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Antinociceptive, Anti-Inflammatory and Antidepressant potential of methanolic extract of *Celosia argentea* Linn

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ABSTRACT

The present study was done to determine the antinociceptive, anti-inflammatory and antidepressant activity of methanolic extract of leaves of *Celosaia argentea (*MECA) by oral administration at doses of 100, 200 and 400 mg/kg/day of body weight to healthy swiss albino mice. The MECA was studied for antinociceptive effect using Eddy's hot plate method and tail flick method in albino mice and anti-inflammatory effect by using carrageenan-induced hind paw edema in mice and the mean increase in paw volume and % inhibition in paw volume was measured plethysmometer at different time intervals after carrageenan injection (1% w/v). The MECA was evaluated for antidepressant effect using forced swim and tail suspension methods in albino mice. The MECA showed antinociceptive effect evidenced by the increase in the reaction time by Eddy's hot plate method and tail flick method in albino mice and anti-inflammatory effect by significant (P<0.001) reduction in the carrageenan-induced paw edema in mice. The MECA showed a significant antinociceptive, anti-inflammatory and antidepressant effect when compared with the standard drugs viz pentazocine, indomethacin and imipramine respectively. The present observation indicated significant (P<0.001) activity of the methanolic extract of *Celosia argentea* in the treatment of pain, inflammation, and depression.

Keywords: *Celosia argentea* Linn*, Antinociceptive, Anti-inflammatory, antidepressant*

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INTRODUCTION

Pain has been officially defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is always a warning signal and primarily protective in nature but often causes a lot of discomforts and leads too many adverse effects[1]. Inflammation is a pathophysiological response of living tissue to injury that leads to the local accumulation of plasmatic fluid and blood cells. Although it is a defense mechanism, inflammatory reaction can be induced, maintain or aggravate many diseases due to the involvement of complex events and mediator[2]. Many components are involved in the inflammation process to name few are edema formation; leukocyte infiltration and granuloma formation are widely noticeable[3]. Depression is a prevalent psychiatric disorder, which affects 21% of the world population. The current drugs can impose a variety of side-effects including cardiac toxicity, body weight gain, and sleep disorder etc. During the last decade, there is a growing interest in the therapeutic effects of natural products on mental disorders[4].

Celosia genus is useful as diuretic, antidysenteric, antiscorbutic and refrigerant; it is also useful in the disorder of the blood. *C. argentea* Linn belonging to Family-Amaranthaceae is annual herb distributed throughout India, tropical Asia, Africa, and America. The seeds are bitter and useful as an aphrodisiac, vulnerary, in diarrhea, blood diseases, mouth sores. The leaves are antipyretic, aphrodisiac, reduce inflammations, and strengthen the liver, useful in gonorrhea. Burnt leaves are styptic. The seeds have a reputation of clearing the vision and healing diseases of the eye[5]. *C. argentea* possesses various activities viz. antidiabetic[6,7], anti-pyretic[8], antioxidant[9,10], antibacterial and diuretic properties[11], anti-inflammatory[12], hepatoprotective[13,14], antidiarrhoeal[15], Antitumor[16,17] and immunomodulatory[18]. Phytochemical investigation revealed various compounds Viz. Saponin, Cyclopeptide, Phenols, fatty acids, amino acids in *C. argentea*[19,20].

The present study was undertaken due to the various folkloric claims and phytochemicals presence to evaluate antinociceptive, anti-inflammatory and antidepressant activity of a methanolic extract of *Celosia argentea.*

MATERIAL AND METHODS

Collection of plant materials and preparation of methanolic extract of *Celosia argentea*

Celosia argentea Linn was collected from Maharashtra. The leaves were then dried under shade at room temperature. Leaves were kept loosely allowing free air circulation. The leaves were ground and extracted with methanol by cold maceration process separately. The extract was filtered and the residue was again extracted with methanol. The filtrate was concentrated and evaporated under reduced pressure and dried in vacuum desiccators. The percentage yields by cold maceration process was 9.2 %.

Laboratory maintenance of animals

Swiss albino mice of either sex, aged 8-12 weeks (body weight 20-25 g) were procured. The animals were maintained separately at 25±2^0 C temperature, 50±15 % relative humidity and normal photoperiod (12h dark/12h light) in plastic cages. The animals were fed standard pellet diet and water *ad libitum*. All the animal experiments were carried out in accordance with the guidelines of CPCSEA, New Delhi and were approved by the Institutional Animal Ethical Committee (IAEC).

Acute oral toxicity

Acute oral toxicity study was performed as per OECD-423 guidelines (acute toxic class method). Swiss albino mice (n =3) of either sex selected by random sampling technique were used for the study. The animals were acclimatized for 5 days. The animals were kept fasting for overnight providing only water, after which the extracts were administered orally at the dose level of 2000 mg/kg body weight by intragastric tube and observed for 14 days[21]. The extract was devoid of any toxicity in rats when given in dose up to 2000 mg/kg by the oral route. Hence, for further studies 100, 200 and 400 mg/kg doses of extract were used.

Evaluation of Analgesic, anti-inflammatory and antidepressant activity

The study design is carried out for every method with thirty Swiss albino mice of either sex were divided into 5 groups, each group consisting of 6 mice.

Study Design					
Activity	**Antinociceptive**		**Anti-inflammatory**	**Antidepressant**	
Group/Method	Tail Flick	Eddys Hot Plate	Carrageenan-induced paw edema	Forced Swim	Tail suspension
I-Negative Control	0.2 ml of 1% w/v carboxymethyl cellulose suspension orally for 7 days				
II-MECA I	100 mg/kg body weight of MECA orally for 7 days				
III-MECA II	200 mg/kg body weight of MECA orally for 7 days				
IV-MECA III	400 mg/kg body weight of MECA orally for 7 days				
V-Positive Control (standard)	10 mg/kg of body weight of pentazocine (sc) for 7 days		10 mg/kg of body weight of indomethacin (i.p.) for 7 days	30 mg/kg of body weight of imipramine (i.p.) for 7 days	

Antinociceptive activity by Tail flick method

The reaction time was recorded using tail flick analgesiometer at 0, 30, 60, and 120 minutes time interval after the drug administration. The temperature was maintained at 50-55^0 C[22,23].

Antinociceptive activity by Eddy's hot plate method

After 1 hour of drug/extract administration, the animals were placed on a Hot plate maintained at 55±1^{0}C. The reaction time was measured in the form of time taken by the animals to lick the fore or hind paw or jump out of the place[22].

Anti-inflammatory activity by Carrageenan-induced paws edema

Acute inflammation was induced in all groups by injecting 0.1 ml of 1% w/v carrageenan into the sub-plantar region of the right hind paw of rats. On the 7th day, paw volume was measured 1 h prior to carrageenan injection using plethysmometer and at 0 and 3 h after the carrageenan injection[24,25]. Mean paw volume increased was measured and percent inhibition was calculated.

$$\text{Percent Inhibition} = 100\ (1 - Vt / Vc)$$

Where, Vc= Edema volume (control), Vt= Edema volume (test / standard).

Forced Swim Test

For the forced swim test (FST), Rats of either sex were individually forced to swim in an open cylindrical container (diameter 10 cm, height 25 cm) containing 19 cm of water at 25±1°c. Treatment was given 60min prior to study as described by study design. All animals were forced to swim for 6 min and the duration of immobility was observed and measured during the final 4 min interval of the test. When each mouse ceased struggling, floating motionless in the water and keeping its head above water was considered as immobile. A decrease in the duration of immobility is indicative of an antidepressant-like effect[26].

Tail Suspension Test

The tail suspension method used in this study[27]. Drug/extract was given 60 min before study as described by study design. Mice were suspended, 50 cm above the floor on the edge of the table with the help of adhesive tape approximately 1 cm placed from the tip of the tail. The immobility induced by tail suspension was recorded during a 6 min of the 10 min period. The Animal did not show any movement of the body was considered to be immobile when it hanged passively and completely motionless.

RESULT

Acute oral toxicity

The MECA was analyzed for the toxicity. Acute toxicity studies revealed the non-toxic nature of the MECA. There were no toxic reactions and no deaths in the female rats observed after administration of the extract at a dose of 2000 mg/kg body weight

Antinociceptive activity by Tail flick method

The antinociceptive activity of MECA viz. 100 mg/kg, 200 mg/kg and 400 mg/kg p.o. determined by using the tail flick method (Table 1). The significant increase in reaction time exhibited by extract was marked central analgesic effect when compared to the control and standard drug pentazocine (10 mg/kg s.c.).

Table 1 Evaluation of antinociceptive activity of methanolic leaf extracts of *Celosia argentea by* Tail flick method

Group	Reaction time in Sec at different time intervals				
	0 min	30 min	60 min	90 min	120 min
1	2.08±0.68	2.12±0.72	2.02±0.75	2.14±0.89	2.06±0.62
2	2.02±0.55	8.62±0.83**	9.82±0.89**	11.28±0.73**	12.12±0.89**
3	2.08±0.66	10.52±0.63**	11.62±0.79**	13.52±0.75**	14.61±0.77**
4	2.06±0.95	12.23±0.88**	14.52±0.61**	15.92±0.54**	17.18±0.82**
5	2.12±0.87	13.23±0.91**	15.32±0.74**	17.22±0.56**	20.02±0.98**

Values are expressed as mean ±SD (n=6). Significance P <0.05 (*), P <0.01 (**) as compared to vehicle control.

Group 1- Vehicle Control (0.1 % CMC)
Group 2- Treated with 100 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 3- Treated with 200 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 4- Treated with 400 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 5- Treated with standard drug Pentazocine 10 mg/kg

Analgesic activity by Eddy's hot plate method

In Hot plate test, (Table 2) the reaction time of the test group increased to a significant level 30 minutes after the treatment. The peak effect was observed at 60 minutes interval. Effect of the extract was persisted up to 120 minutes.

Table 2: Evaluation of antinociceptive activity of methanolic leaf extracts of *Celosia argentea* by Hot plate method

Group	Reaction time in Sec at different time intervals				
	0 min	30 min	60 min	90 min	120 min
1	2.12±0.87	2.18±0.95	2.2±0.48	2.24±0.86	2.18±0.71
2	2.08±0.59	10.18±0.87**	11.22±0.75**	13.28±0.93**	14.26±0.83**
3	2.14±0.61	12.26±0.76**	14.62±0.65**	16.82±0.67**	18.52±0.96**
4	2.18±0.73	14.18±0.74**	16.23±0.93**	18.28±0.99**	19.88±1.02**
5	2.14±0.85	16.22±1.03**	18.42±0.94**	20.42±0.53**	22.16±0.79**

Values are expressed as mean ±SD (n=6). Significance P <0.05 (*), P <0.01 (**) as compared to vehicle control.

Group 1- Vehicle Control (2 ml of 1 w/v % CMC Suspension)
Group 2- Treated with 100 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 3- Treated with 200 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 4- Treated with 400 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 5- Treated with standard drug Pentazocine 10 mg/kg

Anti-inflammatory activity by Carrageenan-induced paw edema

The MECA was observed for anti-inflammatory activity by using carrageenan-induced paw edema and found to be significant at the level of P<0.001 when compared with the vehicle 1% CMC (Control Group) and indomethacin (Standard) (Table 3). The percent inhibition of paw edema of different doses of MECA after 3 hr were found is 18.47 % (100mg/kg p.o.), 26.08 % (200mg/kg p.o.) and 39.13 % (400 mg/kg p.o.) compared with standard drug indomethacin (1 mg/kg p.o.) shows 58.69 %.

Table 3: Evaluation of antinflammatory activity of methanolic leaf extracts of *Celosia argentea* by Carrageenan-induced Paw Edema

Group	0 min.	30 min.	60 min.	120 min.	180 min	Inhibition (%)
I	0.76±0.52	0.89±0.48	0.82±0.51	0.93±0.59	0.92±0.61	---
II	0.8±0.81	1.06±0.73	0.96±0.68	0.81±0.62*	0.75±0.84**	18.47
III	0.76±0.78	0.94±0.72	0.86±0.69	0.74±0.64**	0.68±0.78**	26.08
IV	0.77±0.89	0.9±0.76	0.82±0.85	0.67±0.75**	0.56±0.61**	39.13
V	0.78±0.72	0.82±0.98	0.79±0.79*	0.62±0.84**	0.38±0.68**	58.69

Values are expressed as mean ±SD (n=6). Significance P <0.05 (*), P <0.01 (**) as compared to vehicle control

Group 1- Vehicle Control (2 ml of 1 w/v % CMC Suspension)
Group 2- Treated with 100 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 3- Treated with 200 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 4- Treated with 400 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 5- Treated with standard drug Indomethacine 10 mg/kg

Antidepressant activity

The MECA was observed for antidepressant activity by forced swim test and tail immersion method. In both models MECA significantly reduced ($p<0.01$) immobility period when compared with that of the control group and standard drug imipramine (Table 4).

Table 4 Evaluation of antidepressant activity of methanolic leaf extracts of *Celosia argentea*

Group	Immobility period (sec) by Forced Swim Test	Immobility period (sec) by tail immersion
I	150.54±3.62	148.54±4.32
II	126.26±2.45**	116.26±2.56**
III	119.23±3.24**	99.23±2.74**
IV	93.15±3.28**	83.24±3.32**
V	86.42±3.56**	76.54±3.18**

Values are expressed as mean ±SD (n=6). Significance P <0.05 (*), P <0.01 (**) as compared to vehicle control.

Group 1- Vehicle Control (2 ml of 1 w/v % CMC Suspension)
Group 2-Treated with 100 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 3- Treated with 200 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 4- Treated with 400 mg/kg methanolic leaf extract of *Celosia argentea*.
Group 5- Treated with standard drug Imipramine 30 mg/kg

DISCUSSION

Antinociceptive activity was determined by using tail flick and Eddy's hot plate method. The MECA posse's significant antinocoiceptive activity by an increase in reaction time may be due to the same mechanism. The hot plate test is believed to show the central mechanism. The effect of MECA starts and attains the peak very early; hence it may be used in acute painful conditions. The findings validate the therapeutic use of test drug in different conditions of pain[28].

Anti-inflammatory activity by carrageenan-induced hind paw edema is an appropriate evaluation for appraising anti-inflammatory drugs and to check anti-edematous effect of natural products[29]. The percent inhibition of paw edema after MECA treatment increased significantly after 180 minutes. Flavonoids present in MECA are known to inhibit the enzyme prostaglandin synthetase, more specifically the endoperoxidase and reported to produce anti-inflammatory effects[30].

A decrease in the duration of immobility is indicative of an antidepressant-like effect. Forced swim test (FST) and Tail Immersion method (TIM) are widely used to screen new antidepressant drugs. These tests are quite sensitive and relatively specific to all major classes of antidepressant including tricyclics, 5-HT reuptake inhibitors, MAO inhibitors etc. The FST and TIM induce a state of despair in animals. The immobility referred to as behavioral despair in animals is claimed to produce a condition similar to human depression[31]. MECA significantly reduced immobility.

From the result, it may be said that MECA has potential antinociceptive, anti-inflammatory, and antidepressant activities. There is a need for conducting clinical trials to give promising antinociceptive, anti-inflammatory, and antidepressant drugs.

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