
NATURAL DRUGS

**CNS ACTIVITIES OF *Celesia coromandeliane* Vahl.
IN MICE**

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Abstract: The dried extracts of aerial parts of *Celesia coromandeliane* Vahl. (Scrophulariaceae) were evaluated for CNS activities in mice. The methanol extract of aerial part of *Celesia coromandeliane* (MECC) was found to cause significant depression in general as well as exploratory behavioral profiles in mice. MECC showed reduction in muscle relaxant activity by 30° inclined screen test, as well as potential remarkably the pentobarbitone sodium-, diazepam- and meprobamate-induced sleeping time of mice. The petroleum ether extract of aerial parts of *Celesia coromandeliane* (PECC) showed significant analgesic properties as evidenced by the significant reduction in the number of writhes and stretches induced in mice by 1.2% acetic acid solution. Pretreatment with PECC caused significant protection against strychnine- and leptazol-induced convulsions. All these results were compared with respective controls for the evaluation of significance. The presence of steroids in PECC and saponins in MECC might be responsible for respective CNS activities in mice.

Keywords: *Celesia coromandeliane*, sleeping time, general behavior, analgesic activity, anticonvulsant activity.

Celesia coromandeliane Vahl. (Family: Scrophulariaceae, kukshima in Bengali, gadartambaku in Hindi) is common throughout India, found widely in the plains of West Bengal, growing as shrubs (1). Various parts of this plant were used in tribal medicines for diseases like insomnia, fever, diarrhoea, dysentery and syphilitic eruptions. The juice of the leaves is applied externally for relieving the burning sensations at the hands and feet and used as astringent, a drink in bleeding piles (2). The plant has been found to possess antifertility activities (1, 3). It was found that the petroleum ether extract of aerial parts of *C. coromandeliane* (PECC) showed marked analgesic and anticonvulsant activities and methanol extract of it (MECC) exhibited significant sedative-hypnotic action compared to other extracts in preliminary pharmacological screening (4). However, no detailed study has yet been done regarding the CNS activities of aerial parts of *C. coromandeliane*. Hence, the present communication deals with the various CNS activities of PECC and MECC in mice to substantiate the folklore claim.

EXPERIMENTAL

The aerial parts of *C. coromandeliane* were collected from Panua, Bankura district region of West

Bengal, India and the taxonomic identification was made by the Division of Pharmacognosy, Department of Pharmaceutical Technology, Jadavpur University, Kolkata. The voucher specimen has been preserved in our research laboratory (Ref No: DM1) for future reference. Shade-dried, powdered and sieved (40 mesh size) plant material was extracted in Soxhlet apparatus first with petroleum ether (40-60°C) and then with methanol. Both the petroleum ether and methanol extracts were evaporated to dryness. The trace amount of solvent which might be present within the solid mass of respective extracts was removed under vacuum. The yield of petroleum ether (PECC) and methanol extraction (MECC) were 3.5% w/w and 10.1% w/w, respectively, with respect to the dry starting material.

Chemical investigation of MECC and PECC

The methanol extract of aerial parts of *C. coromandeliane* was dissolved in H₂O and successively portioned with Et₂O and n-BuOH (saturated with H₂O). The n-BuOH fraction was evaporated to afford a crude saponin mixture (5.9% with respect to dried methanol extract) from which a pure fraction A was isolated by preparative TLC using silica gel G as stationary phase and hexane-ethyl acetate (2:3, v/v) as solvent system. Fraction A (R_f 0.38, m.p.

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219-225°C λ_{\max} 230 nm) showed characteristic IR (PERKIN ELMER apparatus) peaks of saponin at 3375 cm^{-1} (for OH group), 1730-1680 cm^{-1} (for ester CO), 1620 cm^{-1} (for unsaturation), 1320 cm^{-1} , 1160 cm^{-1} , 1060 cm^{-1} , and 1040 cm^{-1} . It also gave qualitative positive tests for saponins (foam test, high haemolytic activity) (5, 6, 7). The petroleum ether extract of aerial parts of *C. coromandeliana* (PECC) on preparative TLC using silica gel G as stationary phase and chloroform-acetone (1.7:3, v/v) as mobile phase, gave fraction B (R_f 0.61, m.p. 166°C, λ_{\max} 240 nm) having characteristic IR peaks at 3450 cm^{-1} (OH), 2960 cm^{-1} , 2895 cm^{-1} , 2820 cm^{-1} (CH), 1725 cm^{-1} (C=O), 1645 cm^{-1} (C=C), 1601 cm^{-1} (aromatic), 1445 cm^{-1} , 1375 cm^{-1} , 1260 cm^{-1} , 975 cm^{-1} , 910 cm^{-1} suggesting the structural similarity with stigmaterol derivatives (8, 9). Qualitative tests (Lieberman-Burchard, Salkowski) for steroids were positive for fraction B. For pharmacological studies, PECC and MECC were dissolved in arachis oil (B.D., and Co, India) and propylene glycol (PG) (Ranbaxy Ltd, India), respectively.

Animals and treatment. Adult albino male mice of either sex (22 ± 2 g; Swiss strain) were acclimatized to normal laboratory conditions for one week and given pellet diet (Hindustan Lever Ltd, India) and water *ad libitum*. The experiment was performed under the guidance of the Institutional Ethical Committee.

Toxicity Study

An acute toxicity study related to the determination of the LD₅₀ value was performed with different doses of the extracts in albino mice as per the method described in Ghosh and Kulkarni (10, 11).

Effect on sleeping time

The mice were divided into 5 groups and each group contained 10 mice. The animals of group I and II received normal saline (5 mL/kg, *i.p.*) and vehicle (propylene glycol, 5 mL/kg); Groups III, IV, V received MECC at low, medium and high dose (100 mg/kg, 125 mg/kg and 150 mg/kg, *i.p.*, respectively). Controls and the extracts were injected intraperitoneally 30 min prior to the administration of pentobarbitone sodium (40 mg/kg, *i.p.*), diazepam (3 mg/kg, *i.p.*) and meprobamate (100 mg/kg, *i.p.*). The sleeping time was noted by recording the interval between the loss and regaining of righting reflex (12).

General behavioral tests

This experiment was performed by the methods of Mukherjee *et al.* and Dixit and Verma (13,

14). Swiss albino mice were divided into 6 groups (10 in each group). The first three groups received extract (MECC) at different doses (100, 125, 150 mg/kg body weight), the fourth and fifth group were treated with normal saline (5 ml/kg, *i.p.*) and propylene glycol %5 ml/kg, *i.p.*) for control. The remaining (sixth) group received chlorpromazine (CPZ, 5 mg/kg, *i.p.*) and served as a standard for comparison. All experiments were performed between 8 a.m. to 12 p.m. to minimize circadian influences. The activities were recorded at 30 min intervals during the first hour and at hourly intervals for the next 4 h, for the following parameters. This method gave the effect of MECC on the instinctive hyperactivity seen in animals placed in new surroundings, i.e. explorative hyperactivity (15).

- Spontaneous motor activity: Spontaneous motility of the test animals was determined by a comparison of animals before and after treatment. The animals were placed on a photoactometer and the activity was recorded for 25 min before injection. The same animals were then injected with the extract at the same time the following day and activity was again measured as discussed above (16).

- Awareness and alertness: A mouse was placed in a bell jar and signs of awareness, alertness or stupor were observed. Also visual placing, stereotypy and passivity were observed. It usually shows a moderate degree or inquisitive behavior (17).

- Touch response: It was noted when the animal was touched with a forceps or pencil at various parts (*i.e.*, on the side of the neck, on the abdomen and on the groin) (17).

- Pain response: This response was graded when a small artery clamp was attached to the base of tail (17).

- Righting reflex: A mice was placed gently on its back on an undulated surface made of white iron at 30°C. If the animal remains on its back for 30 sec, loss of the righting reflex are said to occur (10, 11).

- Pinna reflex: It was tested by touching the center of the pinna with a hair of fine instrument. The withdrawal of pinna from the irritating hair was considered to be that response (10).

- Corneal reflex: A stiff hair touched to the cornea, causes the animals to close the eyelids (11).

Muscle relaxant activity

30° inclined screen test. Swiss albino mice (male) 15 min after injection of either propylene glycol (5 mL/kg) or diazepam (10 mg/kg) or MECC (100, 125 and 150 mg/kg) were left on the screen for at least 4 h to observe whether the muscle relaxant effect was severe enough to cause the mice to slide

off the screen (18). Groups of 10 mice were used for each group of control and experimental batches.

Exploratory behavior

Head dip test. The animals (adult female Swiss mice) were divided into 6 groups of 10 for the test. Thirty min after *i.p.* injection of propylene glycol (5 mL/kg), diazepam (10 mg/kg) or the MECC (100, 125 and 150 mg/kg), the mice were placed on a wooden board with 16 evenly spaced holes. The number of time they dipped their heads into the holes during each 3 min trial was counted (19).

Analgesic properties

Writhing test. This method involved *i.p.* injection of freshly prepared 1.2% acetic acid. The number of abdominal constrictions in the following 10 min were noted. For this test PECC was tested at

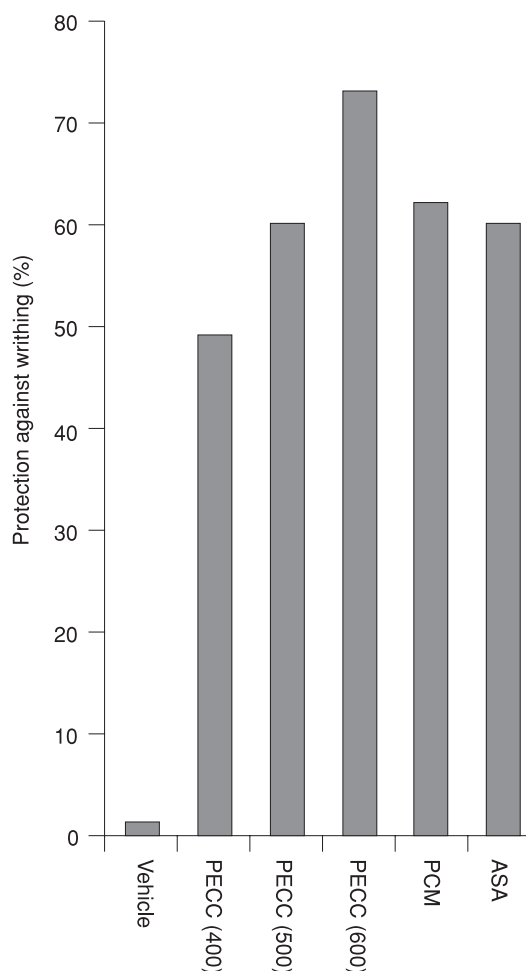


Figure 1. Influence of PECC (400, 500, 600 mg/kg), paracetamol (PCM) (68 mg/kg), acetylsalicylic acid (ASA) (68 mg/kg) and morphine sulphate (M) (1.15 mg/kg) on the writhing and stretching induced in mice by 1.2 % acetic acid (writhing test).

* $p < 0.05$

400, 500 and 600 mg/kg. Acetylsalicylic acid, paracetamol and morphine sulphate were used as reference standard at 68 mg/kg, 68 mg/kg and 1.15 mg/kg, respectively (20-22).

Anticonvulsant activities (20, 23)

The anticonvulsant property of PECC (400, 500 and 600 mg/kg, *i.p.*) was tested against two standard drugs, strychnine (2 mg/kg, *i.p.*) and leptazol (80 mg/kg, *i.p.*). The average survival time (min) and the percentage of mortality after 24 h were recorded.

Statistical analysis (24). Results are expressed as the mean \pm SEM. ANOVA followed by Dunnett's 't' test was performed as a *post hoc* test of significance taking vehicle treated animals as control. The chi-square test was used to assess muscle relaxant activity; $p < 0.05$ was considered significant.

RESULTS

On the basis of the acute toxicity studies, it was observed that the PECC in doses to 1800 mg/kg, *i.p.* did not cause any mortality in mice within a period of 24 h after injection, but the LD₅₀ dose of MECC was 400 mg/kg, *i.p.*

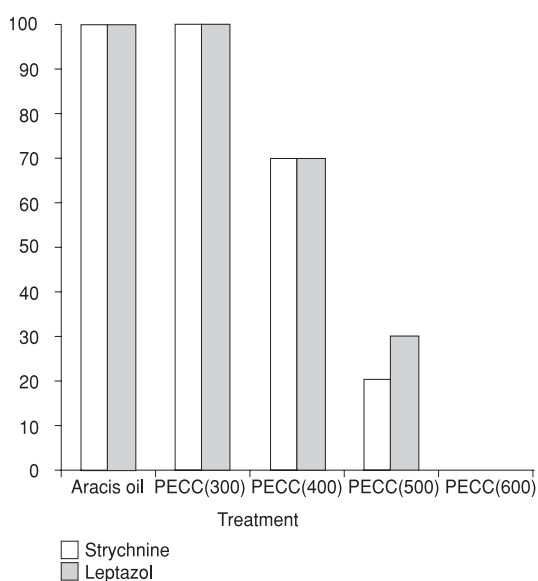


Figure 2. Anticonvulsant effect of PECC in strychnine (2 mg/kg, *i.p.*, b.w.) and leptazol (80 mg/kg, *i.p.*, b.w.) induced convulsion in mice. Results are expressed as percentage of mortality. Respective doses of the extract (mg/kg, *i.p.*, b.w.) are in parenthesis

Table 1. Effect of methanol extract of aerial parts of *C. coromandeliana* Vahl. (MECC) on sleeping time induced by standard sedatives in mice.

Treatment	Sleeping time (min) induced by		
	Pentobarbitone (40 mg/kg, <i>i.p.</i>)	Meprobamate (100 mg/kg, <i>i.p.</i>)	Diazepam (3 mg/kg, <i>i.p.</i>)
Normal saline (5 mL/kg, <i>i.p.</i>)	35.0 ± 1.25	56.7 ± 2.10	68.2 ± 1.75
Vehicle (propylene glycol) (5 mL/kg, <i>i.p.</i>)	39.3 ± 1.55	60.7 ± 1.94	74.0 ± 1.77
MECC (100 mg/kg, <i>i.p.</i>)	72.5 ± 1.77*	93.1 ± 2.02*	102.6 ± 2.05*
MECC (125 mg/kg, <i>i.p.</i>)	79.0 ± 1.90*	101.5 ± 2.11*	118.5 ± 2.25*
MECC (150 mg/kg, <i>i.p.</i>)	88.2 ± 1.99*	115.0 ± 2.28*	140.3 ± 2.48*

Values are mean ± SEM, n = 10; Statistical analyses done by ANOVA followed by post hoc test of significance, Dunnett's 't' test. + p < 0.05 vs vehicle control. PG: propylene glycol. *i.p.* – intraperitoneal.

Table 2. Effect of methanol extract of aerial parts of *C. coromandeliana* Vahl. (MECC) on behavioral profile in mice.

Treatment	Spontaneous motor activity	Awareness and alertness	Touch response	Pain response	Righting reflex	Pinna reflex	Corneal reflex
Normal saline (5 mL/kg, <i>i.p.</i>)	0	0	0	0	0	0	0
Vehicle (PG) (5 mL/kg, <i>i.p.</i>)	0	0	0	0	0	+	0
Chlorpromazine (CPZ) (5 mg/kg, <i>i.p.</i>)	4+	4+	4+	4+	4+	4+	4+
MECC (100 mg/kg, <i>i.p.</i>)	2+	+	+	+	+	2+	2+
MECC (125 mg/kg, <i>i.p.</i>)	3+	2+	2+	2+	+	2+	3+
MECC (150 mg/kg, <i>i.p.</i>)	4+	3+	3+	3+	2+	3+	4+

Key for scoring: 0 = no effect (normal); + = slight depression; 2+ = moderate depression; 3+ = strong depression; 4+ = very strong depression; n = 10; * p < 0.05 vs vehicle control, PG: propylene glycol CPZ: chlorpromazine. *i.p.* – intraperitoneal.

The extract (MECC) at low, medium and high dose level lengthened significantly the sleeping time induced by standard sedatives in the order: sodium pentobarbitone 84.4%, 101%, 124.4%; diazepam 38.6%, 60.1%, 89.6%; meprobamate 53.4%, 67.2%, 89.5% compared with vehicle control mice, respectively (Table 1).

The results obtained from general behavioral profiles are presented in Table 2. Treatment with extract produced a significant reduction in spontaneous motility in test mice. The mean photometer reading in the animals treated with vehicle con-

trol (propylene glycol, 5 ml/kg) was 515 ± 85, but in animals treated with 100, 125 and 150 mg/kg of MECC, the readings were 320 ± 47, 230 ± 28 and 148 ± 22, respectively. It was noted that MECC affected pain and touch responses; altered righting, pinna and corneal reflexes at the dose of 100 mg/kg and above; produced moderate depression in patterns concerned with alertness and awareness when compared to control (propylene glycol, 5 ml/kg). However, chlorpromazine hydrochloride (CPZ) (standard) produced a profound depression of these responses in comparison with MECC. MECC also

Table 3. Effect of methanol extract of aerial parts of *C. coromandeliane* Vahl. (MECC) on exploratory behavior (head dip test) and muscle relaxant activity (30° inclined screen test) in mice.

Treatment	Head dips ¹	30° inclined screen test ϕ
Normal saline (5 mL/kg, <i>i.p.</i>)	27 – 0.84	0
Vehicle (propylene glycol) (5 mL/kg, <i>i.p.</i>)	26 ± 1.91	0
Diazepam (100 mg/kg, <i>i.p.</i>)	8.7 ± 1.11*	100*
MECC (100 mg/kg, <i>i.p.</i>)	18.7 ± 1.14*	41*
MECC (125 mg/kg, <i>i.p.</i>)	14.4 ± 1.27*	60*
MECC (150 mg/kg, <i>i.p.</i>)	13.5 – 1.32*	69*

¹ Values are the number of head dips in 3 min (mean ± SEM).

ϕ values are the percentage of animals showing a negative test. Statistical significance test for comparison of test with control was done using the „Chi-square test“; n = 10; * p < 0.05.

produced a significant loss of motor coordination and muscle tone as evident from the 30° inclined screen test (Table 3).

On the basis of the results obtained from the head dip test, mice treated with low, moderate and high doses of MECC showed a significant decrease (28.1%, 44.6% and 48.1%, respectively) in head dip responses as compared to vehicle control (propylene glycol) (Table 3).

As can be seen in Figure 1, PECC significantly reduced the number of writhes and stretches induced in mice by 1.2% solution of acetic acid,

with a dose of 400 mg/kg, *i.p.*, the percentage of protection being 49%. This dose dependent effect reached 73% with a dose of 600 mg/kg, *i.p.* Analgesic compounds: acetylsalicylic acid (68 mg/kg), morphine sulphate (1.15 mg/kg) and paracetamol (68 mg/kg) gave 60%, 70% and 61% protection, respectively. Table 4 and Figure 2 show that PECC increased the average survival time and decreased the percentage mortality in a dose dependent manner against strychnine- and leptazol-induced convulsions.

DISCUSSION AND CONCLUSIONS

Benzodiazepins are believed to act at specific binding sites which are closely linked to gamma-aminobutyric acid (GABA) receptors, the binding of benzodiazepines enhances GABAergic transmission (25). Although the cause of prolongation of diazepam induced sleeping time is not known, the enhancement of GABAergic transmission might be related to its sedative activity. Prolongation of pentobarbitone induced sleeping time might be due to tranquilizing action as well as CNS depressant action. Although the exact mechanism responsible for the sedative action of meprobamate is not clear, it may be due to CNS depressant action or due to enhancement of GABAergic transmission (25-29). MECC potentiated significantly the duration of diazepam-pentobarbitone and meprobamate-induced sleep in mice, suggesting probable tranquilizing action as well as CNS depressant action (13, 17, 26, 30).

The experimental results indicate that the MECC influences general behavioral profiles, as evidenced in the spontaneous motility, touch and pain responses, awareness, righting, pinna and corneal reflexes. The reduction of pinna reflex may

Table 4. Effect of the petroleum ether extract of aerial parts of *C. coromandeliane* Vahl. (PECC) on average survival time on strychnine- and leptazol-induced convulsions in mice.

Treatment	Survival time (min) after treatment with	
	Strychnine (2 mg/kg, <i>i.p.</i>)	Leptazol (80 mg/kg, <i>i.p.</i>)
Control (Arachis oil, 5 mL/kg, <i>i.p.</i>)	4.3 ± 0.28	10.8 ± 0.21
PECC (300 mg/kg, <i>i.p.</i>)	155.7 ± 1.14***	180.8 ± 1.09***
PECC (400 mg/kg, <i>i.p.</i>)	290.6 ± 2.14***	338.5 ± 2.61***

Values are mean ± S.E.M., n = 10; Statistical analysis done by ANOVA followed by post hoc test of significance, Dunnett's 't' test.

*** p < 0.001 vs control; *i.p.* – intraperitoneal.

be due to stimulation of some part of sensory nerve or the spinal synapses or the efferent pathway (31). The possible CNS activity of MECC was further tested against other common psychopharmacological test (i.e., 30° inclined test). The reduction in exploratory behavior in animals treated with the methanol extract is in keeping with the action of other CNS depressant agents (32).

The profound analgesia produced by PECC is probably mediated by inhibition of a post synaptic specific sensitive mechanisms either by depleting endogenous levels *via* dopamine- β -hydroxylase inhibition or by blocking its effects at the receptor level (33). Analgesic and anticonvulsant activities can also be mediated by other mechanisms. The increase of brain serotonin and GABA level may also be responsible for analgesic and anticonvulsant activities (25, 28, 34). Since various steroids have been reported to possess analgesic (35-38) and anxiolytic (39, 40) activities, the analgesic effects of PECC in mice might be due to the presence of such compounds. Similarly, the sedative activities of MECC might be due to the presence of saponins (41, 42).

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