovery
NJ10	1.4±0.3	6.6±0.6	2.9±0.4	103±0.3	Recovery
NJ11	2.7.± 0.2	12.6±0.5	5.8±0.3	119±0.2	Recovery
NJ12	3.8±0.2	12.8±0.5	7.2±0.3	126±0.2	Recovery
C	4.0±0.3	13.8±0.5	7.8±0.3	133±0.4	Recovery
Sd	-	4±0.7	0.8±0.3	86±1.8	Recovery

* C: control

* Sd : standard (phenytoin)

* - : no activity

Table 05: Effect of Synthesized Compounds on Maximal Electro ShockConvulsion in albino rats. (At 150 mg/kg dose after 4 h)

Code No.	Time(sec) in various phase of convulsion				
	Flexion (mean±SE)	Extensor (mean±SE)	Clonic (mean±SE)	Stupor (mean±SE)	Recovery /Death
NJ1	0.9±0.1	5.9±0.3	2.0±0.2	99±0.2	Recovery
NJ2	1.6±0.2	6.9±0.3	3.1±0.2	112±0.2	Recovery
NJ3	2.8±0.2	11.5± 0.6	6.9±0.3	129±0.2	Recovery
NJ4	3.9±0.3	11.8±0.6	6.9±0.3	128±0.2	Recovery
NJ5	0.6±0.2	4.9±0.7	0.8±0.3	90±0.2	Recovery
NJ6	1.5±0.2	6.5±0.7	3.1±0.2	106±0.3	Recovery
NJ7	2.8±0.3	11.3±0.6	6.8±0.2	125±0.3	Recovery
NJ8	3.8±0.3	13.8±0.6	6.8±0.3	133±0.2	Recovery
NJ9	1.0±0.2	7.1±0.7	3.4±0.2	111±0.2	Recovery
NJ10	2.1±0.2	7.5±0.7	3.9±0.3	121±0.3	Recovery
NJ11	2.6.± 0.2	12.8±0.5	5.9±0.4	121±0.2	Recovery
NJ12	3.9±0.4	13.4±0.4	7.3±0.2	132±0.2	Recovery
C	4.0±0.3	13.8±0.5	7.8±0.3	133±0.4	Recovery
Sd	-	4±0.7	0.8±0.3	86±1.8	Recovery

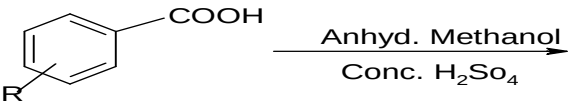
*** C: control**

*** Sd: standard (phenytoin)**

*** - : no activity**

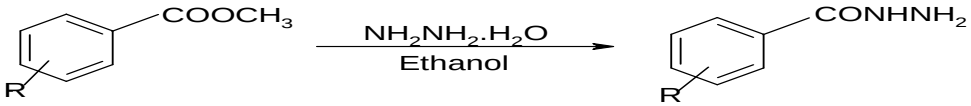
FIGURE-01- SCHEME / CHEMICAL REACTION OF TRIAZOLE DERIVATIVES

(Step-I): Esters *of aromatic acid*

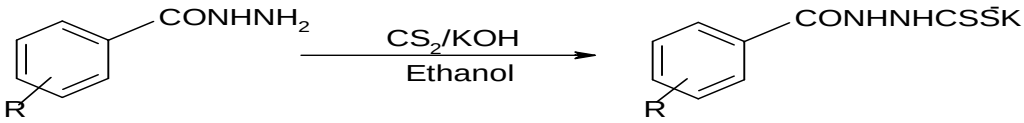


R	R_1& R_2 (Amines)
H	Methyl
H	Ethyl
H	Propyl
H	Isopropyl
CH3	Methyl
CH3	Ethyl
CH3	Propyl
CH3	Isopropyl
OCH3	Methyl
OCH3	Ethyl
OCH3	Propyl
OCH3	Isopropyl

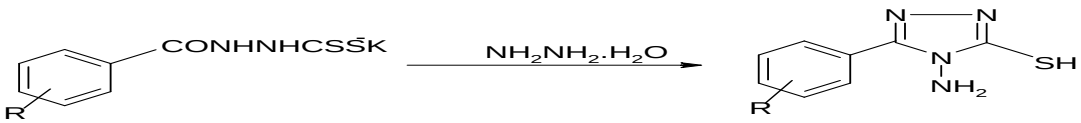
(Step-II): Hydrazide of synthesized ester



(Step-III): Potassium dithiocarbazinate



(Step-IV): 5-aryl-4-amino-3-mercapto-1,2,4-triazole



(Step-V): 5-aryl-4-(chloroacetylamino)-3-mercapto-1,2,4- triazole:

(Step-VI): Amino derivative of 5-aryl-4-(chloroacetylamino) -3-mercapto-1,2,4- triazole:

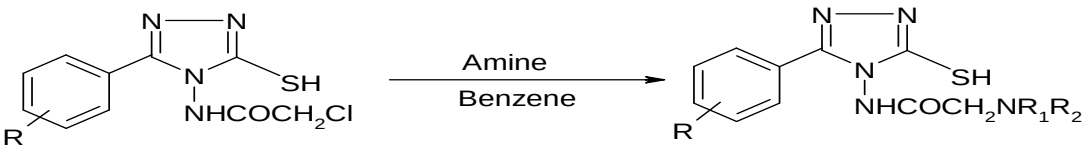


Fig.02 -Combined Anticonvulsant Activity of Synthesized Compounds in MES Model

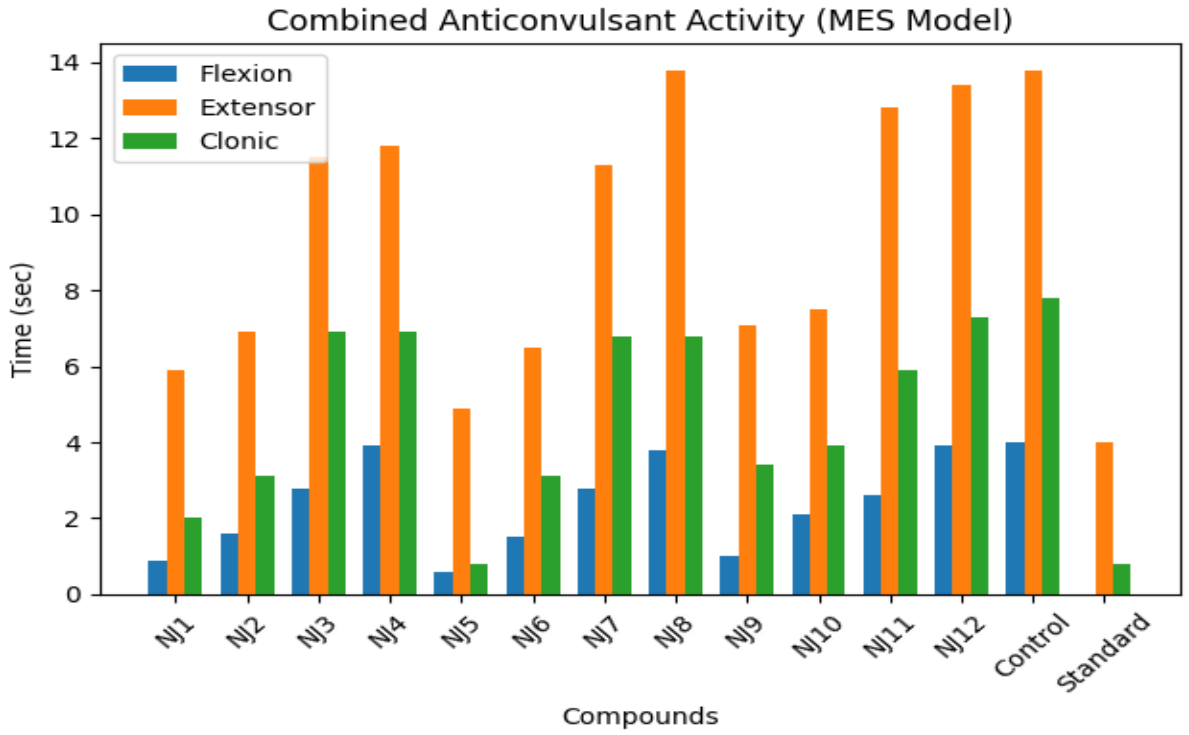
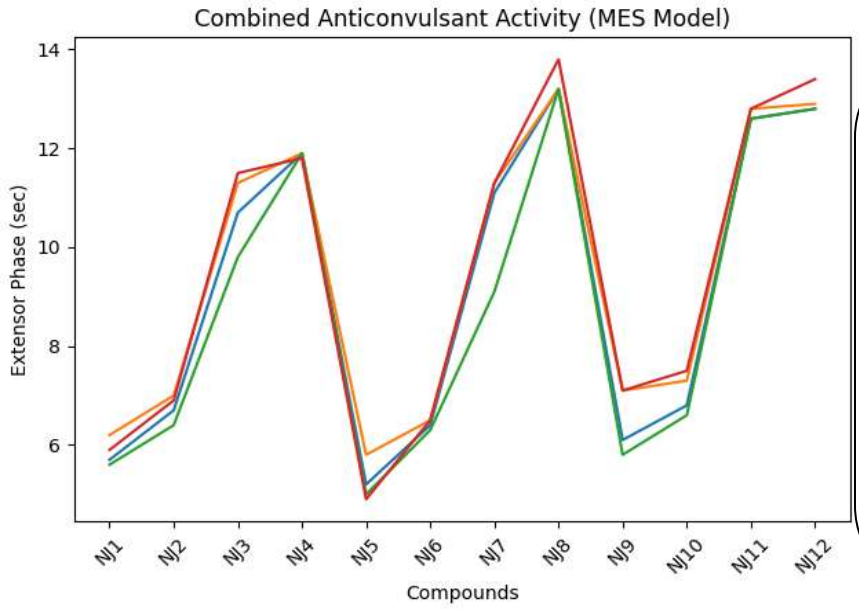


Figure 04: Combined Anticonvulsant Activity of Synthesized 1,2,4-Triazole Derivatives in MES Model



- **X-axis: Compounds (NJ-01 to NJ-12)**
- **Y-axis: Extensor phase (sec)**
- **4 lines represent:**
  - **100 mg/kg (30 min)**
  - **100 mg/kg (4 h)**
  - **150 mg/kg (30 min)**
  - **150 mg/kg (4 h)**