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Central Nervous System Related Studies on *Andrographis paniculata* Nees.

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Abstract
Plants, which include a multitude of medicinal substituent, have served us for millennia with their complex capacity to impede various etiologies. Plants have been exploited for their pharmacological application since ages but their use in the field of neuropharmacological activities are far less explored. Additionally, the questions regarding synthetic drug's, safety on prolonged exercise, economic burden and the other deleterious side effects including the inevitable physical dependency have all paved the way to find an alternate natural treatment strategy. In the present study *A. paniculata* has been investigated to elucidate their influence on CNS by undergoing various tests. The test results revealed that, extracts of *A. paniculata* was not toxic up to 2000 mg/kg of the sample. Although, they did not produce sedative or anesthetic effect, but they hindered seizures thus securing their spot as an Anticonvulsant agent. Further, locomotor activity established it as a CNS depressant. All in all, *A. paniculata* had neuropharmacological activities which can be further explored.

Keywords
A. paniculate, sedative hypnotic activities, locomotor activities, Anticonvulsant activities, local anesthetic activities.

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INTRODUCTION
Central nervous system disorders are one of the leading causes of mortality and morbidity in the world. Since the current updated medications are considered to have negative side effects, there is a strong need to explore newer, stronger, and more reliable methods of mitigating the situation. Of late, lime light has been casted upon the traditional and indigenous system medicine as they are very resourceful. Plants especially, are known to assert physiological and psychological effects on the CNS thus having a positive influence. Significant numbers of studies have been carried to assess the potential of these plants to manipulate CNS [1]. *S. dulcis* is known to possesses strong sedative and hypnotic activities [2]. Extracts of *Bacopa monnieri* and *Benincasa hispida* was known to exhibit anticonvulsant properties [3]. Essential oil extracted from nutmeg demonstrated inhibitory effect on locomotor activity [4].

Andrographis paniculata commonly known as Kalmegh is one of the extensively used healing plants used in both Ayurvedic and Unani system of medicines for the treatment of common cold, tonsillitis, diarrhoea, fever, intestinal sickness, jaundice, as a immunosuppressive , cardiovascular health, ulcers, leprosy, sore throat and as an antioxidant [5].They display various biological properties such as Anti-Inflammatory, Anti-microbial activity, Anti-oxidant activity, Antidiabetic, Hepato - renal protective, Anti- infective, anti-malarial activities etc. [6]. This could be due to the presence of various phytochemicals andrographolide, neoandrographolide, panaculoside, flavonoids,

andrographonin, panicalin, apigenin-7, 4'-di-O-methyl ether, etc [7].

In the present study *A. paniculata* has been explored for their neuropharmacological application to be curated as effective medication for the treatment of psychiatric and neurologic disorders. This was achieved by screening the various extracts of *A. paniculata* for activities including sedative hypnotic, locomotors, anticonvulsant, local anaesthetic activities. Further, is acute toxicity was evaluated to determine the safe dose.

MATERIALS AND METHODOLOGY

Plant material

Plant was collected from wild, and the identity was confirmed with the help of flora and the voucher specimen deposited at the Herbarium of Gulbarga University Gulbarga. The collected specimen was dried in the Tray drier and made into a herbarium with all details of collection entered on the label of Herbarium sheet and deposited in Herbarium of Gulbarga University, Gulbarga with Voucher specimen no. HGUG-268.

Extraction of plant sample

Crude drug was extracted in Soxhlet extractor using solvents like ethanol, Petroleum ether, chloroform and distilled water based on the polarity. Extraction process was continued till the extract decolorized. The extract was evaporated to dryness in a vacuum desiccator. Dry powder was dissolved in distilled water and gum acacia is used as an inert carrier material.

Experimental animal

Totally 24 mice of either sex weighing between 25-30 g were selected and divided into 6 groups of 4 animals each. First 4 groups were treated with various extracts of plants, at 0 min after administering the drugs, retested individual mouse to record the activity. The difference in the activity before and after administration of the drug was noted. Further, rabbits selected and were divided into 2 groups of 5 animals each where one group was treated with the drug and the other behaved as control. The research complied with Ethics Committee on Animal Experiment.

Pharmacological studies

Acute Toxicity:

Twenty-five albino mice were divided into 5 groups of 5 animals each. These animals were fasted for 24 hrs prior to the experiment. Animals of group I-V received 400, 800, 1200, 1600 and 2000 mg/kg of the ethanolic extract respectively. The animals were observed at regular intervals for 24 hrs to see the acute effect of the crude drugs and reading after 60 min. of administration was recorded [8].

Sedative hypnotic activity

The group I-IV of mice 200 mg/kg b.w. of drugs were administered, V group is supplied with vehicle control gum acacia and the VI group is administered with pentobarbital. The righting reflex (sleeping on its back) was observed, and the recovery is also noted [9].

Locomotor activity

Group I-IV was treated with Petroleum ether, chloroform, ethanol (95%) and distilled water extracts respectively. Group V was treated with control (Gum acacia) and Group VI with standard chlorpromazine HCl. Each mouse was individually placed in the activity cage for 10 min and the basal activity as well as the activity after administration of drug was tabulated [10].

Anticonvulsant activity

MES seizures were induced by electro convulsometer (Techno made-60 mA, 0.2 Sec) and phenytoin Na was used as a Standard and dose of 200 mg/kg of various extracts was administered. Presence or absences of reduction in extensor tonic convulsive activity in the hind limb (HLTE) during the seizures were observed [10].

Local anesthetic activity:

The drug (10 mg/ml) was administered into the conjunctiva of the eye and studied the corneal reflex to the pointed object and observations were made at the interval of 10 minutes. Only water extracts were used for this test as organic solvent extracts may cause damage to cornea [11]

RESULTS AND DISCUSSION

Toxicity studies:

Safety and adverse effect of drug were assessed using acute toxicity studies. In the present study alcoholic extract of the whole plant of different concentrations ranging between 400 to 2000 mg/kg body weight was found to be non-toxic and safe. It is evident by the survival of all the animals tested over a period of 24 hrs. However, the cage side observations revealed the CNS depressant activity on the animals as they were lethargic in behaviour, the leg movement was normal but no observable effect on autonomous nervous. Identical results were obtained for the aqueous extract of *A. paniculata* [12].

Sedative hypnotic activity:

In the study conducted on 6 groups of 4 animals each were administered with 200 mg/kg body weight of drug of the plants to study the sedative hypnotic activity. When righting reflex study was made the animals did not respond positively and the animals were normal and active indicating the absence of sedative hypnotic activity on the animals. However,

andrographolide penetrates the blood-brain barrier and concentrates in the brain and spinal cord causing sedative hypnotic activity. It was found that sedation was faster than barbitol. This may indicate that in the crude extracts containing andrographolide and other compounds may not induce sedation. However, if andrographolide is given alone may enter the brain and act upon barbital receptors to bring sedation in animal [13].

Locomotor activity:

The extracts of varying polarity of *A. paniculata* were administered orally to 6 groups of 4 animals each at a dose of 200 mg/kg body weight, showed significant reduction of locomotor activity with petroleum ether (60.62%), ethanol (62.68%) and distilled water (61.45%). This reduction is more significant as compared to the reduction in locomotor activity by the standard chlorpromazine HCl (51.37%). The chloroform extract showed a moderate reduction in the activity of the animals. It is evident that the petroleum ether fraction has pronounced effect on locomotor activity than any other fractions (table 1). Consequently, the drug has CNS depressant activity on mice. Inhibitory locomotor activity was seen in dose dependent fashion by *A. paniculata* when compared with standard lorazepam [14]

Sl. No.	Drug tested	Dose mg/kg (oral)	Avg. of locomotor activity in 10 min.		% Change in activity
1.	Petroleum ether extract	200	320	126	60.62
2.	Chloroform extract	200	384	268	30.2
3.	Alcoholic extract	200	402	150	62.68
4.	Distilled water extract	200	441	170	61.45
5.	Vehicle control (Gum Acacia)	5 ml	412	402	2.427
6.	Standard chlorpromazine HCl	100 mg	436	212	51.376

Table-1: Locomotor activity of various extracts of *A. paniculate*

Anticonvulsant activity:

When 4 different extracts of *A. paniculata* administered orally to 4 different groups of animals for the anticonvulsant activity, it was observed that ethanolic (95%) extract had very short HLTE phase period and recovery period is also very short i.e., 41 seconds as compared to the recovery period of standard phenytoin treated group of animals. Very little protection was seen in petroleum ether extract treated group with a recovery period of 62 seconds after MES induced seizures. Whereas there was no protection against electroshock induced seizures in chloroform and distilled water extracts with a recovery period of 108 and 96 seconds respectively (table 2). The results indicate that the ethanolic (95%) extract of *A. paniculata* is a potent anticonvulsant drug. It was seen that dose lower than 200 mg/kg *A. paniculata* has little to no effect on the induced seizures whereas, dosage of 200 mg/kg significantly lessen the affliction [14]

Sl. No.	Drug tested	Dose mg/kg	Avg. time recorded in sec. in various phases of convulsion and recovery		Died/ Total	
			Flexion	Extensor	Recovery	
1.	Petroleum Ether extract	200	2.5	10.0	62	0/4
2.	Chloroform extract	200	2.5	10.0	108	1/4
3.	Alcoholic extract	200	2.2	6.0	41	0/4
4.	Distilled water extract	200	2.4	9.6	96	0/4
5.	Control (Gum acacia)	5 ml	2.6	10.4	126	4/4
6.	Standard phenytoin Na	100 mg	2.0	3.5	35	0/4

Table-2: Showing anticonvulsant activity of *A. paniculate*

Local anesthetic activity:

The rabbit's right eye was subjected to distilled water extract of *A. paniculata* , the untreated left eye behaved as a negative control and blinking of the eye when cotton swab placed near the cornea indicated positive response inferring the local anesthetic activity of the drug in study. Sample showed negative response when compared to the standard drug Procaine (Table 3).

Sl. No.	Drugs tested	Dose	Local anaesthetic activity after		
		mg/ml	10 min	20 min	30 min
1.	Distilled Water extract	10	-ve	-ve	-ve
2.	Standard Procaine	1% w/v	+ve	+ve	+ve

Table-3: Local anesthetic activity of *A. paniculata*

CONCLUSION

In conclusion, the present study finding gives us a brief overview of various neuropharmacological potential of extract *of A. paniculata* depicting that they possess effective anticonvulsant and locomotor activities. However, additional investigation is deemed necessary to identify and isolate the specific phytochemical/s accountable for this bio-pharmaceutical application.

CONFLICT OF INTEREST:

None

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