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Anticonvulsant Activity of Apasmarari rasa – An Experimental Study

Research Article

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Abstract

Apasmarari rasa, a unique Ayurvedic preparation having hingulottha shuddha parad (HSP), Shuddha Gandhaka (SG) and Shuddha Tuttha (ST) and Bhavana dravya (Trituration) as Tinospora cordifolia (Guduchi) as ingredients. The pharmaceutical processing involved preparation of chakrikas (pellets) by triturating the ingredients and sealing them in Sharava (shallow earthen disc) samputa (uniform smeared and dried) and subjecting the apparatus to Agni. After self-cooling (swangasheeta), the mixture was triturated with kadali kanda swarasa for one day and the final product was subjected to analysis.

Apasmarari rasa was subjected to assess the LD 50 and Anti convulsant activity on Male Albino rats was by means of MES (Maximal Electro convulsing Shock) Method. A supra maximal strength was 150mA in rats for 0.2 seconds and stimulus was applied via ear clip electrodes. The animal dose of Phenytoin (7.2mg/kg), Smriti sagar rasa (18mg/kg) and Apasmarari rasa (5.4mg/ kg) was given orally to different groups. The animals were observed for a period of 180 minutes after being subjected to electro convulsions. Experimental study had shown some significant result when compared to other drugs. No doubt, that both standard drugs also shown good results when it comes to HLE (hind limb extension), but other factors such as time duration of flexion, tonus, clonus, recovery time amongst others in test drug group (Apasmarari rasa) showed significantly better results. Some other observation such as nasal bleeding and orbital bleeding was also absent in test drug group (Apasmarari rasa).

Keywords: Apasmarari rasa, LD 50, Anti convulsant activity, MES Method.

Introduction

Epilepsy is a major neurological disorder and up to 5% of the world population develops epilepsy in their lifetime. As per the present impact of epileptic seizures, it affects nearly 1-5 % of population (1). The current therapy of epilepsy with modern antiepileptic drugs is associated with side effects, dose-related and chronic toxicity, as well as teratogenic effects, and approximately 30% of the patients continue to have seizures with current antiepileptic drugs therapy (2-4). Epileptic seizures have been known to represent an occasional discharge in the nervous tissue (5), characterized by recurrent paroxysmal changes in the neurological function caused by abnormalities in the electrical activity of the brain. Traditional systems of medicine are popular in developing countries and up to 80% of the population relies on traditional medicines or folk remedies for their primary health

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care need. Even herbs used for the treatment of epilepsy (i.e. Carissa carandas Linn.) in different systems of traditional medicine have shown activity when tested in modern bioassays for the detection of anticonvulsant activity.(6) But as Rasaaushadhis are consider to be more persuasive and as it is the need of hour for their endorsements so Apasmarari rasa chosen for this experimental study.

Apasmarari Rasa (7) (ARR) is one among those formulations which is exclusively indicated in Apasmara as explained in Rasakamdhenu (mayoortuttha rasagandho yoryut guduchika toya vimerditam driddham), having minimum ingredients like hingulottha shuddha parad (processed mercury), shudha gandhaka(processed sulphur) and shudha tuttha (processed copper sulphate), and bhavana (Trituration) dravya's like Tinnospora cordifolia (Willd.) Miers. (Guduchi) and Musa paradisiaca linn (kadali kanda swarasa) tuber juice.

Based on the above information, the present study was designed to consider the effect of Apasmarari rasa as an anti convulsant drug, on a well –established MES animal model of convulsion preceded by LD 50 determination. Induction of maximal electroshock seizures (MES), using an electro convulse meter (ECM), is a commonly used model for evaluation of anticonvulsant drugs (8).

Material and Methods:

Animals:

Adult male albino rats weighing between 150-200gms were used in the study. Initially, they were maintained on rat pallet diet and tap water (unless mentioned otherwise) at a 12 hour light dark schedule. They were group housed at a temperature of 25 ± 1 0C. Animals were randomly selected, marked to permit individual identification and kept in their cages for one week prior to dosing to allow for acclimation to the laboratory condition.

DETERMINATION OF LD 50 (TEST COMPOUND) (9) – Fixed dose method (OECD guideline No. 420 of CPCSEA).

The test substance is orally administered in a single dose by using a stomach tube. Animals were fasted for 24 hrs prior to dosing. And observation is made for 24 hours.

TEST PROCEDURE WITH STARTING DOSE OF 2000MG/KG BODY WEIGHT

TABLE-01: Showing dose schedule for LD 50 Determination (Apasmarari rasa)

GROUP	DOSE	ROUTE OF ADMINISTRATION	OBSERVATION
LD – 50	2000mg/kg	Orally	24 hrs
LD – 50	2000mg/kg	Orally	24 hrs
LD – 50	2000mg/kg	Orally	24 hrs

Screening of Anti Epileptic Activity(10):

MES Method:

An electrical stimulus of sufficient intensity to induce maximal seizure is applied by means of an external device stimulator or convulsiometer. A supra maximal strength is 150mA in rats for 0.2 seconds is used .The stimulus is applied via corneal or ear clip electrodes. MES seizures remain the primary screening for potential Antiepileptic activity.

Requirement:

Animals - Healthy Male Wister Albino Rats (150-200 mg)

Drugs - Phenytoin (300mg/ kg) (11) and Smritisagar rasa (12) (1000mg/kg)

Test Drugs - Apasmarari rasa (300mg/kg)

Equipments-Electro-convulsiometer,

Corneal or Ear Electrodes (apply 150mA current for 0.2sec)

Preparation of doses /vehicle:

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The Drug was in powder form so triturated with distilled water.

Administration of doses:

The test substance is orally administered in a single dose by using a stomach tube. Animals were fasted overnight prior to dosing.

Procedure

1. Weigh and number the animals. Divide them into four groups each consisting of 6 rat's first group is used as control and second for drug phenytoin as a standard (A) and third group as Ayurvedic standard drug (B) i.e. Samritisagar rasa to be given, and for fourth test drug Apasmarari rasa should be given respectively.
2. Hold the animal properly, place corneal or ear electrodes on the cornea or ear pinna and apply the prescribed current, note different stages of convulsion i.e. A) Tonic flexion B) Tonic extensor phase C) Clonic convulsions D) Stupor E) recovery or death. Note the time in seconds spent by the animal in each phase of the convulsions. Repeat with other animals of control group.
3. Administer Phenytoin, Samritisagar rasa and Apasmarari rasa orally to different groups. Wait for 180 min and subject the animals to electro convulsions as described earlier.

Note the reduction in time or abolition of tonic extensor of MES convulsions

TABLE NO.02: Showing dose schedule for all groups

GROUP	DRUG	NO. OF RATS	DOSE	ROUTE OF ADMIN.	TIME OF ADMINI.*
Control	DW**	06	1.5 ml/rat	Orally	180 min
SD (A)	Phenytoin	06	7.2mg/kg	Orally	180 min
SD (B)	Samritisagar rasa	06	18mg/kg	Orally	180 min
Test	Apasmarari Rasa	06	5.4mg/ kg	Orally	180 min

* Prior To Induce MES, ** Distilled Water

STATISTICALS STUDY METHOD (13)

Fishers Exact Test:

TABLE NO.03: Showing Effect of therapeutic dose of Apasmarari rasa and its anti convulsant effect with other therapeutic equivalent drugs on MES

SR. NO	DRUG/DOSE	+VE	-VE	%	P VALUE
1	Apasmarari rasa	2	4	66.6	> 0.22
2	Smritisagar rasa	2	4	66.6	>0.22
3	Control	5	1	16.6	< 0.0075
4	Phenytoin	0	6	100	>1

- Control group failed to provide significant protection.
- P> 0.05 denotes insignificant difference as compare to Apasmarari rasa (anticonvulsant dose group)

TABLE NO.04: Master Chart Showing duration of all the stages in seconds

Group/Dose	Sl.No	Flexion	Extension	Clonus	Stupor	Recovery time
Control.	1H	4sec	8 sec	0 sec	120 sec	130 sec
	2N	3 sec	11 sec	Absent	149 sec	165 sec
1.5ml/200gm	3B	1 sec	12 sec	0 sec	200 sec	207 sec
	4T	3 sec	12 sec	66 sec	430 sec	301 sec
	5L	2 sec	Absent	95 sec	145 sec	129 sec
	6UM	2 sec	7 sec	0 sec	120 sec	129 sec
Phenytoin.	1H	12 sec	Absent	0 sec	144 sec	156 sec
7.2mg/200gm	2N	4 sec	Absent	16 sec	122 sec	142 sec
	3B	3 sec	Absent	0 sec	155 sec	158sec
	4T	7 sec	Absent	0 sec	147 sec	154 sec
	5L	14 sec	Absent	24 sec	66 sec	104 sec
	6UM	All stages are absent				
Smritisagar	1H	4 sec	Absent	20 sec	330 sec	624 sec
Rasa.	2N	3 sec	Absent	00 sec	158 sec	161 sec
18mg/200gm	3B	1 sec	Absent	10 sec	158 sec	169 sec
	4T	3 sec	9 sec	8 sec	62 sec	82 sec
	5L	9 sec	Absent	1.29 sec	98 sec	196 sec
	6UM	2 sec	15 sec	8 sec	123 sec	148 sec
Apasmarari	1H	10 sec	3sec	36 sec	173 sec	222 sec
Rasa.	2N	All stages are absent				
5.4mg/200gm	3B	All stages are absent				
	4T	4 sec	4 sec	13 sec	147 sec	168 sec
	5L	13 sec	Absent	8 sec	68 sec	89 sec
	6UM	00 sec	Absent	00 sec	00 sec	00 sec

Discussion

Study showed some significant results in test drug when compared to other two standards. No doubt, that both standard drug also shown good results when it comes to HLE (hind limb extension) ,but if we consider other factors such as time duration of flexion, tonus, clonus, recovery etc. in test drug group these all factors shown better results. Some other observation such as nasal bleeding and orbital bleeding was also absent in test drug group. Abolition of Hind limb Extension, and fast recovery was an experimental observation.

Conclusion

Animal study of Apasmarari Rasa has shown some significant result when compared to other drugs like Phenytoin and Samritisagar rasa. Here one of the main criteria was HLE (Hind Limb Extension) and other factors we found that recovery period and other different stages shown better results with Apasmarari rasa. On the basis of the present results and available reports, it can be concluded that the anti- convulsion activity elucidated by Apasmarari Rasa possesses significant consequence in animals.

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