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Experimental evaluation of *Hingusauvarchaladi Ghrita* and *Saptavartita Hingusauvarchaladi Ghrita* with special reference to their anticonvulsant activity

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Abstract

Incidence of epilepsy is 0.3 to 0.5% in different populations throughout the world, and the prevalence of epilepsy has been estimated at 5 to 10 persons per 1000. Scanning of the Ayurvedic classics reveals that 90% of the formulations mentioned to have action on *sajnavaha srotas* are *ghrita*-based formulations. *Ghrita* because of its *yogavahi guna*, incorporates the qualities of the drugs added to it without losing its own qualities. In the present study *Hingusauvarchaladi ghrita* and *saptavartita Hingusauvarchaladi ghrita* have been selected, to prove their anticonvulsant activity experimentally on albino mice, by the chemoshock method. The observations recorded have been analyzed by one-way ANOVA followed by Scheffe's test, statistically. *Saptavartita Hingusauvarchaladi ghrita* has shown better anticonvulsant activity in comparison to *Hingusauvarchaladi ghrita*.

Key words: *Hingusauvarchaladi ghrita*, Clonus, Seizures, Convulsion, Pentylenetetrazol, *Sneha Kalpana*

Introduction

Convulsion is a sign of panic, which is commonly observed in epileptic and non-epileptic conditions. It often causes transient impairment of consciousness, leaving the individual at risk and is quite often seen in epilepsy. The pathophysiological theories of epilepsy have identified the brain as the site of the problem, and in the mid nineteenth century, the pathological changes in the brain associated with epilepsy were recognized.

As per Ayurvedic classical texts *Akshepa* is a separate disease classified under *Vatananatmaja vyadhi*[1] as well as it has been found as a symptom in different diseases, such as, *Apasmara*, *Apatanaka*, *Apatantraka*[2] and so on, but it is mainly observed in *Apasmara*. In *Madava Nidana* the *samprapthi* of *Akshepa* is clearly mentioned. The Ayurvedic treatise has described the causes, symptoms, and treatment of the disease in detail. In spite of many synthetic drugs introduced in the treatment of convulsions, they develop adverse drug reactions like CNS depression, ataxia, sedation, incoordination, thrombocytopenia, pancreatitis, hepatic dysfunction, tetratogenicity, and so forth.[3] There is still a need for an ideal anticonvulsant medicine with properties like broad spectrum activity, rapid onset of action, very few side effects, good bio-availability, cost effective, and so on.

Some of the drugs and therapies mentioned in Ayurvedic literature have been found to be very effective and offer great hope for a satisfactory treatment of this disease. Today in the era of scientific advances, it is necessary to validate these drugs and therapies experimentally and clinically as well.

Here an attempt has been made to find out the effect of *Hingusauvarchaladi ghrita* and *Sapthavartita Hingusauvarchaladi ghrita* experimentally, to prove their anticonvulsant activity.

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Aims and Objectives

- To revalidate the anticonvulsant activity of the trial drugs, experimentally.
- To compare the anticonvulsant activity of the trial drugs.
- To evaluate the anticonvulsant activity of the trial drugs in comparison to the standard drug sodium valproate.

Materials and Methods

Drugs

The raw drugs necessary for the present study were collected from the local market at Udupi and were identified as genuine samples by the Department of Dravyaguna, A.L.N. Rao Memorial Ayurvedic Medical College Koppa. The entire practical was done in the pharmacy of the Bhaishajya Kalpana Department, A.L.N. Rao Memorial Ayurvedic Medical College, Koppa.

Trial drug 1-*Hingusauvarchaladi ghrita*:

(Ref. *Ashtanga Hrudaya*, *Utharasthana* 6/22-23)

Murchitha ghrita				- 1200 g.
Drava dravya- Gomutra (Cow's urine)				- 4800 ml.
Kalka dravya				
Shoditha Hingu	-	*Ferula foetida* Linn.	Exd.	- 40 g
Sauvarchalalavana	-	(Black salt)		- 40 g
Shunti	-	*Zingiber officinale* Roxb	Rz.	- 40 g
Maricha	-	*Piper nigrum* Linn.	F.	- 40 g
Pippali	-	*Piper longum* Linn.	F.	- 40 g

Trial drug 2 - Saptavartita hingusauvarchaladi ghrita

The process was repeated seven times with the same ingredients of trial drug 1. Concept of *avartana* was adopted.

Experimental study

Selection of animals

Twenty-four albino mice of either sex, weighing between 20 and 25 g, bred in an animal house (Reg. No. 191/CPCSEA) of A.L.N. Rao Memorial Ayurvedic Medical College and P.G. Center were selected for the study, after getting clearance from the Institutional Ethical Committee. Six mice were taken in each group. The animals were housed in groups under 12-hour light / dark cycles, with standard diet and water *ad libitum*, to avoid the 'kindling' effect that occurred as a result of repeated convulsions induced by experimental methods. The animals were not subjected to any experiments for about seven days. The dose was calculated as per the table of Paget and Barne's [Table 1].

Methodology-The chemoshock method by pentylenetetrazol

Pentylenetetrazol[4] is a CNS stimulant. It produces jerky type of clonic convulsions in rats and mice. The convulsive effect of this drug is considered to be analogous with the petitmal type of convulsions in man. In recent times Pentylenetetrazol has been reported to act through GABA – a benzodiazepine receptor mechanism in the brain. It is widely used as a tool in experimental pharmacology to study the convulsive and anticonvulsive actions of the drugs.

Drugs

Pentylenetetrazol (dose 60 mg/kg, i.p)

A stock solution containing 6 mg/ml of the drug was prepared and 1 ml / 100 g of body weight of the mouse was injected. A dose of PTZ 0.25 ml / 25 g body weight of mouse was injected intraperitonially.

The following parameters were observed and recorded as time in seconds:

Table 1: Grouping of animals

Group	No. of animals	Drug	Dose
Control	6	Distilled water	0.1 ml
Standard	6	Sodium valproate	0.32 ml
Trial drug 1	6	Hingusauvarchaladi ghrita	0.16 ml
Trial drug 2	6	Saptavartita Hingusauvarchaladi ghrita	0.16 ml

Seizure duration

- Clonus
- Tonic hind limb flexion
- Tonic hind limb extension
- Postictal depression
- Recovery / Death

Control group

Animals in this group were administered distilled water 0.1 ml orally, and after an interval of 60 minutes, pentylenetetrazol (60 mg/kg body weight) was injected intraperitonially and the different phases of seizures were noted.

Standard group

All the animals in this group were administered sodium valproate 0.32 ml mixed orally and after 60 minutes, pentylenetetrazol (60 mg/kg body weight) was injected intraperitonially to observe the effects of the drug.

Trial group –T1

These animals were administered *hingusauvarchaladi ghrita* for three days at a dose of 0.16 ml orally and on the third day, after administration of the drug, an interval of 60 minutes was maintained, and then they were subjected to chemical shock by injecting pentylenetetrazol in a dose of 60 mg/kg body weight, intraperitonially. The results obtained were recorded.

Trial Group-T2

These animals were administered *saptavartita hingusauvarchaladi ghrita* for three days at a dose of 0.16 ml orally, and on the third day after administration of the drug, an interval of 60 minutes was maintained, and then they were subjected to chemical shock by injecting pentylenetetrazol in a dose of 60 mg/kg body weight, intraperitonially. The results obtained were recorded.

Results

The mean time duration of clonus in the control group, trial T-1 and T-2 was 13.17, 8.5 and 7.16 seconds respectively and abolition of clonus was noted in standard group. In the control group all animals exhibited tonic hind limb flexion, the mean time duration was 9.5 seconds. In standard group except 4, all animals have shown abolition of tonic hind limb flexion and the mean time duration was 2.17 seconds. In trial T- 2 there was abolition of the symptom in one mice .In the control group, all animals exhibited tonic hind limb extension and the mean time duration was 9.17 seconds. In the standard group, all animals except in 3 abolition of tonic hind limb extension was found and the mean time duration was 1.16 seconds. In T-1 and T-2 abolition of tonic hind limb extension was observed in 1 animal and 2 animals respectively [Table 2].

Discussion

In Ayurvedic texts *Akshepa* (convulsion) is a separate disease, classified under *Vatananatmaja Vyadhi* as well as it has been found as a *lakshana* in different diseases like *Apasmara*, *Apatanaka*, *Apatantraka*, and so on, but it is mainly observed in *Apasmara*. The trial drug *Hingusauvarchaladi ghrita* is used as medicine for *Apasmara*. With this background an attempt has been made to prepare *Hingusauvarchaladi ghrita* and *saptavartita*

Table 2: P.T.Z. induced convulsions mean values and standard error mean (parameters are recorded as time in seconds)

Parameters	Control	Standard	Trial 1	Trial 2
Seizure duration Mean (± SEM)	75.66 ± 1.76 ^{bcd}	13.50 ± 1.19^{acd}	40.50 ±2.42^{abd}	31.67 ± 2.41 ^{abc}
Clonus Mean (± SEM)	13.17 ± 1.19 ^{bcd}	0.0 ± 0.0 ^{acd}	8.5 ± 0.76^{ab}	7.16 ± 0.70^{abc}
Tonic hind limb flexion Mean (± SEM)	9.5 ± 0.56 ^{bcd}	2.17 ± 0.74^{ac}	5.83 ±0.79^{ab}	4.5 ± 0.99^{a}
Tonic hind limb extension Mean (± SEM)	9.17 ± 0.60 ^{bcd}	1.16 ± 0.54 ^{ac}	4.00 ± 0.86^{a}	2.83 ± 0.90^{ac}
Extension / flexion ratio (E/F Ratio)	0.9700 ± 0.05	0.1667 ± 0.17^{a}	0.7718 ± 0.18^{b}	0.36 ± 0.16^{a}
Postictal depression Mean (± SEM)	43.00 ± 1.63 ^{bcd}	10.17 ± 0.60^{acd}	22.17 ± 0.60^{ab}	17.17 ± 0.60 ^{abc}
Death (D) / Recovery (R)	D — 4 R — 2	D — 0 R — 6	D — 3 R — 3	D — 2 R — 4

N = 6 albino mice in each group. Statistical method — one-way ANOVA followed by Scheffe's test. a = Statistically significant at ($P < 0.05$) vs. control, b = Statistically significant at ($P < 0.05$) vs. standard, c = Statistically significant at ($P < 0.05$) vs. trial 1, d = Statistically significant at ($P < 0.05$) vs. trial 2

Hingusauvarchaladi ghrita and to find out their anticonvulsant activity. In this method, the criterion noted for evaluation of the anticonvulsant activities of the control, standard, and trial compounds is abolition of the clonus, although criteria such as the tonic hind limb flexion and tonic hind limb extension have also been noted as useful guidelines to assay anticonvulsant activity.

The standard drug and the trial drug T1 and T2 have produced significant ($P < 0.05$) reduction in the seizure duration when compared to the control [Table 2].However, the standard drug abolished the clonus phase, and the trial drugs T1 and T2 significantly reduced its duration when compared with the control group. The standard drug caused a significant reduction in the extensor--flexor ratio (E/F) when compared to the control group. The trial drug 2 also had a significantly reduced E/F ratio. The trial drugs also showed significantly reduced postictal depression when compared to the control group.

From the above results it was concluded that both the trial drugs possessed anticonvulsant activity. On comparing trial drug 1 and trial drug 2, it was concluded that the trial drug 2 possessed better anticonvulsant activity than trial drug 1 [Table 2].

Recovery / death of animals

Death noted in groups C, T1, and T2, four, three, and two, respectively. The remaining animals recovered in all the respective groups. In the standard group all the animals recovered. From this result it could be concluded that trial drug 2 possessed better anticonvulsive activity as compared to trial drug 1.

Probable mode of action

The probable mode of action of the trial drugs can be explained in four angles. *Hingu*, *sauvarchala*, *trikatu*, and *gomutra* are *ushna veerya* and *vatakapha shamaka* drugs.

*Akshepa*ka is a *vata*-predominant disease, where the *sanjavaha srotas* are blocked and the patient goes into an unconscious condition. Here *hingu* is the best *sapjna sthapana* drug [5], thereby it acts as an *Akshepa hara dravya*. *Trikatu* helps to increase the bioavailability of the medicine and moreover removes the *srotorodha* in the cellular level. *Hingu* and *sauvarchala*[6] *lavana* are the best *Anulomana*, *Deepana*, and *pachana dravyas*, which help to subdue the aggravated *vata*. The *kshareeya guna* of *gomutra* and *sauvarchala lavana* are best to remove the *srotorodha*. In this compound formulation *hingu* acts as the activator, *gomutra* and *sauvarchala lavana* act as the potentiators, *trikatu* acts as the bioavailability enhancer, and ghee being the base of the formulation increases the shelf life of the product.

As the active ingredients are mixed with ghee they easily get digested and absorbed. The lipophilic action of the ghee facilitates transportation to the target site.

In general, the blood cerebrospinal fluid and the blood brain barriers are highly permeable to water, carbon dioxide, oxygen, and most lipid soluble substances, and slightly permeable to electrolytes such as sodium chloride and potassium. The more lipophilic the drug is, the more likely it is to cross the blood-brain barrier [7][8].The active principles of *hingu*, *sauvarchala lavana*, *trikatu*, and *gomutra* are lipid soluble, and hence, they cross the blood-brain barrier, to bring about the *sapjna sthapana* of the afflicted person.

Conclusion

The trial drugs 1 and 2, that is, *Hingusauvarchaladi ghrita* and *saptavartita hingusauvarchaladi ghrita*, have a definite demonstrable anticonvulsant action as ascribed by the experimental study conducted on albino mice. The trial drug 1 — *Hingusauvarchaladi ghrita* and trial drug 2 — *saptavartita Hingusauvarchaladi ghrita* have a moderately significant effect against convulsions, when compared with the standard drug. The trial drug 2 — saptavartita *Hingusauvarchaladi ghrita* was more effective than the trial drug 1 — *Hingusauvarchaladi ghrita*.

References

1. Charaka, Charaka Samhita, Sharma PK, Bhagawan Dash, English commentary, Chaukamba Sanskrit Series Office, Varanasi, 2nd ed., 1996, Sutrasthana, 20/9-11.
2. Vagbhata, Ashtanga Hrudaya, Srikantha Murthy KR, English commentary, Krishnadas Academy, Varanasi, 1st ed., 1996, Nidanasthana, 15/17-20.
3. Satoskar RS, Bhandarkar SD, Pharmacology and Pharmacotherapeutics,. Popular Prakashan Pvt. Ltd., Bombay, 19th ed., 2005.
4. Kulkarni SK, Handbook of Experimental pharmacology, Vallabha prakashan, New Delhi, 3rd ed., 1999, p.131-4.
5. Sharma PV, Dravyaguna Vignana, Chaukhambha Bharati Academy, Varanasi, 2001, p.350-4.
6. Sharma S, Rasatharangini, Shastri KN, Hindi commentary, Motilal Banaarisidas, Varanasi, 2004, 14/154-155, p.354.
7. Goodman & Gilman's, The pharmacological basis of therapeutics, Laurence & Brunton, 11th ed., 2006, p.9.
8. Usha KS *et al.*"A clinical study on Apasmara and its management with Maha Pancha Gavya Ghrta", KC 2001, I.P.G.T. & R.A., GAU, Jamnagar.