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ANTI-EPILEPTIC ACTIVITY OF SARVAAPSMARAHARA RASA AGAINST PTZ. INDUCED EPILEPSY IN SWISS ALBINO MICE

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ABSTRACT

Objective: The present study was designed to investigate the anti-epileptic activity of Sarvaapasmarahara rasa against Pentylene tetrazole (PTZ) induced epilepsy in Swiss albino mice. **Materials and Methods:** The Sarvaapasmarahara rasa was screened for its antiepileptic activity against Pentylene tetrazole (PTZ) induced epilepsy. The formulation was given orally at the doses of 125 mg/day for 15 consecutive days prior to the induction of seizure. The protection action against PTZ induced seizure was evaluated by behavioral paradigm. **Results:** In Pentylene tetrazole induced epilepsy model, Sarvaapasmarahara rasa at 125mg/day treated group showed significant increase in onset of action and decrease in death latency, number of convulsions, number of Straub's tail, duration of convulsions, jerking, tonic, clonic, duration of Stupor and Straub's tail was observed. **Conclusion:** Present study shows that the potent Antiepileptic role of Sarvaapasmarahara rasa on Swiss albino mice showed significant changes in behavioral paradigm. Further studies are required to elucidation the potent action of Sarvaapasmarahara rasa on treatment of epilepsy.

KEYWORD: Sarvaapasmarahara rasa, Pentylene tetrazole, antiepileptic, convulsions, seizure.

INTRODUCTION

Epilepsy is a chronic and severe neurological disorder marked by sudden episodes of abnormal, excessive and synchronized neuronal activity within the brain, leading to diverse neurological, cognitive and psychological manifestations. Globally, more than 50 million individuals are affected by epilepsy and about 5–8% of the general population experiences at least one seizure during their lifetime. Various chemical classes of drugs, including barbiturates (e.g. phenobarbitone), succinimides (e.g. ethosuximide) and gamma-amino butyric acid (GABA) analogs, are employed in the management of seizures (Goldenberg, 2010).[1] At present, antiepileptic drugs exhibit limited efficacy and their adverse effects pose challenges in effective patient management (Dalic and Cook, 2016).[2] According to the World Health Organization, nearly 80% of individuals living with epilepsy reside in developing countries. Although several newer Antiepileptic agents—such as vigabatrin, topiramate, zonisamide, levetiracetam, lamotrigine, lacosamide, rufinamide and stiripentol have been developed and are considered relatively safer, representing significant progress in epilepsy treatment (Aneja and Sharma, 2013)[3], their side effects have not been entirely eliminated. Moreover, approximately 30–40% of patients continue to experience seizures despite the use of these newer medications (Ezekiel et al., 2010).[4]

In traditional systems of medicine, numerous medicinal plants employed for the treatment of epilepsy have been scientifically validated to exhibit significant anticonvulsant activity in various experimental screening models.[5] The use of traditional or folk medicinal plants serves as a valuable source of “lead” compounds, offering a more efficient and cost-effective approach for the discovery and development of modern drugs with novel structural frame works.

Sarvaapasmarahara Rasa is a herbo-mineral preparation described in Rasa Tantra Sara Va Siddha Prayoga Sangraha-II. It is classified as a Pottali Rasayana and comprises ingredients such as Rasa Sindoora, Shuddha Surama, Shuddha Vatsanabha, Shuddha Haratala, Shuddha Manashila; Shuddha Somala along with Devadali Swarasa Bhavana. Sarvaapasmarahara Rasa was prepared according to standard guidelines in the Department of Rasashastra and Bhaishajya Kalpana, BVVS Ayurveda Pharmacy, Bagalkot.

MATERIALS AND METHODS

Chemicals

Pentylenetetrazol (PTZ), 70% Alcohol, Lorazepam and all other chemicals were of analytical grade.

Instruments:

- Double beam automated UV-Visible Spectrophotometer UV- 1601 (Shimadzu, Japan).
- Refrigerator,
- Centrifuge (MPW- 350OR, Korea).
- Auto analyzer (Star-21).
- Centrifuge (REMI/R248/99).
- Compound Microscope (Olympus Magnus) was used.

Animals

Young Swiss albino mice of either sex (22-35gms) were procured from the Central Animal House of H.S.K College of Pharmacy Bagalkot. Animals were acclimatized to laboratory conditions at room temperature prior to experimentation. Animals were kept under standard conditions of a12-hour light/12-hour dark cycle with food and water ad- *labium* in groups of plastic cages with soft binding. The protocol was approved by the Institutional Animal Ethics Committee of H.S.K College of Pharmacy, Bagalkot (Ref. No: IAEC/HSKCOP/Feb2025/PG5) and carried out in accordance with the CPCSEA Guidelines for the use and care of laboratory animals.

Preparation of Sarvaapsmarahara rasa[6]

Table 1: Ingredients of Sarvaapsmarahara rasa.

S N	Sanskrit Name	English / Latin Name	Used part	Quantity
1	Shuddha Parada	Hydrargyrum (Hg)	-	1 Part
2	Shuddha Gandhaka	Sulphur(S)	-	1 Part
3	Shuddha Srotoanjana	Grey Antimony (Sb_3S_3)	-	1 Part
4	Shuddha Vatsanabha	Aconitum ferox wall	Root	10 Parts
5	Shuddha Haratala	Arsenic trisulphide (AS_2S_3)	-	1 Part
6	Shuddha Manashila	Arsenic disulphide (AS_2S_2)	-	1 Part
7	Shuddha Gouripashan	Arsenic Trioxide(AS_{2O3})	-	1 Part
8	Devadali swarasa	Luffa echinata Roxb	Leaves	1 Part

The above mentioned ingredients of Sarvaapasmarahara rasa was be procured from Dorle & Sons, Kolhapur and authenticated from Dept of Rasashastra and Bhaishajya Kalpana and Dravya guna. All the shodhana dravya were taken in khalva yantra and mardana was done till homogenous mixture was attained. Lingakara vati was prepared and suspended in dolayantra, Gandhaka paka was given with devadali swarasa and 1 ratti sized vati was prepared and stored in air tight container.

Experimental Design for pentylenetetrazol induced model[7]

Swiss albino mice were divided into 3 groups of 6 animals.

Group I: Control group received normal saline for15days and PTZ on 15th day, (n=6)

Group II: Standard group received Lorazepam 4mg/kg for 15days and PTZon 15th day, (n=6)

Group III: Test group received 125mg/day of Sarvaapasmarahara rasa for 15 days and PTZon 15th day, (n=6)

Mice were administered with respective treatments for15 days and on same day, PTZ 80mg/kg was injected intraperitoneal to mice 60 min after treatment and 30 min after the Lorazepam administration. Immediately after PTZ administration mice were observed for behavioral parameters such as (1)Onset of convulsions(elapsed time from PTZ injection until convulsion occurred) (2) Duration of seizure (Total time how much the animal is in convulsions) (3)Mortality for the duration of 30 minutes, (4)Tonic seizures (5)Clonic seizures (6)Straub's tail(7) Stupor and (8)Jerky moments (Viswanathaetal., 2016).

RESULTS

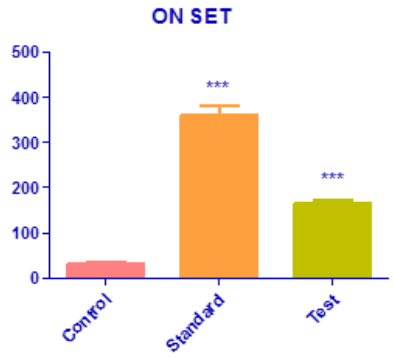
The Effect of Sarvaapsmarahara rasa on PTZ induced epilepsy in mice

The effect of Sarvaapsmarahara rasa on onset of action and death latency against PTZ induced epilepsy, The Sarvaapsmarahara rasa treated group shows significant (p<0.001)increase in Onset of Action and significant (p<0.01) decrease in death latency was observed as compared to Control group (Table 2).

The effect of Sarvaapsmarahara rasa on No. of Convulsion and No. of Straub's tail against PTZ induced epilepsy, The Sarvaapsmarahara rasa treatment group shows significant (p<0.01 to p<0.001) decrease in No. of Convulsion and No. of Straub's tail as compared to Control group (Table3).

Table 2: The Effect of Sarvaapsmarahara rasa on onset of action and death latency against PTZ induced epilepsy in mice.

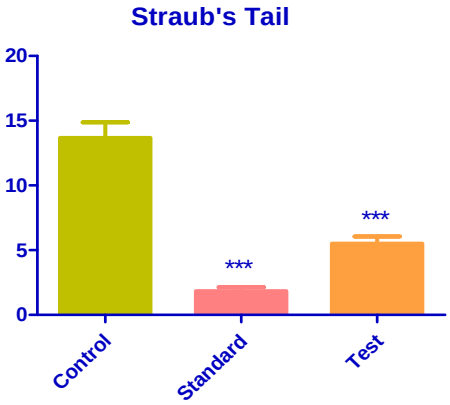
Groups	Time in seconds			
	Onset of Action	Convulsions	Death Latency	Number of Animals Survived
Control	31.67±2.10	5.84±0.74	0/6	0
Lorazepam(4mg/kg)	360.0±21.91***	00±00**	6/6	100
Sarvaapsmarahara rasa (125 mg/day)	165.0±7.63***	00±00**	6/6	100



All the values are expressed as mean ± SEM, n=6, One-way Analysis of Variance (ANOVA) followed by multiple comparisons Dunnett's test. The value significant**p<0.01, ***p<0.001 as compared to control group.

Table 3: The Effect of Sarvaapsmarahara rasa on No. of Convulsion and No. of Straub's tail against PTZ induced epilepsy in mice.

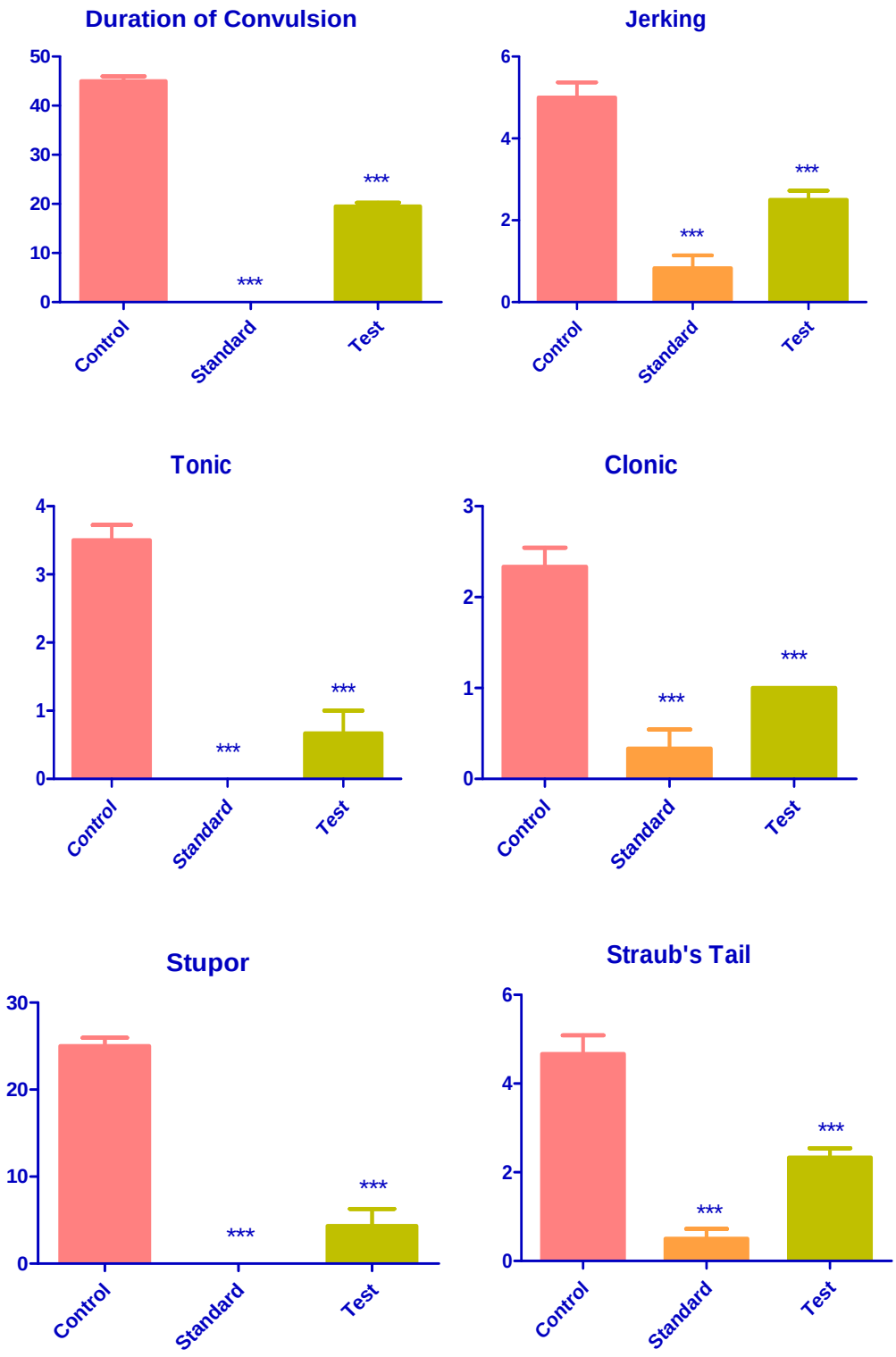
Groups	No. of Convulsion	No. of Straub's tail
Control	1.87±0.23	13.67±1.2
Lorazepam 4mg/kg	00±00***	1.83±0.30***
Sarvaapsmarahara rasa(125mg/day)	0.87±0.12***	5.5±0.50***



All values are expressed as mean ± SEM, n=6, One-way Analysis of Variance (ANOVA) followed by multiple comparisons Dunnett's test. The value significant *p<0.05,* *p<0.01, ***p<0.001 as compared to control group

Table 4: The Effect of Sarvaapsmarahara rasa on Duration of Convulsion, Jerking, Tonic, Clonic, Stupor and Straub's tail against PTZ induced epilepsy in mice.

Groups	Time in Seconds					
	Duration of Convulsion	Jerking	Tonic	Clonic	Stupor	Straub's tail
Control	45.0 ±0.96	5.0±0.3	3.5± 0.2	2.3±0.2	25.0±0.9	4.66 ±0.42
Lorazepam (4 mg/kg)	00±00***	0.8 ±0.3***	00±00***	0.3±0.2***	0.0±0.0***	0.50±0.22***
Sarvaapsmarahara rasa(125 mg/day)	19.50 ±0.76***	2.5 ± 0.2***	0.6±0.3***	1.0±0.0***	4.3±1.9***	2.33±0.21***



All values are expressed as mean ± SEM, n=6, One-way Analysis of Variance (ANOVA) followed by multiple comparisons Dunnett's test. The value significant ***p*<0.01, ****p*<0.001 as compared to control group

The effect of Sarvaapsmarahara rasa on duration of Convulsion, Jerking, Tonic, Clonic, Stupor and Straub's tail against PTZ induced epilepsy, The Sarvaapsmarahara rasa treated group shows significant (*p*<0.001) decrease in Duration of Convulsion, Jerking, Tonic, Clonic, Stupor and Straub's tail as compared to Control group (Table 4).

DISCUSSION

Epilepsy is an important problem in developing countries. GABA potentiating drugs like diazepam,

benzodiazepine, barbiturate, Lorazepam, valproate etc. have been adopted to treat epilepsy. However, prolonged use of such drugs develops tolerance and dependence. Further the side effects like weight gain, insomnia, reflex tachycardia; sexual dysfunction etc. limits the usage of such drugs. As a result of this people worldwide are looking at the alternative system of medicines like Ayurveda, Unani and Homeopathy etc. for remedies to cure the epilepsy (Ekstein and Schachter, 2010). Most of drugs of Sarvaapsmarahara rasa are having tikta rasa pradhana and Medhya in action and Sadhaka pitta is responsible for medhya and buddhi prabodhana. Tikta Rasa helps in correcting Sadhaka pitta thus improves medha. Sarvaapsmarahara Rasa prolonged the onset of convulsions, shorten the duration of epileptic episodes and reduce mortality. These effects may be attributed to the presence of bioactive constituents such as steroids, alkaloids, phenolic compounds and flavonoids in the herbal components. These phyto constituents may act on the GABA calcium channel complex, owing to their structural similarity to benzodiazepines, thereby enhancing its inhibitory effects. Alkaloids possess notable neuroprotective and CNS-modulating properties, while tannins and phenolic compounds contribute to neuronal protection. Steroids play a role in regulating various physiological functions of the central nervous system and carbohydrates provide an essential energy source for the brain. Overall, Sarvaapsmarahara Rasa, being a synergistic blend of minerals and herbs processed through traditional methods, likely enhances therapeutic efficacy and bioavailability through mutual potentiating of its components.

The Sarvaapsmarahara rasa was subjected for preclinical studies using rats there is scope for clinical studies to validate further therapeutic benefits in human volunteers to find out the more detailed mechanism of action of this formulation and ascertaining its isolated constituents responsible for the activity.

CONCLUSION

In the present study, Sarvaapsmarahara Rasa showed Anti-epileptic activity against Pentylenetetrazol induced seizures in mice. Evidenced by decrease in the various phases such as stupor of convulsion in PTZ model and significant increase in onset in duration of seizure, decrease in duration of the seizure and reduced mortality rate in PTZ model in a dose dependent manner. In the PTZ model the effect shown by Sarvaapsmarahara Rasa is similar to standard drug because of reduction in the facilitation of Na^{+}ions to the neuronal area of the brain. So, this may be the reason for shortening in time of both the phases and delay in firing of neurons. Further studies are required to understand the molecular mechanism of this drug.

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