

Psycho-Neuro-Pharmacological Evaluation of Kushmandadi Ghrita

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ABSTRACT : This research is carried out with the aim to study psycho-neuro-pharmacological evaluation of Kushmandadi ghrita which comprises Kushmanda (*Benincasa hispida*), Yashtimadhu (*Glycyrrhiza glabra*) processed in cow's ghee. Among them Kushmanda has been repeatedly mentioned as 'Medhya' and appreciated for its 'Chetasovikaranashanam' effect; Yashtimadhu is included among the four main Medhya Rasayana drugs and also used as routine remedy in the management of the mental illness. Cow's ghee is considered specially nutritive and increased intellectual faculties. Considering these properties, Kushmandadi ghrita was studied on various experimental models such as Gross behavior, Hypnotic potentiation, Anti convulsant activity, Anti psychotic activity, Anti depressant activity, Chronic fatigue syndrome, Anxiolytic activity & Nootropic activity on Charles Foster strain albino rats and Swiss albino mice. The trial drug showed complex pattern of CNS activity, anti-depressant, anti-anxiety and memory and learning enhancement activities. It also produced good effect on chronic fatigue syndrome. It is devoid of anti-convulsant, central muscle relaxant and anti-psychotic activities.

Key words : Kushmandadi ghrita, anxiolytic effect, anti depressant effect, chronic fatigue syndrome.

INTRODUCTION

A number of medicinal plants like *Centella asiatica*, *Bacopa monnieri*, *Nordostachys jatamansi*, *Glycyrrhiza glabra*, *Acorus calamus* have been reported to possess significant CNS activities. However, most of the studies carried out on these plants are on extracts or chemical fractions. In Ayurvedic therapeutics the plants are normally used in combination even when used single plant they are not used as extracts or chemical fractions but as classical Ayurvedic formulations. Thus majority of the pharmacological studies are not in conformity with indications mentioned in Ayurvedic classics. Keeping this fact in the back ground, a series of studies was initiated at IPGT & RA on classical formulations.

Kushmandadi Ghrita contains Kushmanda (*Benincasa hispida*), Yashtimadhu (*Glycyrrhiza glabra*) and Goghrita (Cow ghee). Kushmanda is renowned for its "Chetasovikaranasham", Yashtimadhu is one of the main Rasayana drugs mentioned by Charaka and Goghrita besides being nutritive is also considered to be a Rasayana. Taking the activity profile of the constituent ingredients into consideration the best formulation was evaluated for different psycho-neuro-pharmacological activities in a battery of tests.

MATERIAL & METHODS

Test Drug : Kushmandadi Ghrita comprises Kushmanda swarasa (18 parts) & Yashtimadhu kalka (1/4 part)¹. These are processed in cow's ghee (1part) as per classical Snehapana vidhi in the pharmacy of Gujarat Ayurved University, Jamnagar.

Animals : Charles Foster strain albino rats of either sex weighing between 140g-240g, swiss albino mice of either sex weighing between 20g-40g were randomly selected and maintained in the animal house attached to the Pharmacology laboratory of the institute. They were maintained on "Amrut" brand rat/mice pellets obtained from Pranav Agro Industries, Pune and exposed to ambient temperature, humidity and natural day and night cycles. All-the experiments were carried out between 8:00 am to 12:00 noon hrs of the day.

Experimental models employed were :

1. Gross behavior.²
2. Hypnotic potentiation.³
3. Anticonvulsant activity
Supramaximal electric shock induced convulsion.⁴
4. Antipsychotic activity
Effect on exploratory behavior of mice.⁵
Effect on D-amphetamine stereotypy.⁶
Performance in Cook's pole climbing apparatus.⁷
5. Anti depressant activity
Behavior despair test.⁸
Anti-reserpine test.⁹

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6. Chronic fatigue syndrome test.¹⁰
7. Anxiolytic activity tests
 - ♦ Open field behavior test.¹¹
 - ♦ Elevated plus maze test.¹²
8. Evaluation for nootropic effect.¹³
9. Test for muscle tone and balance by using rota-rod instrument.¹⁴

Ethical Approval :

The research protocol was approved by Institutional Animal Ethics Committee, I.P.G.T. & R.A., Jamnagar.

Groups :

- Group - Normal control - Only tap water
- Group - PG (Vehicle control) - 0.52 ml/kg- test drug
- Group - KG (Kushmandadi ghrita) 0.26 ml/kg- test drug
- Group - KG (Kushmandadi ghrita) 0.52 ml/kg- test drug.
- Group - KG (Kushmandadi ghrita) 01.00 ml/kg Goghrita
- Group - Standard reference drug

The drug treated groups were compared with control group and Goghrita treated group.

Drug administration :

Drug : Kushmandadi Ghrita was prepared by Snehapaka vidhi in the Institutional Pharmacy. It contains 18 parts of Kushmanda swarasa, 1 part Goghrita and 1/4 part Yashtimadhu kalka.

Acute study : Test drug administered one hour prior to the experiment as a single dose.

Chronic study : Test drug administered daily for 7 days continuously one hour prior to the experiment.

Dose calculation :

The dose of the formulation was calculated by extrapolating the therapeutic dose to rat dose on the basis of body surface area ratio (conversion factor 0.18 for rats) by referring to the table of Paget and Barnes (1969)¹⁵ i.e.,

For rats :

Human dose \times 0.018 = X g/200g Rat

$X \times 5 = Y$ g/ kg of rat

For mice :

Human dose \times 0.0026 = X g/20g of mice

$X \times 50 = Y$ g/kg mice

Statistical analysis

The data obtained was analyzed using the student's 't' test, one-way ANOVA with Dunnett's multiple 't' tests for determining the level of significance of the observed effects. In some of the tests that involved awarding subjective scoring non-parametric tests were employed. A 'P' value of less than 0.05 is considered statistically significant.

RESULTS & DISCUSSION

The activity profile obtained has been provided in consolidated form in Table No. 1 to facilitate easy comprehension in the context of the overall study design.

Table No. 1: PSYCHONEUROPHARMACOLOGICAL PROFILE OF KUSHMANDADI GHRITA :

Parameters studied	Goghrita alone *	Kushmandadi ghrita Lower dose **	Kushmandadi ghrita Intermediate dose **	Kushmandadi ghrita Higher dose**
1. Gross behaviour	NSD	NE	Biphasic SD	Biphasic SD
2. Hypnotic potentiation	NSD	NSI	NSI	NSI
3. Anti convulsant activity	NE	NE	NE	NE (Mod prol. Ext)
4. Antipsychotic activity				
a. Exploratory behaviour	SD	NSD	NSD	SI
▪ Motor activity	NSD	NSI	SD	SI
b. d-amphetamine stereotypy	NE	NE	NE	NE
c. CAR	WI	NE	WI	NE
5. Anti depressant activity				
a. Behaviour despair test (Duration of immobility)	SI	SD	NSD	NE
b. Anti reserpine test				
Catatonia	NSD	NSI	NE	NE
Sedation	NSD	NE	NE	NE
Ptosis	SD	SD	SD	SD

Contd....

6. Chronic fatigue syndrome (Duration of immobility 7 days average)	NE	NSD	SD	SD
7. Anxiolytic activity				
a. Open field behavior				
No. of squares crossed	NSD	SI	NSI	SI
No. of rearing	SD	SI	NSI	SI
Duration of freezing	SI	SD	NSD	SD
b. Elevated plus maze - mice time spent in open arm	NE	SD	NSI	NSI
8. Muscle tone (rota rod test)	NE	NE	NE	1/6 affected
9. Analgesic activity tail flick pain threshold				
10. Memory and learning elevated plus maze- mice Clozapine amnesia inhibition	NSD	SD	SD	NSD

NSI=Non significant increase, SI =Significant increase, NSD =Non-significant decrease, SD =Significant decrease,
NE =Not effective, WI =Weak inhibition, CAR =Conditioned avoidance response.

Effect on Hypnotic Potentiation :

TABLE NO. 2: EFFECT OF KUSHMANDADI GHRITA ON PENTOBARBITONE INDUCED SLEEP IN ALBINO MICE :

Group	Dose (ml/kg)	Latency onset of sleep (min)	% Changes	Duration of sleep (min)
Control	-	5.36 ± 0.06	---	192.7 ± 20.9
PG	0.52	4.64 ± 1.10	13.43 ↓	153.6 ± 28.8
KG	0.26	2.15 ± 0.61	59.88 ↓***	206.2 ± 18.5
KG	0.52	4.28 ± 0.36	20.14 ↓**	187.3 ± 28.8
KG	1.00	2.36 ± 0.55	49.19 ↓***	196.3 ± 23.0

ANOVA : non-significant Data : Mean ± SEM, ** p<0.01, ***p<0.001 (Student unpaired 't' test).

Anticonvulsant Activity :

TABLE NO. 3 : EFFECT OF KUSHMANDADI GHRITA ON SUPRAMAXIMAL ELECTRICAL SHOCK INDUCED CONVULSIONS IN ALBINO RATS :

Group	Dose (ml/kg)	Tonic flexion (sec)	%	Tonic Extension (sec)	%	Regaining of R.R. (sec)
Control	-	2.16 ± 0.5	---	13.33 ± 0.73	---	493±75
PG	0.52	2.16 ± 0.3	00.00	12.50 ± 0.49	0.20 ↓	248 ± 56*
KG	0.26	2.83 ± 0.4	03.01↑	13.33 ± 1.38	0.00	230 ± 14 **
KG	0.52	3.01 ± 0.6	38.88↑	11.50 ± 1.48	13.7 ↓	172 ± 70**
KG	1.0	1.83 ± 0.3	15.22↓	16.50 ± 2.60	23 ↑	494 ± 75**

ANOVA : non-significant, Data : Mean ± SEM, * p<0.05, ** p<0.01(Student unpaired 't' test),
‡ p <0.05 in comparison to Goghrita control group, R.R. Righting reflex.

Antipsychotic Activity :

TABLE NO. 4 : EFFET OF KUSHMANDADI GHRITA ON EXPLORATORY BEHAVIOUR OF MICE :

Group	Dose (ml/kg)	No of different tunnel in first min	No of different tunnels entered in 5 min	Total no of tunnels in 5 min
Control	-	0.83 ± 0.17	4.16 + 0.79	7.00 +1.06
GG	0.52	0.83 + 0.30	1.66 + 0.38↓*	4.16 + 0.79
KG	0.26	0.50 + 0.22↓	4.66 + 1.21↑	8.50 + 2.56↑*
KG	0.52	0.50 + 0.22↓	2.33 + 0.50↓*	3.83 + 0.87↓
KG	0.10	1.20 + 0.20↓*	3.33 + 0.69↓	9.00 + 1.30↑*
Chlorpromazine	3mg/kg (ip)	0.33 + 0.33i	1.66 + 0.47↓	1.83 + 0.54↓#

ANOVA : significant, p<0.001 df = 29 F = 4.367, 1.51, Data : Mean ± SEM, # p< 0.05,
‡ p<0.001 (Dunnet 't' test) *p<0.05 (Student unpaired't' test) ◆p<0.001(Student unpaired't' test in comparison to GG)

Antidepressant Activity :

TABLE NO. 5 : EFFECT OF KUSHMANDADI GHRITA ON BEHAVIOUR DESPAIR IN MICE :

Group	Dose (ml/kg)	Duration of immobility time (Sec) Mean + SEM	%
Control	-	143.66 ± 23.57	---
GG	0.52	196.83 ± 11.45*	37.00↑
KG	0.26	102.33 ± 28.41**	28.77↓
KG	0.52	145.33 ± 29.16	01.16↑
KG	0.10	207.16 ± 08.16**	44.20↑
Imipramine	10 mg/kg -(ip)	095.83 ± 16.83	33.29↓

ANOVA : Significant p<0.05 df = 30, F = 4.760, Data : Mean ± SEM, * p < 0.05,
 ** p < 0.01, (Student unpaired 't' test), **a p<0.05 in comparison to Goghrita administered group.

TABLE NO. 6 : EFFECT OF TEST DRUGS ON RESERPINE INDUCED CATATONIA, SEDATION AND PTOSIS :

		Catatonia					Sedation					Ptosis				
		2 nd	3 rd	4 th	5 th	6 th	2 nd	3 rd	4 th	5 th	6 th	2 nd	3 rd	4 th	5 th	6 th
Control	0	0.33± 0.21	1.16± 0.16	2 ± 0	0.33± 0.21	0.16± 0.16	0.16± 0.16	0.83± 0.16	0.66± 0.21	0	1.16± 0.16	0.33± 0.21	0.5± 0.22	0.16± 0.16	0	
GG-0.52	0	0.33± 0.21	0.5± 0.22	0.16± 0.16	0	0	0.33± 0.21	0.33± 0.16	0.3 ± 0.22	0	0	0	0	0	0	
KG -0.26	0	0.5 ± 0.22	0.66± 0.21	1.33± 0.21	0.5± 0.34	0.33± 0.21	0.33± 0.21	0.6 ± 0.22	0.33 0.21	0	0	0	0	0	0	
KG-0.52	0	0.5 ± 0.22	1.33± 0.33	1.17± 1.61	0.33± 0.21	0.33± 0.21	0.3 ± 0.22	0.5 ± 0.22	0.33± 0.22	0	0	0.16± 0.16	0.33± 0.21	0.33± 0.21	0	
KG- 1.0	0	0.33± 0.21	0.33± 0.21	0.16± 0.16	0	0	0.33± 0.21	0.33± 0.21	0.16± 0.16	0	0	0	0	0	0	

Data : Mean ± SEM

Effect on Experimental Chronic Fatigue Syndrome :

TABLE NO. 7 : EFFECT OF KUSHMANDADI GHRITA ON CHRONIC FATIGUE SYNDROME :

Group	Dose (ml/kg)	1	2	3	4	5	6	7 th day	7 days average
Control	---	176.66 ± 19.35	183.33 ± 21.22	182.5 ± 36.8	194.8 ± 18.6	200.4 ± 15.4	183.2 ± 23.7	198.5 ± 20.96	186.81 ± 3.36
G.G	0.52	184.5 ± 19.4	197 ± 13.61	174.33 ± 26.28	210.16 ± 7.157	177.3 ± 11.8	171.16 ± 22	176.5 ± 11.63	184.42 ± 05.38 ↓
KG	0.26	154.5 ± 36.67**	188.5 ± 41.8	172.5 ± 29.3	219.33 ± 11.88	141.8 ± 34.9	185.2 ± 23.3	191.2 ± 20	164.71 ± 21.8 ↓
KG	0.52	155.17 ± 17**	136.6 ± 42.60**	162.2 ± 24.8	104.6 ± 33.6*#	147 ± 32.19	145 ± 28	133.5 ± 48.29*	123.43 ± 19.64↓***
KG	1.0	133.5± 23.50***#	169.5 ± 24.43**	166.33 ± 23.25	127.0 ± 36.25**	156.33 ± 15.3	157.83 ± 22	200.16 ± 9.63	158.66 ± 09.20↓**

ANOVA : Significant, df = 22, F = 3.50, Data : Mean ± SEM, **p < 0.01, ***p< 0.001(Student unpaired't' test),
 # p<0.05, ##p <0.01 (Dunnet't' test), ♦p<0.01 (Student unpaired 't' test in comparison to Goghrita).

Anxiolytic Activity :

TABLE NO. 8 : EFFECT OF KUSHMANDADI GHRITA ON OPEN FIELD BEHAVIOUR OF MICE :

Group	Dose (ml/kg)	On set of activity (sec)	No. of squares crossed	No. of rearing	Freezing time
Control	---	9.6 + 6.74	60.83 ± 10.84	12.5 ± 2.41	28.17 ± 7.76
GG	0.52	1.16 + 0.48	41.66 ± 17.80 ↓	4.83 ± 1.62↓*	171 ± 63.43↑*
KG	0.26	0.16 + 0.17	105 ± 13.75↑**	23 ± 4.06↑**	---
KG	0.52	2.20 + 1.43	70.33 ± 20.18↑	10.33 ± 3.18↓	63.83 ± 47.94↑
KG	1.0	7.83 + 2.50	122 ± 20.6↑**	20 ± 4.19↑**	13.00 ± 05.98↓*
Diazepam	15mg/kg	12.33 + 5.88	28.5 ± 14.30↓	03 ± 1.69↓*	220.8 ± 23.5↑***

ANOVA : Significant, * p <0.05, DF = 30, F = 3.932, 5.754, 22.71, Data : Mean ± SEM, *p < 0.05, ** p < 0.01,
 *** p < 0.001 (Student unpaired't' test), **a p<0.01 in comparison to Goghrita control group

TABLE NO. 9 : EFFECT OF TEST DRUG ON ELEVATED PLUS MAZE TEST :

Group	Dose (ml/kg)	Onset of activity (sec)	Time (in sec) spent in open arm	No entries in open arm (frequency)
Control	Control	0.83 ± 0.30	31.66 ± 10.21	2.67 ± 0.57
GG	0.52	5.5 ± 2.10	(17.00 ± 12.13)	1.83 ± 0.42
KG	0.26	5.5±2.14	00.00	5.17 ± 0.74 ^{aa}
KG	0.52	10.83 ± 8.66	47.5 ± 7.80	0.50 ± 0.5 ^{**}
KG	01.0	1.16 ± 0.75	65.0 ± 13.83	5.17 ± 0.74 ^{aa}
Diazepam	15	14.8 ± 9.18	40 ± 21.32	1.33 ± 0.42

ANOVA : Significant, (Frequency) $p < 0.02$ $df = 30$, $F = 7.74$, Data : Mean ± SEM, * $p < 0.05$, ** $p < 0.01$, # $p < 0.05$ (Dunnett 't' test), *^a $p < 0.01$ in comparison to Goghrita control group.

Effect on Learning and Memory :

TABLE NO. 10 : EFFECT OF KUSHMANDADI GHRITA ON TRANSFER LATENCY ON DIFFERENT DAYS AND AFTER THE TREATMENT OF CLOZAPINE :

Groups	Dose (ml/kg)	Initial Transfer Latency (Sec.)	Transfer Latency (Sec.) after 24 hours	Transfer latency 1 hours after clozapine (72 hours) (Sec.)
Control (Normal-without clozapine)	---	55.00 ± 09.41	20.16 ± 2.51 ^{***a}	19.00 ± 3.16
Control + Clozapine		41.50 ± 09.96	50.16 ± 14.04	129.00 ± 32.83 ^{**b}
KG + Clozapine	0.26	57.83 ± 12.87	28.83 ± 10.48	15.16 ± 2.38 ^{**c}
KG + Clozapine	0.52	54.50 ± 11.57	19.00 ± 8.13	18.16 ± 7.43 ^{**c}
KG + Clozapine	1.00	52.83 ± 10.47	70.16 ± 28.70	90 .00 ± 29.08
GG + Clozapine	0.52	75.16 ± 09.44	62.33 ± 16.37	94.33 ± 29.67

^{***a} $p < 0.01$ in comparison to Initial value in the same group (paired't' test),

^{**b} $p < 0.01$ in comparison to normal control animals,

^{**c} $p < 0.01$ in comparison to Control + Clozapine group.

In Goghrita administered group a moderate decrease in the CNS activity was observed and in contrast to this a bi-phasic effect was observed in the Kushmandadi ghrita administered group. In which an initial depression followed by stimulation was observed. This indirectly indicates that the Kushmanda *per se* has CNS stimulation effect. To obtain further clarification the results obtained with hypnotic potentiation test were analyzed. A moderate non-significant shortening was observed in Goghrita administered group in comparison to normal control. This moderate shortening was found to be reversed in Kushmandadi ghrita administered groups. This shows that Goghrita *per se* has complex effect that cannot be simply classified as CNS depressant and the same inference holds good for different doses of Kushmandadi ghrita. The latency of onset of PBN sleeping was found to be significantly shortened in lower and higher dose Kushmandadi ghrita administered group (Table-2) indicating facilitation of the entry of the drug in to the CNS. (Table-2)

The test drugs did not protect the experimental animals against the electro-convulsions indicating that they do not possess anti-convulsant effect of any significance.

The duration required for the regaining of the righting reflex after exposure to electric shock was significantly shortened in Goghrita and Kushmandadi ghrita administered group (lower and intermediate dose) in comparison to normal control group (Table-3). This may perhaps be indicative of anti-stress or adaptogenic effect in the formulation and ghrita *per se* enhancing the general resistance power of the animal. This effect was surprisingly not observed at higher dose level. (Table-3).

Analysis of the data obtained in d-amphetamine stereotypy and CAR test clearly indicate that at the dose level studied the test formulations do not have any anti-psychotic activity. In the tunnel board test- Goghrita *per se* had no effect on the exploratory behavior at the first minute of observation but significant decrease was observed when the data of different tunnels entered during the entire observation period is taken into consideration (Table-4). This indicates exploratory behavior suppression effect in Goghrita *per se*. This suppression was found to be reversed by the administration of Kushmandadi ghrita at different dose levels. At higher dose level Kushmandadi ghrita produced increased exploratory activity. In Goghrita administered group a moderate decrease in the

total number of tunnels entered was observed. This indicates CNS depression. This was not seen in lower and higher dose.

In Kushmandadi ghrita administered groups, at intermediate dose no effect was observed. At higher dose the observed increase in the total number of tunnels entered was found to be statistically significant in comparison to Goghrita alone administered group. Increase in the total number of tunnels entered is indicative of CNS stimulation. This indicates that the test drug has complex effects on CNS sometimes producing stimulation and sometime producing depression depending the dose and experimental condition. Taking all the parameters into consideration it may be suggested that the test preparation has no anti-psychotic activity but produces complex behavioral changes, which cannot be easily categorized into CNS depression or stimulation.

In the behavioural despair test in Goghrita administered group prolongation of mice immobility was observed. In Kushmandadi ghrita administered group, (at lower dose a significant shortening of the duration of mice immobility, at intermediate dose a moderate) but statistically non-significant shortening and at higher dose level a non-significant prolongation was observed (Table-5). Significant shortening is indicative of presence of anti-depressant activity. Based on this it can be suggested that the test drug Kushmandadi ghrita possess significant anti-depressant activity at lower dose level, moderate anti-depressant activity at intermediate dose level and no anti-depressant activity at higher dose level. Thus this effect is dose dependent. Being compound preparation it is possible that at higher dose level the concentration of active principle that may interfere with the anti-depressant effect may become dominant counter acting the anti-depressant activity observed at lower dose levels. In reserpine effect reversal test ptosis was completely antagonized (this was seen with Goghrita alone administered group) and sedation was moderately antagonized (Table-6). If we take into consideration the activity profile in both the tests it can be suggested that the test preparation possesses moderate to significant anti-depressant activity. Probable mechanism(s) of antidepressant effect of the test preparation could be suggested as follows : a) Inhibition of uptake of monoamines, b) increased monoamine transmission by binding to the monoamine transporter, c) by increasing monoamine release from their vesicles, d) inhibition of MAO, e) stimulation of A1-neurosteroids receptor, f) blocking of NK, neurokinin receptor further studies on the plant constituent for these mechanisms would be quite rewarding.¹⁶

A significant decrease in the duration of immobility when taken as an average of 7 days reading which can be considered as the index of chronic fatigue syndrome was observed especially at intermediate and higher doses (Table-7). This shows that the preparation could be of significant benefit in the treatment of chronic fatigue syndrome.

CFS has multifactor etiology, important among them are abnormality of hypothalamic - pituitary - adrenal axis; mild hypocortisolism of central origin, decrease in the plasma level of catecholamine metabolites and increase in the basal level of plasma 5-HT metabolites. It can be suggested that the test drugs by acting at several sites in the CNS modulate the factors that are responsible for the appearance of CFS (Table-7).

In the elevated plus maze test, at the lower dose level a pro-anxiety activity, whereas at intermediate dose a moderate anti-anxiety activity and at higher dose level a significant anti-anxiety activity was observed (Table-9) which indicates dose dependent anti-anxiety activity of the test drug. In the open field behavior test freezing time was significantly prolonged by Goghrita. This prolongation was shown to be significantly decreased at lower and higher dose level whereas a moderate decrease was observed at the intermediate dose (Table-8). Taken the result of both test together it can be suggested that the test formulation has dose dependent anti-anxiety activity.

Benzodiazepines are the widely used drugs for the treatment of anxiety. They produce their pharmacological effect by binding to the site specific for them situated adjacent to the receptor of GABA¹⁷. Among the other mechanisms involved in anxiolytic activity expression is stimulation of 5-HT_{1A} - receptor. This is an inhibitory autoreceptor that reduces the release of 5-HT and other mediators and causes anxiety suppression. Many other neurotransmitters and receptors have been implicated in anxiety and panic disorders like noradrenaline and neuropeptide such as cholecystokinin and substance P. It can be suggested that the test formulation produces anti-anxiety activity by modulating selectively the above-mentioned factors. (Table-8, 9).

The effect of test drugs on memory was evaluated by noting their performance on elevated plus maze. Here the protocol of 3 consequent days was followed, in which on first day acquisition was noted. On the second day, the retention / consolidation (memory) was examined by noting the difference between the transfer latencies of 2nd and 1st day. Afterwards on third day effect on drug induced amnesia in elevated plus maze was noted.

In clozapine administered control group the transfer latency, unlike the shortening observed in normal control, was not affected indicating that it is interfering with the acquisition of memory. This effect was significantly reversed by the lower and intermediate doses of the Kushmandadi ghrita; surprisingly the reversal was not significant at higher dose level (Table-10). This activity profile is a clear indication of the fact that the test formulation by interfering with the amnesic effect of clozapine shows that it has memory enhancing and learning facilitating effect.

Administration of Goghrita has no effect on the performance of the mice on the rota rod in comparison to control group. At lower and intermediate dose levels Kushmandadi Ghrita did not produce any effect on muscle tone and balance. At higher dose level effect of one mouse was affected at 40 minute and 3 hour after drug administration.

CONCLUSION

Kushmandadi ghrita produces a complex pattern of CNS activity. The effect cannot be easily categorized in to CNS stimulation or depression on the basis of gross behavior test. In some of the tests the observed effect is dose dependent. The data generated during the study indicate presence of significant anti-depressant, anti-anxiety and memory and learning enhancement activities. It also produced very good effect in the experimental model representing chronic fatigue syndrome which should be considered as a significant finding of the present study. The formulation is devoid of anti-convulsant, central muscle relaxant and anti-psychotic activities.

REFERENCES

1. Vagbhata, Ashtanga Hridaya, Uttara sthana 7/28, edited by Pt. Hari Sadashiv Shastri Padarakara, Chaukhambha Surabharati Prakashan, Varanasi, 2002.
2. Clara Morpurgo Arzaeim - Forsch 21(1), 1727 "New design for the screening of CNS active drugs in mice", 1971, P-1727-1734.

3. Gaitonde B.B., Kulkarni M.J., Joglekar S.N., Nabar S.D., 1980, Bull Medico, Ethno. Bot. Res.1(2) : 240.
4. Goodman L.S., Grewal M.S. Brown B.C., Swinyard E.A., "Comparision of maximal seizure evoked by pentylenetrazol and electric shock in mice and their modification by anti convulsants", 1953, J. Pharmc. Exp. Ther., 108, 168-176.
5. Shillito E. "A method for investigating the effect of drugs on the exploratory behavior", 1970, British Journal of Pharmacology, 40, 113.
6. Valame S.P., Gupta K.G., "Effect of clonidine on amphetamine induced stereotype" 1981, Ind. J. Pharmac. 13(2), P-203-204.
7. Maffi. G. 1958 "The secondary conditioned response of rats and the effect of some psycho-pharmacological agents." Journal of Pharmacy and pharmacology, Vol.11, P-129-139.
8. Porsolt R.D. Bartin A., Jalfre M. "Behavioural 'despair' in mice - A primary screening test for anti depressants" 1977, Arch. Int. Pharmacodyn, 229, 327-336.
9. Sheth U.K., Dadkar N.K., Kamath U.G. 1972 in selected Topics in Experimental Pharmacology, ISI, Kothari Book Depot, Bombay.
10. Kaur G. and Kulkarni S.K., "Reversal of forced swimming induced chronic fatigue in mice by anti depressant and herbal psychotropic drugs." (1998) Ind. Drugs 35, 771.
11. Bhattacharya et. al. 1993, Manual Pre-conference workshop on Research Methodology in Pharmacology, 3.
12. Pellow, S., Chopin, P., File, S.E. and Briley, M., J.Neurosci. Meth. 14: 149-167, 1985.
13. Kulkarni S.K., 2003, in Hand book of Experimental Pharmacology, 54, Vallabh Prakashan, Delhi.
14. Bansinath M. Chandra Bose A, Hema S, Guruswamy MN. Interaction of metamizol with some hypnotic in rats. Arch Int Pharmacodyn 1977; 229: 327-336.
15. Paget G. E., Barnes J. M.; 1969 Evaluation of drug activities, pharmacometrics eds. Lawrance D. R. and Bacharach A.L. Vol. 1. Academic press New York), 170.
16. Kramer M.S., Catler N., Feighner J., Shrivastava R., Carmen J., Sramek J.J., Knowles E., et al. The journal of Pharmacology and Experimental Therapeutics, Vol.281, 1640-1645, 1998.
17. Mycek M.J. 2000, Lippincott's Illustrated Reviews Pharmacology 2090, 2nd edition 89, 99, 199, Lippincott Williams and Wilkins, Philadelphia.
18. Sandford J.J.; Aggyropoulos S.U.; Natt D. J. (2000); the Psychobiology of anxiolytic Drugs, Part I Basic Neurobiology, Pharmacol. Thera.; 88; 1497; 1952.

हिन्दी सारांश

कूष्माण्डादि घृत का केन्द्रीय नाड़ी संस्थान के क्रिया-कलापों पर प्रायोगिक अध्ययन

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प्रस्तुत शोधपत्र कूष्माण्डादि घृत (कूष्माण्ड, यष्टिमधु, गोघृत) का प्रायोगिक जन्तुओं के केन्द्रीय नाड़ी संस्थान की विभिन्न क्रियाओं पर अध्ययन को दर्शाता है। यह शास्त्रीय औषध योग-कूष्माण्डादि घृत नाड़ी संस्थान पर औषध मात्रा के अनुसार प्रभावकारी है। अध्ययन के सांख्यिकीय परीक्षण से स्पष्ट होता है कि कूष्माण्डादि घृत में निश्चित रूप से चित्तोद्देग और अवसाद विरोधी प्रभाव है। साथ ही साथ यह औषध योग थकावट, स्मृति और मस्तिष्क की क्रियाओं को उत्तेजित कर सीखने की प्रक्रिया में भी सहायक है। आयुर्वेद में मानसरोगों में इसका सफलतापूर्वक प्रयोग किया गया है।

