

Neuropharmacological study of some Ayurvedic medicinal plants

JMA Hannan¹, Masum Shahriar^{2*}, M Naimul Islam³, Mafruhi Sattar³, Sabera Haque³ and MSK Choudhuri³

¹Department of Pharmacology, Research Division, BIRDEM, Dhaka-1000; ²Department of Pharmacy, Gono Bishwabidyalay, Nayarhat, Savar, Dhaka-1344; ³Ethnopharmacology Laboratory, Department of Pharmacy, Jahangirnagar University, Savar, Dhaka-1342

SUMMARY

Water extract (kwath) of six different widely used Ayurvedic medicinal plants were tested in mice for possible neuropharmacological efficacy. In the present experiments it was observed that a number of plant tested causes a significant level of Central Nervous System (CNS) depression, in that it significantly decreased the spontaneous Motor activity, and also lowered the exploratory behavior of the treated animals. *Terminalia chebula* (HAA), *Terminalia bellerica* (BHA), *Emblica officinalis* (AA), *Piper longum* L. (PP). exhibited depressant action of on the CNS. Apart from them a mild to moderate degree of depression was evident as a consequence of administration of *Zingiber officinale* Rosc (SUT), *Piper nigrum* L. (MRC). However, none of the plant tested did not exhibit significant effects on pentobarbital induced narcosis, and this indicated that the sedating effects of the drug was not associated with the risk of fatal consequences on overdose.

Key Words: Neuropharmacological; Triphala; Trikatu; *Terminalia chebula*; *Emblica officinalis*; *Terminalia bellerica*; *Piper nigrum*; *Piper longum*; *Zingiber officinale*

INTRODUCTION

Three fruits of the plants namely Haritaki (*Terminalia chebula* Retz), Bahera (*Terminalia bellerica* Roxb), and Amlaki (*Emblica officinalis* Gaertn. syn. or *Phyllanthus emblica* Linn., Euphorbiaceae are essential constituents of drugs called 'triphala'. There are various kinds of triphalas used for the cure of various ailments like the disease of the Central Nervous System, brain, eye, nose and ear. These are also effective for relieving constipation, strengthening the intestine, stomach and liver. *Emblica officinalis* (*Phyllanthus emblica*) is considered to be a refrigerant, diuretic, laxative and purifier of the humors of the body. It is also applied externally on account of its cooling and astringent properties. It is the richest source of Vitamin C and is used as an antidote against scurvy. The raw fruit is aperient and the dried fruit is useful in hemorrhage, diarrhoea and dysentery.

In combination with iron, it is used in anaemia, jaundice and dyspepsia (Said, 1978). *Terminalia chebula* is considered to be a powerful alternative. tonic, laxative and stomachic. Seven varieties of 'Haritaki' are described which are nothing more than the same fruit in different stages of maturity. The ripe fruits are chiefly used as purgative and is considered to be able to remove bile and phlegm (Dymock, 1972). *Terminalia bellerica* is considered to be an astringent, tonic, palliative, and aperient. It is used as a remedy against flatulence, dyspepsia and other digestive disturbances where drugs, increasing the secretion of bile, are generally indicated. Effects (Tariq, 1977) of alcoholic extracts of fruits of *Emblica officinalis* and *Terminalia bellerica* (1 g/kg., p. o. on two consecutive days) were studied in rats after isoproterenol induced (85 mg/kg., s. c. on 2 days) myocardial necrosis. The effects of the extract were studied 48 hours after the first injection of isoproterenol. There was a marked decrease in cardiac glycogen and rise in levels of serum enzymes in the group treated with isoproterenol. Cardiac glycogen level significantly decreased in

*Correspondence: Masum Shahriar, Lecturer, Department of Pharmacy Gono Bishwabidyalay, Gonoshayasthya Kendra, Savar, Dhaka1344 Bangladesh. Tel: 8802-7708004; E-mail: smasum@bdcom.com

the group treated with *E. officinalis*. Levels of serum GOT, GPT and LDH were significantly less in groups treated with *E. officinalis* and *T. belerica*. The extracts also produced marked changes in serum fatty acids. Phyllembin (ethyl gallate) obtained from the fruits of *E. officinalis* has been found to potentiate some of the pharmacological actions of adrenaline (Said, 1969) in vitro and in vivo. Besides it shows a mild depressant action on central nervous system and has spasmolytic activity. Chebulin, which is present in the fruits of *T. chebula* (Inamdar *et al.*, 1962) has depressant actions on the myocardium and blood vessels of rabbit. There is a vasodilatation in the coronary artery and on the peripheral blood vessels of rabbits and rats. A moderate fall in blood pressure, in anaesthetized cats as well as in the spinal cat, was observed. It has antispasmodic action on the intestine of cat, rabbit and guinea pig. The pharmacological actions of water extract, alcohol extract and phyllembin (ethyl gallate) of the fruit of *T. belerica* (Siddiqui, 1963) was studied on nembutal anaesthetized dogs. The alcoholic extract was found to increase the bile secretion while the water extract and phyllembin had hardly any effect. The alcoholic extract also increased the total solid content in bile. Increase in the total solid content in bile may be useful in digestive disorder. The relaxation of the intestine may slow down the peristalsis and thereby assist in better digestion of the food and absorption of the resulting materials. The alcoholic extract has a muscular relaxation activity similar to papaverine. It also produced a fall in blood pressure. The drug was found to be non-toxic up to a dose equivalent of 5 gm/kg, when given orally to mice. Bile salts are formed in the body, by liver, from cholesterol in the blood. Normally these bile salts are reabsorbed through the gut wall and recycled with a loss of only up to 15 to 20 percent of the total content, each day. So far, the constituents responsible for the curative properties of the three fruits have not been identified. It is observed that the water extract of *T. belerica* had no activity, whereas alcoholic extract increased the bile flow. The above observation indicates that the active constituents of *T. belerica* are not soluble in cold water, may be that these are soluble in boiling water. Till the active constituents are identified, it is

better to use the three fruits in powder form. Beta-sitosterol (Edgar, 1972) also lowers cholesterol level. This is present in *T. belerica* and may also be responsible for the hypocholesterolemic activity of the plant. The other two plants namely *T. chebula* and *E. officinalis* have not been tested for this activity. Triphala is reputed to be useful for lowering blood pressure.

Piper nigrum, *P. longum* and *Zingiber officinale* individually or in combination are very frequently included in a large number of Ayurvedic prescriptions. In combination this three plants are popularly known as Trikatu. To investigate the possible scientific basis of the extensive usage of these three herbals, their effects were studied on bioavailability of vasicine. Trikatu, as a whole, influenced bioavailability to a greater extent. Individually, *P. longum* as well as *P. nigrum* were found to be almost equi-effective in enhancing the bioavailability of vasicine in rats, while piperine (suspension) in 40 mg/kg dose, when co-administered orally with vasicine enhanced the bioavailability of the latter by more than 300 percent (Atal *et al.*, 1981; Zutshi & Kaul, 1982). Atal *et al.* (1984, 1985), studied the biochemical basis of enhanced drug bioavailability by piperine, through the interaction of piperine with enzymatic drug biotransforming reactions in hepatic tissue in vitro and in vivo. Piperine inhibited arylhydrocarbon hydroxylation, ethylmorphine-N-demethylation, 7-ethoxycoumarin-O-demethylation, and 3-hydroxy-benzo(a)pyrene glucuronidation in rat postmitochondrial supernatant in vitro in a dose dependent manner. The studies demonstrated that piperine is a non-specific inhibitor of drug metabolism showing little discrimination between different cytochrome P₄₅₀ form. Oral administration of piperine in rats strongly inhibited the hepatic arylhydrocarbon hydroxylase (AHH) and UDP-glucuronyltransferase activities. The maximal inhibition of AHH was observed within one hour was restored to normal value in six hours. Pretreatment with piperine prolonged hexobarbital sleeping time and zoxazolamine paralysis time in mice. In an investigation with six volunteers, Trikatu extract did not enhance the bioavailability of rifampicin. On the other hand, the bioavailability was reported to be reduced (Dahanukar *et al.*, 1982). In another investigation with six human volunteers, Trikatu powder, showed

an effect similar to that of the extract on the bioavailability of rifampicin. The powder, however, appeared to bring about more uniformity in absorption of rifampicin (Dahanukar *et al.*, 1983). In a double-blind clinical study carried on 240 children (age ranging from neonatal period to 12 years) suffering from bronchial asthma were administered orally with *P. longum* for two to three total courses. Each course constituted a gradual daily increase of the dose of *P. longum* from a minimum of 1 gm to a maximum of 30 gm (depending on the age) and then the daily dose was gradually reduced to the original level. In 60 patients, significant effect in controlling the frequency and severity of the asthmatic attacks was observed (Fernandez *et al.*, 1980). In another open trial on 20 paediatric patients of asthma (aged 1-2 years) *P. longum* (powder in capsules) was administered with milk, in a gradually increasing dose for a period of 5 weeks. The serum IgE levels estimated in 6 patients did not yield any conclusive results. At the end of 1 year, 3 out of 20 patients failed to show satisfactory response. Three others who had a history of allergy to certain food items could consume these very food items and tolerate them well after this treatment (Dahanukar *et al.*, 1984).

MATERIALS AND METHODS

Following nine plants are used in this experiment:

Scientific name	Local name	Part used	Human dose
1. <i>Emblica officinalis</i> Gaertn. (AA)	Amloki	Fruit rind	6 gm
2. <i>Terminalia chebula</i> Retz. (HH)	Hari-taki	Fruit rind	6-12 gm
3. <i>Terminalia bellerica</i> Roxb. (BHA)	Bahera	Fruit rind	3 gm
4. <i>Piper longum</i> L. (PP)	Pepul	Fruit	0.5 gm
5. <i>Piper nigrum</i> L. (MRC)	Marich	Fruit	0.5 gm
6. <i>Zingiber officinale</i> Rosc. (SUT)	Shut	Rhizome	0.5 gm

Experimental animals

The experimental animals, used in this research work, were mostly mice [crl: CFW (Swiss Webster) BR]. They were kept in cages having dimensions of 30×20×13 cm and soft wood shavings were employed as bedding in the cages. The animals were fed with

“mouse chow” (prepared according to the formula developed in the BCSIR, Dhaka) and were provided with tap water. All animals were given four days rest, before being employed in different tests, to adjust themselves with the new environment and to get over the food and water restrictions incurred during transit.

Preparation & feeding of the drugs

All the plants AA, BHA, HAA, MRC, SUT, PP were fed to the test animal as kwath (water extract). 25 gm powder of these drugs were added to 400 ml of distilled water and boiled till the volume was reduced to one quarter of the original. The kwath was filtered through thick cloth. Each of these kwath was given in dose of 1 cc/25 gm of body weight. The Control group of animals were simultaneously fed with equal volume of 0.9% normal saline.

Experimental procedure:

1. Spontaneous motor activity test

For this experiment, brick chip displacement method, a modified version of the sand displacement method of Siegmund and Wolf (1952), was employed. The displaced brick chips, through the wire nettings, due to the spontaneous motor activity of the animals, were recorded with 5 minutes interval for a period of one hour.

2. Amphetamine induced hyperactivity test

This experiment was also carried out by the previously described method of spontaneous motor activity test (Siegmund, 1952). The test drugs were administered one hour prior to administration of amphetamine in a stimulant dose of 4 mg/kg (Vane *et al.*, 1961).

3. Climbing out test

This experiment was carried out by the method of Sandberg (1957) The animals were put in a cage with dimension of 60×50×30 cm and having dark walls. Animals were supplied with a ladder and the time taken to climbs out of the cage was recorded for a maximum period of 10 minutes.

4. Open field test

In this experiment, the method of Gupta (1971) was

employed. The floor of an open field of half square meter was divided in to a series of squares, each alternatively coloured black and white. The apparatus had a wall of 40 cm. The number of squares, travelled by the animal, was recorded for a period of two minutes.

5. Hole board test

This experiment was carried out by the method of Nakama (Nakama *et al.*, 1972). 16 holes, each 3 cm in diameter were presented to the mouse in a flat space of 25 square centimeter. Each animal was transferred carefully to the corner of the field and the number of holes passed, head dipping and the number of fecal boluses excreted, was recorded for a period of two minutes.

6. Hole cross test

In this experiment, the method of Takagi *et al.* (1971) was employed. In a box having dimension of 30×20×14 cm, a hole of 3 cm in diameter at a height of 4.5 cm from the floor was constructed on the dividing wall. Spontaneous movement of the animals through the hole from one chamber to the other, was counted for a period of 2 minutes. The observation was conducted 30, 60, 120 and 240 minutes after oral administration of test drugs and was compared with control animal administered with normal saline.

7. Hot plate test

To study the narcotic analgesic activity of test drugs, the hot plate test was carried out by the method of Woolfe and MacDonald (1944). The animals were exposed to a hot plate with a temperature of 55±1°C and true taken to experience the heat, indicated by paw-licking or jumping was record.

8. Pentobarbital sleeping time test

In this experiment the method of Tedeschi and Tedeschi (1968) was employed. The drugs were administered p.o. and 60 minutes later pentobarbital, in a sub-hypnotic dose of 45 mg/kg was administered by the i.p. route. The time interval between the loss of righting reflex and the recovery of reflex was recorded for each mouse and thus the average sleeping time was determined.

9. Sedative ataxia test

This experiment was carried out by the method of Bastian (1961). The animals were observed for tolerance of back or side position, for their ability to grasp and to slide down from a vertical pole (39.4 cm high and 0.95 cm thick) and for their ability to walk on a wire net. The animals were scored according to their performance on these three instruments by the following method.

Score	Toleration of side or back position	Activity on vertical pole	Activity on inclined screen
0	No	Grasps pole and walks down	Moves actively on screen
1	No	Grasps pole and slides down	Moves actively on screen
2	No	Grasps pole and slides down	Cannot move or only sluggishly
3	No	Cannot grasp pole	Cannot move or only sluggishly
4	No	Cannot grasp pole	Cannot hold on to screen
5	Yes	Cannot grasp pole	Cannot hold on to screen

Statistical analysis

The mean and Standard error of the mean (SE.) of the results were calculated and a student's t-test or paired t-test was applied: $p=0.05$ was taken to be the significant level. (Glasnapp and Poggio, 1985).

RESULT AND DISCUSSION

Spontaneous motor activity test

General behavior may be considered to be the result of integration of inputs deriving from the environment, impinging upon the central nervous system and thus the peripheral capacity of an organism to deliver a response or a coordinated sequence of responses (Valzelli, 1973). A common technique, employed by the ethologists in evaluating behavioral effects of a drug, is to observe its effect on the spontaneous motor activity. As such, the first test performed was on the central nervous system and was involving the spontaneous motor

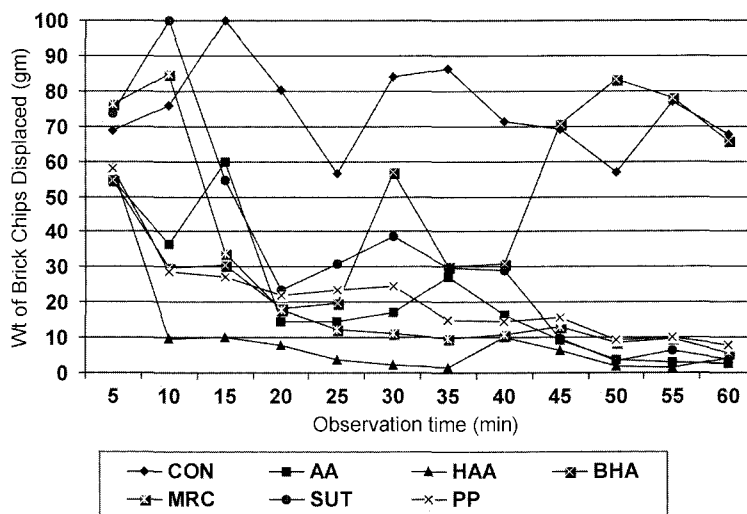


Fig. 1. Graphical presentation of spontaneous motor activity test.

activity test.

The experimental data (Fig. 1) shows that HAA, AA, BHA reduced spontaneous locomotor activity. Of these HAA reduced spontaneous locomotor activity more significantly ($p < 0.01$). MRC, SUT and PP also markedly reduced locomotor activity. The locomotion effect of PP was found to be more prominent.

Amphetamine induced hyperactivity test

Once it was established that some of tested components possess a retarding effect on the

spontaneous motor activity, interest was focused on whether these drugs have any effect on the locomotor activity of the excited animals. The amphetamine induced hyperactivity experiment was designed to find out whether the drug can suppress the hyperactivity, in animals induced by amphetamine. The experimental data (Fig. 2) suggests that AA, BHA and HAA exhibited a marginal reducing effect, although the effects were found to be statistically insignificant on the amphetamine induced locomotion. PP produced reducing effect on spontaneous movement of the amphetamine

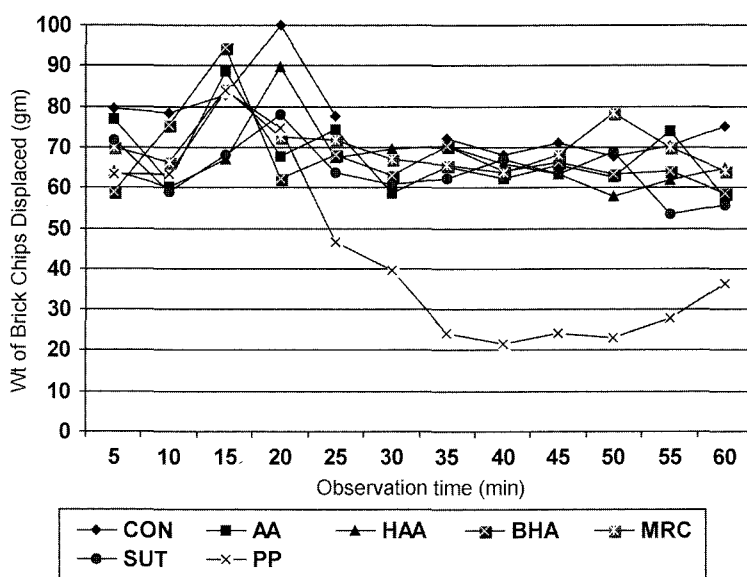


Fig. 2. Graphical presentation of amphetamine induce hyperactivity test.

treated mice. However the effects of MRC and SUT were found to be insignificant.

Climbing out test

Exploration is a broad category of behavior, the consequence of which are to provide the organism with information about the exteroceptive environment (Berlyne, 1960). Any changes in the surrounding lead to a marked increase in exploratory behavior, so that an effective way of inducing a high level of activity, on demand, is to place the animal on unfamiliar or partly familiar environment. This served as the basis of the experiments performed to investigate the effect of the drug on exploration. Here special task is assigned. Data from the climbing out test (Table 1) show that all of the three constituents of Triphala (AA, BHA and HAA) reduced the exploratory behavior of the treated animals. More pronounced action was observed after 1 hour of the drug administration of HAA and BHA. Whereas after 2 hour of the administration of AA, highly significant ($p < 0.001$)

effect was observed. MRC, SUT and PP also showed significant reduction in the exploratory behaviour of the treated animals.

Open field test

It has been experimentally proven that, in the absence of a special task to perform, the behavior of a given animal tend to maintain that inner activation level that is, at times, inconsistent with the actual level of activation of the animals. In order to get as accurate a picture as possible, on the effect of the drug on exploration, the open field test was performed. AA, BHA and HAA reduced exploration in the open field test. However, only the effect of HAA was found to be significant. MRC and PP produced marked reducing effect on the exploration. After half an hour of the drug administration of MRC and after one hour in case of PP, both of them produced a mark reducing effect on the exploration. SUT produced negligible effect on treated animals. Result of this test was presented in Table 2.

Table 1. Tabular presentation of climbing out test

Groups	Time of study				
	0 min Mean \pm S.E.	+ 30 min Mean \pm S.E.	+60 min Mean \pm S.E.	+120 min Mean \pm S.E.	+240 min Mean \pm S.E.
Control	89.83 \pm 16.78	90.16 \pm 14.54	76.67 \pm 11.70	92.83 \pm 14.79	112.30 \pm 18.69
AA	66.67 \pm 8.63	154.20 \pm 42.48	282.5 \pm 94.68	581.3 \pm 17.04 ^a	383.6 \pm 17.04
HAA	142.0 \pm 14.21	151.8 \pm 49.13	347.3 \pm 93.51 ^c	83.33 \pm 194.5	165.0 \pm 45.37
BHA	40.37 \pm 6.01	59.67 \pm 11.94	242.7 \pm 104.5	135.3 \pm 84.94	160.8 \pm 80.88
MRC	54.0 \pm 16.73	600.0 \pm 0.0 ^a	600.0 \pm 0.0 ^a	574.2 \pm 23.58 ^a	525.0 \pm 68.46
SUT	46.0 \pm 7.53	270.8 \pm 98.62	508.7 \pm 60.64 ^b	426.2 \pm 91.04 ^c	386.5 \pm 91.44 ^c
PP	61.16 \pm 8.04	273.7 \pm 98.23	243.2 \pm 88.06	318.5 \pm 88.06	147.2 \pm 82.79

^aindicates $p < 0.001$, ^bindicates $p < .01$, ^cindicates $p < 0.05$

Table 2. Tabular presentation of open field test.

Groups	Time of study				
	0 min Mean \pm S.E.	+ 30min Mean \pm S.E.	+60min Mean \pm S.E.	+120min Mean \pm S.E.	+240 min Mean \pm S.E.
Control	87.33 \pm 3.57	80.17 \pm 6.63	66.33 \pm 6.35	48.33 \pm 4.61	49.67 \pm 3.13
AA	82.17 \pm 11.16	73.39 \pm 9.40	63.17 \pm 6.55	26.83 \pm 5.28 ^b	16.17 \pm 5.18
HAA	98.83 \pm 8.36	48.17 \pm 7.14	36.67 \pm 4.17	29.50 \pm 4.56 ^b	12.17 \pm 1.95 ^b
BHA	108.5 \pm 3.88	51.17 \pm 5.45	45.17 \pm 6.29	46.67 \pm 3.8	30.67 \pm 2.57
MRC	93.83 \pm 5.75	2.83 \pm 1.12 ^a	1.67 \pm 0.90 ^a	0.67 \pm 0.45 ^a	2.67 \pm 1.15 ^a
SUT	84.67 \pm 6.57	76.50 \pm 7.54	66.00 \pm 3.74	42.33 \pm 3.34	51.00 \pm 4.51
PP	76.33 \pm 4.21	18.00 \pm 2.71 ^a	7.50 \pm 1.22 ^a	27.17 \pm 1.96 ^c	49.33 \pm 9.19

^aindicates $p < 0.001$, ^bindicates $p < .01$, ^cindicates $p < 0.05$

Hole board test

The Hole Board Test is somewhat related to the open field situation, but here animals are provided with a stronger stimulus for exploratory behavior, represented by the holes, which the animals explore by inserting their head into them. A pattern of behavior characterized by exploration, (head dipping through the holes), locomotion (ambulation past the holes) and emotional defaecation are evoked in the hole-board test. The result of the hole board test are given in Fig. 3, 4 and 5. A significant decrease in ambulation was observed in animals treated with AA, BHA, SUT and PP. No significant decreasing effect, except for a marginal reduction, was observed in, HAA, treated animals. A decrease in the exploratory head dipping was observed in

the group treated with AA, BHA, SUT and PP however this reduction is not statistically significant. No significant effect on head dipping was observed in the group treated with HAA. Most of the tested drug did not exhibit any significant effect on the defaecation.

Hole cross test

This test is also designed to evaluate effects on the exploratory behavior. In order to further investigate the effects of the drug on the exploratory behavior of the treated animals, this test was performed. Result of this test are given in Table 3. AA, HAA, BHA, C significantly reduced the exploratory activity of the treated animal and the animals showed less interest in crossing the hole, in

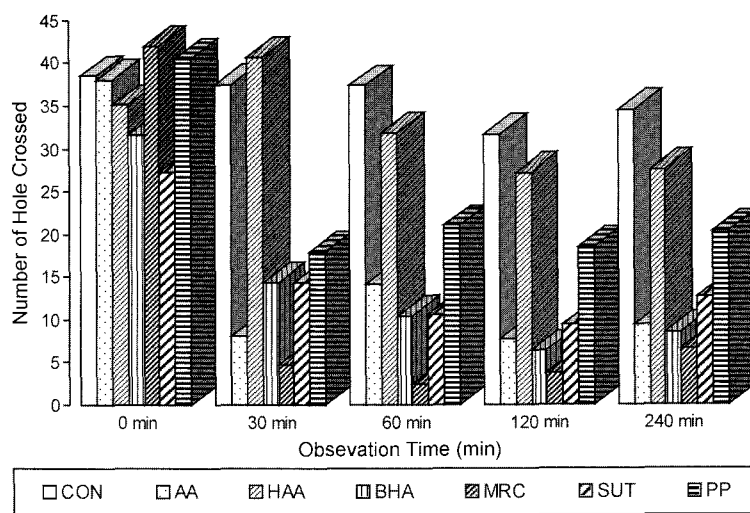


Fig. 3. Graphical presentation of hole board test (Ambulation).

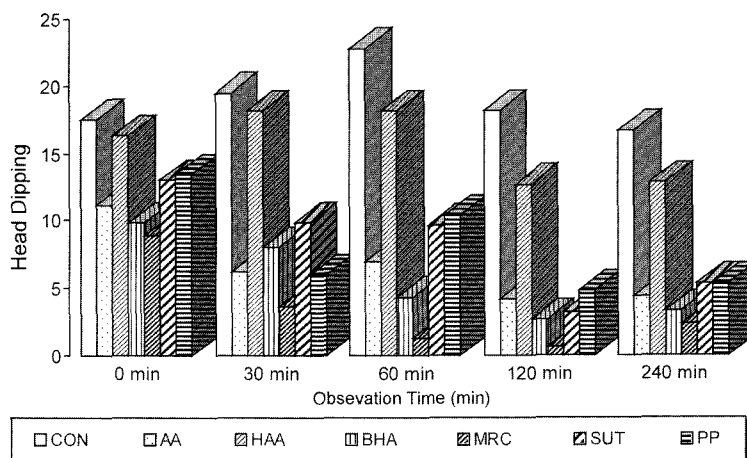


Fig. 4. Graphical presentation of hole board test (Head dipping).

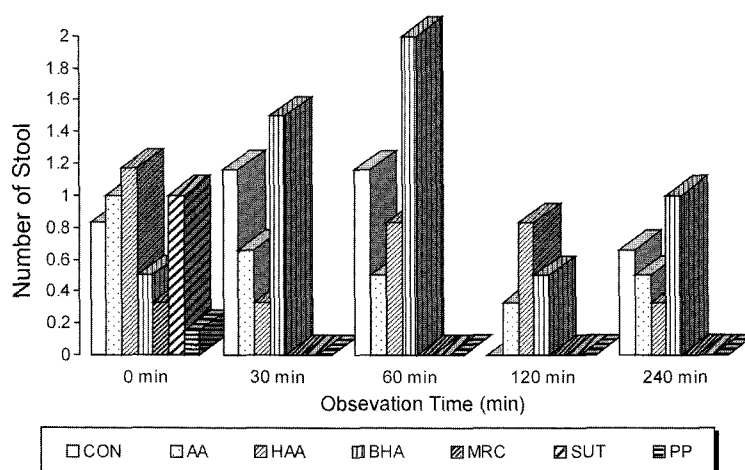


Fig. 5. Graphical presentation of hole board test (Defecation).

Table 3. Tabula presentation of hole cross test

Groups	Time of study				
	0 min Mean \pm S.E.	+ 30 min Mean \pm S.E.	+60 min Mean \pm S.E.	+120 min Mean \pm S.E.	+240 min Mean \pm S.E.
Control	6.38 \pm 0.44	5.67 \pm 0.93	5.83 \pm 0.77	6.13 \pm 0.68	5.17 \pm 0.86
AA	6.67 \pm 0.56	4.33 \pm 0.19	2.67 \pm 0.56	1.00 \pm 0.33 ^c	1.5 \pm 0.66 ^c
HAA	3.83 \pm 0.43	4.16 \pm 0.44	2.83 \pm 0.76	3.0 \pm 0.84	3.33 \pm 0.80
BHA	7.17 \pm 0.60	4.33 \pm 0.77	3.67 \pm 0.56	3.33 \pm 0.51	2.33 \pm 0.19
MRC	5.83 \pm 0.43	0.50 \pm 0.31 ^c	0.33 \pm 0.19 ^b	0.33 \pm 0.19 ^b	0.33 \pm 0.19 ^b
SUT	4.83 \pm 0.54	7.16 \pm 0.83	2.00 \pm 0.62	0.83 \pm 0.36 ^c	1.163 \pm 0.43 ^c
PP	6.33 \pm 0.69	0.33 \pm 0.19 ^b	0.50 \pm 0.31	2.17 \pm 0.83	5.83 \pm 1.04

^aindicates $p < 0.001$, ^bindicates $p < .01$, ^cindicates $p < 0.05$

comparison to that of the control animals. After 30 minutes of drug treatment MRC and PP showed significant ($p < 0.001$) lowering effect on exploratory behavior, but at that time SUT produced inverse effect and with the passage of time, the animals showed reduced interest in crossing the hole.

Pain perception test

The chances of a central nervous system depressant to produce analgesic activity by depressing the sensory afferent nerve fibers of the central neurons, is not very slim and as a consequence of that, the effects of the drugs on the pain perception time, were also evaluated. The experimental data, presented (Table 4) show that the drug BHA and PP produced a noticeable degree of analgesia, indicated by the increase in the time taken for pain perception. After 30 minutes of the study, PP exhibited a marked analgesic effect ($p < 0.01$). The

rest of the constituents did not show any significant analgesic effect.

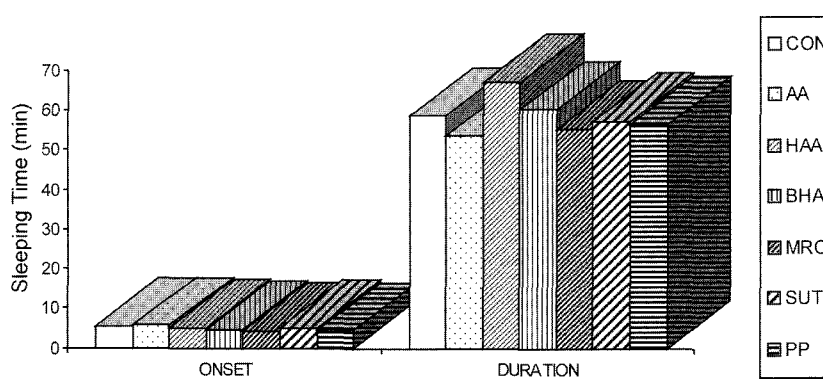
Pentobarbital induced sleeping time test

Many a central depressant elicit their effect by interfering with the functions of the cerebral cortex. A most important method of investigating the probable cortical manifestation of a drug is to check its effect on the pentobarbital narcosis as pentobarbital has multifarious effects on the cerebral cortex (Bowman and Rand, 1980). The pentobarbital sleeping time test was performed to find out whether the water extract of the plants have any effect on the cerebral cortex. The experimental data, presented (Fig. 6) show that most of the plants have no significant effect on both the onset and the duration of the action of pentobarbital.

Table 4. Tabular presentation of pain perception

Groups	Time of study (Sec)				
	0 min Mean ± S.E.	+30 min Mean ± S.E.	+60 min Mean ± S.E.	+120 min Mean ± S.E.	+240 min Mean ± S.E.
Control	12.33±0.38	13.50±0.39	12.0±0.47	12.17±0.54	13.16±0.54
AA	14.16±0.64	7.83±0.43	13.5±0.69	9.83±0.68	13.33±0.83
HAA	17.16±1.53	11.66±1.09	16.66±0.38	14.00±1.15	13.5±0.39
BHA	17.00±0.66	18.33±1.21	17.66±1.59	16.17±1.8	18.33±1.3
MRC	12.00±0.52	8.66±0.5	3.83±0.28	7.33±0.45	8.6±0.31
SUT	11.6±0.67	12.00±1.2	11.5±0.9	14.16±1.34	14.16±1.32
PP	14.8±0.65	36.4±4.7 ^a	29.83±2.71 ^a	30.17±2.38 ^a	30.00±3.42 ^a

^aindicates $p < 0.001$, ^bindicates $p < .01$, ^cindicates $p < 0.05$

**Fig. 6.** Graphical presentation of petobarbital induced sleeping time test.**Table 5.** Tabular presentation of sedative ataxic score

Groups	Time of study (Sec)				
	0 min Mean ± S.E.	+30 min Mean ± S.E.	+60 min Mean ± S.E.	+120 min Mean ± S.E.	+240 min Mean ± S.E.
Control	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0
AA	0.0±0.0	0.0±0.0	0.83±0.15	0.0±0.0	0.33±0.19
HAA	0.0±0.0	0.5±0.2	0.33±0.19	0.17±0.05	0.83±0.16
BHA	0.0±0.0	0.33±0.19	0.33±0.16	0.19±0.04	0.33±0.19
MRC	0.0±0.0	0.66±0.19	0.83±0.15	0.86±0.15	0.5±0.2
SUT	0.0±0.0	0.0±0.0	0.5±0.2	0.17±0.08	0.0±0.0
PP	0.0±0.0	0.33±0.14	0.5±0.19	0.5±0.2	0.17±0.05

^aindicates $p < 0.001$, ^bindicates $p < .01$, ^cindicates $p < 0.05$

Sedative ataxic score

In order to find out the presence of any muscular relaxant effect of the drugs, as happens with many a central depressants, the effect of the drugs on the sedative ataxic score was performed. The experimental results (Table 5) indicate that none of the plant tested produce any noticeable degree of ataxia in the treated animals.

REFERENCES

- Atal CK, Dubey RK, Singh J. (1985) Biochemical Basis of Enhanced Drug Bioavailability by Piperine: Evidence That Piperine is a Potent Inhibitor of Drug Metabolism. *J. Pharmacol. Exp. Therapeut.* **232**, 258.
- Atal CK, Zutshi U, Paro PG. (1981) Scientific Evidence on the Role of Ayurvedic Herbal on Bioavailability

- of Drugs. *J. Ethnopharmacol.* **4**, 229.
- Atal CK, Dubey RK, Singh J. (1984) Biochemical Basis of Enhanced Drugs Bioavailability by Piperine: Evidence that Piperine is a Potent Inhibitor of Mono Oxygenase System. Abstr of papers presented at XVI Ann Conf Dec 28-30, 1983. *Indian J. Pharmacol.* **16**, 52.
- Bastian JW. (1961) Classification of CNS Drugs by a Mouse Screening Battery. *Arch. Int.l Pharmacodyn Thera.* **133**, 347-364.
- Berlyne DE. (1960) Conflicts, Arousal and Curiosity, McGraw- Hill Publications Inc., New York, 147.
- Bowman WC, Rand MJ. (1980) Text Book of Pharmacology, 2nd edn. Black Well Scientific Publications, New York, 21.3.
- Cahen RL, Tvede K. (1952) Homatropine Methyl-bromide: A Pharmacological Reevaluation. *J. Pharmacol. Exp. Ther.* **105**, 166-177.
- Chakravarti HS. (1961) Cited in Advances in Research in Indian Medicine - 1970. B.H.U. Varanasi, 203.
- Chatterjee TK. (1993) Hand Book on Laboratory Mice and Rats, Department of Pharmaceutical Technology, 1ST edn, Jadavpur University, 157.
- Dahanukar SM, Kapadia AB, Karandikar SM. (1982) Influence of Trikatu on Rifampicin Bioavailability. *Indian Drugs.* **19**, 271.
- Dahanukar SA, Kapadia AB, Karandikar SM. (1983) Influence of Trikatu Powder on Rifampicin Bio-availability. *Indian Drugs.* **20**, 402.
- Dahanukar SA, Karandikar SM, Desai M. (1984) Efficacy of *Piper longum* in Childhood Asthma. *Indian Drugs.* **21**, 384.
- Dymock W. (1972) Pharmacographia Indica, Hamdard Foundation, Dhaka.
- Edgar SL. (1972) Beta-sitosterol: The Cholesterol of Plants. *Manufacturing Chemist.* **11**, 59-62.
- Fernandez A, Tavares F, Athavale VB. (1980) Asthma in Children: A Clinical Controlled Study of *Piper longum* in Asthma. *Paediatr. Clin. India.* **15**, 45.
- Glasnapp DR, Poggio JP. (1985) Essentials of Statistical Analysis for the Behavioral Sciences. Charles E. Merrill Publishing Company, London.
- Goel FG, Bham MK, Azamy S, Ahrary R, Srivastava RN. (1981) *Ind J. Pediatr.* **18**, 643-646.
- Gupta BD, Dandiya PC, Gupta ML. (1971) A Psycho-Pharmacological Analysis of Behavior in Rat. *Jpn J. Pharmacol.* **21**, 293-298.
- Ikram M. (1984) Triphala: A Unani Medicine. *Hamdard Medicus.* **23**, 133-137.
- Inamdar MC, Rajarama RMR. (1962) Constituent of *Terminalia chebula*. *J. Sci. Industr. Res.* **21c**, 345-348.
- Lands AM. (1947) The Pharmacology of N-alkyl Homologous of Epinephrine. *J. Pharmacol. Exp. Ther.* **90**, 110-119.
- Mcomic WA. (1947) Local and Systemic Effects of 2-methyl -2,4 pentanediol (Hexylene glycol). *Fed. Proc.* **6**, 357.
- Nakama M, Ochiai T, Kowa Y. (1972) Effects of Psychotropic Drugs on Emotional Behavior: Exploratory Behavior of Naive Rats in Holed Open Field. *Jpn J. Pharmacol.* **22**, 767-775.
- Said HM. (1969) Hamdard Pharmacopoeia of Eastern Medicine. Hamdard Foundation, Dhaka.
- Said HM. (1978) Eastern Medicine in Changing World. *Hamdard Medicus.* **21**, 7-21.
- Sandberg F. (1959) Comparative Quantitative Study of the Central Depressant, Effects of Seven Clinically Used Phenothiazine Derivatives. *Arzneimittel Forschung.* **9**, 203-206.
- Santhakumari G, Rathinam K, Seshadri C. (1978) Anticoagulant Activity of Plumbagin. *Indian J. Exp. Biol.* **16**, 485-491.
- Schumacher HR. (1988) Rheumatoid Arthritis. J.B. Lippincott Co., Philadelphia, 2. 1 .
- Setniker I. (1960) Amino-methylchromes, Brain Stem Stimulants and Pentobarbital Antagonists. *J. Pharmacol. Exp. Ther.* **128**, 176-181.
- Sharkawi M. (1970) Effects of Some Centrally Active Drugs on Acetylcholine Synthesis in Rat Brain. *Pharmacologist.* **12**, 294-298.
- Siddiqui HH. (1963) Pharmacological Study of Water Extract, Alcohol Extract and Phyllembin of the Fruit of *Terminalia bellerica*. *Indian J. Phann.* **25**, 297-302.
- Siegmund PN, Wolf M. (1952) Displacement of Sand Method for the Determination of Locomotor Activity. *Arch. Exp. Pathol. Pharmacol.* **216**, 232-235.
- Tedeschi DW, Tedeschi RE. (1968) Importance of Fundamental Principles of Drug Evaluation. Raven Press, New York, 307.
- Takagi K, Watanbe M, Saito H. (1971) Studies of the Spontaneous Movement - of Animals by the Hole Cross Test: Effect of 2-dimethylminoethanol and Its Acylesters on the Central Nervous System. *Jpn. J. Pharmacol.* **21**, 797-810.
- Tariq M, Hossain ST, Arif M, Jannan M. (1977) Effect of Alcoholic Extracts of Fruits of *Emblca officinalis* and *Terminalia bellerica*. *Indian Exp. Biol.* **15**, 485-6.
- Valzelli L. (1973) Psychopharmacology. Spectrum Publications Inc., New York, 16.
- Vane JR. (1961) Tryptamine Receptors in the Central Nervous System. *Nature.* **191**, 1068-1069.
- Woolfe G, Macdonald AD. (1944) The Evaluation of the Analgesic Action of Pethidine Hydrochloride (Demerol). *J. Pharmacol. Exp. Ther.* **80**, 300-307.
- Zutshi U, Kaul JL. (1982) The Impact of Ayurvedic Herbals on Drug Bioavailability. *Indian Drugs.* **19**, 476.