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CNS Activity Of An Ayurvedic Preparation: Asthamangal Ghrita

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Abstract: Asthamangal Ghrita is a compound formulation of herbal drugs extracted in the butter fat (Ghee) of cow's milk. It is classified as ghrita in Indian system of medicine called Ayurvedic Medicine. Butter fat acts as both a vehicle as well as an active ingredient by virtue of its several properties claimed in the old Indian scriptures. Along with butter fat present are Acorus calamus, Brassica campestris, Centella asiatica, Hemidesmus indicus, Piper longum, Saussurea lappa and Rock salt. All of these drugs along with ghee are claimed to have CNS actions, mostly as calming, sedative, memory enhancing etc. So, it was thought worthwhile to validate the said activities by modern pharmacological screening methods.
In the present study, Asthamangal ghrita was studied for its effect on Behavioural activity, Sleeping time, pain, convulsions, locomotor activity etc. and it was found to be effective in CNS related disorders in mice.
Key Words: Asthamangal Ghrita, CNS activity, Ayurvedic preparation.

Introduction

In recent years there has been an upsurge in the clinical use of indigenous drugs. Polyherbal preparations, originally used in the traditional system of medicine, are now being investigated and effectively tried in a variety of pathophysiological states[1]. Side effects and expenses associated with allopathic drugs have provoked the need for research into drugs, which are without side effects, especially those belonging to the traditional systems of medicine like Ayurveda[2].

Ghrita is a Kasthaushadhi type of Ayurvedic preparation i.e. compound formulation containing butter fat obtained from cow's milk along with other active ingredients from natural origin. Ghee (butter fat) in such preparations act as both, a vehicle for extracting and holding the active therapeutic principles from the drugs and an active ingredient due to its many actions claimed in Ayurveda.

Asthamangal ghrita is a compound formulation containing ghee along with Acorus calamus having carminative[3], sedative and tranquilizing effects[4], Brassica campestris having anti-inflammatory and anti-epileptic properties[5], Centella asiatica for its brain growth and effect on learning and memory[6], Hemidesmus indicus with anti-epileptic effects[7], Piper longum for use in insomnia[8], Saussurea lappa [9,10]and Rock salt. These drugs are claimed to have CNS actions particularly Centella asiatica and Hemidesmus indicus are very widely used in marketed preparations sold for memory enhancing purposes. Ghee is claimed to have many properties and by virtue of having fatty acids and lipophilic nature, it is hypothesized that it can enter the otherwise strong Blood Brain Barrier (BBB).

Present study was an attempt to illustrate the CNS activities of Asthamangal ghrita, since it is claimed in Ayurvedic literature as memory enhancer in young people.

Materials and Methods

Asthamangal Ghrita: It was prepared according to the method described in Ayurvedic texts taking the herbs from the medicinal garden of Birla Institute of Technology, Ranchi and the Rock salt was purchased from the local market. Ghee was purchased from the Goras Bhandar, Wardha, India.

Animals: Male Swiss albino mice weighing 25-30 g were used. They were housed in groups of 5-6 under standard laboratory conditions (temperature 23±1^{o}C, relative humidity 55±5% and lighting 08:00-20:00 h) with food (Lipton India Ltd. pellets) and water ad libitum. The animals were transferred to the laboratory at least 1h before the start of the experiment. The experiments were performed during day (08:00-16:00 h). The institutional animal ethical committee approved the study protocol.

Behavioural effect: Behavioural effects of Asthamangal ghrita (50 mg/kg and 100 mg/kg) were assessed by the method described by Irwin [11]. The animals were observed continuously for the presence of behavioural, autonomic, neurological and other signs up to 2 h after treatment.

The animals were also fed with 2000 mg/kg of the formulation and were observed for one week for detection of mortality, if any.

Vehicle controls were also maintained simultaneously. All the experiments were commenced at 9:00 am.

Pentobarbitone-induced sleeping time: The animals were divided in four groups (n=6). Group I served as control and received vehicle orally and pentobarbitone sodium (45 mg/kg i.p.). Groups II, III and IV were injected with pentobarbitone sodium (45 mg/kg i.p.), 30 minutes after oral administration of test formulation (100, 200, and 300 mg/kg). The time elapsed between loss and recovery of righting reflex was recorded as sleeping time and recorded for control and pre-treated animals [12].

Spontaneous locomotor activity: The animals were divided in four groups (n=5). Group I served as control and received vehicle orally and groups II, III and IV were treated with test formulation (100, 200 and 300 mg/kg) orally. The spontaneous locomotor activity was recorded using Actophotometer wherein interruption of beam of light generated a pulse which was recorded on digital counter using the method described by Turnar in 1965. The locomotor count for each animal was recorded for 5 minutes at 30 minutes interval for 1.5 h.

Amphetamine antagonism: The animals were divided in four groups (n=5). Group I served as control and received vehicle orally and groups II, III and IV were treated with test formulation (100, 200 and 300 mg/kg) orally 30 minutes before amphetamine administration (2 mg/kg i. p.). The motor activity count was recorded in actophotometer for 5 minutes at 30 minutes interval for 1.5 h after the injection of stimulant.

Analgesic activity: The experimental animals were divided in four groups (n=5). Group I animals were treated with vehicle only. Animals of groups II, III and IV were treated with the test formulation at the dose level 100, 300 and 500 mg/kg respectively. Basal reaction time to radiant heat was noted by placing the tip of the tail on radiant heat source. The tail withdrawn from the heat source was taken as end point. The cut off period of 10-12 seconds was taken to prevent the damage to tail.

Motor coordination test: The animals were administered orally the test formulation (100, 200, and 500 mg/kg) and effect on motor coordination was evaluated by the method described by Dunham and Miya [13]. The animals were trained on rota-rod apparatus to remain for 3 minutes on rotating rod at the speed of 25 rpm. 24 hours later the test formulation was administered orally to group of mice (n=6) in the doses given above. The control group received only the vehicle and the ability of mice to remain on the rotating rod were assessed before and 60 mins. after the treatment. The fall off time of each animal from rod was noted.

Maximal electroshock (MES) - induced seizures: The animals were divided into six groups (n=8), treated with either test formulation (100, 300 and 500 mg/kg p.o.) or vehicle or diazepam (4mg/kg i.p.). They all received current of 42 mA for 0.2 sec duration through electroconvulsiometer (Techno, India) using corneal electrodes, after 60 minutes of oral administration of test formulation. The incidence and duration of extensor tonus was noted. A complete abolition of hind limb extension was considered as100% protection [14].

Pentylenetetrazole (PTZ) - induced seizures: The animals were divided into six groups (n=8), treated with either test formulation (100, 300 and 500 mg/kg p.o.) or vehicle or diazepam (4mg/kg i.p.). They were all treated with PTZ (80 mg/kg s.c.) 60 minutes later and observed for the occurrence of seizures and presence or absence of clonic convulsions. Animals devoid of seizures were considered protected [15].

Statistics: The data was subjected to student't' test or one way analysis of variance (ANOVA) followed by Dunnett 't' test. The level of significance was set at $p<0.5$.

Results

3.1-Behavioural effects

The formulation Asthamangal ghrita was found to safe after oral administration upto the dose of 2 g/kg. No mortality was observed in this dose upto 48 hours. The animals were observed for 2 hours after oral administration of test formulation (50 and 100 mg/kg). During the observation period various behavioural scores were noted as shown in Table 1. There was decrease in alertness, spontaneous locomotor activity and reactivity to touch stimuli. The animals did not show loss of righting reflex, and body position was normal and no stereotypy and lacrimation was observed.

Table1: Behavioural Effects of Asthamangal Ghrita

S. No.	Behavioural Signs	Asthamangal ghrita mg/kg	
		50	100
1.	Alertness	√	↓
2.	Passivity	√	√
3.	Stereotypy	-	-
4.	Grooming	√	√
7.	Locomotion	√	↓
8.	Righting reflex	√	√
9.	Grip strength	√	√
10.	Straub tail	-	-
11.	Respiration	√	√
12.	Convulsions	-	-

3.2-Pentobarbitone- induced sleeping time

The pre-treatment with the formulation Asthamangal ghrita significantly potentiated pentobarbitone induced sleep. The results are shown in Fig. 1. Asthamangal ghrita potentiated pentobarbitone sleeping time from 68.4+-3.725 to 92.8+-7.68, 97.8+-6.59 and 148.6+-9.5 .

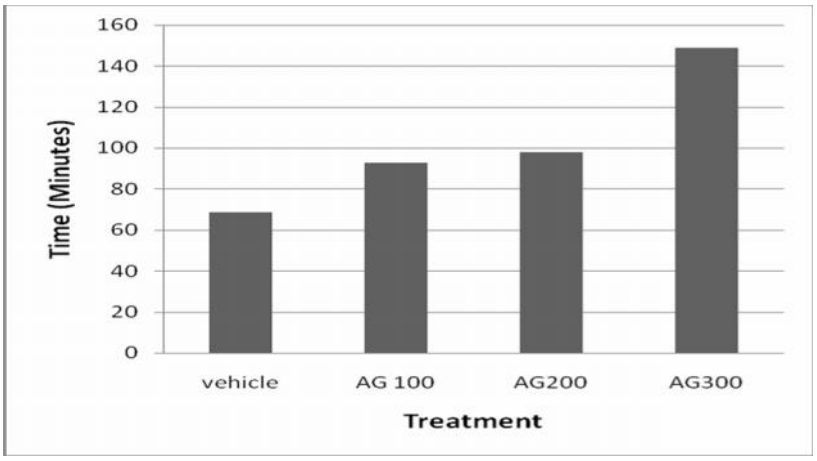

Fig. 1 Effect of Asthamangal ghrita on Pentobarbitone-induced Sleeping time

3.3-Spontaneous locomotor activity

Asthamangal ghrita exhibited significant decrease in spontaneous locomotor activity in mice. (Fig. 2)

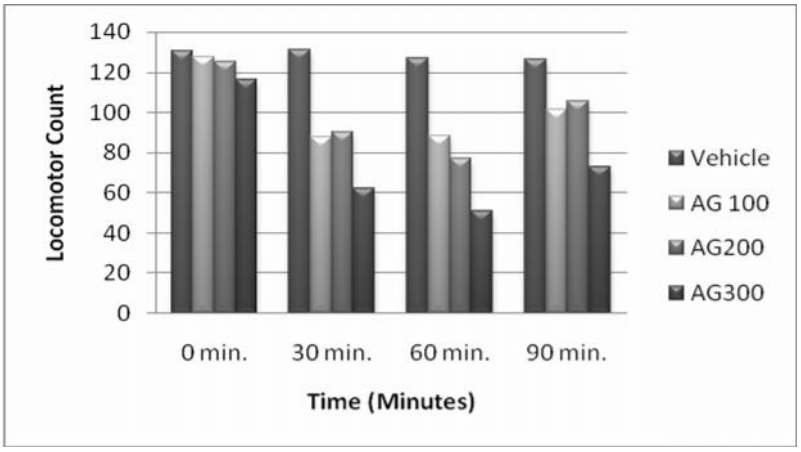

Fig. 2 Effect of Asthamangal ghrita on Spontaneous locomotor activity

3.4-Amphetamine antagonism

The formulation antagonized the hyperactivity induced by CNS stimulant drug amphetamine (2 mg/kg i. p.) in the dose of 200 and 300 mg/kg orally (Fig. 3).

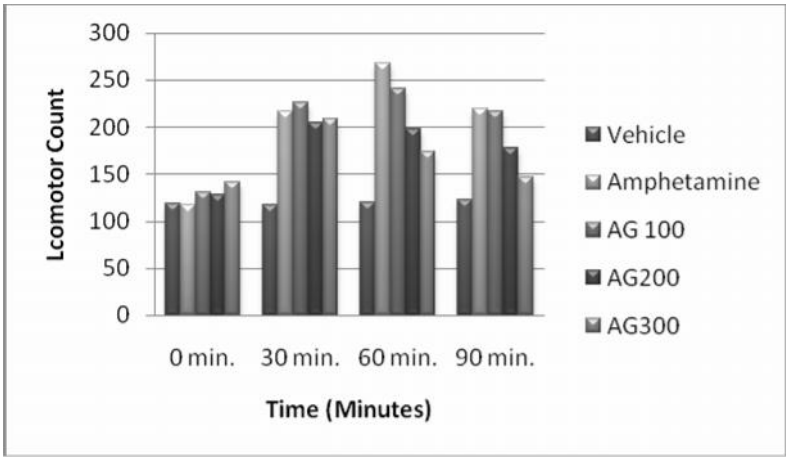

Fig. 3 Effect of Asthamangal ghrita on Amphetamine antagonism

3.5-Analgesic activity

Asthamangal ghrita significantly increased pain threshold in mice in dose dependent manner (Fig. 4).

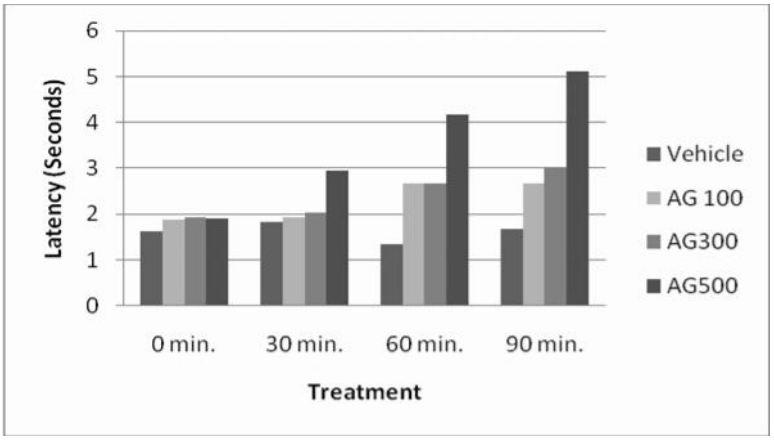

Fig. 4 Effect of Asthamangal ghrita on Analgesic activity

3.6-Motor coordination test

The animals treated with Asthamangal ghrita remained for 3 minutes in rotating rod at all the doses levels. The data was not found statistically significant. The formulation did not induce any motor in-coordination.

3.7-Maximal electroshock (MES) - induced seizures

Asthamangal ghrita produced dose dependent decrease in the duration of hind limb extensor phase. The maximum decrease or incidence of convulsions was noticed at 500 mg/kg p.o. The results are shown in Table 2.

3.8-Pentylenetetrazole (PTZ) - induced seizures

The formulation delayed or abolished clonic seizures induced by PTZ and reduced mortality in the dose 500 p.o. (Table 3).

Table 2: Effect of Asthamangal ghrita on maximal electroshock -induced seizures

S. No.	Treatment (mg/kg)	Duration of tonic hind limb extension (sec.) +- S.D.	Percent of animals protected
1.	Vehicle	14.39+-0.52	00
2.	AG 100 p.o.	12.78+-1.003	00
3.	AG 300 p.o.	9.225+-0.825	25
4.	AG 500 p.o.	7.28+-0.83	50
5.	Diazepam 4 i.p.	0.0+-0.0	100

Table 3:Effect of Asthamangal ghrita on PTZ- induced seizures

S. No.	Treatment (mg/kg)	Onset of Spasm (sec.) +- S.D.	Death of Animals
1.	Vehicle	46.89+-2.55	8/8
2.	AG 100 p.o.	46.96+-2.01	8/8
3.	AG 300 p.o.	73.93+-3.38	7/8
4.	AG 500 p.o.	106.84+-3.8	6/8
5.	Diazepam 4 i.p.	-	0/8

Discussion

Asthamangal ghrita was shown to decrease the locomotor activity and alertness in the mice with overall calmness. It potentiated the sleeping time in dose-dependent manner induced by pentobarbitone which substantiates the evidences of behavioural effects. It was further confirmed by performing the spontaneous locomotor activity on the actophotometer. Asthamangal ghrita antagonizes the activity of amphetamine which suggests it to be used as CNS depressant.

It showed a very good analgesic activity and did not show any motor in-coordination. It clearly suggests that this particular ghrita can be successfully used as a CNS agent for the treatment of over excitation. Asthamangal ghrita was also shown to have anticonvulsant effect in higher doses.

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