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IN EVALUATION OF ANTI -EPILEPTIC ACTIVITY OF CHLOROFORM ROOT EXTRACT OF ACONITUM HETEROPHYLLUM BY PENTYLENETETRAZOLE (PTZ) MODEL

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ABSTRACT

The aim of the present study is to evaluation of antiepileptic activity of chloroform root extract of aconitum heterophyllum. The antiepileptic activity of chloroform extract of *A.* heterophyllum at the doses of 75 and 150 mg/kg, p.o. was evaluated by Pentylenetetrazole (PTZ) and Sodium Valproate induced convulsions in albino wistar rats. Statistical analysis was carried out by one-way analysis of variance followed by Dunnett's test In case of PTZ induced convulsion, the result of the present study shows that the chloroform extract of Aconitum heterophyllum, at doses 75 and 150 mg/kg significantly reduced the duration and also delayed the onset of convulsion when compared to control group. PTZ may be exerting convulsant effect by inhibiting the activity of GABA at GABAA receptors. The results revealed that the Chloroform root extract of aconitum heterophyllum (CEAH) possess anticonvulsant activity. The chloroform extract exhibited significant and dose-dependent antiepileptic activity, which may be due to the presence of antioxidant principles like flavanoids.

INTRODUCTION:

Epilepsy is one of the major neurological disorders affecting approximately 0.8% of the population. There has been considerable progress in the pharmacotherapy of epilepsy over the last few decades, including the introduction of new antiepileptic drugs such as felbamate, lamotrigine, etc. However, current drug therapy of epilepsy is complicated by side-effects, teratogenic effects; long term toxicity and about a third of patients are refractory to pharmacotherapies. Furthermore, there is currently no drug available which prevents the development of epilepsy e.g. after head trauma and all currently available AEDs drugs are synthetic molecules. Epilepsy can be caused by stroke, brain injury, brain tumors, infections (such as: meningitis, brain abscess, AIDS), but most of the time the cause of epilepsy is not known. A seizure can be defined as "an episodic disturbance of movement, feeling, or consciousness caused by sudden synchronous, inappropriate, and

excessive electrical discharges in the cerebral cortex". Epileptic convulsions are expected to have negative consequences on the patient's psychological and social life such as relationships, education and employment. Uncontrolled seizures are associated with physical and psychosocial morbidity, dependent behavior, poor quality of life and an increased risk of sudden unexpected death. If seizures do not persist after the underlying cause is corrected, the person is not considered as being epileptic [1]. Epilepsy is not a single entity but rather a collection of different and often distinct disorders that have in common the occurrence of seizures [2, 3]. GABA plays an important role in regulation of neuronal excitability and impairment of GABA function produces seizures. Compounds that enhance GABA-mediated inhibition are convulsants. GABA exerts its major inhibitory effect via GABAA receptor (which is a ligand-gated ion channel) by increasing neuronal membrane conductance for chloride ions causing membrane hyperpolarization resulting in reduced neuronal excitability and most rapid inhibition in brain. GABA exerts its major inhibitory effect via GABAA receptor (which is a ligand-gated ion channel) by increasing neuronal membrane conductance for chloride ions causing membrane hyperpolarization resulting in reduced neuronal excitability and most rapid inhibition in brain. GABA A receptor is target for many important neuroactive drugs including antiepileptic drugs benzodiazepines and barbiturates. GABAA receptor consists of five subunits that form a chloride ion channel. The subunits consist of various subtypes and pharmacological studies have shown that individual subunits and subtypes confer different sensitivities to agents acting on GABAA receptors. GABAA receptor-mediated miniature IPSCs play important physiological role in preventing the development of neuronal hyper excitability [4]. Plant Aconitum heterophyllum family Ranunculaceae has the antiepileptic activity due to presence of alkaloids like heterophylline, heterophyllidine, heterophyllisine, hetidine [5]. Seeds are also thought to have diuretic properties which help in alleviating the burning sensation in urinary tract and increase the intensity of urine [6]. Medicinal plants used for the therapy of epilepsy in traditional medicine have been shown to possess promising anticonvulsant activities in animal models of anticonvulsant screening [7]. Various studies shows that the active principle alkaloids having a crucial role in treatment of epilepsy. Aconitum heterophyllum is rich in Diterpene alkaloids [8].

MATERIAL AND METHOD

Collection and authentication of plant material

The root powder of the Aconitum heterophyllum was collected in local area of Gwalior in January 2025 and was authenticated at the Department of Botany, Jiwaji University, Gwalior MP.

Extraction of the plant material

The extraction is done by using Soxhlet apparatus. The coarse powder of the roots were first extracted with petroleum ether. Obtained defatted material is again extracted with chloroform. After extraction, the chloroform extract were evaporated or concentrated by using rotary evaporator and dried at room temperature to give a viscous mass. The obtained crude extracts were weighed and stored at 40C for the further analysis.

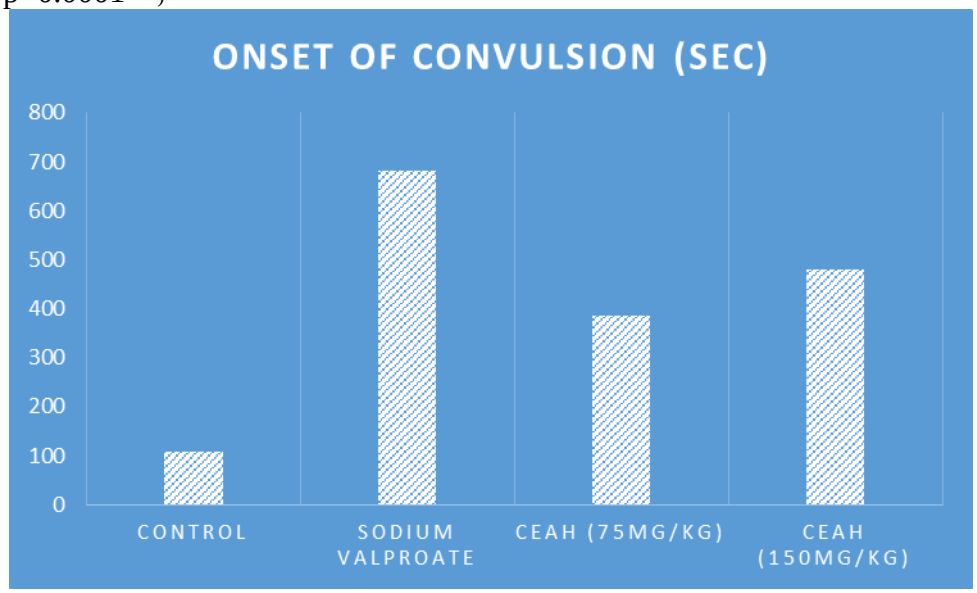
Pharmacological study animals and management: Healthy adult Wistar albino rats of either sex weighing 180-250g will be selected. The animals will be housed in large, spacious, hygienic cages during the course of experimental period. The animal house will be well maintained and the animals will have 12 ± 1 hour day and night schedule with a temperature [64-79°F] maintained at standard experimental condition. The animals will be fed with standard rodent pellet feed and water ad libitum. The animals will be fasted 12 hours prior to the experiment with free access to only water. The experimental procedure was approved by IAEC (Institutional animal ethical committee, governed by CPCSEA, Government of India.)

Evaluation of antiepileptic activity

Table 1- Effect of Chloroform extract of Aconitum heterophyllum on PTZ induced seizures Models (Onset of Convulsion)

S.NO	GROUPS	ONSET OF CONVULSION (SEC)
1	control	107.4±1.32
2	Sodium Valproate	680.6±1.28
3	CEAH (75MG/KG)	384.4±2.29
4	CEAH (150MG/KG)	478.8±1.35

Statistical comparison: One way ANOVA, followed by Dunnet's multiple comparison test. Standard, CEAH (low dose) and CEAH (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)



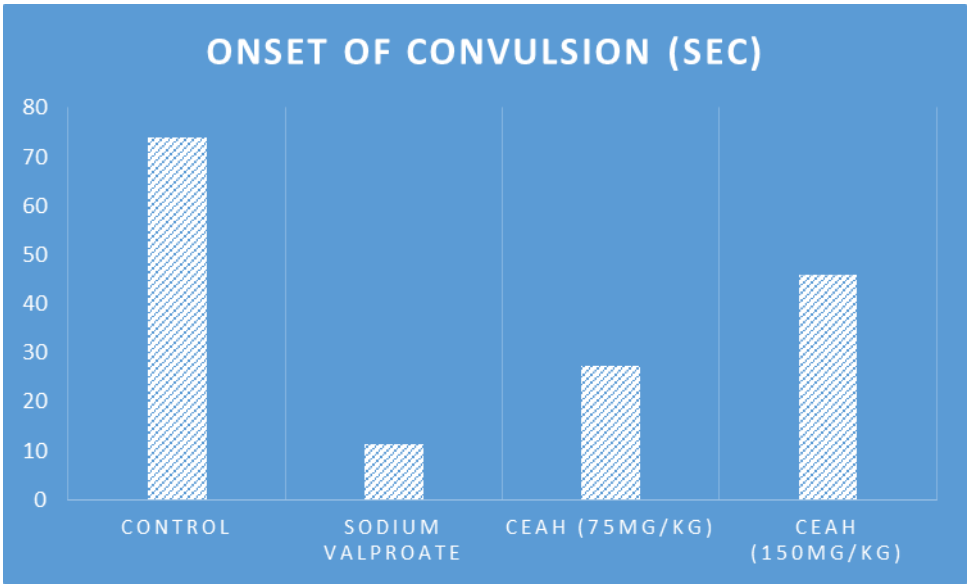
Statistical comparison: One way ANOVA, followed by Dunnet's multiple comparison test. Standard, CEAH (low dose) and CEAH (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)

Figure 1- Effect of Chloroform extract of Aconitum heterophyllum on PTZ induced seizures Models (Onset of Convulsion)

Table 2- Effect of Chloroform extract of Aconitum heterophyllum on PTZ induced seizures Models (Duration of Convulsion)

S.No	Groups	Duration of Convulsion (Sec)	Recover/Mortality
1	Control	74.00±1.41	Mortality
2	Sodium Valproate	11.20±0.37	Recovery
3	CEAH (75MG/KG)	27.40±0.67	Mortality
4	CEAH (150MG/KG)	45.80±0.73	Recovery

Statistical comparison: One way ANOVA, followed by Dunnet's multiple comparison test. Standard, CEAH (low dose) and CEAH (HIGH DOSE) are compared with control ($p<0.05$-*, $p<0.001$**, $p<0.0001$***)



Statistical comparison: One way ANOVA, followed by Dunnet's multiple comparison test. Standard, CEAH (low dose) and CEAH (HIGH DOSE) are compared with control ($p<0.05$-* , $p<0.001^{**}$, $p<0.0001^{***}$)

Figure 2- Effect of Chloroform extract of Aconitum heterophyllum on PTZ induced seizures Models (Duration of Convulsion)

Acute toxicity study

Rats were kept overnight fasting prior to drug administration. A total of five animals were used which received a single oral dose (2000mg/kg) of chloroform extract of the root of Aconitum heterophyllum. After administration of the test extract, food was withheld further 3–4hr. Animals were observed individually at least once during the first 30min after dosing, periodically during the first 24hr (with special attention during the first 4hr) and daily thereafter for a period of respiratory rate, circulatory (heart rate and blood pressure), autonomic (salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation) and central nervous system (ptosis, drowsiness, gait, tremors and convulsion) changes. Mortality, if any, was determined over a period of 2 weeks. LD50 was done as per OECD guidelines for fixing the dose for biological evaluation.

Evaluation of antiepileptic activity:

Animal Selection: Wistar albino rats weighed around 150-250g were used for the study. Rats were divided into four groups of 5 animals each.

Procedure: Animals in the control group [Group 1] will be administered equivalent volume of normal saline by i.p route. Animals in Group 2 will be administered standard drug Sodium Valproate. . In Groups 3 and 4 Aconitum heterophyllum low dose and high dose will be administered by oral route in 1% Sodium lauryl sulphate solution respectively. After 30 minutes of administration of above drugs, all the animals will be given Pentylenetetrazol [PTZ] and the various parameters will be recorded.

Statistical Analysis: The data's of all the parameters were analyzed using the software Graph pad Prism 5. Analysis of variance (ANOVA); one way ANOVA followed by Dunnet's test was performed. The values were expressed as Mean ± SEM.

RESULTS

Pharmacological Investigations

Acute Toxicity Study: In the acute toxicity study, Chloroform root extract of aconitum heterophyllum (CEAH) was found to be toxic at a dose of 2000 mg/kg, 1000 mg/kg, 900 mg/kg and 800mg/kg p.o. body weight in albino wistar rat and CEAH was found to be safe up to 750 mg/kg, p.o. So, 750 mg/kg body weight were selected for the evaluation of antiepileptic activity.

DISCUSSION

In case of PTZ induced convulsion, the result of the present study shows that the chloroform extract of Aconitum heterophyllum, at doses 75 and 150 mg/kg significantly reduced the duration and also delayed the onset of convulsion when compared to control group. PTZ may be exerting convulsant effect by inhibiting the activity of GABA at GABAA receptors. The results revealed that the CEAH possess anticonvulsant activity.

CONCLUSION

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. Approximately 30% of the patients continue to have seizures with current antiepileptic drug therapy. Natural products from folk remedies have contributed significantly in the discovery of modern drugs and can be an alternative source for the discovery of antiepileptic drugs with novel structures and better safety and efficacy profiles. The chloroform extract of *Aconitum heterophyllum* delayed the onset and reduced the duration of convulsion in PTZ induced convulsion model and can be used as an adjuvant therapy against cognitive deficit in convulsions. Further studies are needed to explore the mechanism as well as the active principle responsible for the anticonvulsant activity of *Aconitum heterophyllum.*

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Conflicts of interest: None

REFERENCES

1. A. S. Serruys, Antiepileptic natural product discovery using a zebra fish seizure model. Group Biomedical Sciences, Faculty of Pharmaceutical Sciences, Laboratory for Pharmaceutical Biology. Vrijdag. 2012.19.
2. Kamdod, Experimental evaluation of anticonvulsant activity of hydrocotyle asiatica Linn (centella asiatica) in albino mice. Department of pharmacology Karnataka institute of medical sciences, hubli-22. 2011.15.
3. Ghazi Ahmed, Characterization of response to antiepileptic drugs. University of Glasgow. 2010. 24-26.
4. Sarah Ward, The development of exogenous anticonvulsants and endogenous uracil based antiepileptic agents. Dalhousie University Halifax, Nova Scotia, Canada. 2011. 19-21.
5. David Abasiwani Alagpulinsa, Anticonvulsant and Neurobehavioral Effects of the Aqueous Leaf Extract Of Leea Guineensis G. Don (Family: Leeaceae). Kwame Nkrumah University of Science & Technology, Kumasi .2010. 20-23.
6. http://www.indianmedicinalplants.info/d2/Aconitumheterophyllum (Ativisa%20). html
7. http://www.who.int/mental_health/neurology/Epilepsy_disorder_rev1.pdf
8. Bhavna Gupta, Medicinal plants as agent of anticonvulsant activity, Int. J. Res. Dev. Pharm. L. Sci, 1 (2012)126-134.