

ROLE OF CESTRUM NOCTURNUM ON AROMA IN THE MANAGEMENT OF DEPRESSION AND LEARNING DEFICITS

Dr. Ravish Kumar Sahu, Ms. Sheetal Yadav, Mr. Puspendra Singh Thakur,
Mr. Bhanu Prakash Patel, Mr. Yogesh Rahul

SVN Institute of Pharmacy and Research, Swami Vivekanand University, Sagar

Abstract:

Major depression is characterized by symptoms like sad mood, loss of interest and pleasure, low energy, worthlessness, guilt, psychomotor retardation or agitation, change in appetite and/or sleep, melancholia, suicidal thoughts, etc. Brain lesions cause memory to break down in several distinct ways in people. First, cortical lesions cause disturbances in short-term memory. Second, other cortical lesions disturb the retrieval of previously well-established semantic and episodic memories. Aromatherapy is currently used worldwide in the management of depression, anxiety, some cognitive disorders, insomnia and stress-related disorders. Although essential oils have been used, reputedly effectively, for centuries as a traditional medicine, there is very little verified science behind this use. *Cestrum nocturnum* is a garden shrub commonly known as "lady of the night" which is used as a remedy for different health disorders. This sprawling shrub has glossy simple leaves, vine like stems, greenish-creamy white tubular flowers and fleshy berries. Behavioral parameters are the primary evidence to confirm depression as well as anti-depressant of treatments. All the parameters are based on pathophysiology of depression because depression is evaluated through stress or immobilization of animal like mice and rats. The plant *Cestrum nocturnum* shows the richness of phytochemicals except Carbohydrates. As per study of various behavior parameters and biochemical estimation of essential oil of *Cestrum nocturnum* it concluded that the plant *Cestrum nocturnum* shows the positive response for antidepressant activity and learning/ memory impairment as compare to negative control but the response is not better than standard drug response. The response of plant *Cestrum nocturnum* is better than negative control group comparatively.

Keywords: *Cestrum nocturnum*, Aroma therapy, Mice, Depression, Learning and memory

1. Introduction

Major depression is characterized by symptoms like sad mood, loss of interest and pleasure, low energy, worthlessness, guilt, psychomotor retardation or agitation, change in appetite and/or sleep, melancholia, suicidal thoughts, etc. In bipolar disorder cycles of mood swings from mania to depression occur over time. The mood change may have a psychotic basis with delusional thinking or occur in isolation and induce anxiety. On the other hand, pathological anxiety may lead to depression ⁽¹⁾. While many brain regions have been implicated in regulating emotions, we still have a very rudimentary understanding of the neural circuitry underlying normal mood and the abnormalities in mood that are the hallmark of depression. This lack of knowledge is underscored by the fact that even if it were possible to biopsy the brains of patients with depression, there is no consensus in the field as to the site of the pathology, and hence the best brain region to biopsy ⁽²⁾.

Brain lesions cause memory to break down in several distinct ways in people. First, cortical lesions cause disturbances in short-term memory. Second, other cortical lesions disturb the retrieval of previously well-established semantic and episodic memories. Third, frontal cortex dysfunction seems to be related to a memory syndrome caused by a breakdown in the ability to plan and carry out elaborative processing. Fourth, and most explored, is the amnesic syndrome(s), caused by limbic system or diencephalic lesions. ⁽³⁾

Aromatherapy is currently used worldwide in the management of depression, anxiety, some cognitive disorders, insomnia and stress-related disorders. Although essential oils have been used, reputedly effectively, for centuries as a traditional medicine, there is very little verified science behind this use. The pharmacology of the essential oils and/or their single chemical constituents, therefore, remains largely undiscovered. However, accumulating evidence that inhaled or dermally applied essential oils enter the blood stream and, in relevant molecular, cellular or animal models, exert measurable psychological effects, indicates that the effects are primarily pharmacological ⁽⁴⁾.

2. Plant Profile

Cestrum nocturnum is a garden shrub commonly known as "lady of the night" which is used as a remedy for different health disorders. This sprawling shrub has glossy simple leaves, vine like stems, greenish-creamy white tubular flowers and fleshy berries. ⁽⁵⁾ Common names of plant are Lady of the Night, Night Jessamine, Night Jasmine, Night Blooming Jessamine, family Solanaceae. ⁽⁵⁾ Phytochemical tests of the extracts of *cestrum nocturnum*

leaves revealed the presence of carbohydrates, proteins, saponins, flavonoids, alkaloids, cardiac glycosides, tannins and sterols. The various extracts were evaluated for the presence of carbohydrates, proteins, flavonoids, tannins, cardiac glycoside, saponins and alkaloids using standard procedures. Stem and Flowers extract exhibit higher concentration in phenolic contents rather than stem extract. The absorbance of the ethanolic (96%). stem, leaves, and flowers were 0.1569, 0.1896, and 0.1497, which correspond to 3.01, 3.17 and 3.74 mg GAE/g respectively. ⁽⁶⁾

3. Materials and Methods

The herb has been collected from local market, with the help of field Botanist. The herb has been authenticated by Dr. H. S. Gaur University, Department of Botany, Sagar (M.P). Herbarium number Bot/Her/B1/1364, (Ref. no. Bot/179).

Hydro-diffusion consists of extracting the essential oil with steam that circulates through the plant material. At laboratory scale, we bring a few liters of water to a boil, and steam rises in a column containing the more or less finely ground plant. The vapor phase is then directed to a condenser, and the liquid is collected in a graduated burette. Thanks to a bended connection at the base of the burette, the hydrosol flows to the left in the beaker, while the essential oil remains in the burette. After typically 2 h of extraction (calculated from the first condensed drop), we can measure the volume of oil recovered and calculate the yield from the mass of plant introduced. This technique has the advantage of allowing us to recover the hydrosol. It also allows us to perform extractions on larger quantities of plants ⁽⁷⁾.

Description of groups

Total 09 groups, 06 animals in each group for statistical significance result

Control Group (Vehicle Treated)

Negative Control (Disease Induced)-

- (i) For depression
- (ii) For learning/memory impairment

Standard

- (i). For depression
- (ii). For learning/memory impairment

Test group-1 (*Cestrum nocturnum* 100mg/kg)

- (i) For depression
- (ii) For learning/memory impairment

Test group-II (*Cestrum nocturnum* 200mg/kg)

- (i) For depression
- (ii) For learning/memory impairment

Animal: Mature Sprague-Dawley Mice (20–25gm) were used for the study. All animal were kept in standard plastic polypropylene cages with stainless steel coverlids and wheat straw will be used as bedding material. The animal were facilitated with standard environment of photoperiod (12:12 hr dark: light cycle) and room temperature (23 ± 20 C). The animal assists free to feed and purified water ad libitum. All experiment were according to CPCSEA guidelines and approved by IAEC (CPCSEA/2022/137).

Animal model:- (*Stress induced depression by immobilization*) Animals were immobilized (IMO) for 3 hr. by taping all the four limbs on board by putting them on their backs using zinc oxide hospital tape. The animals were released by unraveling the tape after moistening with acetone in order to avoid pain and discomfort. In unstressed group, the mice were handled without any stress. ⁽⁸⁾

Drug induced memory impairment:- Repeatedly exposed to psychomotor stimulant drug for 07 days repeated dose (two times a day), amphetamine (AMP, 3.0mg/kg i.p.), developed cognitive and behavioral abnormalities that are similar to those associated with paranoid schizophrenia. In the experiments reported, we were examining the long-term effects of repeated intermittent injections of AMP on frontal cortex DA activity ⁽⁹⁾.

4. Pharmacological Screening

Table. 4.1. For Depression Values are expressed MEAN \pm SEM, n=6, ** = P<0.01, *** = P<0.001 when compared to normal control group, b = ns when compared to normal control group, a*** = P<0.001 when compared to negative control group, c= ns when compared to standard group. Standard = Amitriptyline (4mg/kg).

S. No.	Groups	Force swim test	Hole board test	Open field test	
				No. of Squire Cross	No. of Rearing
1	Positive Control	75 \pm 2.6457	45 \pm 2.0816	61 \pm 1.5270	48 \pm 1.5916
2	Negative Control	23 \pm 1.1547	11 \pm 1.1547	19 \pm 0.7302	11 \pm 2.3094
3	Standard	60 \pm 1.5275* *	36 \pm 1.5275* **	54 \pm 1.9832**	46 \pm 1.0645* **

4 .	Test Group-I (100mg/kg)	33±2.0816*	16±1.1547*	31±1.1254*	26±1.1909*
5 .	Test Group-II (200mg/kg)	51±1.7320* *	26±1.7320* *	46±2.6451**	36±2.1602* *

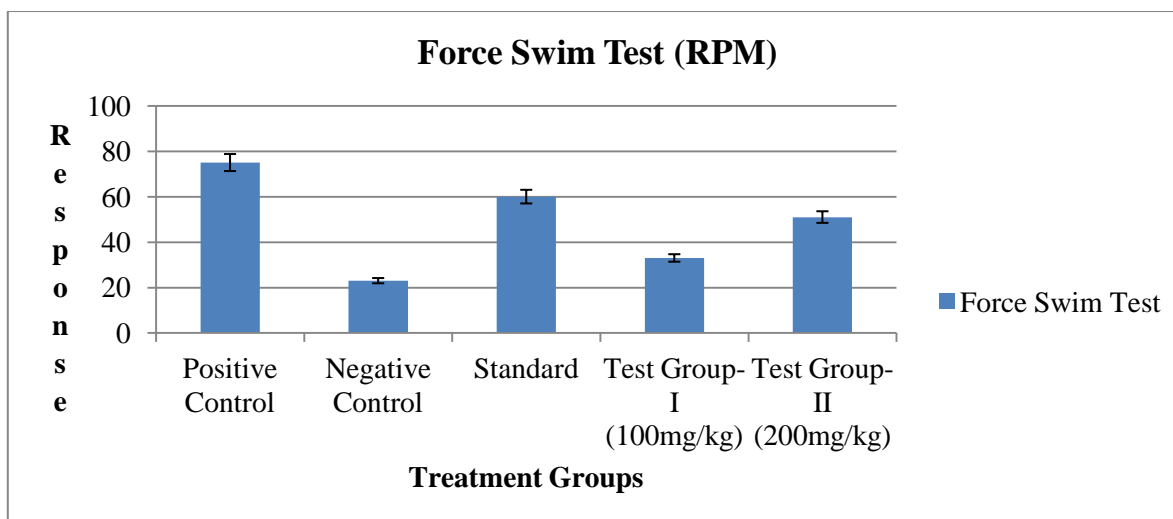


Fig. 4.1. Effect of *Cestrum nocturnum* on Force Swim Test

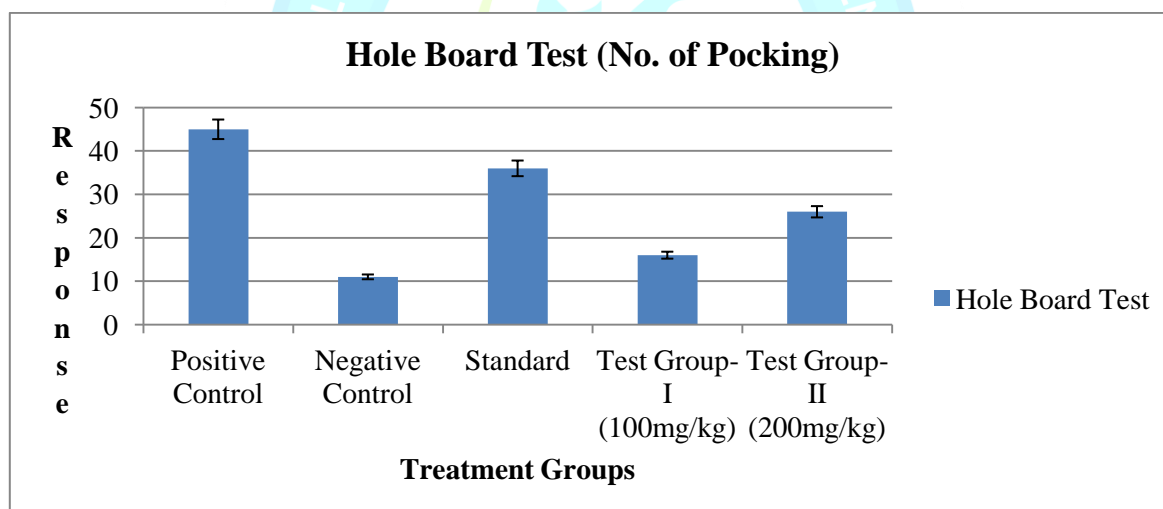


Fig. 4.2. Effect of *Cestrum nocturnum* on Hole Board Test

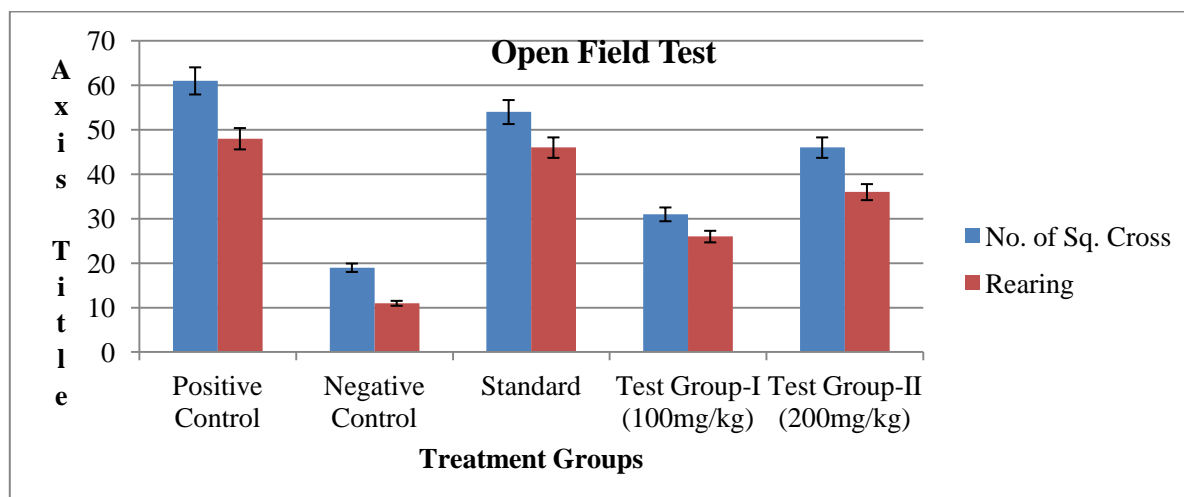


Fig. 4.3. Effect of *Cestrum nocturnum* on Open Field Test

Table 4.2. For Learning/Memory Impairment activity Values are expressed MEAN \pm SEM, n=6, ** = P<0.01, *** = P<0.001 when compared to normal control group, b = ns when compared to normal control group, a*** = P<0.001 when compared to negative control group, c = ns when compared to standard group. Standard = Chlopromazine (10mg/kg).

S. No.	Groups	Pole Climbing Test	Actophotometer activity	Staircase activity
1.	Positive Control	192 \pm 2.5166	80 \pm 1.0026	51 \pm 1.5271
2.	Negative Control	58 \pm 2.2304	28 \pm 2.3094	15 \pm 1.4864
3.	Standard	169 \pm 3.7854**	69 \pm 3.0012* **	48 \pm 1.2870**
4.	Test Group-I (100mg/Kg)	109 \pm 2.0906*	41 \pm 2.0816*	23 \pm 1.0076*
5.	Test Group-II (200mg/Kg)	155 \pm 2.5094**	59 \pm 1.7320* *	28 \pm 1.9840*

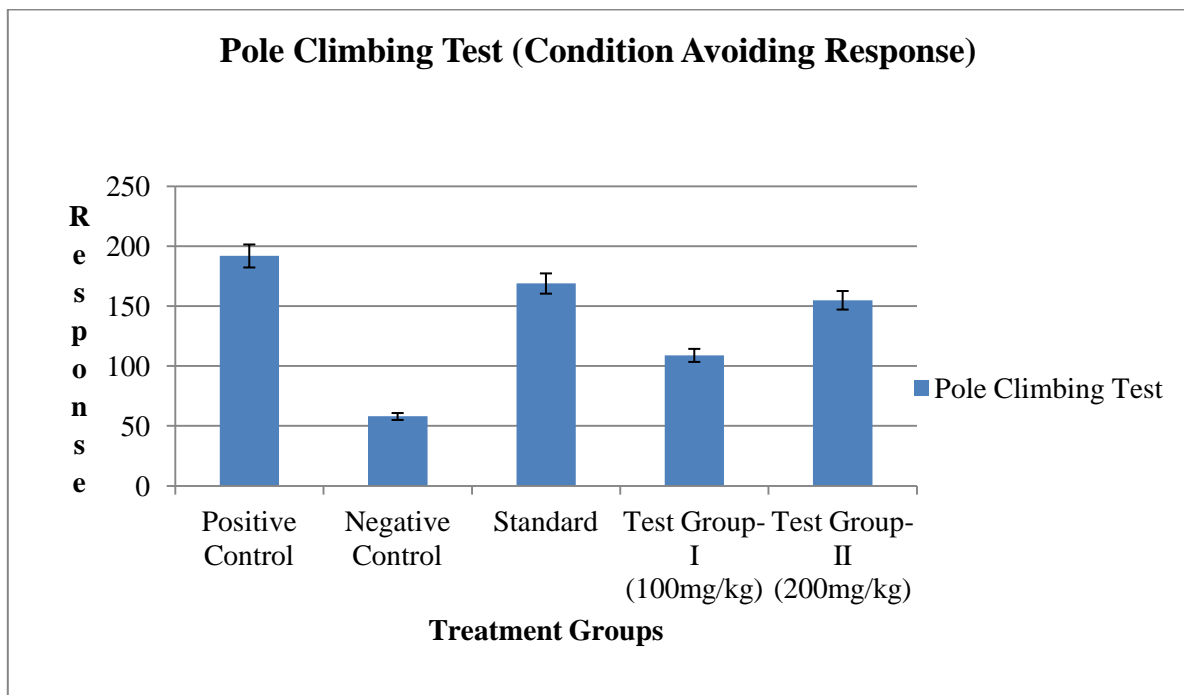


Fig. 4.4. Effect of *Cestrum nocturnum* on pole Climbing Test

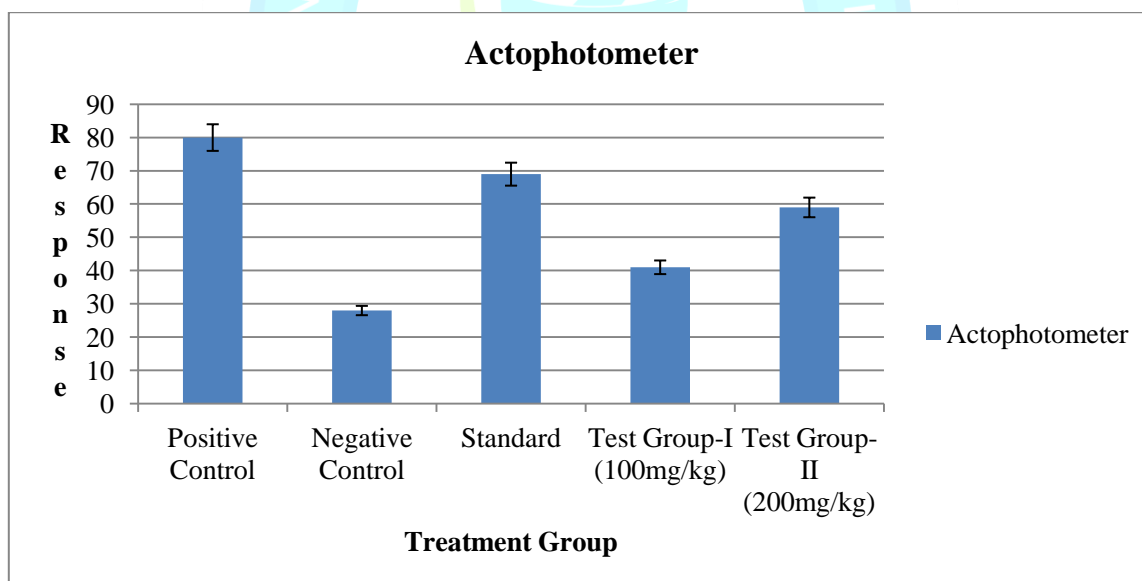


Fig. 4.5. Effect of *Cestrum nocturnum* on Actophotometer

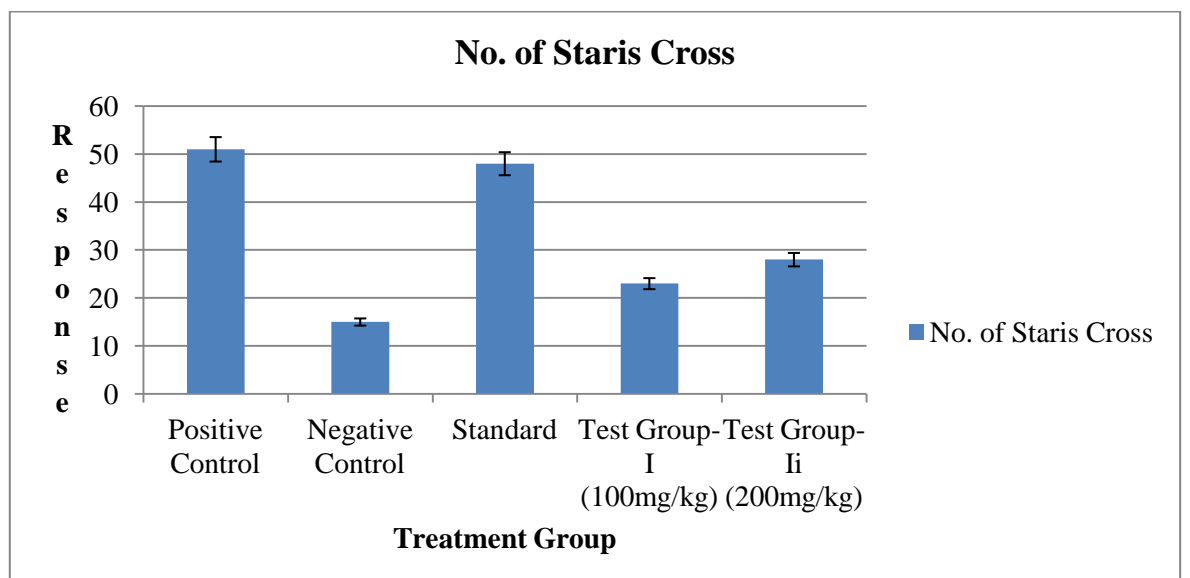


Fig. 4.6. Effect of *Cestrum nocturnum* on Staircase Test

5. Discussion and Conclusion

Behavioral parameters are the primary evidence to confirm depression as well as antidepressant of treatments. All the parameters are based on pathophysiology of depression because depression is evaluated through stress or immobilization of animal like mice and rats.

Forced Swim test is the most commonly used preliminary screening tests for characterizing potential antidepressant drugs. In these models *Cestrum nocturnum* at doses of 100 mg/kg, and 200 mg/kg, showed significant increase in the motor activity of mice which elevate depressed mood by decreasing immobility time of mice. The parameters observed in this model are immobility time of mice. Drugs which decrease immobility time leads to increase in the motor activity of mice which inhibit depression developed due to swimming of mice in these tests and offer protection against depression induced by these methods. In the present study, *Cestrum nocturnum* (100 & 200 mg/kg,) has shown a significant dose dependent activity i.e. increase in the dose of the drug proportional to decrease in the immobility time threshold and offers good percentage protection as compared to control group. The highest significant increase ($P < 0.001$) was observed for CF at 200 mg/kg.

The holeboard test is mainly used for assessing exploratory behaviors in rodents. The animal is placed on an arena with regularly arranged holes on the floor. Both frequency and duration of spontaneous elicited hole-poking behavior are then measured during a short period of time. *Cestrum nocturnum* treated mice showed a significant increase in the number

of head dipping compared to the negative control (at 100 and 200 mg/kg, respectively). The number of head-dipping also increased significantly ($P < 0.001$) in marketed drug treated mice compared to the control, as did treatments with HF and CF at both doses. The highest significant increase ($P < 0.001$) was observed for CF at 200 mg/kg.

OFT is the test to evaluate anti-anxiety effect as well as to compare the statistics with actophotometer because each square in OFT is 10x10cm and each electrode's difference in actophotometer is 6 cm so the reading should be double in OFT. Animal in control group were shows significant walk fullness in OFT (61 ± 1.5270). After administration of Aqueous extract of *Cestrum nocturnum* at dose of 200mg/kg, the animal was shows significant effect ($P > 0.001$). Rearing is the parameter in OFT which shows alertness of animal. After administration of Aqueous extract of *Cestrum nocturnum* at dose of 200mg/kg, the animal as shows significant effect ($P > 0.001$) in OFT (54 ± 1.9832) compared with standard group.

Pole climbing equipment is designed in such a way to climb the pole when stimulus is generated. Prior to the experiment, animals were trained. Training and testing is conducted in a $25 \times 25 \times 40$ cm chamber that is enclosed in a dimly light, sound attenuated box. Scrambled shock is delivered to the grid floor of the chamber. A smooth stainless steel pole, 2.5 cm in diameter, is suspended by a counter balance weight through a hole in the upper centre of the chamber. A micro switch is activated when the pole is pulled down by 3 mm. A response is recorded when a mice jumps on the pole and activates micro switch. The activation of light and speaker together is used as conditioned stimulus. After administration of Aqueous extract of *Cestrum nocturnum* at dose of 200mg/kg, the animal was shows significant effect ($P > 0.001$). After administration of *Cestrum nocturnum* at dose of 200mg/kg, the animal was shows significant effect ($P > 0.001$) in pole climb (155 ± 2.5094) compared with standard group (169 ± 3.7854).

The locomotor activity of drug can be studied using actophotometer which operates on photoelectric cells which are connected in circuit with a counter when the beam of light falling on photocell is cut off by the animal, then a count is recorded. Locomotor activity after administration of Aqueous extract of *Cestrum nocturnum* at dose of 200mg/kg, the animal was shows significant effect. After administration of *Cestrum nocturnum* at dose of 200mg/kg, the animal was shows significant effect in locomotor activity (59 ± 1.7320) compared with standard group (69 ± 3.0012).

In CNS activity two parameters were measured: the number of steps climbed for

locomotor activity assessment and the number of rearing events for exploratory behavior evaluation. A step is considered climbed only if the mouse places all four paws on it, and rearing was defined as each instance the mouse stood on his two back feet. CNS activity after administration of Aqueous extract of *Cestrum nocturnum* at dose of 200mg/kg, the animal shows significant effect. After administration of *Cestrum nocturnum* at dose of 200mg/kg, the animal shows significant effect in CNS activity (28 ± 1.9840) compared with standard group (48 ± 1.2870).

The plant *Cestrum nocturnum* shows the richness of phytochemicals except Carbohydrates. As per study of various behavior parameters and biochemical estimation of essential oil of *Cestrum nocturnum*. It concluded that the plant *Cestrum nocturnum* shows the positive response for antidepressant activity and learning/ memory impairment as compared to negative control but the response is not better than standard drug response. The response of plant *Cestrum nocturnum* is better than negative control group comparatively.

6. Acknowledgements

The authors would like to acknowledge the support of colleagues and institutions that provided guidance and resources during the preparation of this review.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

8. References

1. Rayner H.S.; Thomas M. and Milford D.V. "Kidney Anatomy and Physiology". Springer International Publishing Switzerland, 2016; 1(1): 1-10.
2. Coe F. L.; Evan A. and Worcester E. "Kidney stone disease," Journal of Clinical Investigation, 2005; 115(10): 2598–2608.
3. Chhiber N.; Sharma M.; Kaur T. and Singla S. "Mineralization in health and mechanism of kidney stone formation," International Journal of Pharmaceutical Science Invention, 2014; 3(1): 25–31.
4. Han H.; Segal A.M.; Seifter J.L. and Dwyer J.T. "Nutritional Management of Kidney Stones (Nephrolithiasis)". Clinical Nutrition Research, 2015; 4(3): 137–152.
5. Skolarikos A.; Straub M. and Knoll T., "Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines," European Urology. 2015; 67(4): 750–763.

6. Phillips, R.; Hanchanale, V. S.; Myatt, A.; Somani, B.; Nabi, G. & Biyani C. S. "Citrate salts for preventing and treating calcium containing kidney stones in adults" Cochrane Database of Systematic Reviews, 2015; (10) 1-42.
7. Barbasa C.; Garciaa A.; Saavedraa L. and Muros M. "Urinary analysis of nephrolithiasis markers," Journal of Chromatography, 2002; 781(1-2): 433–455.
8. Griffith D.P.; "Struvite stones," Kidney International. 1978; 13(5): 372–382.
9. Ngo T. C. and Assimos D. G. "Uric acid nephrolithiasis: recent progress and future directions," Reviews in Urology, 2007; 9: 17–27.
10. Kumar S.B.N.; Kumar K.G.; Srinivasa V. and Bilal S. "A review on urolithiasis," International Journal of Universal Pharmacy and Life Sciences, 2012; 2(2): 269–280.
11. Ahmed K.; Dasgupta P. and Khan M.S. "Cystine calculi: challenging group of stones," Postgraduate Medical Journal, 2006; 82(974): 799–801.
12. Vijaya T.; Kumar M.S.; Ramarao N.V.; Babu A.N. and Ramarao N. "Urolithiasis and Its Causes- Short Review". The Journal of Phytopharmacology, 2013; 2(3): 1-6.
13. Daudon M.; Vincent Frochot V.; Bazin D. and Paul Jungers P. "Drug-Induced Kidney Stones and Crystalline Nephropathy: Pathophysiology, Prevention and Treatment" Springer International Publishing AG, part of Springer Nature, 2017; 5(78): 1- 40.
14. Dursun M.; Otunctemur A.; and Ozbek E. "Kidney stones and ceftriaxone," European Medical Journal of Urology, 2015; 3(1): 68–74.
15. Khan S.R.; Pearle M.S.; Robertson W.G.; Gambaro G.; Canales B.K.; Doizi S.; Traxer O.; Tiselius H.G.; "Kidney stones". Nat Rev Dis Primers. 2016; 25(2): 1-50.
16. Alelign T. and Petros B. "Kidney Stone Disease: An Update on Current Concepts". Adv Urol. 2018; 1-12.
17. Noble H. and Walsh L.K.; "Kidney Stone: Pathophysiology, diagnosis and management" British journal of nursing. 2016; 25(20):1112-1116.
18. Debra Sullivan N.E. "Kidney stones". The healthline editorial team. 2018; 12: 1-12
19. Dawson C.H.; Tomson C.R.; "Kidney stone disease: pathophysiology, investigation and medical treatment". Clin Med (Lond). 2012 Oct; 12(5):467-71.
20. Harmacek D.; Blanchard A.; Wuerzner G.; Maillard M.; Jeunemaitre X.; "Azizi M and Bonny O. "Acute decrease of urine calcium by amiloride in healthy volunteers under high-sodium diet". Nephrology Dialysis Transplantation, 2022; 37(2): 298–303.