ISSN (Online) 2249-6084 (Print) 2250-1029

International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR)
[Impact Factor – 0.852]

Journal Homepage: www.eijppr.com

Research Article

The Role of *Elettaria cardamomum* (L.) Maton in Inflammatory, Gastrointestinal and Stress Disorders

Mehjabeen[1]*, Mansoor Ahmad[2], Noorjahan[3], Farah-Saeed[4], Asif Bin Rehman[5]
[1]Department of Pharmacology, Faculty of Pharmacy, Federal Urdu University of Arts, Science and Technology, Karachi-75300, Pakistan.
[2]Research Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Karachi, Karachi-75270, Pakistan.
[3]Department of Pharmacology, Dow College of Pharmacy, Dow University of Health Sciences Karachi, Pakistan.
[4]Department of Pharmacognosy, Dow College of Pharmacy, Dow University of Health Sciences Karachi, Pakistan.
[5]Department of Pharmacology, Hamdard college of Medicine and Dentistry, Hamdard University Karachi, Pakistan.

Article info

Article History:
Received 26 December 2014
Accepted 13 March 2015

Keywords:
Analgesic, Anti-inflammatory, Neurophamracology, *E. cardamomum*

Abstract

At present there are many anti-inflammatory, antipsychotic and anti-ulcer drugs available but their undesirable effects limiting the use in chronic state of disease. *Elettaria cardamomum* (L.) Maton is one of the traditionally used medicines which contain volatile oil and other active constituents. This study was made to determine the altered behavior, gastrointestinal and inflammatory disorders in mice. The drug showed antidepressant potential followed by sedative effect at the dose of 300 and 500mg/kg, whereas at 200mg/kg the crude extract showed anxiolytic effect. The analgesic effect through tail flick and hot plate and acetic acid induced writhing methods exhibited dose dependant increase in reaction time. *E. cardamomum* extract displayed mild insecticidal activity that is 20-40%. The anthelmintic activity was also found significant. The drug at a dose of 50mg/2ml showed 5 hour death time. In gross organ toxicity test non-significant toxic effects were observed. The gastrointestinal results showed the decrease in intestinal motility and softness of stool with increase diuresis. Significant anti-inflammatory results were found at the dose of 300 and 500mg/kg in mice. All of the results were compared with the standard reference drugs to evaluate the efficacy of crude extract of *E. cardamomum*. These results generally provide an idea how to improve our knowledge of the consequences of stress, inflammation and gastrointestinal trouble with the possible way of treatment.

1. INTRODUCTION

Stress and inflammation have close association with gastrointestinal problems. Chronic inflammation may also lead to altered behaviour as well as other psychological problems[1,2]. Since multiple drug therapy not only increases the cost of treatment, but complicates the disease also thus it is again important to treat the disease by single drug therapy. Therefore, these studies have been carried out on *Elettaria cardamomum* medicinal plant in order to evaluate and investigate its role in stress, inflammation and depression.

Elettaria cardamomum (L.) Maton (Zingiberaceae) has a wide range of chemical constituents which play an important role for the pharmacological action[3]. It contains terpineol, terpinene, cineol, limonene, sabinene etc. Volatile oil is present in the seeds gives specific aroma. These are myrcene (1.4), D-limonene, methylheptenone (0.03), β-pinene, linalool acetate, terpinyl acetate, α-terpineol[4]. It is expensive spice through out the world. Traditionally it is used in infections, bronchial inflammation, gastrointestinal troubles, cardiac problems[5,6].

2. MATERIALS AND METHODS

Whole fruit of *E. cardamoum* is purchased from local market and a voucher specimen (001116-03) was deposit in the herbarium of Department of Pharmacognosy, Research Institute of Pharmaceutical Sciences, University of Karachi, Pakistan. The conventional extraction procedure was used to get the crude extract later it was used for pharmacological and other studies[3].

Corresponding Author:
Dr. Mehjabeen
Department of Pharmacology, Faculty of Pharmacy,
Federal Urdu University of Arts,
Science and Technology, Karachi-75300, Pakistan
Email: mehjabnn1@gmail.com

2.1 Pharmacological analysis

a) *Anti-inflammatory activity*

Formalin and Carrageenan test

These test were performed according to modified method describe by Hunskaar and Hole1987and Rathi et al., 2003, Vishnukanta and Rana, 2008, Liu et al., 2005). The animals were divided in to 5 groups (each group consist of five animals (Rats/mice). The control group received saline solution[7-10].

b) *Analgesic activity*

Tail immersion, Hot plate and Acetic acid induce writhing test

These tests were carried out in mice according to the methods described by Owoyele *et al*. (2004), Dharmasiri *et al*. (2003) and Koster *et al.* (1959)[11-13].

c) *Neuropharmacological assessment* *(Open field, head dip, rearing test, cage cross, traction and forced induce swimming test)*

These tests were performed to evaluate the crude extract action at the dose of 200, 300 and 500 mg/kg in the animal model (mice). These studies were conducted by the modified method of Irwin *et al.* (1968), Debprassad *et al*. (2003), Kennett (1985) and Florence (2000)[14-17].

d) *Insecticidal and Anthelmintic activity*

In insecticidal activity test *Tribolium castaneum* and *Sitophilus oryzea* were used as test insects. Permethrin was used as standard drug. The percentage of mortality was calculated with reference to control (Collins, 1998)[18]. For anthelmintic activity determination a modified method described by Kumar and Shivkar (2003) was used[19]. The test was performed on *Lumbricus terrestris* (Earth worms). The mean paralysis and death time were noted. Vermox drug was used a reference standard.

e) Laxative and Diuretic activity

Effect of *E. cardamomum* extract on gastrointestinal tract was evaluated by the modified method of Capasso *et al*. (1986). In this method mice were divided in to four groups of each 5 animals. Group I (control) received 0.5 ml saline only. Group II and III received crude extract of *E. cardamomum* 300 and 500mg/kg respectively. Group IV received reference standard drug Agar-Agar 300 mg/kg. After 4, 8 and 24 hours numbers of fecal out put was measured[20].

Diuretic activity was performed by the modified method reported by Sripanid kulchai *et al*., (2001). Each animal (divided in to four groups; Group I: control, Group II: 300 mg/kg of *E. cardamomum* extract: Group III, 500mg/kg, Group IV: reference drug Furosemide 20mg/kg g) was kept separately in to the metabolic cages and 24 hours urine (ml) is collected in to the tubes fitted to the bottom of the metabolic cage[21].

2.2 Statistical analysis

All results are calculated by using student "t" test at $p<0.05$ and presented with Standard error mean (SEM).

3. RESULTS AND DISCUSSION

E. cardamomum has wide range of medicinal application such as it is effective in stomachic, kidney problems, infectious disease, headache, convulsion[22].

Table 1 shows the results of formalin and carrageenan induced inflammation. Crude extracts *of E. cardamomum* (200, 300 and 500mg/kg p.o.) produced dose independent inhibition of neurogenic (0–15 min) and inflammatory (15–30 min) phases of formalin-induced licking. The effects were significant in 500mg/kg dose in second phase. The extract also showed a significant percentage of inhibition in carrageenan induced edema (25.1%; 36.7%; 40.7%, 30.3%; 34.3%; 44.3%, 22.39%; 29.5%; 44.7% respectively at 200, 300 and 500mg/kg oral dose).

Table 1: Effect of Crude extract of *E. cardamomum* on Formalin and carrageenan induce inflammation

Treatment of *E. cardamomum* Crude extract	% of Formalin induced pain inhibition		% of inhibition of rat paw edema induced by carrageenan		
	1st phase	2nd phase	1 hr	2hr	3hr
Control	-	-	-	-	-
200mg/kg	45.45	50	25.1	36.66	40.71
300mg/kg	38.18	38.46	30.3	34.28	44.26
500mg/kg	16.36	84.61	22.3	29.52	44.66
Aspirin	36.36	26.92	26.3	28.09	35.57

Mean ± S.E.M; N = 5; Significance with respect to control (= Significant results, ** = highly significant results)*

In analgesic activity the analgesiometers (hot plate and water bath) were used to measure the delayed pain response in animal. The results of *E. cardamomum* extract exhibited a significant increased in latency time (Table 2 and 3). The significant response was observed with 500mg/kg in 1 hour 30 minutes in comparison to control and aspirin treated groups.

Table 2: Effect of crude extract of *E. cardamomum* on water bath (tail flick) in mice

Group	Time in sec ±SEM				
	0hr	1hr	2hrs	3hrs	4hrs
Control	1.8 ±0.09	1.80±0.09	1.6±0.12	1.00 ±0.06	1.2±0.15
E. cardamomum 200 mg/kg	2.4 ±0.13	3.00* ±0.32	3.8*±0.24	2.60 ±0.13	2.4±0.13
E. cardamomum 300 mg/kg	1.8 ±0.19	5.2**±0.21	5.6**±0.32	3.6* ±0.24	3.8**±0.29
E. cardamomum 500 mg/kg	1.2 ±0.25	4.2**±0.25	6.1**±0.39	3.6* ±0.24	3.4* ±0.22
Aspirin 300mg/kg	1.00 ±0.05	3.8* ±0.24	5.6*±0.35	3.8* ±0.24	2.4±0.19

Mean ± S.E.M; N = 5; Significance with respect to control (= Significant results, ** = highly significant results)*

Table 3: Effect of crude extract of *E. cardamomum* on Hot plate Analgesiometer in mice

Group	Time in sec ±SEM				
	0hr	1hr	2hrs	3hrs	4hrs
Control	11.6± 1.029	11.8± 1.583	12.6± 1.777	11.6± 1.024	11.6± 1.013
E. cardamomum 200 mg/kg	11.2± 0.862	14.8 ± 0.862	16.4 ± 0.929	15.2± 1.070	11± 1.07
E. cardamomum 300 mg/kg	12.8± 0.862	24.2 ± 1.116	26.8± 0.862	25± 0.709	12.8± 1.53
E. cardamomum 500 mg/kg	14± 1.228	24.4± 1.211	24.2± 0.584	19.8± 1.070	12.4± 1.49
Aspirin 300mg/kg	15 ± 1.43	38 ± 0.82	44* ± 0.51	33 ± 0.81	22± 0.91

Mean ± S.E.M; N = 5; Significance with respect to control (= Significant results, ** = highly significant results)*

Results of acetic acid induced writhing tests were given in table 4. The results of hot plate test of *E. cardamomum* extract were given in Table 19 and graph 4D at three different doses. The increased in latency time was observed at 200, 300 and 500 mg /kg means ± SEM at $p \leq 0.05$. The results were highly significant with 300 mg/kg in 2.5hours. Reduction in abdominal cramps in first phase was 54%; 62.9%, 64.4%; 70.4% and 70.4%68.9% and 72.2% in second phase at 200, 300 and 500mg/kg dose. Different other studies suggested that the essential oil of *E. cardamomum* causes the inhibition of cyclooxygenase and lipoxygenase pathways and produces ulcer healing activity[23-24], so it may be possible that the anti inflammatory and analgesic effects may be due to the inhibition of cyclooxygenase, lipoxygenase and other chemical mediators of the arachidonic acid pathway[12].

Table 4: Assessment of analgesic activity of crude extract of *E. cardamomum* (Acetic acid induced writhing)

Treatment	Dose mg/kg orally	Mean No. of Writhes ± S.E.M		Inhibition (%)	
		1st phase	2nd phase	1st phase	2nd phase
Control	0.5 ml Saline	87± 5.67	54 ± 4.67	-	-
Crude extract *E. cardamomum*	200mg/kg	40±1.13	20±0.73	54.0	62.9
	300mg/kg	31±1.81	16±1.72	64.4	70.4
	500mg/kg	27±1.18	15±1.32	68.9	72.2
Aspirin	300mg/kg	50.6±1.35	14± 0.45	41.8	74.1

Mean ± S.E.M; N = 5; Significance with respect to control (= Significant results, ** = highly significant results), CE: crude extract of E. cardamomum*

Results of different neuro-pharmacological parameter were presented in table 5. The means ± SEM on the open field were 95±0.58; 137±0.71 and 151.6±1.51 for 200, 300 and 500 mg/kg doses respectively and for the control received 0.5ml saline was 250±0.71. It showed a slight stimulated effect at low dose and at high dose the drug produced stimulatory response followed by sedative effect. Over all the extract increased the locomotor effect and acted as anxiolytic remedy. The effect of *E. cardamomum* at 200mg/kg was significantly decreased the activity of head dip box. The results were compared with standard drugs Diazepam 2mg/kg, Imipramine 15 mg/kg, Codeine sulphate 50, 100 and 150 mg/kg and Caffeine 15 mg/kg. Highly significant results were observed as they initially improved the strength of muscles followed by relaxation. *E. cardamomum* extract showed the mobility time of 2.76±0.45, 2.24±0.014; 2.15±0.013 at 200, 300 and 500 mg/kg respectively at oral dose ($p \leq 0.05$). Initial CNS stimulating effect of *E. cardamomum* may be because of reflex of dopamine receptor stimulation at GIT which trigger the release of some stimulating neurotransmitters in the brain[3].

Table 5: Effect of Crude extract of *E. cardamomum* on different neuropharmacological parameters

Treatment Dose mg/kg orally	Mean no. of observations ± S.E.M					
	Open field activity	Head dip activity	Cage cross activity	Rearing activity	Mobility time	Traction time in sec. (after 1 hr)
Control0.5 ml saline	250 ± 0.71	51 ± 5.04	50.4 ±5.28	49.6 ± 1.93	2.76 ± 0.45	14.05 ± 2.05
CE 200	95.8±0.58	19.6±0.93	19.4±1.08**	28±0.71	-	10± 0.86
CE 300	137± 0.71*	33±0.71*	18 ± 0.71**	23.8± 0.86*	2.242±0.014**	10± 0.93
CE 500	151.6 ± 1.51**	39.8 ± 0.86**	16.4 ± 0.93**	13.6 ± 0.93**	2.146±0.013**	01± 0.51
Diazepam 2 mg/kg	41 ± 1.12	11 ± 1.12	39 ± 1.12	06 ± 1.12**	2.15 ± 1.12	16f ± 0.0082
Imipramine 15 mg/kg	353.5 ± 1.04	93.5 ± 1.04	78.5 ± 1.04**	53.5 ± 1.04	4.7±0.18	-
Codeine sulphate 50	98 ±3.67	08 ± 2.17	21± 2.01*	32± 1.04*	2.20± 0.01	-
Codeine sulphate 100	101 ±5.67	06 ± 2.07	16± 0.17**	19± 0.14*	02±0.03	-
Codeine sulphate 150	39.30 ± 3.12	01 ± 2.17	07± 1.04**	09± 1.32**	2.28 ± 0.07	-
Caffeine 10mg/kg	267 ± 0.89	81.6 ± 4.86	27 ± 2.99*	13± 1.14*	-	-

Mean ± S.E.M; n = 5; Significance with respect to control
(= Significant results, ** = Highly significant results), CE: crude extract of E. cardamomum*

Table 6: Insecticidal and anthelmintic effect of *E. cardamomum*

Treatment	No. of Fecal out put			Urine out put (ml)
	4 hours	8 hours	24 hours	
Control 0.5 ml saline	02±0.02	04±0.01	08±0.04	1±0.02
E. cardamomum 300 mg/kg	09±1.04**	12±0.30**	06±0.02	1.45±0.03*
E. cardamomum 500 mg/kg	14±1.09**	09±0.12*	06±0.05	1.95±0.12**
Agar-Agar 300 mg/kg	06±0.01*	07±0.31	05±0.02	-
Furosemine 20 mg/kg	-	-	-	2.2±0.22**

Mean ± S.E.M; n = 5; Significance with respect to control
(= Significant results, ** = Highly significant results), CE: crude extract of E. cardamomum*

Similarly the results of insecticidal and anthelmintic effects are given in table 6. Different doses of *E. cardamomum* crude extract showed a significant percentage of mortality against insects and worms. These results suggested the effective use of drug as an insecticidal and anthelmintic agent. Vermox and Permethrin were used as reference standard drugs.

In case of gastrointestinal effect, *E. cardamomum* laxative action was investigated with standard drug (Agar-Agara). The crude extract of *E. cardamomum* showed increase in fecal output at 4 hours, followed by gradual decreased and attain normal condition (table 7). Highly significant result was observed at 500 mg/kg with respect to control and reference drug. The number of fecal output of 500 mg/kg crude extract at 4, 8 and 24 hours were 14±1.09, 09±0.12 and 06± 0.06 respectively. The diuretic activity was also found significant at 500 mg/kg; 1.95±0.12 when compared with positive control; 1±0.02 and standard drug Furosemide 20mg/kg; 2.2±0.22. These results indicated that *E. cardamomum* has laxative potential as well as moderate diuretic effect.

Table 7: Laxative and Diuretic effect of *E. cardamomum*

Concentration mg/2ml	Insecticidal activity		Anthelmintic activity			
	Tribolium castaneum	*Sitophilus oryzae*	Crude extract *E. cardamomum*		standard drug Vermox	
	% Mortality	% Mortality	Mean paralytic time	Mean Death time	Mean paralytic time	Mean Death time
1 mg	0	0	-	-	-	-
5mg	0	0	-	-	-	-
10mg	0	0	-	-	-	-
25mg	20	20	4-5hr	Alive	-	-
50mg	30	10	1-2hr	2:30hr	4-6hr	-
75mg	40	20	1:20hr	1:25hr	4-5hr	-
100mg	40	40	15min	1:05hr	4hr	-
Permethrin (copex) 235.9 µg/cm^2	100	100				
Negative control solvent	0	0				

More over the crude extract of fruit of *E. cardamomum* contains some important active constituents[25] which are involve in its anti-inflammatory, analgesic, laxative and anxiolytic effects.

4. CONCLUSION

Crude extract of *E. cardamomum* showed a significant analgesic and anti-inflammatory drug. Its anxiolytic and muscle relaxing effect gives an additional effect for the use of stress related gastric troubles.

REFERENCES

1. Anisman, H. and Merali, Z. (2002) Cytokines, stress and depressive illness. Brain, Behavior, and Immunity, 16, 513–524.
2. Bourdeau I, Bard C, Forget H, et al. Cognitive function and cerebral assessment in patients who have Cushing's syndrome. Endocrinol Metab Clin North Am 2005; 34:357.

3. Mehjabeen (2009). Studies on the anti-inflammatory action of *Cinnamomum camphora*, *Cuscuta reflexa*, *Elettaria cardamomum* and *Solanum nigrum* on different organs in model experiments. Ph.D. thesis University of Karachi, Karachi.
4. Rastogi R. P. and Mehrotra B. N. 1991. *Compendium of Indian Medicinal Plants*. Vol. II. Central Drug. Research Institute, Lucknow and Publications and Information Directorate, New Delhi 2; 292.
5. Palatty A. S. and Shivanna1 K. R. 2007. Pollination ecology of cardamom (*Elettaria cardamomum*) in the Western Ghats, India. *Journal of Tropical Ecology*, 23; 493–496.
6. Ravindran, P. N., Shylaja M., Babu K. N. False cardamoms. 2002. *Medicinal and Aromatic Plants--Industrial Profiles,* 30(Cardamom); 330-340.
7. Hunskaar S., Hole K. 1987. The formalin test in mice: dissociation between inflammatory and non-inflammatory pain. *Pain.,* 30(1); 103–114.
8. Rathi N., Recta K. H., Mediratta P. K., Jain H., Cough C., Mahajan P., Sharma K. K. 2003. Effect of oxytocin in formalin induced pain response in mice. *Indian J. Pharmacology,* 35; 128-136.
9. Vishnukanta and Rana A. C. 2008. Analgesic and anti-inflammatory activity of Hydroalcoholic extract of leaves of *Plumbago zeylanica*. *Pharmacognosy Magazine*, 4(15); S133-136.
10. Liu S.Y., Shieh J. P., Tzeng J. I., Chia-Hui H., Yen-Ling C., Huang K. L., and Wang J. J. Novel 2005. Depots of Ketorolac Esters Have Long-Acting Antinociceptive and Antiinflammatory Effects. *Anesth Analg*, 101; 785–92.
11. Owoyele B. V., Olaleye S. B., Oke J. M. and Elegbe R. A. 2004. Anti-inflammatory and analgesic activities of *Nothospondias* staudtii. Nigerian Journal of Physiological Sciences, 19(1-2); 102-105.
12. Dharmasiri, M.G., Jayakody, J.R.A.C., Galhena G., Liyanage S.S.P. and Ratnasooriya. 2003. Anti-inflammatory and analgesic activities of mature fresh leaves of *Vitex negundo*. Journal of *Ethnopharmacology*, 87; 199-206.
13. Koster, R., Anderson, M., De, Bear E.J. Acetic acid for analgesic screening. *Fed. Proceed.,* 1959;18:412-416.
14. Irwan S., Taber R. I., Fox J. A., Roth F.E. 1968. Comparison of Perphenazine and Fluphenazine enanthates in rats. *Psychopharmacology*, 12; 441-447.
15. Debprasad C., Arunachalam G., Subhash C., Mandal R. B., Mandal A. B. 2003. CNS activity of methanol extract of Mallotus peltatus (Geist) Muell Arg. leaf: an ethnomedicine of Onge. *Journal of Ethnopharmacology*, 85; 99-101.
16. Kennett G. A., Dicknison S.L., Curzon G. 1985. Central serotonergic responses and behavioural adaptation to repeated immobilization, the effect of corticosterone synthesis inhibitor metyrapone. *Eur. J. Pharmacol*, 119; 143-152.
17. Florence C., James R. M., Mohlar H. and Rudorlph U. 2000. Mechanism of the hypnotic zolpidem *invivo*. *British Journal of Pharmacology*, 131; 1251-1254.
18. Collins, P. J. 1998. Inheritance of resistance to pyrethroid insecticides in *Tribolium castaneum* (Herbst) (Coleoptera: Tenebrionidae). *J. Stored Prod. Res.,* 34; 395–401.
19. Kumar, V.L., Shivkar, Y.M. Wormicidal activity of latex of Calotropis procera. *Indian Journal of Pharmacology,* 2003;35:128-136.
20. Capasso F., Mascolo N., Autore G. and Romano V., Laxatives and the production of autocoids by rat colon, J. Pharm. Pharmacol, 13, 1986, 627-629.
21. Sripanid kulchai Bungorn., Wongpanch Varima, Laupattarakasem Pisamai, Suwansaksri jamsai, jirakulsomchok Dusit. Diuretic effects of selected Thai indigenous medicinal plants in rats. J. *Ethnopharmacol*., 2001; 75: 185-190.
22. Gurdip S., Kiran S., Marimuthu P., Isidorov V., Vinogorova Vera. 2008. Antioxidant and antimicrobial activities of essential oil and various oleoresins of *Elettaria cardamomum* (seeds and pods). *Journal of the Science of Food and Agriculture*, 88(2); 280-289.
23. Jamal A, Farah, Aisha S, Aslam M, Javed K and Jafri MA. 2005. Antiulcerogenic activity of Elettaria cardamomum Maton. And Amomum subulatum Roxb. Seeds. Indian Journal of Traditional Knowledge, 4(3); 298-302.
24. Rainsford KD. 1987. The effect of 5-lipoxygenase inhibitors and leukotriene antagonist on the development of gastric lesions induced by non steroidal anti-inflammatory drugs in mice, Agents Actions, 21; 316.
25. Anonymous. 2005-06. *Hand on Unani Medicines*: *E. cardamomum*, NIIR board of consultants and Engineers. Asia Pacific Business Press, Dehli, India, 145-153.