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SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF CARBONYL DERIVATIVES OF ADENINE

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Abstract:

Objective: *In this study, a variety of adenine semicarbazide derivatives were created using adenine as a starting material followed by synthesis of their semicarbazone derivatives.*

Methods: *The antibacterial activity was assessed using a cup-plate method. Analgesic, anticonvulsant activity, and neurotoxicity of the compounds were assessed using a model of chemically induced convulsions; acetic acid induced writhing response model and the rotarod test on male albino mice.* ***Results:*** *The compounds AA2, AA3, AA4, AA5 and AA10 were found to be good peripheral analgesics showing % analgesic activity 67, 55.5, 54.1, 47.5 and 88.4% respectively & compound AA10 was the most active among all the derivatives tested for the central analgesic activity. AA3, AA7 and AA10 were found to be exhibiting good antibacterial activity. The findings showed that the compounds 2-(2-oxoindolin-3-ylidene)-N-(9H-purin-6-yl) hydrazinecarboxamide (AA3) and 2-((E)-3-phenylallylidene)-N-(9H-purin-6-yl) hydrazinecarboxamide (AA10) were the most active, powerful, and least poisonous ones.*

Conclusion: *The present work involves pharmacological evaluation of adenine derivatives. The outcomes obtained from the work are significant for further research concentrating on examining prospective options for treatments for epilepsy.*

Keywords: *Epilepsy, Anticonvulsant, Analgesic, Adenine, antiepileptic.*

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INTRODUCTION:

One of the most prevalent and dangerous brain disorders is epilepsy. Seizures frequently result in temporary impairment of awareness, putting the person at danger for physical damage and frequently interfering with learning and working[1]. People of different ages, races, social levels, and geographic places can suffer from epilepsy, one of the most prevalent neurological illnesses[2,3]. The hallmarks of epilepsy include an enduring (persistent) propensity to cause seizures, unprovoked by any immediate injury to the central nervous system, as well as the neurobiologic, cognitive, psychological, and social effects of seizure recurrences[4,5]. A recent study estimates that 70 million people globally suffer from epilepsy, with over 90% of those persons living in developing nations. Epilepsy is thought to affect 2.4 million people worldwide annually[6,7]. There are many heterocycles in medicinal substances. The pyrimidine moiety belongs to a significant group of N-containing heterocycles that are crucial constituents of pharmacological medicines[8, 9]. Due to their biological potential, thiazolopyrimidine derivatives—which are thia-analogs of the natural purine bases adenine and guanine—have grown in significance in the field of medicinal chemistry. Pharmacological actions include antiepileptic, analgesic, anti-inflammatory, anti-arrhythmic, anti-parkinsonian, and anti-cancer actions are known to be displayed by them. Numerous businesses and research facilities are still actively engaged in the quest for novel antiepileptic drugs. For the creation of new medicines, the pyrimidine and its fused heterocyclic derivatives investigated for a variety of pharmacological activities like antimalarial, anti-bacterial, antifungal, anthelmintic, cardio-tonic, anticonvulsant, anti-inflammatory, and analgesic activity represent a key class of substances. As a result, these compounds have been produced by numerous researchers as target structures, and their biological activities have been assessed[10–19]. Also, there are already many antibiotics available to treat infections brought on by E. coli and other strains, but due to resistance that has developed against these antibiotics, research is always being conducted to produce novel antibiotics in order to address this issue[20]. In pursuing our research on antibacterial, anticonvulsant and analgesic activity we found that many derivatives of adenine ring shows antibacterial, anticonvulsant and analgesic activity. In the current paper we report the antibacterial, anticonvulsant and analgesic activity of ketone and semicarbazide derivatives of adenine.

MATERIALS AND METHOD:

Chemistry:

Adenine derivatives (AA1-AA11) were synthesized (Fig 1) according to the given scheme 1. The drug was dissolved in glacial acetic acid and diluted with water. To this solution, sodium cynate was dissolved and crystals were collected. To the product thus obtained, equimolar concentration of hydrazine hydrate was added and it was made alkaline using sodium hydroxide followed by refluxing for 1.5 hrs. The product was collected. To the product obtained in the second step, glacial acetic acid was added and pH kept between 5-6. To this solution, an equimolar quantity of different ketones/aldehydes were added and refluxed for 30 minutes, filtered and recrystallized from ethanol. The physicochemical properties and spectral characterization was done for the synthesized compounds. The compounds were evaluated for their antibacterial, analgesic and anticonvulsant activity.

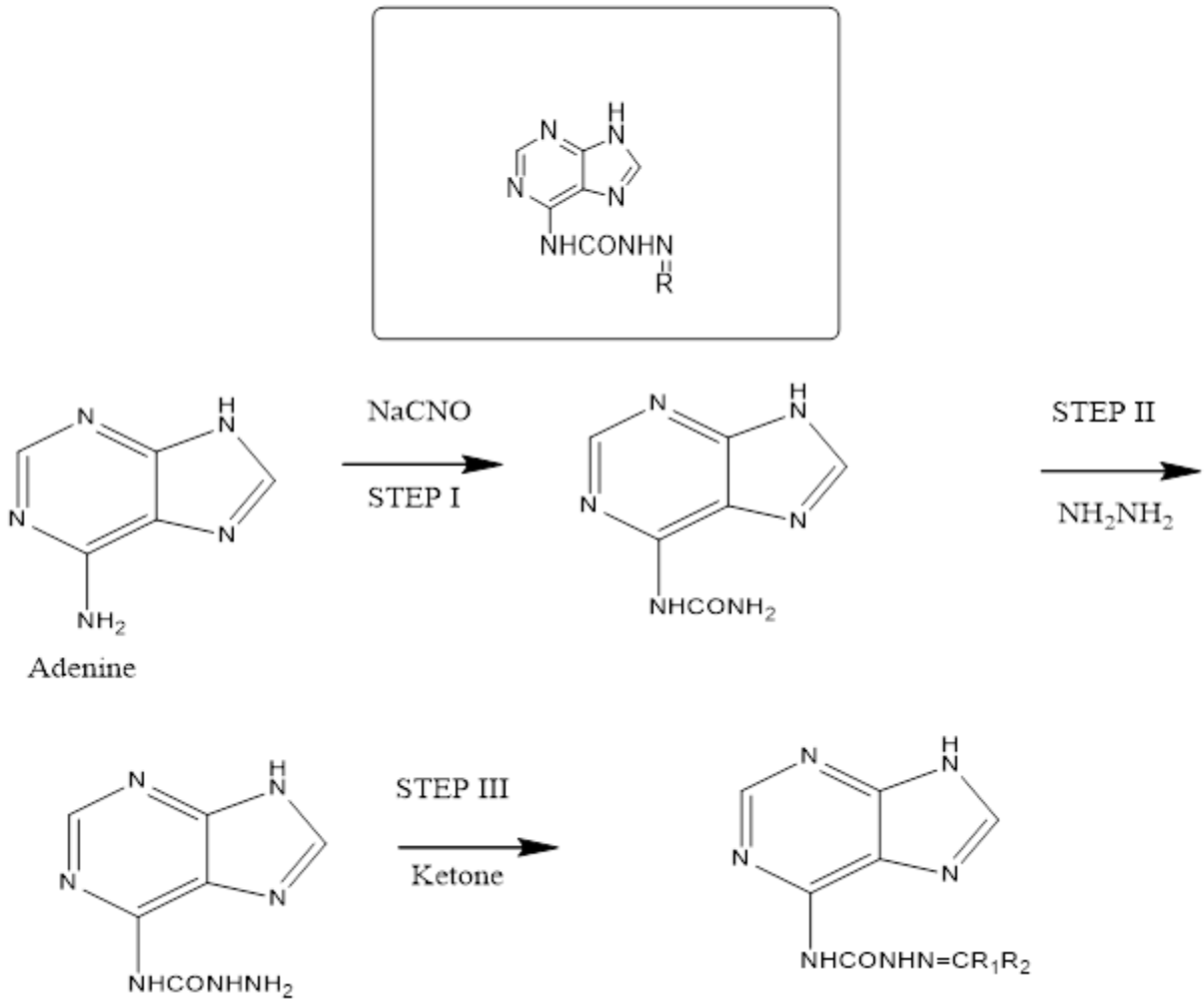
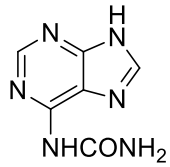
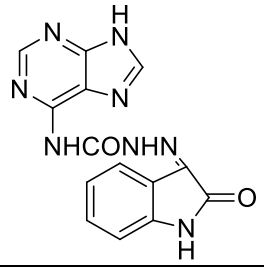
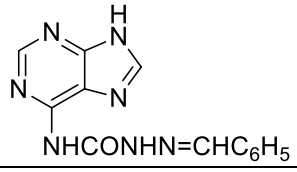
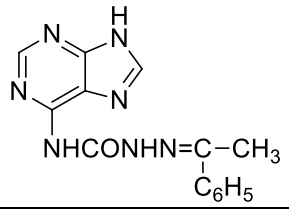
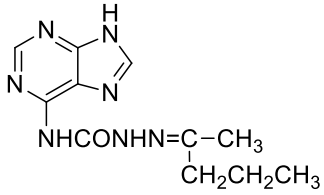
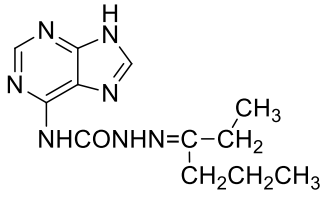
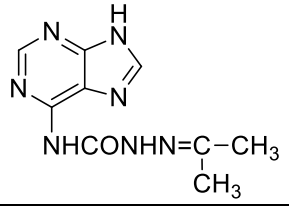


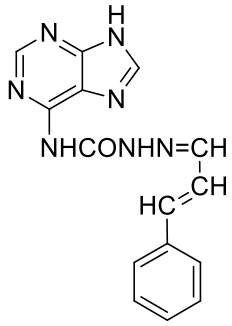
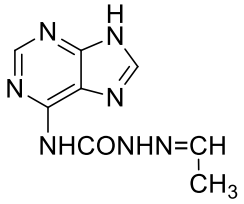
Fig.1: Designed Compounds- urea, semicarbazide and semicarbazone derivatives of adenine.

Scheme: Method for preparation of proposed compounds. Reagents and conditions (a) sodium cynate, glacial acetic acid (b) Hydrazine hydrate, NaOH (c) glacial acetic acid, ethanol, appropriate ketone.

Table 1: Physical data of adenine derivatives (AA1-AA11)

S.no.	Compd Code	Compound	Ketone	Mol. formula	M.W	MP	%yield
1.	AA1		-	$C_6H_6N_6O$	178.06	290^{0}C	77%
2.	AA2		-	$C_6H_7N_7O$	193.17	310^{0}C	90%

3.	**AA3**		Isatin	$C_{14}H_{10}N_8O2$	322.28	140^0C	87%
4.	**AA4**		Benzaldehyde	$C_{13}H_{11}N_7O$	281	335^0C	80%
5.	**AA5**		Benzophenone	$C_{19}H_{15}N_7O$	357.37	345^0C	61%
6.	**AA6**		Acetophenone	$C_{14}H_{13}N_7O$	295.12	330 ^{0}C	71%
7.	**AA7**		2-Pentanone	$C_{11}H_{15}N_7O$	261.28	250^0C	75%
8.	**AA8**		3-Hexanone	$C_{12}H_{17}N_7O$	275.31	70^0C	80%
9.	**AA9**		Propanone	$C_9H_{11}N_7O$	233.23	85^0C	88%

10.	**AA10**		Cinnamaldehyde	$C_{15}H_{13}N_7O$	307.31	92^0C	95%
11.	**AA11**		Acetaldehyde	$C_8H_9N_7O$	219.20	90^0C	85%

Pharmacology:

Animals:

For the investigation, healthy, 25–30 g Swiss albino mice of both sexes were used. Throughout the experimentation, the animals were housed in a large, clean cage. The animals were housed in rooms that were kept at a constant 22°C with a 12h light/dark.

Anticonvulsant screening:

Utilizing male albino mouse models of strychnine, thiosemicarbazide, and 4-amino pyridine-induced convulsions, all the produced compounds were tested for their anticonvulsant efficacy (20–25g). Diazepam is utilized as a conventional medication and PEG-400 as a carrier.

Chemical induced models:

Ten mice of either sex, weighing 22–25g, were administered the test substances intraperitoneally, or the standard (for example, diazepam 10 mg/kg i.p.). Only the vehicle was given to the controls. The mice received subcutaneous injections of 300 mg/kg strychnine, 20 mg/kg thiosemicarbazide, and 13.3 mg/kg body weight of 4-aminopyridine 30 minutes after receiving i.p. therapy. After 0.5 hours, 1 hour, 2 hours, and 4 hours, respectively, clonic seizures, tonic seizures, and death or recovery were seen.

Neurotoxicity Screening:

Rotorod test:

The rotorod test was used on mice to assess minimal motor impairment[21]. The mice were trained to

Remain on a rotating object that accelerates and revolves at a speed of 6 revolutions per minute.

The rod had a 3.2 cm diameter. The animal's inability to stay balanced on the rod for at least one minute

during each of the three trials was a sign of neurotoxicity. It was observed at what dosage the animals

were unable to grasp the rotorod[22].

Analgesic activity:

Analgesic activity using hot plate test:

Glassman's approach was used to conduct the experiment, and hot plate apparatus with a temperature of 550.5 0C was used[23]. In total, there were 14 groups of six mice each. The mice's response time to the thermal stimulation was measured as the amount of time between being placed above the hot plate and jumping or licking its rear paws. Prior to administering synthetic chemicals and drugs, the reaction time was measured (0 min). Group 1 served as the standard control. Mice in groups 2- 14 received subcutaneous injections of the produced compounds at a dose of 5 mg/kg. Using mice from group 14 as a control, morphine sulphate 5mg/kg was administered. Using mice from group 14 as a control, morphine sulphate 5mg/kg was administered. At 0, 30, 60, and 90 min after the treatment, the reaction time was once more tested. The cut-off period for the reaction to the thermal stimuli was chosen at 60 sec to prevent tissue injury to the mice's paws. It was estimated how much the reaction time increased compared to the control.

Analgesic activity (acetic acid induced writhing response model):

Following the method of Koster et al., the compounds were chosen to investigate their analgesic effectiveness in acetic acid produced writhing reaction in Swiss albino mice. The experiment included 14 groups of mice, each with six. The first group functioned as the control and solely received the test chemicals; groups 2 through 12 received the vehicle. The final two groups were given aspirin and at a dose of 10 mg/kg and diclofenac at a dose of 20 mg/kg as reference medications. Each mouse received 0.6% of an acetic acid aqueous

solution (10mL/kg) after 30 minutes, and the mice were then housed in clear enclosures for observation. Twenty minutes after the injection of acetic acid, the number of writhes was tallied. Each treated group's number of writhes was compared to that of the control group. The number of writhes was counted, and the percentage of protection was calculated[24].

$$(\%\ \text{protection} = (\text{control mean} - \text{treated mean} / \text{control mean})\ 100)$$

Antibacterial Activity:

Determination of antimicrobial activity:

Antimicrobial activity of synthesized compounds (AA1-AA11) was determined by the cup plate method and zones of inhibition of synthesized compounds were measured from the circumference of the well to the circumference of the inhibition zone (clear zone). Zones of inhibition of test samples were recorded by measuring the diameter (mm) of clear zone from the circumference of the well and compared with standard antibiotic Ciprofloxacin[25–27].

Preparation of solution of synthesized compound:

100mg of each synthesized compound (AA1-AA11) was transferred separately to 100 ml volumetric flasks. These compounds were dissolved in 5 mL DMSO and then volume was made up to 100 ml with sterile distilled water. These solutions (each with conc. 1000µg\mL) were used as a stock solution. 0.5 mL, 1.0 mL and 1.5 mL of these solutions were transferred to 10 mL volumetric flasks and volume was made upto 10 mL with sterile distilled water and each flask contained 50, 100. 150 µg synthesized compound per mL of distilled water.

Preparation of stock solution of standard antibiotic (Ciprofloxacin):

100 mg of Ciprofloxacin was weighed accurately, transferred and dissolved in 5 mL of DMSO and volume was made up to 100 mL with sterile distilled water. 0.5 mL and 1.0 mL of these solutions were transferred to 10 mL volumetric flasks and volume was made upto10 mL with sterile distilled water and each flask contained 50 and 100 µg Ciprofloxacin per mL of distilled water.

Sterilization of glassware:

Culture tubes, pipettes, petri plates were packed and sterilized at 160 ºC for 2 hrs in a hot air oven.

Preparation of nutrient media:

All the ingredients listed in table were weighed and dissolved in 1000 mL of distilled water in conical flask by heating for 10 minute, filtered and the pH was adjusted to 8.0 – 8.5 using 5M sodium hydroxide and finally sterilized in autoclave at 15 lb/inch^2 pressure (121ºC) for 30 minute[28].

Preparation of nutrient broth for bacteria:

Table 2: Nutrient broth for bacteria

S. no.	Ingredients	Quantity
1	Beef extract	10.0g
2	Peptone	10.0g
3	Sodium chloride	5.0mg
4	Distilled water	1000mL

Table 3: Nutrient agar media for bacteria

S. No.	Ingredients	Quantity
1	Beef extract	10.0g
2	Peptone	10.0g
3	Agar	15.0g
4	Sodium chloride	5.0mg
5	Distilled water	1000mL

Procedure: Beef extract, peptone and sodium chloride were weighed and dissolved in 1000 mL of distilled water with the aid of heat and the pH was adjusted to 8.0-8.5 using 5M sodium hydroxide and agar was dissolved by boiling for 10 minute with occasional shaking, filtered and finally sterilized in autoclave 15 lb/inch^2 pressure (121ºC) for 30 minute.

EXPERIMENTAL:

Synthesis procedure

Procedure for synthesis of AA1

0.01 mol of drug(adenine) was dissolved in 10 ml glacial acetic acid and diluted to 50 ml with water. To this solution, equimolar (0.01 M) Sodium cynate in 50 ml of warm water was added with stirring. The mixture was allowed to stand for 30 min and crystals were collected. Then it was recrystallized with ethanol.

Procedure for synthesis of AA2

To the substituted adenine (urea derivative) in 100 ml of ethanol, an equimolar quantity of hydrazine Hydrate was added. It was made alkaline by adding sodium hydroxide and refluxed for 1.5 hours and then cooled in ice. The resultant product was filtered and recrystallized from ethanol.

Procedure for synthesis of (AA3-AA11)

To the adenine (semicarbazide derivative) in ethanol, 1-2 ml of glacial acetic acid was added to maintain the PH between 5-6. To this solution, an equimolar quantity of different ketones/aldehydes were added and refluxed for 30 minutes, filtered and recrystallized from ethanol.

Table 4: Characterization

Compound Name	IR Spectra (KBr)cm^{-1},	^{1}HNMR(CDCl$_3$)	Elemental Analysis
AA1	1670(C=O), 3062 (N-H), 1530(C=N).	δ 11.0(s,N-H,purine),6.0(s,N-H,urea), 8.10-8.68(m, 2H,purine),6.0(s,2H,NH$_2$)	C (73.72), H (6.19), N (115.63), O (4.46)
AA2	1672(C=O), 3060 (N-H), 1532(C=N).	δ11.2(s,N-H,purine),6.2(s,2H,N-H,urea), 2.0(s,2H,NH$_2$,amine),8.12-8.69(s, 2H, C-H,purine).	C (37.31), H (3.65), N (50.76),O (8.28)
AA3	1672(C=O), 3060(N-H), 1532(C=N).	δ 11.5(s,N-H,purine),6.0(s,N-H,urea), 8.0(d,N-H,sec.,amide),7.0-7.7(m,4H, C-H,purine),7.0(s,N-H,hydrazid),8.02-8.70(s, 2H, purine).	(52.17), H (3.13), N (34.77), O (9.93)
AA4	1670(C=O),3060 (N-H), 1530(C=N).	^{1}HNMR(CDCl$_3$); δ 11.0(s,N-H,purine), 6.0(s,2H,N-H,urea),8.12-8.60(s,2H, C-H,purine).	C (55.51), H (3.94), N (34.96) O, 7.12
AA5	1650(C=O), 3062 (N-H), 1540(C=N).	^{1}HNMR(CDCl$_3$); δ 11.6(s,N-H,purine), 6.0(s,N-H,urea),8.20-8.60(s,2H,C-H ,purine),7.4-7.8(s,10H,Ar-H),7.2 (s,N-H,hydrazid).	C (63.86), H (4.23), N (27.44) O, 8.13
AA6	IR(KBr)cm^{-1}, 1670(C=O), 3060(N-H), 1530(C=N).	^{1}HNMR(CDCl$_3$); δ 11.0(s,N-H, purine),6.4(s,N-H,urea),8.10-8.80 (s,2H,C-H,purine),7.3-7.6(s,5H,Ar-H), 7.4(s,N-H,hydrazid),0.9(s,3H,CH$_3$).	C (56.94), H (4.44), N (33.20) O, 6.22
AA7	IR(KBr)cm^{-1}, 1620(C=O), 3055(N-H), 1540(C=N).	^{1}HNMR(CDCl$_3$); δ 11.8(s,N-H, purine),6.2(s,N-H,urea),8.20-8.90 (s,2H,C-H,purine),7.1-7.7(s,5H,Ar-H), 7.5(s,N-H,hydrazid),0.95(s,3H,CH$_3$).	C, 50.56; H, 5.79; N, 37.53; O, 6.12
AA8	IR(KBr)cm^{-1}, 1615(C=O), 3050(N-H), 1530(C=N).	^{1}HNMR(CDCl$_3$); δ 11.08(s,N-H, purine),6.3(s,N-H,urea),8.15-8.75 (s,2H,C-H,purine),7.1-7.5(s,5H,Ar-H), 7.4(s,N-H,hydrazid),0.7(s,3H,CH$_3$).	C, 52.35; H, 6.22; N, 35.61; O, 5.81
AA9	IR(KBr)cm^{-1}, 1625(C=O), 3050(N-H), 1535(C=N).	^{1}HNMR(CDCl$_3$); δ 11.9(s,N-H, purine),6.8(s,N-H,urea),8.11-8.50 (s,2H,C-H,purine),7.2-7.8(s,5H,Ar-H), 7.9(s,N-H,hydrazid),0.8(s,3H,CH$_3$).	C, 46.35; H, 4.75; N, 42.04; O, 6.86
AA10	IR(KBr)cm^{-1},	^{1}HNMR(CDCl$_3$); δ 11.2(s,N-H,	C, 58.63; H, 4.26;

	1628(C=O), 3060(N-H), 1542(C=N).	purine),6.3(s,N-H,urea),8.15-8.85 (s,2H,C-H,purine),7.7-7.8(s,5H,Ar-H), 7.5(s,N-H,hydrazid),0.9(s,3H,CH_3).	N, 31.90; O, 5.21
AA11	IR(KBr)cm^{-1}, 1630(C=O), 3040(N-H), 1548(C=N).	^{1}HNMR($CDCl_3$); δ 11.2(s,N-H, purine),6.2(s,N-H,urea),8.20-8.90 (s,2H,C-H,purine),7.4-7.8(s,5H,Ar-H), 7.7(s,N-H,hydrazid),0.8(s,3H,CH_3).	C, 50.56; H, 5.79; N, 37.53; O, 6.12

RESULT AND DISCUSSION:

Anticonvulsant activity:

All the synthesized compounds were evaluated for their anticonvulsant activity using various chemical induced convulsion models on male albino mice (20–25g). PEG-400 was used as a vehicle & Diazepam 10mg/kg b.w. as a standard drug. All the synthesized derivatives were evaluated at the dose of 30mg/kg body weight & have shown good anticonvulsant activity & the compounds AA3, & AA10 were found to be most active amongst all the screened compounds using Strychnine induced model, & against thiosemicarbazide induced model respectively and none of the compound showed anticonvulsant activity using 4-amino pyridine.

Neurotoxicity screening:

Activity of the drugs interfering with motor coordination was checked by the rotorod test. None of the compound was found to be neurotoxic at a dose of 30mg/kg b.w. amongst all the tested compounds.

SAR:

Chemical model of epilepsy is based on the application of or withdrawal from, chemical substances with consequent appearance of epileptic symptomatology. Different chemical models of epilepsy, which mimic different clinical seizure types, dealing with different mechanisms and acute versus chronic epileptic phenomena were used to screen the synthesized derivatives of adenine. The result showed that the most of the derivatives were active anticonvulsant against hydrazides as convulsant & they share a common action namely facilitation of GABA synthesis which was prevented by the Hydrazides via inhibition of glutamic acid decarboxylase. The derivatives were found to act as convulsant in a K^+ channel antagonism. The adenine derivatives substituted with isatin and/or cinnamaldehyde are more potent anticonvulsant agents. Different derivatives of semicarbazone are found to be more active as compared to semicarbazone.

Table 5: Table of anticonvulsant activity:

Compound code	**Strychnine induced model 0.5h**	**1h**	**2h**	**Thiosemicarbazide induced model 0.5h**	**1h**	**2h**	**4aminopyridine induced model 0.5h**	**1h**	**2h**	**Neurotoxicity Testing 0.5h**	**4h**
control	----	----	----		----	---	death	----	-----	30mg	----
AA1	30mg			30mg			death			30mg	
AA2	30mg			30mg			death			30mg	
AA3	30mg	30mg	30mg	30mg	30mg	30mg	death			30mg	
AA4	30mg	30mg		30mg			death			30mg	
AA5	30mg	30mg		30mg			death			30mg	
AA6	30mg	30mg		30mg	30mg		death			30mg	
AA7	30mg	30mg		30mg	30mg		death			30mg	
AA8	30mg	30mg		30mg	30mg		death			30mg	
AA9	30mg	30mg		30mg	30mg		death			30mg	
AA10	30mg	30mg	30mg	30mg	30mg	30mg	death			30mg	
AA11	30mg	30mg		30mg			death			30mg	
Diazepam	10mg	10mg	10mg	10mg	10mg	10mg	death			30mg	

Analgesic activity:

The derivatives of Adenine were screened for their analgesic activity using both central analgesic and peripheral analgesic assays. The compounds AA2, AA3, AA4, AA5 & AA10 were found to be good analgesic when compared with reference drug i.e., Diclofenac & even more active than another reference drug Indomethacin using peripheral analgesic assay. The compound AA2 was found to be most active among all the screened compounds using acetic acid induced writhing test. The evaluation of all the synthesized derivatives against hot-plate test revealed that the compounds AA1, AA2, AA3 & AA10 were active central analgesics & compound AA10 was the most active among all the derivatives tested for the central analgesic activity.

Table 6: Percent analgesic activity (Peripheral, writhing test).

GROUPS	DOSE(mg/kg)	NO.OF WRITHINGS RESPONSE IN MICE	% ANALGESIC ACTIVITY
Control	30	14.3±1.06	--------
AA1	30	8.8±0.37	28.4%
AA2	30	6.8±0.53	67%
AA3	30	6.3±0.37	55.5%
AA4	30	5.5±0.37	54.1%
AA5	30	7.5±0.68	47.5%
AA6	30	9.5±0.64	13.6%
AA7	30	7.1±0.53	32.3%
AA8	30	10.1±0.87	19.2%
AA9	30	5.8±0.48	50.8%
AA10	30	8.8±0.37	88.4%
AA11	30	6.8±0.53	50.2%
Diclofenac		6.67±0.30	89.24%
Indomethacin		21.83±0.28	64.47%

Each value represents the mean ±SEM (n=6)

Significant levels *p<0.01 as compared with respective control

Table 7: Central analgesic activity (hot-plate test)

GROUPS	REACTION TIME (SEC) 0 Min	REACTION TIME (SEC) 30 Min	REACTION TIME (SEC) 60 Min	REACTION TIME (SEC) 90 Min
Control	10.0±0.24	10.00±0.24	10.3.00±0.30	11.00±0.19
AA1	15.6 ±1.04	42.6±4.79	25.3±1.1	26.0±1.3
AA2	17±0.73	36.8±1.9	28.1±1.4	26.6±1.5
AA3	17.3±1.09	34.6±4.96	27.5±1.4	18.8±1.2
AA4	14.3±0.99	35.16±2.4	29.1±0.84	20.3±0.87
AA5	12±0.95	34.8±2.9	26.8±1.4	18.3±1.2
AA6	10.3±0.88	36.0±3.6	20.8±1.5	15.1±1.0
AA7	19±0..46	32.8±2.28	27.8±1.6	24.5±1.4
AA8	13.8±0.58	31±2.29	26.8±2.6	25.8±1.4
AA9	18 ±0.76	29±2.15	25.1±1.4	20.6±0.99
AA10	15.6 ±1.04	42.6±4.79	25.3±1.1	26.0±1.3
AA11	17±0.73	36.8±1.9	28.1±1.4	20.1±1.5
Morphine	3.33±.19	9.00±0.24**	12.50±0.20**	9.8±0.28**

Values represent the mean ± SEM of six animals for each group.

*significant at p<0.05 , **significant at p<0.01 (Dunnett's test)

Antibacterial activity:

All synthesized compounds were screened for antibacterial activity against *E. coli*, ***Pseudomonasaeruginosa, S. aureus*** **and** ***B. subtilis*****.** Most of the compounds showed moderate activity at low concentration. **Against *E. coli***, almost all the titled compounds were not found to have moderate activity. **Compounds AQ7** was found to have significant activity than other titled compounds against a no. of bacterias. But none of the activity was comparable to standard.

P.aeroginosa ATCC 27853 - 3 µg/ml
Stap. aureus - 0.45 µg/ml
E.coli. - 0.30 µg/ml
S. Flexneri ATCC 12022SAR - 0.30 µg/ml

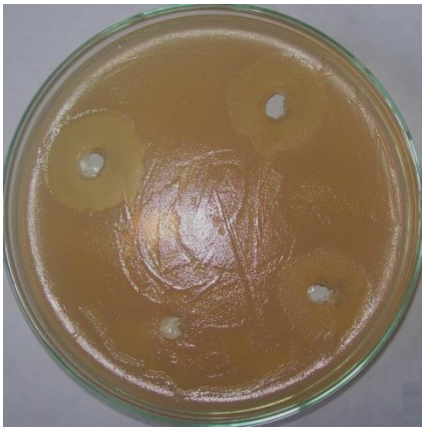
SAR

All synthesized compounds were screened for antibacterial activity against *E. coli, Pseudomonas aeruginosa, S. aureus* and *S. Flexneri ATCC 12022***.** Most of the compounds showed moderate activity at low concentration. The compounds having Norfloxacin moiety are found to be more active as compared to other compounds.

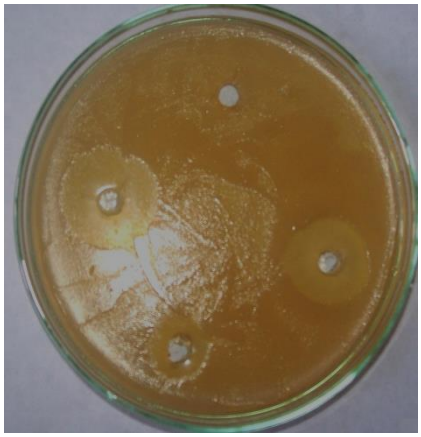
Table 8: Antibacterial activity:

COMPOUND NO.	**MIC range (µg/mL)**			
	E. coli	***Pseudomonas aeruginosa***	***s.aureus***	***S. Flexneri ATCC 12022***
AA1	400	400	400	400
AA2	400	400	400	400
AA3	0.30	3.0	0.55	1.0
AA4	400	400	400	400
AA5	400	400	400	400
AA6	400	400	400	400
AA7	0.30	3.0	0.45	1.0
AA8	400	400	400	400
AA9	400	400	400	400
AA10	0.30	3.0	0.45	1.0
AA11	400	400	400	400
Ciprofloxacin	0.15	0.20	0.01	0.25

Measurement of zones of inhibition



Zones of inhibition of compound AA10 against *B. subtilis*



Zones of inhibition of compound AA10 against S. *aureus*

Fig.2: Antibacterial activity of compound AA10

CONCLUSION:

The present work involves pharmacological evaluation of adenine derivatives. The findings from this study showed that the compounds (AA3) and (AA10) were the most active, powerful, and least poisonous anticonvulsant agents. The compounds AA2, AA3, AA4, AA5 & AA10were found to be good peripheral analgesics & compound AA10 was the most active among all the derivatives tested for the central analgesic activity. AA3, AA7 and AA10 were found to be exhibiting good antibacterial activity. The outcomes obtained from the work are significant for further research concentrating on examining prospective options for treatments for epilepsy.

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REFERENCES:

1. Das M, Sehgal VK, Singh H. Case Report ADVERSE DRUG REACTIONS OF ANTI-EPILEPTIC DRUGS IN PEDIATRIC AGE GROUP IN A TERTIARY CARE TEACHING HOSPITAL ; A CROSS-SECTIONAL STUDY. 2022;15(3):2–5.
2. Allers K, Essue BM, Hackett ML, Muhunthan J, Anderson CS, Pickles K, et al. The economic impact of epilepsy: A systematic review. BMC Neurol [Internet]. 2015;15(1). Available from: http://dx.doi.org/10.1186/s12883-015-0494-y
3. Sander JWAS, Shorvon SD. Incidence and prevalence studies in epilepsy and their methodological problems: A review. J Neurol Neurosurg Psychiatry. 1987;50(7):829–39.
4. Kotsopoulos IAW, Van Merode T, Kessels FGH, De Krom MCTFM, Knottnerus JA. Systematic review and meta-analysis of incidence studies of epilepsy and unprovoked seizures. Epilepsia. 2002;43(11):1402–9.
5. Beghi E. The Epidemiology of Epilepsy. Neuroepidemiology. 2020;54(2):185–91.
6. Ngugi AK, Bottomley C, Kleinschmidt I, Sander JW, Newton CR. Estimation of the burden of active and life-time epilepsy: A meta-analytic approach. Epilepsia. 2010;51(5):883–90.
7. Singh A, Trevick S. The Epidemiology of Global Epilepsy. Neurol Clin. 2016;34(4):837–47.
8. Selvam TP, Karthick V, Kumar PV, Ali MA. Antiepileptic Activity of Novel 2- (substituted benzylidene) -7- (4- vatives. 2013;3:204–11.
9. Guan L, Sui X, Chang Y, Yan Z, Tong G, Qu Y. Design , Synthesis and Anticonvulsant Activity Evaluation of 7-Substituted –[1 , 2 , 4] -Triazolo [4 , 3- f] Pyrimidine Derivatives. 2012;3:1076–83.
10. Prakash CR, Raja S. Design, synthesis and antiepileptic properties of novel 1-(substituted benzylidene)-3-(1-(morpholino/piperidino methyl)-2, 3-dioxoindolin-5-yl) urea derivatives. Eur J Med Chem. 2011;46(12):6057–65.
11. Said SA, Amr AEGE, Sabry NM, Abdalla MM. Analgesic, anticonvulsant and anti-inflammatory activities of some synthesized benzodiazipine, triazolopyrimidine and bis-imide derivatives. Eur J Med Chem. 2009;44(12):4787–92.
12. Shalaby AFA, Abdulla MM, Amr AEGE, Hussain AA. Synthesis, reactions, and anti-arrhythmic activity of substituted heterocyclic systems using 5-chloroanisic acid as starting material. Monatshefte für Chemie-Chemical Mon. 2007;138(10):1019–27.
13. Abd El-Latif NA, Amr AE-GE, Ibrahiem AA. Synthesis, reactions, and pharmacological screening of heterocyclic derivatives using nicotinic acid as a natural synthon. Monatshefte für Chemie-Chemical Mon. 2007;6(138):559–67.
14. Hammam AEFG, Fahmy AFM, Amr AGE, Mohamed AM. Synthesis of novel tricyclic heterocyclic compounds as potential anticancer agents using chromanone and thiochromanone as synthons. Indian J Chem - Sect B Org Med Chem. 2003;42(8):1985–93.
15. Amr AE, Abdulla MM. Synthesis and pharmacological screening of some new pyrimidine and cyclohexenone fused steroidal derivatives. Indian J Heterocycl Chem. 2002;12(2):129–34.
16. Amr AGE, Mohamed AM, Mohamed SF, Abdel-Hafez NA, Hammam AEFG. Anticancer activities of some newly synthesized pyridine, pyrane, and pyrimidine derivatives. Bioorganic Med Chem. 2006;14(16):5481–8.
17. Amr A-GE, Hegab MI, Ibrahiem AA, Abdulla MM. Synthesis and reactions of some fused oxazinone, pyrimidinone, thiopyrimidinone, and triazinone derivatives with a thiophene ring as analgesic, anticonvulsant, and antiparkinsonian agents. Monatshefte für Chemie/Chemical Mon. 2003;134(10):1395–409.
18. Amr AE-GE, Sabry NM, Abdulla MM. Synthesis, reactions, and anti-inflammatory

activity of heterocyclic systems fused to a thiophene moiety using citrazinic acid as synthon. Monatshefte für Chemie-Chemical Mon. 2007;138(7):699–707.
19. Spear BB. Pharmacogenetics and antiepileptic drugs. Epilepsia. 2001;42:31–4.
20. Gupta A. Synthesis of novel methoxy substituted benzothiazole derivatives and antibacterial activity against escherichia coli. Asian J Pharm Clin Res. 2018;11(9):416–9.
21. Sridhar SK, Pandeya SN, Stables JP, Ramesh A. Anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin derivatives. Eur J Pharm Sci. 2002;16(3):129–32.
22. Verma M, Pandeya SN, Singh KN, Stables JP. Anticonvulsant activity of Schiff bases of isatin derivatives. Acta Pharm. 2004;54(1):49–56.
23. Jerome M. Glassman. Agents with analgesic activity and deprndence liability. In: edited by Robert Turner PH, editor. Screening Methods in Pharmacology: Volume II, Volume 2. revised. Elsevier, 2016; p. 227–45.
24. Vogel HG. Drug discovery and evaluation:pharmacological assays,Berlin. New York: Berlin; 2002. 696–713 p.
25. Pandeya SN, Sriram D, Nath G, De Clercq E. Synthesis and antimicrobial activity of Schiff and Mannich bases of isatin and its derivatives with pyrimidine. Farm [Internet]. 1999;54(9):624–8. Available from: https://www.sciencedirect.com/science/article/pii/S0014827X99000750
26. Pandeya SN, Sriram D, Nath G, De Clercq E. Synthesis and antimicrobial activity of Schiff and Mannich bases of isatin and its derivatives with pyrimidine. Farmaco. 1999;54(9):624–8.
27. Pandeya SN, Sriram D, Nath G, DeClercq E. Synthesis, antibacterial, antifungal and anti-HIV activities of Schiff and Mannich bases derived from isatin derivatives and N-[4-(4′-chlorophenyl) thiazol-2-yl] thiosemicarbazide. Eur J Pharm Sci. 1999;9(1):25–31.
28. Pandeya SN, Sriram D. Synthesis and screening for antidacterial activity of schiff's and mannich bases of isatin and its derivatives. ACTA Pharm Sci. 1998;40(1).