



Potentiation of Phenobarbitone Induced Hypnosis by *Celosia Argentea* Leaves

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Received: 1 April 2014, Accepted: 24 May 2014, Published Online: 10 June 2014

Abstract

The present study was planned with the rationale of evaluating the hypnotic potentiating activity of *celosia argentea* (200mg/kg, P.O) leaf methanolic extract against Phenobarbitone induced hypnosis in albino rats. Onset of sleep and Duration of sleep were the parameters measured in rats for the present study. Control group rats exhibited duration of sleep for a period of 871 minutes (14.5 hours) with phenobarbitone 50mg/kg. Rats pretreated with *celosia argentea* leaves extract exhibited a potentiation in sleep time induced by phenobarbitone with increase in duration of sleep for a period of 1123 minutes (18.71 hours) compared to sleep time in control rats. However *celosia argentea* leaves hypnotic potentiation effect is less in comparison to standard Clonazepam (0.5mg/kg). *Celosia argentea* leaves have no effect on the onset of sleep induced by phenobarbitone. onset of sleep was the time elapsed between administration of phenobarbitone and the loss of lighting reflex, while total sleeping time was measured as the duration between the loss and regain of righting reflex. Preliminary phytochemical screening of *celosia argentea* leaves reveals the presence of flavonoids, glycosides, alkaloids and steroids in methanolic extract. Hence the following hypnotic potentiating effect of methanolic extract of *celosia argentea* leaf may be attributed to these active constituents.

Keywords: *Celosia argentea*, methanolic extract, hypnotic potentiation effect

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Manuscript ID: IJMPR2064



PAPER-QR CODE

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1. Introduction

Hypnotics also known as soporific drugs are the drugs which induce sleep resembling to the natural sleep and are widely used in the treatment of insomnia¹. The currently available allopathic hypnotic drugs are habit forming and they have a destructive impact on sleep pattern. Hence it is recommended that hypnotics should be used for a short period of time². Many medicinal plants have been used for treatment of insomnia in Asia which has less impact on sleep pattern. However, scientific evidence and precise mechanism for their sedative-hypnotic activity have not been

fully investigated³. CNS depressant activity has been observed in many plants and many plants can potentiate the CNS depressant activity of other drugs. Hence the present study was undertaken to evaluate the hypnotic potentiation effect of *celosia argentea* leaves by using phenobarbitone 50mg/kg induced hypnotic model in rats. Since there are no reports of hypnotic activity of plant *celosia argentea*, the present study is planned to exploit the hypnotic potentiation activity of *Celosia argentea* leaves by phenobarbitone induced hypnotic model in rats.

2. Materials and Method

Fresh leaves of *celosia argentea* were collected from the surrounding gardens of the Guntur district, Andhra Pradesh, India. After the leaves were authenticated by a botanist, leaf specimens have been deposited at the museum of the college for future reference. Fresh mature leaves were shade dried at room temperature, coarse powdered and extracted with methanol by Soxhlet's extraction method. Thereafter, the extract was concentrated by placing them in a china dish and allowing them for evaporation of solvent at room temperature until semisolid extract is formed. The percentage yield of the leaf extract was found to 9.8%. The extract was stored in airtight container in refrigerator below 10°C. Appropriate concentration of stock solution of extract were prepared using distilled water and used for the following studies.

Preliminary phytochemical screening⁴

Preliminary phytochemical tests were performed for the methanolic extract of *Celosia argentea* leaf to detect the presence of phytochemicals by following the standard methods described in the practical pharmacognosy of Kokate and Khandelwal. The results have been tabulated in table I.

Experimental animals

Male albino rats (150-200g) were used in the experiments. They were procured from Sainath agencies, Musheerabad. After randomization into various groups and before initiation of experiment, the rats were acclimatized for a period of 10 days. Animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding and maintained under standard environmental conditions such as temperature ($26 \pm 2^\circ\text{C}$), relative humidity (45-55%) and 12hr dark/light cycle. The animals were fed with rodent pellet diet (Golden Mohur Lipton India Ltd.) and water *ad libitum*. The study protocol was approved from the institutional animal ethics committee (IAEC) before commencement of experiment (1230/a/08/CPCSEA).

Determination of acute toxicity

The *celosia argentea* methanolic extract was studied for acute toxicity study at a dose of 5 mg/kg, 50mg/kg, 300 mg/kg, and 2000 mg/kg P.O in albino mice. For each dose 3 mice were used (up and down procedure, OECD guidelines No. 425). The methanolic extract was found safe in all mice at 5, 50, 300 & 2000mg/kg doses. Further the mice were subjected to a dose of 5000 mg/kg. At 5000 mg/kg all the mice were died exhibiting mortality and confirming acute toxicity of the extract. Hence a cut off dose of 2000mg/kg is selected as safer dose and 1/10th of 2000mg/kg i.e 200mg/kg of *celosia argentea* extract was selected for our *in vivo* study.

Effect of *celosia argentea* leaves on Phenobarbitone induced hypnosis in rats^{5,6}

Hypnosis was induced in control group animals (consisting of 6 rats) by per oral administration of phenobarbitone 50mg/kg. The test and standard rats (each group consists of 6 rats) received methanolic extract of *celosia argentea* 200mg/kg and clonazepam 0.5mg/kg per orally one hour prior to the administration of phenobarbitone. The parameters measured in the present study are onset of sleep and duration of sleep i.e the time for onset of sleep was the time duration between the loss and regain of righting reflex elapsed between administration of phenobarbitone and the loss of lighting reflex, while total sleeping time was measured as the duration between the loss and regain of righting reflex.

Statistical Analysis

The values are represented as mean \pm S.E.M, and statistical significance between treated and Control groups was analyzed using One way ANOVA, followed by Dunnett's test where $P < 0.001$, $P < 0.01$ and $P < 0.05$ was considered statistically significant.

3. Results and Discussion

Results of the preliminary phytochemical investigation of methanolic extract of *celosia argentea* leaves are shown in table. I. The results obtained by phenobarbitone induced hypnotic model in rats (Table II) indicates that per oral administration of *Celosia argentea* leaf extract before hypnosis induction increases the duration of sleep induced by phenobarbitone 50mg/kg i.e from 871 minutes (control rats) to 1123 minutes (*celosia argentea* extract treated rats). This indicates that *celosia argentea* leaves have sleep (hypnotic) potentiating activity. However the hypnotic potentiation effect of *celosia argentea* leaves extract was less in comparison to standard hypnotic drug clonazepam (duration of sleep is 1219 minutes). The exact mechanism of hypnotic potentiation effect of *celosia argentea* leaves is not understood. However it may be hypothesized that *celosia argentea* leaves methanolic extract (200 mg/kg) exhibits hypnotic potentiation effect by enhancing the GABA transmission in the brain, thereby preventing neuronal firing (depolarization) of brain neurons.

Table 1. Phytochemical Investigation of Celosia Argentea Leaf Methanolic Extract Phytoconstituents
Methanolic extract of *Celosia argentea*

Phytoconstituents	Methanolic extract of <i>Celosia argentea</i>
Carbohydrates	-
Steroids	+
Glycosides	+
Flavonoids	+
Alkaloids	+
Tannins	-

(-) Absent, (+) present

Table 2. Phenobarbitone induced hypnotic potentiation by *Celosia Argentea*

Groups of rats	Time In Minutes	
	Onset of Sleep	Duration of Sleep
Control	325± 1.13 minutes	871 ± 0.11minutes
Test	331±0.53 minutes	1123±0.06* minutes
Standard	323±1.02 minutes	1219±1.44** minutes

* Significant at p< 0.05; ** highly significant at p<0.01; *** Very highly significant at p<0.001



Figure 1. Phenobarbitone Induced Sleep in Rats

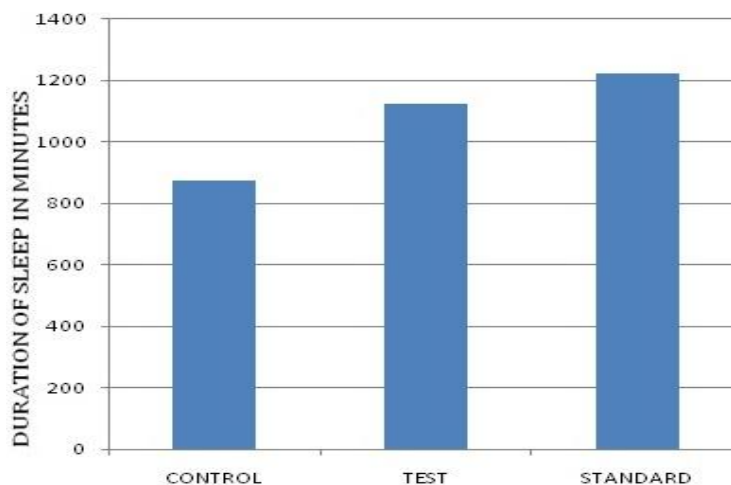


Figure 2. Graphical Representation of Effect of *Celosia Argentea* on Phenobarbitone Induced Hypnotic Model in Rats

Control = distilled water, **Test**= Methanolic Extract of *Celosia Argentea* (200mg/kg), **Standard** = Clonazepam (0.5mg/Kg In 2% Gum Acacia)

4. Conclusion

The Results of the present study describes that the celosia argentea leaves methanolic extract at 200mg/kg possessed significant hypnotic potentiating activity and thus supports the use of Celosia argentea leaves in treatment of insomnia. Insomnia is a common problem that occurs due to enhanced neuronal excitation in the brain and celosia argentea leaf extract is thought to inhibit neuronal excitation by increasing GABA levels in the brain.

5. Acknowledgement

The authors are grateful to the management and staff of Vijaya College of Pharmacy, Hyderabad for providing the facilities for our Research.

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