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Research article

Anxiolytic, antidepressant and anticonvulsant activity of mucuna pruriens seeds

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ABSTRACT

Behavioral models such as the elevated plus maze (EPM), light and dark method, Hole-board method, and Marble burying method were used to assess Methanolic extract of Mucuna pruriens seeds (MEMP) for anxiolytic function. MEMP in a dose of 200 and 300 mg/kg, p.o. was found to possess significant anxiolytic activity. In TST and FST, MEMP showed a substantial reduction in the time of immobility, indicating antidepressant action. MEMP significantly increased the latency for straub tail, extensor, myoclonic jerk, clonic convulsion and stupor in pentylenetetrazol (PTZ) and isoniazid-induced convulsion models. MEMP may be interfering with the level of monoamines; L-dopa, serotonin and histamine and produced antidepressant activity.

Keywords: anxiolytic, convulsion, depression, Elevated plus maze, Forced swim method, Pentylenetetrazol, Tail suspension method

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INTRODUCTION

Mucuna pruriens Linn (Fabaceae), also known as cowhage fruit, kapikacho, or kevach, is the most commonly used ayurvedic drug. Mucuna spp. (velvet beans) is native to Asia (including Malaysia), America, and Africa. Traditional Nigerian therapists have recommended the beans as an oral antidote to snakebites.(1) Methanolic extract of M. pruriens roots possesses anti-epileptic and anti-neoplastic activity.(2) M. pruriens exhibited various activities including analgesic and anti-inflammatory,(3) anticoagulant,(4) anti-diabetic, anti-microbial and anti-oxidant,(5) aphrodisiac.(6)

Seeds of M. pruriens revealed presence of alkaloidal constituents(7) viz., mucunadine, mucunine, prurienidine, prurienine(8) and epoxy fatty acids viz., cis-epoxyoctadec-trans-9-cis-acid, cis-12, 13-epoxyoctadectrans-9-enoic acid.(9) Numerous seeds-derived formulations are used to treat a various free radical-mediated diseases, including ageing, rheumatoid arthritis, asthma, atherosclerosis, male infertility, and nervous disorders. Being good source of L-dopa, it is also used in the management of Parkinsonism. (10) According to the research, the hot water extract (HWE) of M. pruriens seeds contracted the guinea-pig ileum dose-dependently. This underline that M. pruriens seed extract contains potent histamine receptor stimulants. (11) According to Yokoyama et al., (2009), (12) the drugs or plant extract acting as agonists on H_3 receptors may have anxiolytic-like effects. Oxidative stress may be the cause for various neurodegenerative disorders. M. pruriens has potent in vitro and in vivo antioxidant activity.(13) Hence, the study's aim is to explore the anxiolytic, antidepressant, and anticonvulsant properties of M. pruriens seeds.

MATERIALS AND METHODS

Plant material and extraction

Authentication of Mucuna pruriens Seeds (1 kg) purchased from Ayurvedic Seva Sangh College, Nashik, was done by Dr. S. L. Dasari, Ayurvedic Seva Sangh College, Nashik. Defatting of powdered seeds was done with petroleum ether (60-80ºC) using Soxhlet's extractor, and further successively extracted with methanol. The filtrate was concentrated under vacuum at 60ºC and air-dried (MEMP) (yield: 4.6 % w/w).

Animals

Swiss albino mice (22-25 gm) of either sex were obtained from Bharat Vaccines and Serum Limited, Thane. Institutional Animal Ethics Committee (IAEC), M. G. V.'s Pharmacy College, Nasik, approved all of the experimental techniques and protocols used in this study.

Drugs

Diazepam (Calmpose, Ranbaxy, India), Imipramine (Antidep, Torrent Ltd., India), Pentylenetetrazol (Sigma Chemicals) and Isoniazid (Solonex, Mecleods, India) were used in this study.

Treatment schedule

Mice received MEMP (100, 200 and 300 mg/kg) orally 1 h prior to observation period. Thirty minutes before the test, through intra peritoneal route animals received diazepam (1 mg/kg) in anxiolytic study, imipramine (15 mg/kg) in antidepressant activity and diazepam (10 mg/kg, i.p.) in anticonvulsant study as a reference standard drug. Animals were divided in 5 groups (n=5) for all activities.

Anxiolytic activity

Elevated plus maze [14, 15]

The elevated plus-maze (EPM) for mice consisted of two diagonal open arms and two parallel closed arms. The mouse was positioned in the middle of the plus-maze facing one closed arm after Diazepam and MEMP treatment, and the number of entries and time of permanence in the open arm were measured for 5 minutes.

Light/dark transition [16]

Assessment of mice is inhibited by bright illumination in the light-dark model, which is highly aversive for rodents. A partition divides the light and dark compartments, with a tunnel providing passage from one to the other compartment. After the treatment with Diazepam and MEMP, the mouse was placed at the centre of the lit area, facing the tunnel's opposite wall. During 5 minutes, the total time spent and the total number of entries in the light compartment was counted.

Marble-burying [17]

A 2 cm coating of sawdust was spread over the box's floor (42 cm x 26 cm x 15 cm), and 25 glass marbles were scattered inside. The male mice were separately placed in the cage for 10 minutes after being administered with Diazepam and MEMP, and the burying response was assessed by measuring the amount of marbles that were more than two-thirds coated in sawdust. The burying response is reduced, indicating a positive anxiolytic reaction.

Hole-board [18]

The hole-board apparatus was placed 3.5cm above the ground and consisted of a wooden floor (40 x 40 cm) with nine holes (1.5 cm diameter) spaced symmetrically in a diamond pattern. Mice were separately placed in the apparatus for 5 minutes after being treated with Diazepam and MEMP. The number of head-pokes was counted, with a higher number indicating a positive anxiolytic effect.

Anti-depressant activity

Forced swim test (FWT) [19]

After treatment with imipramine and MEMP, mice were subjected to a swimming test in a transparent Plexiglas cylinder (20 cm height and 12 cm diameter) filled to a 15 cm depth of water (24 ± 1□C). The immobility time was measured during the test session. Apart from the actions required to keep its head above water, the mouse's immobility period is defined as the time when it made no further attempts to escape.

Tail suspension test (TST) [20]

After treatment with Imipramine and MEMP, mice were suspended for a 6 minute period on the edge of a table 50 cm above the floor using adhesive tape affixed one cm from the tail tip. [21]

Anticonvulsant activity

Pentylenetetrazol (PTZ)-induced seizures [22]

Mice of either sex were assigned to the various groups at random. Pentylenetetrazol (60 mg/kg, s.c.) was given to the mice in the control group. In standard group, Pentylenetetrazol was administered after 30 min of diazepam administration. In test group, animals received Pentylenetetrazol 1 h after the MEMP. Onset to straub tail, myoclonic jerk, hind-limb extension, clonic convulsion and stupor was recorded. Mice are considered protected if they did not convulse 30 minutes after receiving Pentylenetetrazol.

Isoniazid-induced convulsions in mice [23]

Animals received isoniazid (iso-nicotinic acid hydrazide) (300 mg/kg, s.c.) after MEMP or diazepam. Control group received vehicle only. Latency for myoclonic jerk, hind-limb extension, clonic convulsion and stupor was recorded.

Statistics analysis

The data was provided as a mean with a standard error of the mean (SEM). The results were evaluated using one-way ANOVA, followed by Dunnett's multiple comparison test. The significance of a P0.05 value is regarded statistically significant.

RESULTS

Anxiolytic activity

Elevated plus maze

In comparison to control, diazepam and MEMP (200 and 300 mg/kg) significantly improved time spent and number of entries in open arm while MEMP (100 mg/kg) shows significantly improved time spent in open arm (Figure 1 and 2).

Figure 1. Effect of methanolic extract of Mucuna pruriens seeds on time spent in open arms of elevated plus maze.

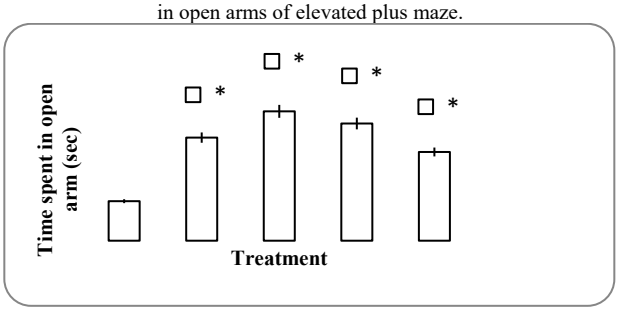
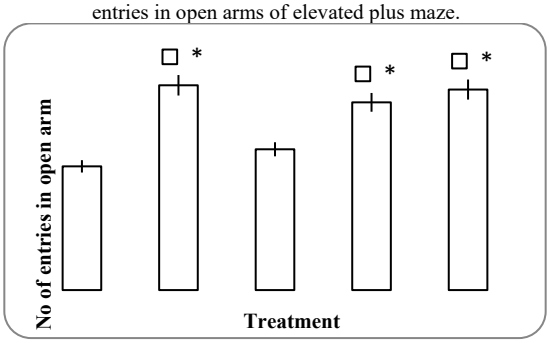


Figure 2. Effect of methanolic extract of Mucuna pruriens seeds on number of entries in open arms of elevated plus maze.



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Light-Dark transition test

In comparison to control, diazepam and MEMP (200 and 300 mg/kg) significantly increased the frequency of entries and time spent in the light cage (Figure 3 and 4).

Figure 3. Effect of methanolic extract of Mucuna pruriens seeds on time spent in light compartment in light and dark model.

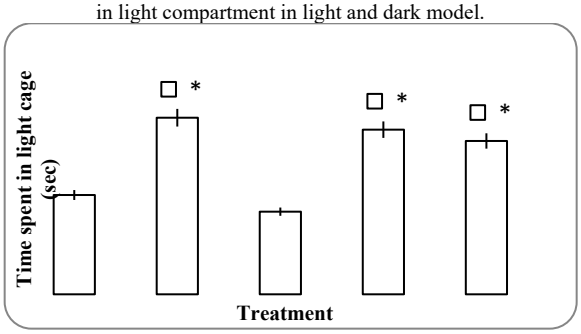
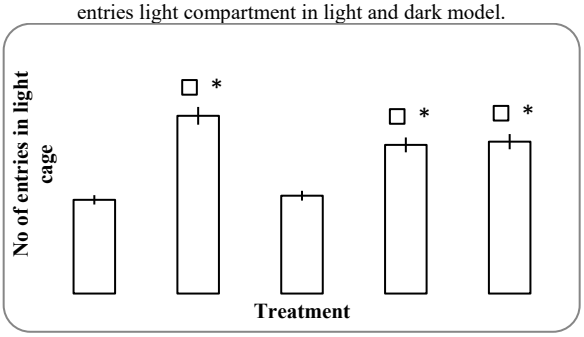


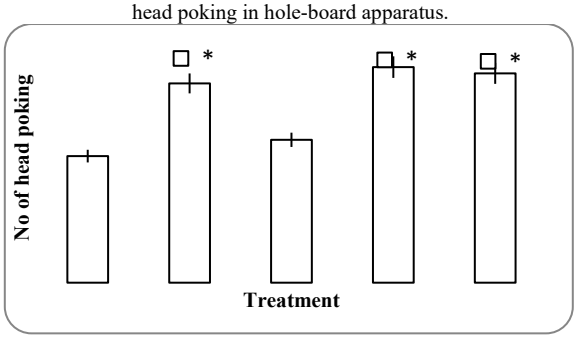
Figure 4. Effect of methanolic extract of Mucuna pruriens seeds number of entries light compartment in light and dark model.



Hole-board test

In comparison to control, diazepam and MEMP (200 and 300 mg/kg) significantly increased number of head poking (Figure 5).

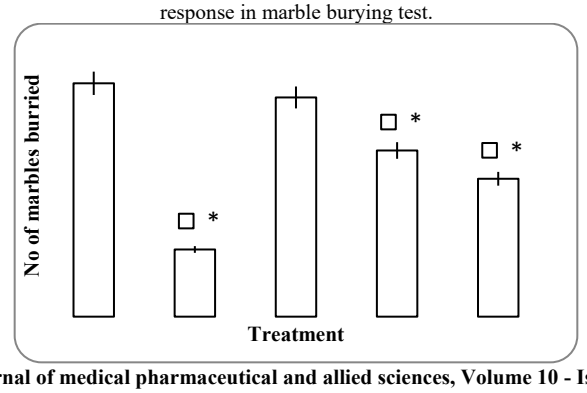
Figure 5. Effect of methanolic extract of Mucuna pruriens seeds on number of head poking in hole-board apparatus.



Marble burying test

In comparison to control, Diazepam and MEMP (200 and 300 mg/kg) significantly reduced number of marbles buried (Figure 6).

Figure 6. Effect of methanolic extract of Mucuna pruriens seeds on burying response in marble burying test.



Antidepressant activity

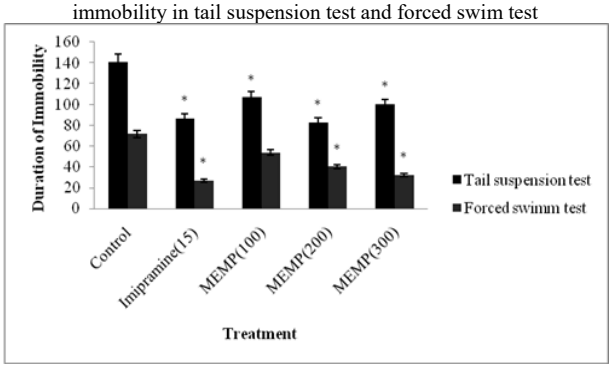
Tail suspension test

In comparison to control, Imipramine and MEMP reduced duration of immobility significantly (Figure 7).

Forced swim test

In comparison to control, Imipramine and MEMP (200 and 300 mg/kg) significantly reduced duration of immobility (Figure 7).

Figure 7. Effect of methanolic extract of Mucuna pruriens seeds on duration of immobility in tail suspension test and forced swim test

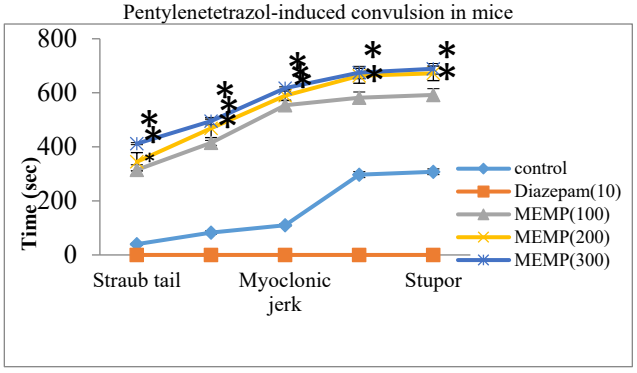


Anticonvulsant activity

Pentylenetetrazol-induced convulsion

In comparison to control, Diazepam does not show any sign of convulsion. Significant increase in the latency for straub tail, extensor, myoclonic jerk, clonic convulsion and stupor was observed after MEMP treatment (Figure 8).

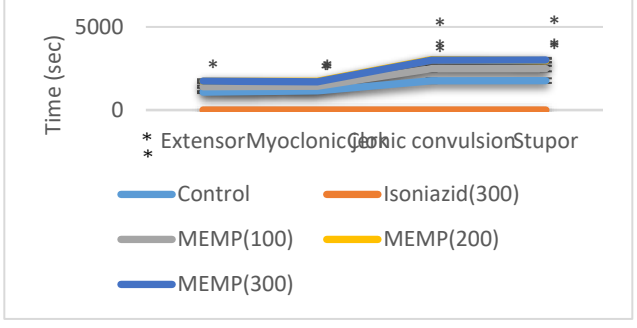
Figure 8: Effect of methanolic extract of Mucuna pruriens seeds on Pentylenetetrazol-induced convulsion in mice



Isoniazid-induced convulsion in mice

In comparison to control, Diazepam does not show any sign of convulsion. Significant increase in the latency for extensor, myoclonic jerk, clonic convulsion and stupor was observed after MEMP treatment (Figure 9).

Figure 9. Effect of methanolic extract of Mucuna pruriens seeds on isoniazid-induced convulsion in mice.



DISCUSSION

Anxiety is a type of behavioral inhibition that arise as a consequence of novel environmental effects. It has been identified that many plant secondary metabolites are used in the treatment of psychotic disorders, especially anxiety, in traditional medicine practice, with the majority of them affecting the noradrenaline, serotonin, GABA neurotransmitters activities in the central nervous system directly or indirectly.[24,25,26] Disorders of anxiety are most common psychiatric problems.[27]

Psychological and pharmacological therapies in clinical trials have been crucial in defining and validating effective interventions for a variety of anxiety disorders. [28]

Depression is one of the most common mental illnesses, with symptoms including persistently depressed moods, reduced physical activity, feelings of helplessness, and slow thinking and cognitive function. The TST and FST are the most commonly used screening and assessment models for antidepressant-like activity in mice. [19, 21, 29, 30]

Epilepsy is the most common of the chronic neurological conditions, and it is the most difficult to treat. Epilepsy may be a symptom of a number of diseases, and the mortality rate varies depending on the disease. The history etiology of epilepsy, such as tumours, trauma, degenerative disorders, or cerebrovascular diseases, is likely to be the cause of death.[31] GABA is the brain's key inhibitory neurotransmitter, and its suppression is considered to play a role in epilepsy.[32] Petitmal epilepsy resembles isoniazid and pentylenetetrazol-induced seizures.[33] In both laboratory and clinical settings, evidence suggests that a disproportion between excitatory and inhibitory neurotransmission in the brain is a major contributor to seizure progression.[34]

MEMP shows significant increase in the time spent and number of entries in open arm of EPM as well as in light area of light and dark cage, and significantly delayed onset of extensor phase, myoclonic jerk, clonic convulsion and stupor in PTZ and INH-induced convulsions i.e. MEMP protects animals against PTZ and INH-induced convulsions. Anxiolytic activity may be due to the activation and facilitation of GABA at the GABAA receptor.

This study indicates that plant extract contains chemical constituent that facilitate GABAergic transmission. This suggests that there is involvement of GABA receptors in the anxiolytic and anticonvulsant activity. The administration of MEMP significantly decreased the duration of immobility in TST and FST. There is evidence of involvement of L-dopa in antidepressant activity of M. pruriens. Previous studies suggested dose-dependent contraction of guinea-pig ileum with hot water extract (HWE) of M. pruriens seeds suggesting presence of potent histamine receptor stimulants. [35]

CONCLUSION

The findings have demonstrated that MEMP has anxiolytic, antidepressant, and anticonvulsant activity, may be mediated through the GABAergic, dopaminergic, and histaminergic nervous systems. However, the basic mechanism of action needs to be elucidated.

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