International Journal of Chemistry and Pharmaceutical Sciences

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R E S E A R C H A R T I C L E

Anticonvulsant Activity of Various Synthetic Compounds on Experimental Animals

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A B S T R A C T

Anti-convulsion drugs are intended for the treatment of convulsive disorders in living system. Convulsions may arise due to many reasons most of the animal techniques used for evaluating anti – epileptic drugs. 7-phenylcarbamoylheptanoic acid, 7-(4 – Methyl – 2-oxo–2H–chromen–6–ylcarbamoyl) – heptonic acid, 4-[(pyridine-3-ylmethoxy carbonyl amino)-methyl]-benzoic acid, 4-(Benzyloxycarbonylamino-methyl)-benzoic acid were synthesized from laboratory. In this experiment, the entire synthesized drugs (CMP I – CMP IV) exhibited anticonvulsant activity. The test is started 30 min after i.p. injection. Male Swiss albino mice are stimulated through pinna electrodes the resultant seizure in normal mice shows a tonic phase of limb flexion around 2 seconds, followed by full tonic extension phase around 10 -13 seconds and a few clonic jerks there after the number of post – tonic as physical death are noted.

Keywords: Anti convulsant activity, CMP I-CMP IV, MES, Seizures.

A R T I C L E I N F O

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PAPER-QRCODE

A R T I C L E H I S T O R Y: Received 21 February 2019, **Accepted** 28 March 2019, **Available Online** 27 April 2019

Citation: Mani Mala Velayutham, *et al. Anticonvulsant Activity of Various Synthetic Compounds on Experimental Animals*. *Int. J. Chem, Pharm, Sci.*, 2019, 7(4): 105-107.

C O N T E N T S

1. Introduction. 105
2. Materials and Methods 106
3. Results and Discussion 106
4. Conclusion. 107
5. References. 107

1. Introduction

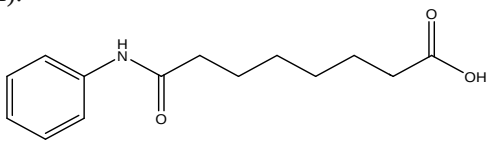
Epilepsy is a sickness of high prevalence, being well known since thousands of years as “morbus sacer”. In spite of intensive investigations, the pathophysiology of epilepsy is still poorly understood. Learn with a variety of mammal models have provided ample proof for heterogeneity in the mechanisms of epileptogenesis [1]. Seizure is a convulsive event that is due to irregular, extreme and hyper synchronous release from an aggregate of central nervous system neurons. Epilepsy is the second most frequent disorder of the central nervous system after stroke and up to

5% of world population expands epilepsy in their lifetime [2]. New evidence derives from investigations of kindling, which involves the delivery of brief, initially subliminal, electrical or chemical stimuli to a range of region of the brain. After 10 to 15 days of once-daily stimulation, the period and intensity of after-discharges reach a stable maximum and a characteristic seizure is produced [3]. Subsequent stimulation then regularly elicits seizures. Excitatory receptors have been divided into subtypes according to the events of specific agonists or antagonists. Mediators which reduce GABAA synaptic function provoke convulsions. More than a few biochemical theories have been advanced, involving the inhibitory GABAergic system and the system of the excitatory amino acids glutamate and aspartate. A convulsive condition is inducing by the straight blockade of GABAA receptors (e. g. to the action of bicuculline) or a reduction in the GABA-mediated opening of the chloride ion channel (e. g. by picrotoxin). One major factor in epileptogenesis seems to be a decreased function of GABAA synapses [4-6].

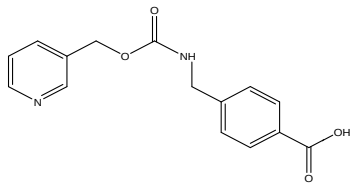
2. Materials and Methods

All the test compounds were synthesized from our laboratory [7-10]

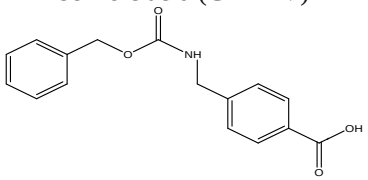
Compound Name: 7-phenylcarbamoylheptanoic acid (CMP-I).



Compound Name: 7- (4 – Methyl – 2- oxo – 2H – chromen – 6 –ylcarbamoyl) – heptonic acid (CMP - II)



Compound name: 4-(Benzyloxycarbonylamino-methyl) benzoic acid (CMP-IV)



Animal : Male Swiss albino mice (25 – 30 g)
Drugs : standard (Phenytoin (25 mg / kg))
Test : Synthetic drugs (50 mg / kg)
Instrument : Electro convulsiometer model, Ki – 9531

Experimental animals:

Male Swiss albino mice of 8-10 weeks old, weighing about 25-30 g were used in experiments. Animals were housed in polypropylene cages maintained under standard condition (12 hours light and 12 hours dark cycle; 25 ± 30oC, 45-65% humidity) and had free access to standard feed and water ad libitum. All the animals were acclimatized to laboratory condition for a week before commencement of experiment. All pharmacological activities were carried out as per CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) norms after obtaining the approval from the Institutional Animal Ethics Committee of the Department of Pharmacology, Arulmigu Kalasalingam College of Pharmacy.

Acute toxicity study:

All animals used in this experiment were observed for 48 h and mortality of animals recorded where present for each group at the end of observation period.

Supra Maximal Electrical Method:

The electro shock assay in mice is used primarily as an indication for compounds which are effective in grandmal epilepsy. Healthy male swiss albino mice weighing from 25 – 30 g were selected. They were kept in separate cages, fed with balanced diet, water and libitum [11,12]. Then the animals were divided into 6 groups each groups containing six animals. The first groups of animals were served as control, which received 10ml/kg normal saline solution. Second group served as standard which received phenytoin sodium (25 mg/kg). Third group treated with synthetic compound CMP-I (50 mg/kg). Fourth group treated with synthetic compound CMP-II (50 mg/kg). Fifth group treated with synthetic compound CMP-III (50 mg/kg). Sixth group treated with synthetic compound CMP-IV (50 mg/kg). All the test compounds were dissolved in 0.5ml DMSO and administered through intra-peritoneal route. The test is started 30 min after i.p. injection [13]. Male Swiss albino mice are stimulated through pinna electrodes (12mA, 50Hz for 0.2 s) The resultant seizure in normal mice shows a tonic phase of limb flexion around 2 seconds, followed by full tonic extension phase around 10 -13 seconds and a few clonic jerks there after the number of post – tonic as physical death are noted [14-16].

Statistical analysis

All the values are expressed as mean ± SEM. Statistical differences between means were determined by one way ANOVA followed by Newman Keul's multiple range tests. $p<0.05$ was considered as significant.

3. Results and Discussion

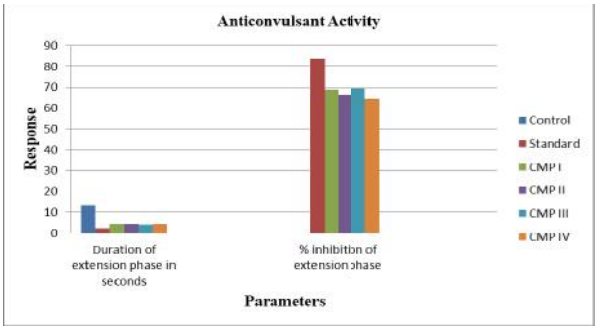


Fig 1: Anticonvulsant activity

Discussion

The maximal electroshock test is broadly used animal model in the discovery of antiepileptic drug, because seizure initiation is easy and the predictive value for notice clinically effective antiepileptic is high. The maximal

electroshock test identifies mediator with activity against generalized tonic clonic seizures using clinically established antiepileptic drugs. In present study data's shown that both synthesized compounds such as CMP-I and CMP-III possess significant Anti convulsant activity at P<0.01 than CMP-II and CMP-IV compare with standard. Both compounds were reducing the duration of extensor phase significantly**.**

Table 1: Anticonvulsant Activity of Various Synthetic Compounds

Treatment	Body Wt.	Drug	Dose	Duration of extension phase in seconds	% inhibition of extension phase
Group I	200 – 230 gm	Normal saline	10 ml / kg	13.52 ± 2.12	
Group II	200 – 230 gm	Phenytoin sodium	25 mg / kg	2.2 ± 0.45	83.72 %
Group III	200 – 230 gm	CMP-I	50 mg / kg	4.22 ± 0.96	68.78 %
Group IV	200 – 230 gm	CMP-II	50 mg / kg	4.29 ± 0.98	66.28 %
Group V	200 – 230 gm	CMP-III	50 mg / kg	4.12 ± .0.95	69.52 %
Group VI	200 – 230 gm	CMP-IV	50 mg / kg	4.31 ± 0.96	64.31 %

4. Conclusion

In this experiment, the entire synthesized drugs (CMP I – CMP IV) exhibited anticonvulsant activity. The test is started 30 min after i.p. injection. Male Swiss albino mice are stimulated through pinna electrodes the resultant seizure in normal mice shows a tonic phase of limb flexion around 2 seconds, followed by full tonic extension phase around 10 -13 seconds and a few clonic jerks there after the number of post – tonic as physical death are noted.The maximal electroshock test identifies mediator with activity against generalized tonic clonic seizures using clinically established antiepileptic drugs. In present study data's shown that both synthesized compounds such as CMP-I and CMP-III possess significant Anti convulsant activity at P<0.01 than CMP-II and CMP-IV compare with standard. Both compounds were reducing the duration of extensor phase significantly**.**

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