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Anticonvulsant efficacy of *Mucuna pruriens* in Pregnant Female Albino wistar Rats using Maximal Electroshock induced Epilepsy

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Abstract

Background

The worldwide occurrence of epilepsy is increasing and it is more challenging in pregnant woman. The challenges are to maintain a balance between benefits and potential risks of pharmacotherapy to avoid the teratogenecity associated with prenatal exposure to AEDs for a developing fetus and the need for effective treatment of maternal health conditions. Epileptic women patients may also be at greater risk for suboptimal prenatal care owing to altered hemodynamic and volume of distribution during pregnancy.

Main body of abstract

This study used the Maximal Electroshock technique in an experimental rat model to compare the anticonvulsant characteristics of *M. pruriens* to safer alternatives that were prescribed to pregnant females. The study comprises of following groups Control, *M. pruriens* (100 mg/kg), and standard medication as per global guidelines i.e., Lamotrigine (20 mg/kg), in female Albino wistar rats.

Conclusion

The MES results indicated significant anticonvulsant activity as compared to standard drug utilized in the experimental model.

Keywords: *Mucuna pruriens*, Maximal electroshock method, Anticonvulsant, Pregnancy, Epilepsy.

Background

Recurrence of spontaneous seizures is a hallmark of the brain disease linked to epilepsy. Prognosis generally refers to the likelihood of achieving seizure independence with therapy, and the natural history of the untreated illness is not well understood [1]. A brief review of evidence pertaining to Anti-epileptic drug (AED) use in pregnancy is conducted, along with an exploration of lessons learned from rarer epilepsies regarding the connection among epilepsy type, causes, and choice of antiepileptic medicines (AED) [2].

Up to two-thirds of people may have a suppression of seizures when taking anti-seizure medication, although the long-term prognosis remains same [3].Antiepileptic drug exposure during pregnancy may raise the likelihood of physical abnormalities and neurodevelopmental impairment, according to mounting data. Neurodevelopmental disability can be temporary or persistent into adulthood, and is defined by a single defect or a constellation of abnormalities affecting cognitive, motor, and social skills. It is crucial to recognize, reduce, and make these possible dangers understandable to women who have epilepsy [4].

An antiepileptic drug's pharmacokinetics is affected during pregnancy due to alterations in the drug's volume of distribution and clearance capacity. These modifications may have an impact on the fetus's exposure to antiepileptic medication and the frequency of seizures that occur during pregnancy [5].

Levetiracetam and Lamotrigine are related to lesser likelihood of malformation; however, the neuro-developmental effects of levetiracetam are based on a small sample, which is little to no evidence addressing the applicability of other AEDs on neurodevelopment during gestation. Young female patients should have teratogenic concerns taken into account as soon as treatment is started [6].

Conversely, pregnancy-related changes in pharmacokinetics lay elevated threat of seizures along with adverse effects on fetus [7].

The extract from *Mucuna pruriens* may be drug of choice as an antiepileptic and anti-cataleptic medication [8], however, this herbal plant is known to possess varied properties like aphrodisiac, treatment of male infertility and neurological disorders. Research has demonstrated that the seeds of this plant may have significant medical value [9& 10].

Rats are frequently utilized in many various fields of research, such as teratogenicity effect screening, behavioral aspects of reproduction, and studies on fecundity and fertility. Comprehending the typical reproductive characteristics and behavior of rats is essential for several scientific domains [11]. Because of their short gestation period (20–22 days), short estrous cycle (4–5 days), litter size of approximately 7–9, weaning age of approximately 21 days, and relatively short period of sexual maturity (7–8 weeks) [12]. From the first day of birth until weaning, each pup/offspring will undergo motor and cognitive tests to assess their neurobehavioral potential post MES exposure during gestation period.

The aim of this research work is to compare *Mucuna pruriens* anticonvulsant impact to Lamotrigine in the context of maximal electroshock-induced convulsions in pregnant female albino wistar rats.

Material and Methods:

Chemicals

Lamotrigine purchased from Ranbaxy Lab Ltd., New Delhi, India.

Experimental Animals

Eight male and twenty-four female healthy 6-to 8-week-old Albino wistar rats weighing 150–250 grams each were included in the investigation. According to the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), all experiments were conducted as per Good Laboratory Practice (GLP) and CCSEA (earlier known as CPCSEA) guidelines. The Institutional Animal Ethical Committee (IAEC) of Subharti Medical College Delhi Haridwar by Pass Road Meerut, Uttar Pradesh - 250005, INDIA approved the study with reference no. (1204/Po/Re/S/08/CPCSEA/23-01).

Collection of plant and preparation of plant extract:

The herbal extract *M. pruriens* (70% L-Dopa) was procured from GPPL Pvt. Ltd. Indore Madhya Pradesh and was authenticated via letter number GPPL/COA/23/122.

Grouping

The pregnant Albino wistar rats were grouped in three sections, Group 1 (n=8; Standard) received Lamotrigine (20 mg/kg) orally, Group 2 (n=8; Test) received test drug Mucuna pruriens (100mg/kg) orally and Group 3 (n=8; Control) received water.

Preparation of animals

Acclimatization

Before initiation of the experiments, all the animals were maintained in their cages for a minimum of five days to enable them to become acclimated to the laboratory environment. They were also randomly picked and coded to enable individual identification [13].

Breeding method

All the animals (female albino wistar rats) were acclimatized and aligned for at least 4 hours daily with Male rats where three female rats and one viable sexually active male rat were placed in cage as per *harem* (3:1) mating method as mentioned in figure 1. After four hours, the female rats were separated. In order to count the days after confirmation of conception using vaginal smear analysis and copulatory plug assessment, the rats were labeled and that day was designated as day 0 of their pregnancy upon copulatory plug inspection for confirmation of mating [15&16]. The pregnant rats divided in three groups of eight each and kept individually in separate cages labeled with the day of conception as Standard (Group 1), Test (Group 2) and Control (Group 3).

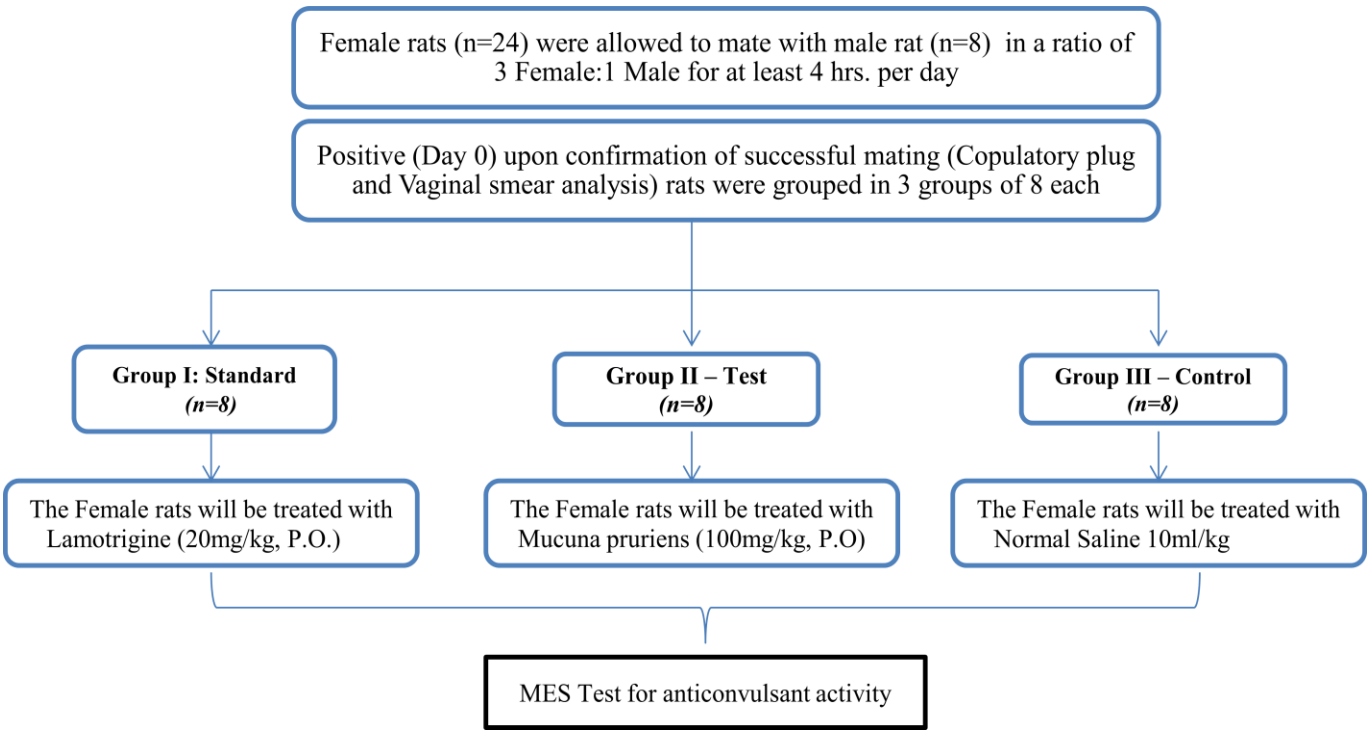

Figure1. Flow chart of breeding method in female wistar rat. The females were allowed to mate with male rats for at least 4 hours. Post confirmation of possible mating, female rats were housed in a group of 8 each. The female rats were subjected to MES test during Gestational day 14 till 21. Post delivery, one male and one female pup were included for neurobehavioral study. On the day 21 post delivery 1 male and 1 female pup were included from each mother in this study and till all offspring were weaned they were housed in group of 3 in each cage until the completion of studies.

Evaluation of Anti-epileptic activity of *Mucuna pruriens*

Maximal Electroshock (MES) method

The maximal electroshock seizure (MES) test is frequently employed in preclinical assessments of the anticonvulsive qualities of the potential antiepileptic drugs [17].An electric stimulus (an alternating current 10Hz. 0.1 sec) produced by a rodent shocker and applied via ear-clip electrodes caused convulsions. The endpoint was determined to be tonic hind limb extension, or the hind limbs of animals extended 180˚ to the plane of the body axis [18]. The medicine under test has a median effective dosage (ED50) that prevents 50% of mice from having their maximal electroshock-induced seizures. In order to establish the drug's ED50, a minimum of three animal groups were administered increasing dosages of the antiepileptic medication Lamotrigine and *Mucuna pruriens*, followed by a maximum electroshock test [19 & 20].

The lengths of different phases of epilepsy, such as Phases of clonic convulsions, tonic limb extension, tonic limb flexion, stasis, and recovery or death were noted as mentioned in Figure 2.

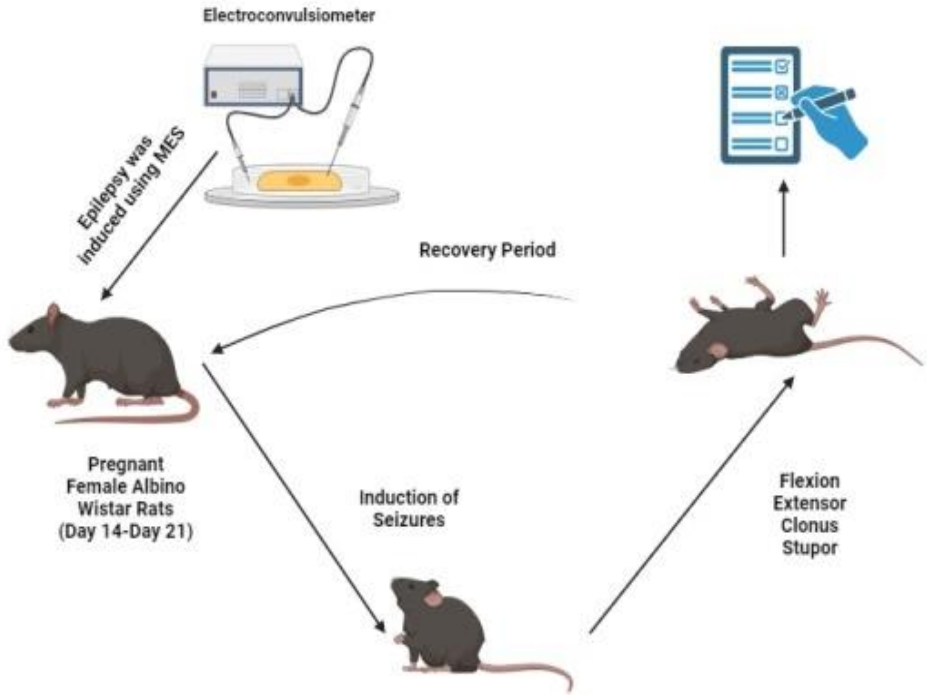

Figure2. The Pregnant female rats were exposed to MES using electroconvulsiometer and various stages of Epilepsy and were record for interpretation.

Result:

Significant variations in the various MES model parameters across the treatment groups were revealed by the statistical test one-way ANOVA followed by Dunnett's test.

Table -1 Comparison of parameters of MES model among treated groups

Groups	**Flexion**	**Extensor**	**Clonus**	**Stupor**	**Recovery time**
Test Group (*M. pruriens*)	17.33 ± 5.51	14.75± 6.35	16.46±6.69	36.75±4.64	48.17±3.88
Standard Group (Lamotrigine)	16.79 ± 3.92	2.25±3.52	15.75±4.19	26.46±5.92	39.33±8.38
Control	17.75±6.23	20.63±5.06	22.58±5.47	37.00±4.54	64.00±6.63

Data expressed as Mean ± SEM. One-way ANOVA with Dunnett's test –
*: $p<0.01$ drug treatment vs. MES control

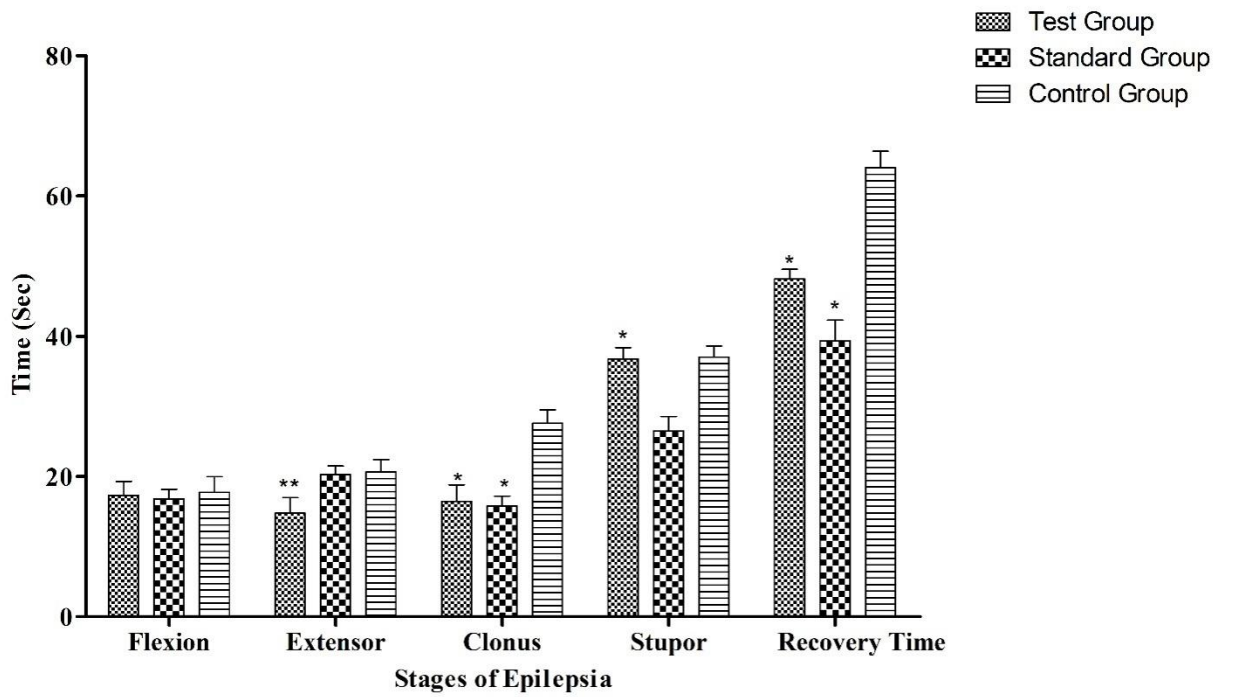

Figure3. The above graph depicts different stages of epilepsy post treatment of Control (*Normal Saline 10g/kg)*; Test (*Mucuna pruriens 100mg/kg*) and Standard treatment (*Lamotrigine 20 mg/kg*) on pregnant female albino wistar rats using Convulsiometer and their recovery time was monitored.

Discussion

Various models may be employed to assess anticonvulsant activity. In this experimental research work MES model was utilized to assess the anticonvulsant efficacy of *Mucuna pruriens* and compare it with the established standards. In this investigation, Lamotrigine was selected as the standard drug. The results demonstrate that *Mucuna pruriens* exhibited outcomes comparable to those of lamotrigine with regards to seizure latency, as it delayed the onset of seizures. Consequently, we infer that *Mucuna pruriens* (100 mg/kg), possesses statistically significant anticonvulsant activity in the MES model.

The flexion response, a significant indicator of motor function, is crucial in understanding the efficacy of pharmaceutical interventions in various conditions. In this study, we explore and compare the flexion responses induced by *Mucuna pruriens*, Lamotrigine, and a control treatment in albino wistar rats. The flexion response elicited by *M. pruriens* (17.33 ± 1.95) exhibits a notable prominence in comparison to Lamotrigine (16.79 ± 1.39). This suggests a potentially heightened impact of *Mucuna pruriens* on motor function. The observed variance emphasizes how crucial it is to look into alternate therapeutic options for illnesses that impact motor responses. Interestingly, while *Mucuna pruriens* demonstrates a more pronounced flexion response compared to Lamotrigine, its similarity to our control treatment is noteworthy. The mechanisms behind *Mucuna*

pruriens effects and the effectiveness of conventional pharmacological therapies are intriguingly called into doubt by this result.

The extension response during epileptic episodes is crucial for evaluating the efficacy of anti-epileptic drugs and control interventions. In this discussion, we compare the extension responses elicited by Lamotrigine (LMT) and a control treatment, shedding light on their effects on hind limb extensions in epileptic animals. This study reveals a similarity in the extension response between Lamotrigine (20.25 ± 1.24) and the control treatment (20.63 ± 1.79). The findings suggest that during epileptic episodes both the therapies showed similar response on the extension parameter. The animals exhibited reduced extension of hind limbs during stages of epilepsy. This observation suggests a potential limitation in the efficacy of both interventions in mitigating the severity of epileptic episodes, particularly hind limb extension.

Clonus and stupor are significant indicators of neurological activity and responsiveness to pharmacological interventions. In this discussion, we compared the clonus response elicited by Lamotrigine (LMT), *Mucuna pruriens* (MP), and a control group, shedding light on their efficacy in managing these neurological manifestations. A notable difference in clonic activity between Lamotrigine (15.75 ± 1.48) and the control group (27.58 ± 1.93). The significantly reduced clonic activity in the Lamotrigine group suggests its effectiveness in mitigating this aspect of neurological dysfunction compared to control intervention. *Mucuna pruriens* (16.46 ± 2.36) exhibits a clonus response similar to that of the control group. This finding suggests that *Mucuna pruriens*, despite being an herbal drug, does not significantly alter clonic activity when compared with control intervention.

The recovery period after a neurological event or intervention is a critical parameter for reflecting the effectiveness of treatments in restoring normal neurological function. In this discussion, we compare the recovery periods observed with *Mucuna pruriens* (MP), Lamotrigine (LMT), and a control group, shedding light on their respective effectiveness in promoting neurological recovery. *Mucuna pruriens* significantly shortened the recovery duration (48.17 ± 1.37) in comparison with the control group (64.00 ± 2.34). This finding suggests that MP has a beneficial impact on neurological recovery, highlighting its potential as a therapeutic agent for enhancing post-neurological event rehabilitation. Lamotrigine (39.33 ± 2.96) demonstrates a shorter recovery period compared to *Mucuna pruriens*. It shows the LMT exerts is more efficacious in promoting neurological recovery than MP. The superior effectiveness of Lamotrigine underscores its established role as a standard pharmacological intervention for neurological disorders.

Conclusion:

When compared to the standard medicine, the herbal extract of *Mucuna pruriens* demonstrated comparable activity during the stages of flexion and clonus. However, the extensor response was noticeably superior to the currently available product, Lamotrigine and Control therapy. Comparing the MP to Standard and test treatment, it took longer for the patient to recover from the

stages of reduced consciousness and responsiveness, or stasis (Stupor) and recovery time. Overall, the *Mucuna pruriens* suggested that the MES test carried out in the animal model had resulted in considerable suppression of tonic clonic seizures. This activity might be due activity on voltage-gated sodium ion channels or via neuroprotective activity of L-DOPA. Given the above promising responses, further investigations can be planned to evaluate efficacy at the molecular and sub-molecular level.

Abbreviations

AEDs – Anti-Epileptic Drugs
MES - Maximal Electro Shock
LMT - Lamotrigine
MP - *Mucuna pruriens*
ED - Effective Dose
L-Dopa - l-3,4-dihydroxyphenylalanine

References

1. Sirven JI (2015) Epilepsy: A Spectrum Disorder. Cold Spring Harb Perspect Med. 5(9):a022848. doi: 10.1101/cshperspect.a022848.
2. Komal K, Cleary F, Wells JSG, Bennett L (2024) A systematic review of the literature reporting on remote monitoring epileptic seizure detection devices. Epilepsy Res.201:107334. doi: 10.1016/j.eplepsyres.2024.107334. Epub 2024 Feb 27.
3. Chen Z, Brodie MJ, Ding D, Kwan P (2023) Editorial: Epidemiology of epilepsy and seizures. Front Epidemiol. 30; 3:1273163. doi: 10.3389/fepid.2023.1273163.
4. Umamageswari J, Balasubramanian S, Krishnakumar K, et al (2020) A simple and rapid staining technique to confirm mating in Wistar rats. Journal of Entomology and Zoology Studies. 8(5):820–3.
5. Beghi E (2020) The Epidemiology of Epilepsy. Neuroepidemiology.54(2):185–91.
6. Zahra W, Birla H, Singh SS, et al (2022) Neuroprotection by *Mucuna pruriens* in Neurodegenerative Diseases. Neurochemical Research. 47(7):1816–29.
7. Symonds JD, Zuberi SM, Johnson MR (2017) Advances in epilepsy gene discovery and implications for epilepsy diagnosis and treatment. Current Opinion in Neurology. 30(2):193–9.
8. Lampariello LR, Cortelazzo A, Guerranti R,et al (2012) The Magic Velvet Bean of *Mucuna pruriens*. Journal of Traditional and Complementary Medicine. 2(4):331–9.
9. Benson R, Pack A. Epilepsy. Handbook of Clinical Neurology. 2020 Jan 1; 172:155–67.
10. Duarte GM, de Araújo FEA, da Rocha JMC, et al (2023) Neuroprotective Potential of Seed Extracts: Review of In Vitro and In Vivo Studies. Nutrients. 27;15(11):2502. doi: 10.3390/nu15112502.

11. Borgelt LM, Hart FM, Bainbridge JL (2016) Epilepsy during pregnancy: focus on management strategies. Int J Womens Health.19; 8:505-517. doi: 10.2147/IJWH.S98973.
12. Ochiogu IS, Uchendu CN, Ihedioha JI (2006) A new and simple method of confirmatory detection of mating in albino rats (Rattus norvegicus). Animal Research International.3(3):527-30.
13. Turner PV, Brabb T, Pekow C, et al (2011) Administration of substances to laboratory animals: routes of administration and factors to consider. J Am Assoc Lab Anim Sci. 50(5):600-13.
14. Nevalainen T (2014) Animal husbandry and experimental design. ILAR J.55 (3):392-8. doi: 10.1093/ilar/ilu035.
15. Burns CJ, McIntosh LJ, Mink PJ, et al (2013) Pesticide exposure and neurodevelopmental outcomes: review of the epidemiologic and animal studies. J Toxicol Environ Health B Crit Rev.16(3-4):127-283. doi: 10.1080/10937404.2013.783383. Erratum in: J Toxicol Environ Health B Crit Rev.; 16(6):395-8.
16. Holson RR, Pearce B (1992) Principles and pitfalls in the analysis of prenatal treatment effects in multiparous species. Neurotoxicol Teratol. 14(3):221-8. doi: 10.1016/0892-0362(92)90020-b.
17. Banach M, Rudkowska M, Sumara A, et al (2021) Amiodarone Enhances Anticonvulsive Effect of Oxcarbazepine and Pregabalin in the Mouse Maximal Electroshock Model. Int J Mol Sci. 21; 22(3):1041. doi: 10.3390/ijms22031041.
18. Nirmala M, Suhasini GE, Venkata Lakshmi K, et al (2014)Maximal Electroshock (MES) Induced Convulsions Model for Evaluating Anti Epileptic Activity of New Isatin Derivative -N'- (7- Chloro- 2- Oxo -2, 3-Dihydro-1H - Indol- 3-yl) Benzohydrazide. *Int. J. Res. Pharm. Sci. 5*, 329-334.
19. Madhyastha M, Shenoy S, Ramachandra VH, et al (2016) A Study of Effect of Acute and Chronic Administration of Aqueous Extract of Calotropis Procera Leaves on Maximal Electroshock Induced Seizures in Rats. *Int J Basic Clin Pharmacol* ; *6*, 1-4.
20. Xavier S, Soch A, Younesi S, et al (2021) Maternal diet before and during pregnancy modulates microglial activation and neurogenesis in the postpartum rat brain. Brain Behav Immun. 98:185-197. doi: 10.1016/j.bbi.2021.08.223.