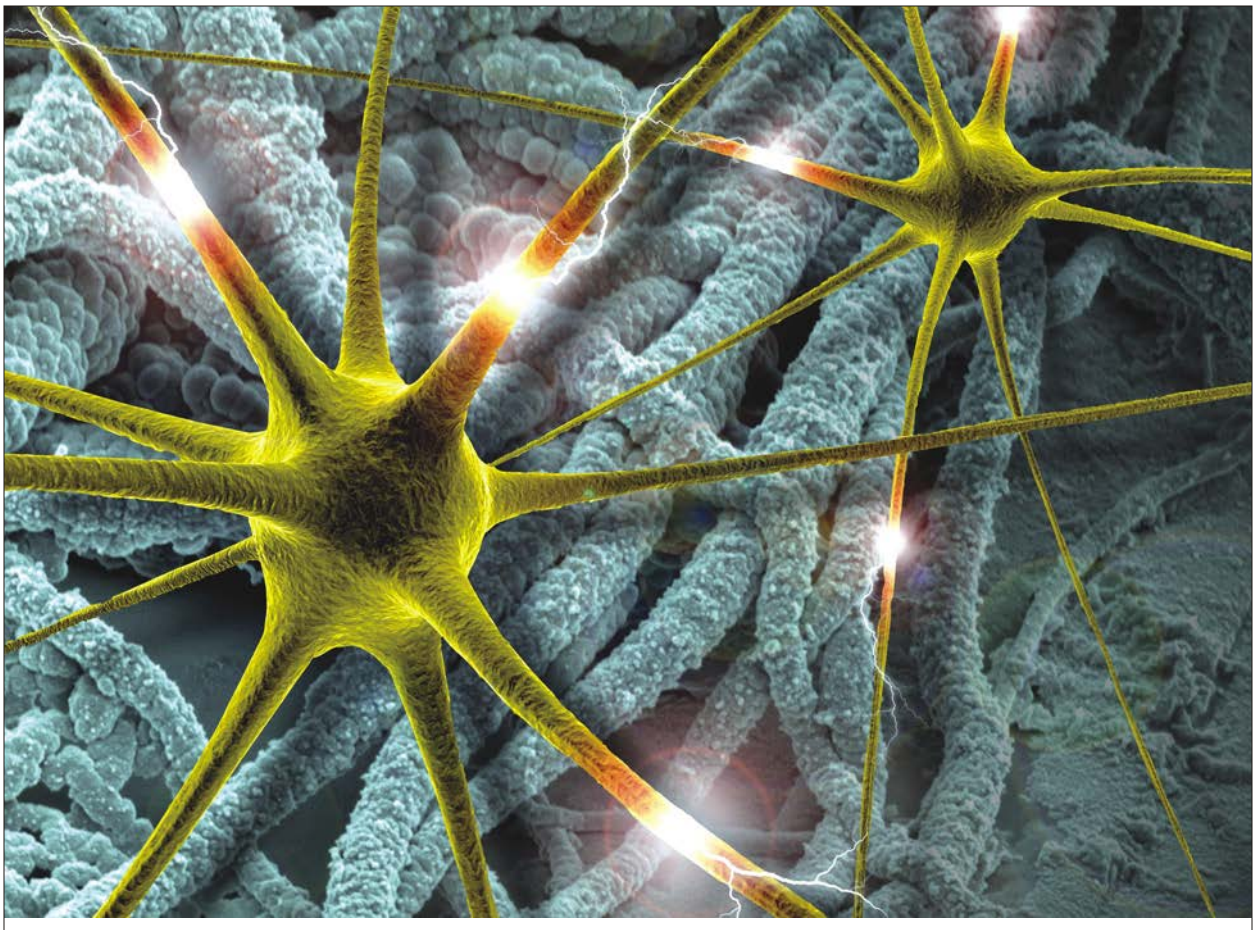

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Evaluation of Central Nervous System Activities of *Cyperus rotundus* L. Extract on Rodents

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ABSTRACT

Cyperus rotundus Ethanolic Extract (EECR) investigated for antidepressant, anxiolytic, anticonvulsant and hypnotic and muscle relaxant activities in two different animal models to find out its scientific values. Oral administration of EECR at doses of 200 and 400 mg kg^{-1} on various behavioural models such as tail suspension, hole-board, elevated-plus-maze, locomotor, strychnine, maximal electroshock induced seizure, pentylenetetrazole, rotarod, climbing an inclined screen in mice and forced swim light-dark box models in rats was utilized. In the open field test, EECR (200 and 400 mg kg^{-1}) ($p<0.05$, $p<0.01$) increased in numbers of rearing. However, the number of central motor and ambulation reduced. The number of entries and the time spent in the open arm were increased while the number of locomotion was decreased ($p<0.01$) in elevated-plus-maze and actophotometer test, respectively. The EECR (200 and 400 mg kg^{-1}) protected the mice against the pentylenetetrazole and strychnine induced convulsions; it causes significant ($p<0.05$ and $p<0.01$) dose dependent increase in latency of convulsion. Treatment with EECR decreased the duration of the tonic hind limb extension induced by electroshock. The EECR treatment also significantly increased the hypnotic's time and decreased motor co-ordination of experimental animals. These findings are consistent with the hypothesis that *C. rotundus* treatment triggers immobility behavior, time spent in light, locomotor and climbing time in rat and mice model. Further studies will confirm the mechanism of action of *C. rotundus* for CNS drug development.

Key words: Anxiety, *Cyperus rotundus*, pentobarbital, open field test

INTRODUCTION

Central nervous system plays a vital role in the physiological organization of the completely human body. Modern world, everyday people suffered by depression, anxiety, epilepsy and restlessness (Moreno *et al*., 2014). While, majority of commercial drugs, benzodiazepines, diazepam, zolpidem, zopiclone and zaleplon caused adverse side effects like tiredness, weight gain, nausea, dry mouth, sexual dysfunction, amnesia, sedation, headache and wooziness (Dhingra and Sharma, 2006). Previous reports point out the herbal medicines played a vital role in CNS disorders (Carlini, 2003). *Cyperus rotundus* L. (Cyperaceae) is perennial invasive weeds originally to India, after that widely found in tropical and temperate regions of Asia, South Africa and South America (Gordon-Gray, 1995). The roots and rhizomes of *C. rotundus* used to treat chronic diarrhea, bowel

disorders, skin rashes and excess bleeding. It also exhibited anti-estrogenic, antimicrobial, anthelmintic, antihistaminic, antiemetic, antipyretic and antidiabetic activities (Shivakumar *et al*., 2009). The bioactive compounds in the tubers of *C. rotundus* are responsible for spicy aroma of black pepper, such as α-cyperone, β-selinene, cyperene, sugeonol, isokobusone and rotundone (Siebert *et al*., 2008). Based on review and issues of commercial drugs, the present study aimed to evaluate central nervous system activities of *C. rotundus* of using Wistar albino rats.

MATERIALS AND METHODS

Drugs and chemicals: The experimental drug pentobarbitone obtained from Rhone-Poulenec, (Mumbai, India). All other chemicals used were of analytical grade obtained from (Sigma Aldrich, USA).

Plant material: Tubers of *C. rotundus* collected from outskirts of Erode, Tamil Nadu, India during January 2011. The plant was identified and authenticated by Botanical Survey of India, Tamil Nadu Agricultural University Campus, Southern Regional Centre, Coimbatore and (Voucher No. BSI/SRC/775/23/2012-13/Tech) has been deposited in the herbarium for future references.

Extraction: Five hundred grams of tubers washed with fresh water to remove adhering dirt and foreign particles. After that, the material of *C. rotundus* was shade dried, crushed and grinded to get coarse powder. The powdered material extracted with 80% ethanol for 72 h in a cold percolation method. The menstruum collected, concentrated by vacuum distillation. The air-dried dark gray residue used to further experiment.

Experimental animals: The Swiss mice (18-22 g) and Wistar rats (180-220 g) were procured from Central Animal House, IRT Perundurai Medical College, Tamil Nadu, India. Animals housed at a temperature of 24±2°C and relative humidity of 30-70% at 12:12 light: dark cycle followed. All animals permitted to free access to water and pellet fed (M/s. Hindustan Lever Ltd. Mumbai). The experimental events and protocols used in this study followed by NIN and approved by the Institutional Animal Ethics Committee (Reg. No. 688/02/NCP/CPCSEA) of Nandha College of Pharmacy and Research Institute, Tamil Nadu, India.

Acute toxicity study: Acute toxicity of *C. rotundus* Ethanolic Extract (EECR) evaluated according to the method described by an Organization of Economic Cooperation and Development Guideline (OECD) 423 (Ecobichon, 1997). The animals were kept fasting overnight. The EECR administered orally at a dose of 5 mg kg^{-1} (0.5% CMC) initially to separate groups of mice and mortality observed for 3 days. If mortality observed in 4/6 or 6/6 animals, then the dose administered considered as toxic dose. However, if the mortality was found in single mice out of 6 animals, then the dose was repeated with higher 50, 300, 500, 1000 and 2000 mg kg^{-1} b.wt. Control mice given 10 mL kg^{-1} of water. Behavioural changes and mortality of experimental mice observed for 24 h. After that, continued observations composed to the 14th day.

Treatment schedule: The 24 mice and 24 rats were divided into eight groups of six animals each. First four groups contain experimental Swiss mice and last four groups contain Wistar rats. Group 1, served as control, treated with 0.5% Carboxymethylcellulose (CMC) solution (10 mL kg^{-1}); Group 2 treated with diazepam (1 mg kg^{-1}); Group 3 and 4 treated with EECR by doses of 200 and

400 mg kg^{-1}; Group 5, served as control rats, treated with 0.5% CMC solution (10 mL kg^{-1}); Group 6 treated with Diazepam (1 mg kg^{-1}); Group 7 and 8 treated with EECR by doses of 200 and 400 mg kg^{-1}, respectively.. The drugs were administered orally by suspend in 0.5% CMC 30 min before the initiation of experiment. Forced swim test Imipramine (20 mg kg^{-1}) used as the standard drug.

Antidepressant, anxiolytic, anti convulsant, hypnotic and muscle relaxant activities of EECR in Swiss mice model

Tail suspension test: The tail suspension test conducted in accordance with the method described by Steru *et al*. (1985).

Elevated plus maze: The elevated plus maze test is the most extensively used to access the anxiety that depend upon the study of spontaneous behavior. After treatment with EECR (200 and 400 mg kg^{-1}), the animals were placed in the centre of the elevated plus maze and noticed the number of open and closed arm entries and time spent on open and closed arm in the mice (Herrera-Ruiz *et al*., 2007).

Loco motor activity: The locomotor test is usually involved forced confrontation of a rodent with the situation (Flint *et al*., 1995). Mice can travel between compartments through an opening (7.5×7.5 cm) located at floor level in the centre of the partition involving two compartments. The test initiated by placing the mouse into the white, aversive partition to increasing aversion of anxiety behavior. The time spent in the compartments monitored for 5 min.

Hole-board test: The poking of the nose into a hole is the usual behavior of mice indicating the definite degree of curiosity (Takeda *et al*., 1998). After treatment with EECR (200 and 400 mg kg^{-1}) animals were located in the center of the hole-board and allowed freely to explore the equipment for 5 min. The number of heads dipping recorded by visual examination. Head dip scored if both eyes disappeared keen on the hole (Sheik *et al*., 2014a).

Pentylenetetrazole induced convulsions: The experiment mice are considered a model of human absence epilepsy and myoclonic seizure. After treatment, the animals noticed for duration of convulsion induced by Pentylenetetrazole were recorded (Amabeoku *et al*., 2007).

Strychnine induced convulsions: The convulsing exploitation of strychnine is due to interfering with postsynaptic inhibition mediated by glycine. After treatment, the animals observed for a period of convulsion induced by strychnine was recorded (Yemitan and Salahdeen, 2005).

Electro-shock induced seizure model: The electroshock attempt in mice primarily used as a sign for extracts in grand mall epilepsy. Followed by the treatment, mice were noticed for the incidence and duration of extensor tonus was noted (Achliya *et al*., 2005).

Pentobarbitone induced sleeping time: The test used to reveal CNS active properties of extracts. The loss of righting reflexes measured as a decisive factor for the duration of pentobarbitone induced sleeping time. After treatment, the effects of EECR (200 and 400 mg kg^{-1}) was recorded as follows: Time beyond among the administration of pentobarbitone until loss

righting reflex the sedative action was recorded as the time from the lose to its revival was measured as the duration of sleep (Herrera-Ruiz *et al*., 2007).

Rota-rod method: The test used to evaluate the activity of EECR (200 and 400 mg kg^{-1}) interfere with motor coordination. The equipment consists of a horizontal metal rod covered with rubber to 3 cm diameter attached to a motor with speed accustomed to rotations min^{-1}. The number of animals falling from the roller during this time counted.

Climbing test: The mice formed to climb a chain of (6 cm long) floating from a clamp of a retort stand (100 cm above ground). Only those mice that climb the chain within 10 sec selected for the test. After treatment with EECR (200 and 400 mg kg^{-1}), experimentation took place for 10 min, the climbing capability was observed.

Inclined screen test: The inclined plane test is to determine the skeletal muscle relaxant activity (Sheik *et al*., 2014b).

Antidepressant and anxiolytic activities of eecr in wistar rat model

Forced swim test: The test carried out according to a modification of the traditional method described by Porsolt *et al*. (1977) and Cryan *et al*. (2002) for rats.

Light-dark box test: The testing initiated by placing the mice into the white, aversive partition to increasing aversion to the light partition and to increase the sensitivity of measuring anxiety behavior and the time spent in the compartments were monitored for 5 min (Zanoli *et al*., 2000).

RESULTS

Toxicity studies: Acute toxicity of EECR did not produce any mortality orally up to 2000 mg kg^{-1} observed for 5 h after administration. There were no visible signs of delayed toxicity and mortality observed for 14 days.

Antidepressant effect of eecr in mice: Table 1 represents the result of climbing time and tail suspension test. A decrease in the duration of immobility was regarded with the standard drug and EECR ($p<0.01$) in all the tested doses as opposed to the control. The EECR in doses of 200 and 400 mg kg^{-1} produced a greater decrease in the duration of immobility as compared to the standard drug imipramine.

Anxiolytic effect of EECR in mice: Extract at doses of 200 and 400 mg kg^{-1} produce a low number of entries in the closed arm, while control (10 mL kg^{-1}) had the highest closed arm entry value of 11.38±0.29. The effects of EECR and diazepam resulted in potential increases in the total number of entries into the two arms (Table 2). In the hole board test, there was a

Table 1: Antidepressant activity of EECR in mice using climbing counts and tail suspension test

Groups	Climbing counts (numbers)	Tail suspension test (Immobility time in TST)
Control (0.5% CMC)	8.25	171.87
Diazepam (1 mg kg^{-1})	4.11	106.12
EECR (200 mg kg^{-1})	7.09*	169.77*
EECR (400 mg kg^{-1})	6.87**	156.75**

Values are Mean±SD (n = 6). *$p<0.05$, **$p<0.01$ significantly different compared to normal control

Table 2: Anxiolytic activity of EECR in mice using elevated plus maze

	Elevated plus maze			
Groups	Entries in open arm (sec)	Time spent in open arm (sec)	Entries in closed arm (sec)	Time spent in closed arm (sec)
Control (0.5% CMC)	3.07±0.03	71.07±0.70	11.38±0.29	219.73±90.0
Diazepam (1 mg kg^{-1})	12.09±0.08*	272.62±4.21*	2.11±0.05*	50.12±0.22*
EECR (200 mg kg^{-1})	8.19±0.17**	210.31±1.70*	6.17±0.17**	80.79±0.83*
EECR (400 mg kg^{-1})	9.15±0.12**	220.41±1.16**	5.91±0.06**	77.75±1.13**

Values are Mean±SD (n = 6). *p<0.05, **p<0.01 significantly different compared to normal control

Table 3: Anxiolytic activity of EECR in mice using locomotor and hole board test

	Locomotor		Hole board head dips (numbers)	
Groups	Rearing	Crossing	Head dips in 30 min	Head dips in 60 min
Control (0.5% CMC)	19.57	47.24	3.11	2.07
Diazepam (1 mg kg^{-1})	26.3	59.04	11.10	13.12
EECR (200 mg kg^{-1})	23.48*	54.26*	8.52**	6.58*
EECR (400 mg kg^{-1})	24.19**	56.88**	6.18*	7.13**

Values are Mean±SD (n = 6). *p<0.05, **p<0.01 significantly different compared to normal control

significant ($p<0.01$) decrease in the number of head dips 13.12±0.04 of Diazepam (1 mg kg^{-1}), EECR (400 mg kg^{-1}) compared to control group 2.07±0.03-6.58±0.07 (Table 3).

Convulsion effect of EECR in mice: Pentylenetetrazole produced tonic seizures in the entire animals used. A dose of 100 mg kg^{-1} of EECR protected 33.33% of the animals against seizures and did not affect the onset (latency) of seizures to any noteworthy extent. The EECR the dose of 200 and 400 mg kg^{-1} protected 22.84±0.41 and 20.30±0.17 of the mice against seizures and significantly ($p<0.05$ and $p<0.01$) increased the latency of the seizures. Strychnine elicited clonic convulsions in experimental animals. The normal control group produced convulsion and showed latency of 21.57±0.08s. The EECR (200 and 400 mg kg^{-1}) significantly ($p<0.05$ and $p<0.01$) delayed the duration of strychnine induced seizures from 50.75±0.25s in control to 22.55±0.32 and 20.23±0.10 sec, respectively and shows dose dependent increase in the anticonvulsant activity. Similarly, diazepam 5 mg kg^{-1} pre-treatment significantly ($p<0.05$) increased the latency of strychnine-induced seizures from 55.25±0.50 sec to 14.28±0.20 with 100% protection. Maximal electroshock produced hind limb tonic extension in all the animals. The vehicle treated rats showed tonic hind limb extension for the duration of 15.16±0.22 sec. Administration of EECR (200-400 mg kg^{-1}) showed a dose dependent increase in the delay of the onset time of seizures induced by maximal electroshock induced convulsion and decreased duration of tonic hind limb extension (Fig. 1a).

Hypnotic effect of EECR in mice: The oral treatment of mice with EECR (200-400 mg kg^{-1}) 1 h before the sodium pentobarbital injection did not modify the latency to induce sleep but this treatment significantly increased duration of the hypnosis induced by the drug as indicated in Fig. 1b.

Muscle relaxant effect of EECR in mice: Treatment with EECR (200 and 400 mg kg^{-1}) showed significant ($p<0.05$) reduction in the time spent on the rotarod test by the animals on revolving rod when compared to control. The standard drug Diazepam also showed an effect when compared to control ($p<0.05$). Low dose of EECR (200 mg kg^{-1}) was showed significant effect ($p<0.05$). The results of climbing test, indicated the time taken to climb the chain was also found to be delayed in the EECR treated groups ($p<0.05$ at 200 mg kg^{-1} and $p<0.01$ at 400 mg kg^{-1} dose levels) than

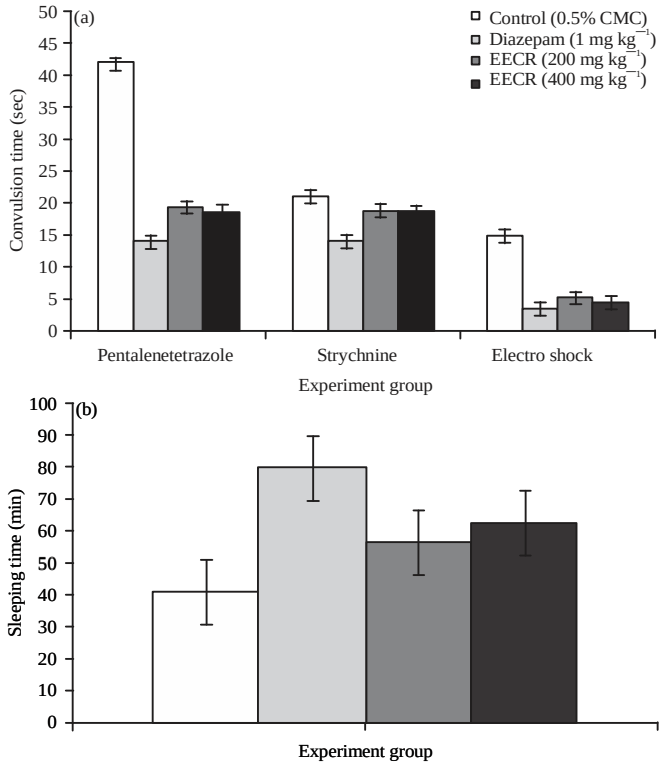

Fig. 1(a-b): Effect of oral administration of EECR on (a) Convulsion time and (b) Sleeping time in experimental animals. *p<0.05 and **p<0.01 indicate significant difference from control

Table 4: Antidepressant activity of EECR in rats using forced swim test

	Forced swim test	
Groups	Immobilization time in FST	Swimming time
Control (0.5% CMC)	240.57	129.96
Diazepam (1 mg kg^{-1})	178.93	219.61
EECR (200 mg kg^{-1})	228.81*	171.36*
EECR (400 mg kg^{-1})	233.36**	180.87**

Data represent the Mean±SD (n = 6). *p<0.05, **p<0.01 significantly different compared to normal control

the control (Fig. 2a). Treatment with EECR at a dose of 200 and 400 mg kg^{-1} and Diazepam decreased sliding time of experimental animals. The result obtained from both standard and EECR treated groups was reported to the control group. The result from the rota rod, climbing and inclined test showed that the 400 mg kg^{-1} of EECR significantly (p<0.01) reduced the motor co-ordination of the tested animals (Fig. 2b).

Antidepressant effect of EECR in rats: The effect of EECR and imipramine was on active behaviors in the FST of rats. Treatment with EECR (200 and 400 mg kg^{-1}) significantly shortened the immobility time in comparison to control values. This effect was associated with a significant increase in climbing behaviour after EECR administration of 200 and 400 mg kg^{-1}. Imipramine, a selective serotonin re-uptake inhibitor, markedly decreased the immobility time during the 5 min test session, while inducing a corresponding increase in swimming behavior. There was slight significant difference between the effects of EECR and imipramine on the immobility time (Table 4).

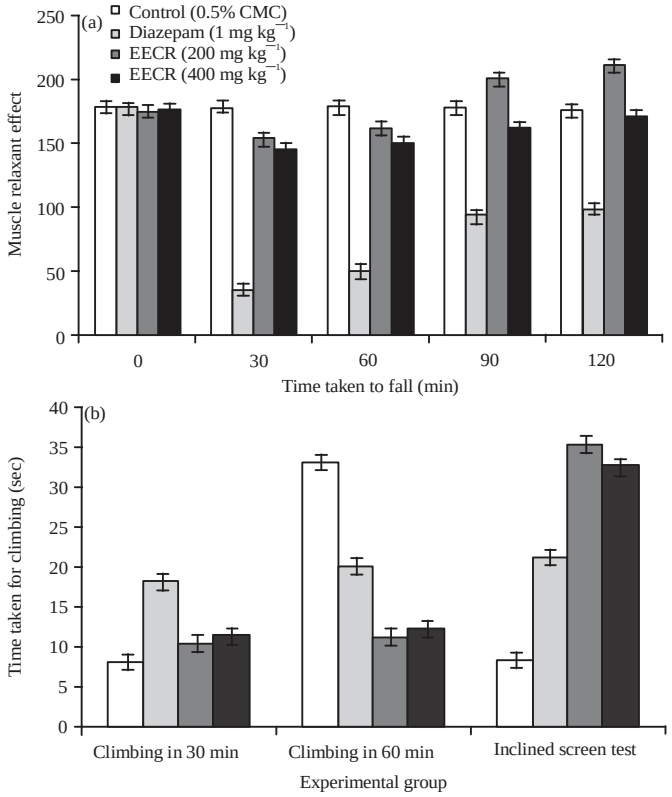

Fig. 2(a-b): Muscle relaxant activity of EECR (a) Rotarod method and (b) Climbing and inclined screen test. The data represent the Mean±SD (n = 6). *p<0.05, **p<0.01 significantly different compared to normal control

Table 5: Anxiolytic activity of EECR in rats using light and dark test

	Light-dark box test	
Groups	Time spent in light (sec)	Time spent in dark (sec)
Control (0.5% CMC)	110.33±1.37	189.67±1.37
Diazepam (1 mg kg^{-1})	180.33±1.63*	119.67±1.63*
EECR (200 mg kg^{-1})	151.83±2.99*	148.17±2.99*
EECR (400 mg kg^{-1})	162.67±3.27**	137.33±3.27**

Values are Mean±SD (n = 6). *p<0.05, **p<0.01 significantly different compared to normal control

Anxiolytic effect of EECR in rats: Diazepam (1 mg kg^{-1}) and 400 mg kg^{-1} EECR significantly (p<0.01) increased time spent in the light area 180.33±1.63 and 162.67±3.27 and decreased in dark area viz., 119.67±1.63 and 137.33±3.27. The number of crossings considerably increased in Diazepam and EECR compared to control group. Treatment with EECR (200 and 400 mg kg^{-1}) to the rats, causes increases in the frequency of the open arm entries. Significant (p<0.01) and dose dependent increase in the duration of time spent in the open arm were observed in EECR (400 mg kg^{-1}) treated rats (Table 5).

DISCUSSION

At present, number of chemotherapeutic drugs was available for the treatment of mental disorders. While, using synthetic drug, patients cannot stand the side effects or loss their response during the handling period. Recent researches focused on herbal drugs, which have lower side

effects and increased the success rate of patients (Akhondzadeh and Maleki, 2006). *Cypeus rotundus* regularly known as "Nutgrass and Motha" it offered good source of remedy to various sickness. Based on the characteristic feature of cheapness, forcefulness and reliability, we selected TST and FST behavioural model for evaluation of antidepressant activity of EECR. Swimming is sensitive to serotonergic composite (Detke *et al*., 1995). Some studies evaluated the magnitude of the antidepressant effect of *Cassia occidentalis* compared to fluoxetine treated group. Similarly, Herbal oil of *C. scariosus* exhibited significant anti-depressant activity (Bhawna *et al*., 2013). In the present study, the ethanolic extract of tuber effectively reduced the immobility time without modifying swimming duration compared to the control. Secondary metabolites of plants might be interacting with natural endogenous mediators in the physiological system to exert their anxiolytic action. De Almeida *et al*. (2012) observed the frequency and time spent in open arms is the major indexes of anxiety in the plus maze model, given the fact that rodents to an open area. In the present study, diazepam increased the number of entries and time spent in the open arms demonstrating the characteristic of synthetic anxiolytic drug, benzodiazepine. Thakur and Mengi (2005) point out the locomotor activity measured through an index of alertness and decrease in the locomotors score. Both doses of EECR have a selective anxiolytic effect with significantly modifying the locomotor activity. Also in the case of hole board model, the head dips were minified in experimental animals that received EECR. Comparable results observed in *Oxalis corniculata* ethanolic extracts of 200 and 400 mg kg^{-1} (Sampath *et al*., 2011). The seizure induced models, such as pentylenetetrazole; strychnine and electro-Shock are effective to evaluate the anticonvulsant activity of the medicinal plants. Among these, the PTZ interacted with GABA neurotransmitters and its receptor complex to raise seizure. Anticonvulsant effect of EECR protect and significantly prolonged the onset of seizure in mice against PTZ induced seizure by modifying excitatory and inhibitory neurotransmission through voltage gated ion channels, GABA (A) receptors and glutamate mediated excitatory neurotransmission (Sierra-Paredes, 2008). Selective competitive antagonist strychnine, blocks the inhibitory effect of glycine amino acids at all receptors (Ishola *et al*., 2013). The EECR treated animals increased the seizures onset significantly in a dose dependent manner, which reflects its anticonvulsant activity. Similarly, ethanolic extracts of *C.rotundus* reported to reduce the hind limb extension and duration of convulsion then compared to standard drug phenytoin and diazepam. The EECR nearer to the action of Diazepam which belongs to benzodiazepine group, it has a binding site on the GABA receptor type ionophore complex and decreases the activity (Huang *et al*., 2007). The frequently employed prognostic test for asses the sedative hypnotic properties are phenobarbitone-induced sleeping assays (Perveen *et al*., 2009). Pre-treatment of experimental animals with EECR showed dose dependent reduction in latency time and effective sleeping duration of phenobarbitone induced sleeping time test. The reduction in the amplitude of motion attributed to sedative action of EECR. The plant extract act as an enzyme inhibitor, as increased the action of hexobarbitone by preventing its metabolism. *Boerhaavia diffusa* posed significant hypnotic activity through the GABAA-chloride ion channel complex prolongs pentobarbital induced sleep duration (Venkateswarlu and Rao, 2013). The presence of flavonoids might be responsible for CNS activity by resembling endogenous metabolites, ligands, or neurotransmitters on human models.

CONCLUSION

In conclusion, the present study evidenced that the ethanolic extract of *C. rotundus* demonstrated potential CNS activity. These findings are consistent with the hypothesis that

C. rotundus treatment triggers immobility behavior, time spent in light, locomotor and climbing time in rat and mice model. Further studies will confirm the mechanism of action of *C. rotundus* for CNS drug development.

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REFERENCES

Achliya, G.S., S.G. Wadodkar and A.K. Dorle, 2005. Evaluation of CNS activity of *Bramhi ghrita*. Indian J. Pharmacol., 37: 33-36.

Akhondzadeh, S. and J. Maleki, 2006. Herbal medicines in the treatment of psychiatric and neurological disorders. Iran J. Psychiatry, 1: 1-11.

Amabeoku, G.J., I. Green and J. Kabatende, 2007. Anticonvulsant activity of *Cotyledon orbiculata* L. (Crassulaceae) leaf extract in mice. J. Ethnopharmacol., 112: 101-107.

Bhawna, K., S.S. Kumar, S. Lalit, M. Sharmistha and S. Tanuja, 2013. *Cyperus scariosus*: A potential medicinal herb. Int. Res. J. Pharmacy, 4: 17-20.

Carlini, E.A., 2003. Plants and the central nervous system. Pharmacol. Biochem. Behav., 75: 501-512.

Cryan, J.F., A. Markou and I. Lucki, 2002. Assessing antidepressant activity in rodents: Recent developments and future needs. Trends Pharmacol. Sci., 23: 238-245.

De Almeida, A.A.C., J.P. Costa, R.B.F. de Carvalho, D.P. de Sousa and R.M. de Freitas, 2012. Evaluation of acute toxicity of a natural compound (+)-limonene epoxide and its anxiolytic-like action. Brain Res., 1448: 56-62.

Detke, M.J., M. Rickels and I. Lucki, 1995. Active behaviors in the rat forced swimming test differentially produced by serotonergic and noradrenergic antidepressants. Psychopharmacology, 121: 66-72.

Dhingra, D. and A. Sharma, 2006. A review on antidepressant plants. Nat. Prod. Radiance, 5: 144-152.

Ecobichon, J.D., 1997. The Basis of Toxicity Testing. 2nd Edn., CRC Press, Boca Raton, ISBN-13: 9780849385544, Pages: 240.

Flint, J., R. Corley, J.C. DeFries, D.W. Fulker, J.A. Gray, S. Miller and A.C. Collins, 1995. A simple genetic basis for a complex psychological trait in laboratory mice. Science, 269: 1432-1435.

Gordon-Gray, K.D., 1995. Cyperaceae in Natal. National Botanical Institute: Pretoria, South Africa, pp: 45-76.

Herrera-Ruiz, M., C. Gutierrez, J.E. Jimenez-Ferrer, J. Tortoriello, G. Miron and I. Leon, 2007. Central nervous system depressant activity of an ethyl acetate extract from *Ipomoea stans* roots. J. Ethnopharmacol., 112: 243-247.

Huang, F., Y. Xiong, L. Xu, S. Ma and C. Dou, 2007. Sedative and hypnotic activities of the ethanol fraction from *Fructus schisandrae* in mice and rats. J. Ethnopharmacol., 110: 471-475.

Ishola, I.O., S.O. Olayemi and A.R. Idowu, 2013. Anticonvulsant, anxiolytic and hypnotic effects of aqueous bulb extract of *Crinum glaucum* A. chev (Amaryllidaceae): Role of GABAergic and nitrergic systems. Pak. J. Biol. Sci., 16: 701-710.

Moreno, L.C.G.A.I., G.Z. da Silva Oliveira, I.M.F. Cavalcanti, N.S. Santos-Magalhaes, H.M.L. Rolim and R.M. de Freitas, 2014. Development and evaluation of liposomal formulation containing nimodipine on anxiolytic activity in mice. Pharmacol. Biochem. Behav., 116: 64-68.

Perveen, T., S. Haider, S. Kanwal and D.J. Haleem, 2009. Repeated administration of *Nigella sativa* decreases 5-HT turnover and produces anxiolytic effects in rats. Pak. J. Pharm. Sci., 22: 139-144.

Porsolt, R.D., M. le Pichon and M. Jalfre, 1977. Depression: A new animal model sensitive to antidepressant treatments. Nature, 266: 730-732.

Sampath, T.S., P. Santosh, L. Mangala, P. Ajaygodwin, S.P. Kumar and A. Lingesh, 2011. Anxiolytic effect of ethanolic extract of *Oxalis corniculata* L. in mice. Int. J. Pharma Bio Sci., 2: 281-290.

Sheik, H.S., N. Vedhaiyan and S. Singaravel, 2014a. Evaluation of central nervous system activities of *Citrus maxima* leaf extract on rodents. J. Applied Pharm. Sci., 4: 77-82.

Sheik, H.S., N. Vedhaiyan and S. Singaravel, 2014b. Evaluation of *Abelmoschus moschatus* seed extract in psychiatric and neurological disorders. Int. J. Basic Clin. Pharmacol., 3: 845-853.

Shivakumar, S.I., H.M. Suresh, C.S. Hallikeri, B.C. Hatapakki, J.S. Handiganur, K. Sankh and B. Shivakumar, 2009. Anticonvulsant effect of *Cyperus rotundus* Linn rhizomes in rats. J. Nat. Rem., 9: 192-196.

Siebert, T.E., C. Wood, G.M. Elsey and A.P. Pollnitz, 2008. Determination of rotundone, the pepper aroma impact compound, in grapes and wine. J. Agric. Food Chem., 56: 3745-3748.

Sierra-Paredes, G., 2008. Recent advances in the neurochemistry of epilepsy. Eur. Neurol. Rev., 3: 96-98.

Steru, L., R. Chermat, B. Thierry and P. Simon, 1985. The tail suspension test: A new method for screening antidepressants in mice. Psychopharmacology, 85: 367-370.

Takeda, H., M. Tsuji and T. Matsumiya, 1998. Changes in head-dipping behavior in the hole-board test reflect the anxiogenic and/or anxiolytic state in mice. Eur. J. Pharmacol., 350: 21-29.

Thakur, V.D. and S.A. Mengi, 2005. Neuropharmacological profile of *Eclipta alba* (Linn.) Hassk. J. Ethnopharmacol., 102: 23-31.

Venkateswarlu, B. and Y.R. Rao, 2013. Anxiolytic-hypnotic activity of whole plant extract of *Boerhaavia diffusa*. Int. J. Phytother., 3: 33-36.

Yemitan, O.K. and H.M. Salahdeen, 2005. Neurosedative and muscle relaxant activities of aqueous extract of *Bryophyllum pinnatum*. Fitoterapia, 76: 187-193.

Zanoli, P., R. Avallone and M. Baraldi, 2000. Behavioral characterisation of the flavonoids apigenin and chrysin. Fitoterapia, 71: S117-S123.