Bull. Pharm. Sci., Assiut University, Vol. 45, Issue 1, 2022, pp. 129-137.

Bulletin of Pharmaceutical Sciences
Assiut University
Website: http://bpsa.journals.ekb.eg/
e-mail: bullpharm@aun.edu.eg

NEUROPHARMACOLOGICAL ACTIVITIES OF METHANOLIC EXTRACT OF LEAVES OF VISCUM CAPITELLATUM SMITH.

Varsha S. Jadhav[1], Vilas B. Ghawate[1], Ramchandra B. Jadhav[2], Sanjay J. Surana[3] and Mohan G. Kalaskar[3*]

[1]*Department of Pharmacognosy, MES College of Pharmacy, Sonai, Ahmednagar, India*
[2]*Department of Pharmacognosy, SVPM'S College of Pharmacy, Malegaon(BK), Pune, India*
[3]*Department of Pharmacognosy, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule India*

In present study, Viscum capitellatum Sm., hyperparasite was investigated for various neuropharmacological activities such as locomotor activity, skeletal muscle relaxation activity, antianxiety and sleep potentiation using Swiss Albino mice. The effects of methanol extract of V. capitellatum (MEVC)on anxiety, depression, rota rod performance and pentobarbital-induced sleep time were evaluated. The anxiolytic activity of MEVC at lower dose (100 mg/kg) was characterized by increased time spent and number of entries in open arms in the elevated plus maze paradigm as compared to control group. The MEVC (100, 200, and 400 mg/kg, i.p.) showed dose-dependent significant increase in motor coordination in rota rod performance test. The MEVC at the doses 500 mg/kg, i.p. was found to produce a significant prolongation of pentobarbital-induced sleeping time. The phytochemical estimation revealed the presence of significantly high amount of polyphenols. The results of the study showed that the V. capitellatum possesses neuropharmacological activity, confirming the traditional claims.

Key words: *Viscum capitellatum, neuropharmacology, Hyperparasitic plants, polyphenols.*

INTRODUCTION

Anxiety and depression are the most common psychiatric disorders. There are450 million people worldwide, 121 million of whom suffer from depression, and approximately 50 million people have epilepsy.[1] In developed countries, herbal medicines are used by 70% to 80% of the population to treat ailments. More than 53% of patients with depression and anxiety utilize complementary and alternative plant-related medicines.[2] This could be attributable to various factors, including a desire to avoid side effects as well as take advantage of the safety, effectiveness, and greater quality control of today's phytomedicines.[3] In the development of pharmaceuticals, medicinal plants have proven to be an important resource. Plants are responsible for approximately 25% of today's prescribed drugs, either directly or indirectly.[4] A considerable number of herbal medicines are recognized as active in the central nervous system (CNS). As such, some researchers are focusing on medicinal plants to elucidate compounds that are similarly effective but with fewer side effects. It has become an important area of research interest in psychopharmacology during this decade.

There are approximately 100 species of Viscum, the which are often native in Africa and Madagascar, with a few in South Asia. The genus *Viscum* is now classified as a member of family Viscaceae.[5&6] *Viscum* has about 100 species, most of them in Africa and Madagascar and a small number in southern Asia. *Viscum capitellatum* Smith (Viscaceae) is an herbaceous growing shrub parasitic on *Dendrophthoe falcata* Linn (Loranthaceae), which is itself parasitic on *Mangifera indica*

Received in 11/11/2021 & Accepted in 16/2/2022

*Corresponding authorMohan G. Kalaskar, E-mail: kalaskar.mohan@gmail.com

Linn (Anacardiaceae).[7] Predominantly, *V. capitellatum* is distributed throughout the Western Ghats region, India. The only host so far reported is *Dendropthoe falcata* Linn. (Loranthaceae). Because of their strange habitat, mistletoes remain the source of their mystical and medicinal use in different cultures. Several other mistletoes have been used and evaluated for its efficacy in CNS diseases in folklore and traditional practice.[8, 9] However, except for the European mistletoe *Viscum album*, no other mistletoe has been investigated systematically for its CNS related activities. By considering the phylogenetic relationship, we undertook the study to evaluate the neuropharmacological activities of *V. capitellatum* by using different animal models.

MATERIALS AND METHODS

Collection of plant material

V. capitellatum parasitic plant grown on *D. fulcata* was collected from the Western Ghats region (Latitude 17° 55' 0N and Longitude 73° 40' 0E and at an altitude of 1352 m). The plant specimen of *V. capitellatum* (Voucher no. RBJ1311) was authenticated by Dr. C.B. Salunkhe (Department of Botany, Krishna Mahavidyalaya, Rethare, India).

Extraction

The plant material was dried in the dark at room temperature, powered and extracted with methanol (100%) by the cold maceration technique. The liquid extract was dried by removal of the solvent under vacuum. The percent extract was found to be 9.86%w/w. it stored in closed container in desiccator and used in the pharmacological experiments.

Quantitative chemical investigations

Total phenolic content

The total phenolic content (TPC) of methanolic extract of *V. capitellatum (MEVC)* was determined by the Folin-Ciocalteau phenol reagent colourimetric assay.[10] In Brief, 0.1 mL of extract (100µg/mL) was mixed separately with 0.2 mL of Folin-Ciocalteu reagent (1:5 with distilled water). After this, 2 mL of distilled water and 2 mL of 15% Na_2CO_3 were added to the mixture. After 10 minutes of an incubation period at 50°C in a water bath, absorbance was measured at 660 nm using a UV-visible spectrophotometer (Shimadzu, UV-2450). The total phenolic contents in the extracts were calculated using the gallic acid standard calibration curve. The total phenolic content is expressed as mg/gm of gallic acid equivalents (GAE).

Total flavonoid content

In brief, each 0.5 ml of MEVC (100 µg/mL) were thoroughly mixed with 1.5 mL of ethanol, 0.1 mL of 10% Al $(NO_3)_3$, 0.1 mL of 0.1M CH_3COONa and 2.8 mL of water. The resultant mixture was incubated for 40 min at room temperature. The absorbance of the reaction mixture was measured at 415 nm using UV-spectrophotometer (Shimadzu, UV-2450).[11] The Total flavonoid content (TFC) of the extract was calculated by using the standard quercetin calibration curve. Results were expressed as mg/gm quercetin equivalents (QE).

Total proanthocyanidin content

The total proanthocyanidin content of MEVC was determined using a reported method.[12] In brief, 1ml of extract (100 µg/ml) was mixed with 2 mL of freshly prepared vanillin solution (1% vanillin in 70% H_2SO_4) and maintained for 15 min at 20^oC. The absorbance was measured at 500 nm. A calibration curve was drawn using aqueous solution of epicatechin as a reference standard. Total proanthocyanidins were expressed as mg/gm of epicatechin equivalent.

Animals

In both acute toxicity studies and neuropharmacological assays, Swiss albino mice weighing 30-36 gm were used. The animals were housed in community cages and maintained under regular laboratory conditions (23 ± 1^oC temperature, 55.5% relative humidity, 12-h light-dark cycle, free access to water and standard rodent chow: Lipton India Ltd).[13] All animals were acclimatized for 3 weeks prior to initiation of the test. The experiments were conducted in a special adjacent noise-free room with controlled illumination.

Acute toxicity study

For the determination of acute toxicity by the oral route, Swiss albino mice were divided into two groups (n= 6) and sequentially dosed to determine the oral toxicity of MEVC as per Organization for Economic Co-operation and Development (OECD) guideline 425.[14] The test group received MEVC (5-2000 mg/kg body weight) suspended in 0.5% carboxymethyl cellulose (CMC) orally, while the control group received only 0.5% CMC. After the test extracts administration, food or water was withheld for the next 1-2 hrs. Animals were closely observed after dosing of text extracts for the initial 4 hrs after dosing, followed by neurobehavioral, changes for 14 days.

Open Field Test

The open field area was comprised of transparent acrylic walls and a black floor (30 x 30 x 15 cm) divided into nine squares of equal size. One hour before the test, the mice were treated with MEVC (100, 200 and 400 mg/kg, i.p), diazepam (4 mg/kg, i.p., as a positive control) and normal saline (vehicle, i.p., control group). The open field test was used to evaluate the locomotor activity of mice. The observed parameters included the number of squares crossed. The spontaneous motor activity was recorded 30 min after extract/drug administration.[15] The results of the treated groups were compared with those of the saline control.

Motor Co-ordination test

The rota rod used in this test was a rubber-coated metallic rod (3 cm in diameter) connected to a motor. The rod was rotated at a constant speed, i.e. 9 rpm, and was placed about 60 cm above the table in order to prevent the mice from jumping off the roller. Mice were exposed to the rota rod as a pretest before the experiment and only those mice included in the study were those that remained on the rod for 5 min at a speed of 9 rpm. All the groups (n= 10) were treated with diazepam (4 mg/kg), saline water (10 mL/kg) and MEVC (100,200 and 400 mg/kg, i.p.). Each mouse was exposed for 5 min at 0 and 30 min after the drug administration on the revolving rod and the time spent on the rod was recorded.[16]

Elevated Plus Maze test

The EPM test is the most frequently employed model for the assessment of the anxiolytic activity of novel substances.[17] The maze consisted of a central platform (10 x 10 cm) with two open (12 x 5 cm) and two closed arms (12 x 5 cm) and 12 cm high walls. The maze was elevated 38.5 cm from the room's floor. The experimental animals were divided into five (n=10). The mice were treated 30 min prior to the test with diazepam (4 mg/kg, i.p., positive control), while normal saline (vehicle, i.p., control group) and MEVC (100,200 and 400 mg/kg, i.p., test group). Each animal was placed at the center of the maze facing one of the open arms. The number of entries and the time spent in the enclosed and open arms were recorded during the 5 min test. After each test, the maze was carefully cleaned with wet tissue paper (10% ethanol solution).

Pentobarbitone induced sleep potentiation

The pentobarbitone-induced sleep potentiation test was performed as per the reported method.[18] The mice were divided into five groups (n=10). The MEVC (100, 200 and 400 mg/kg, i.p., test group) and normal saline 1% (vehicle, p.o., control group) were administrated 1 h prior to the test, and diazepam (45 mg/kg, i.p., positive control) was administered 30 min before the test. In this experiment, after the administration of pentobarbitone (30 mg/kg, i.p.), the mice were placed separately in transparent Plexiglas cages (25 × 15 × 10 cm) to observe the hypnotic effect, which was considered to be the time interval between the disappearance (latency) and reappearance (duration) of the righting reflex.

Statistical analysis

All the data were expressed as mean ± SEM from five animals. The data obtained was analyzed using the one-way ANOVA followed by Dunnett's test for determining the level of significance and $p< 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Quantitative phytochemical analysis

Table 1 displays the total phenolic, flavonoid and proanthocynidine contents of MEVC. Amongst the all determinations, MEVC found content highest total phenolic content (47.84 ± 4.12 mg/g GAE), followed total flavonoid AEB-*ChF* (29.25 ± 2.20 mg/g QE) and total proanthocynidine (15.59 ± 1.81 mg/g EE).

Table 1: Quantitative phytochemical estimations

Phytochemicals	MEVC
Total phenolic content (mg/g of GAE)	47.84 ± 4.12
Total flavonoid (mg/g of QE)	29.25 ± 2.20
Total proanthocynidine (mg/g of EE)	15.59 ± 1.81

Values (n=3) are mean ± SD

Open field exploratory test

Mice treated with MEVC (100, 200 and 400 mg/kg), did not showed dose dependent change in the total crossing. 100 mg/kg showed the least changes in the parameters of total crossing compared with the control group (p> 0.05). The MEVC at a higher dose has shown significant percent inhibition comparing with the control group (p< 0.01). In the case of animals treated with a dose of 400 mg/kg of MEVC exhibited a decrease in the number of total crossings (p< 0.01) (Table 2).

Motor Co-ordination test

The data shows that, the animals treated MEVC (100, 200 and 400 mg/kg i.p.) were able to maintain equilibrium on the rotating rod and stayed on longer without falling. The rota rod activity of all groups is shown in table 3. The time spent on the revolving rod was significantly reduced by diazepam, in comparison with the control group.

Table 2: Effect of MEVC on locomotor activity by using Actophotometer.

Group	Group &Dose (i.p.)	Crossings		% inhibition
		'0'min	'30' min	
1.	Control (10 ml)	454.3 ± 31.23	349.2 ± 36.35	---
2.	Diazepam (4 mg/kg)	361.4 ± 13.81	35.90 ± 7.521	89.59
3.	MEVC (100 mg/kg)	420.2 ± 27.60	257.4 ± 41.60	26.28
4.	MEVC (200 mg/kg)	303.8 ± 38.54**	161.9 ± 13.41**	53.63
5.	MEVC (400 mg/kg)	293.3 ± 35.22**	89.00 ± 13.78**	74.51

All results are expressed in terms of Mean ± S.E.M., n=6, Data processed by one-way ANOVA followed by Dunnett's test, * p<0.05, ** p<0.01 compared to vehicle treated group. MEVC-Methanolic extract of *V. capitellatum.*

Table 3: Effect of methanolic extract of *V. capitellatum* (VCM) on muscle relaxant activity in rotarod performance.

Group	Group & Dose (i.p.)	Fall off time (Sec)	
		Before drug	After drug
1.	Control (10 ml)	300	300 ± 1.52
2.	Diazepam (4 mg/kg)	300	59.60 ± 8.017**
3.	MEVC (100 mg/kg)	300	107.9 ± 19.37*
4.	MEVC (200 mg/kg)	300	181.6 ± 4.167**
5.	MEVC (400 mg/kg)	300	200.9 ± 13.33**

All results are expressed in terms of Mean ± S.E.M., n=6, Data processed by one-way ANOVA followed by Dunnett's test, * p<0.05, ** p<0.01 compared to vehicle treated group. MEVC-Methanolic extract of *V. capitellatum*

Elevated plus maze test

The anxiolytic diazepam induced a significantly increased number of entries to open arms and the of time spent in the arms in the MEVC, when comparing to control group ($p< 0.05$) at lower dose (100 mg/kg, i.p.). Surprisingly the mice treated with MEVC in the dose of 200, 400 mg/kg, showed reduced entries and time in open arm with respect to the control group (Table 4).

Pentobarbitone induced sleep potentiation

In the pentobarbitone induced sleep potentiation, the extract at doses, 100, 200 and 400 mg/kg showed a significant reduction in the time of onset of sleep in a dose-dependent manner (Table 4). The effect of the extract (400 mg/kg) on the onset of sleep was comparable to that of the standard. All doses of the extract potentiated the duration of pentobarbitone induced sleeping time in test animals compared to controls (Table 5).

Table 4: Effect of MEVC on mice in antianxiety activity by using Elevated Plus Maze Apparatus.

Group	Group & Dose (i.p.)	Open arm	
		No. of entries	Avg. time spent (s)
1.	Control (10 ml)	6.7 ± 1.106	12.0 ± 2.338
2.	Diazepam (4 mg/kg)	7.7 ± 1.38*	14.8 ± 2.215
3.	MEVC (100 mg/kg)	7.4 ± 0.65*	10.2 ± 1.482
4.	MEVC (200 mg/kg)	4.9 ± 0.95*	7.1 ± 1.215
5.	MEVC (400 mg/kg)	4.1 ± 0.74*	5.4 ± 0.686

All results are expressed in terms of Mean ± S.E.M., n=6, Data processed by one-way ANOVA followed by Dunnett's test, $^{*}p<0.05$, $^{**}p<0.01$ compared to vehicle treated group. MEVC-Methanolic extract of *V. capitellatum*

Table 5: Effect of MEVC on pentobarbitone induced sleep time potentiation.

Group	Group & Dose (i.p.)	Onset of sleep (min.)	Total sleep time (min.)	% Potentiation
1.	Control (10 ml)	49.30 ± 2.89	81.40 ± 4.08	----
2.	MEVC (100 mg/kg)	23.90 ± 1.17**	94.40 ± 4.67	51.52
3.	MEVC (200 mg/kg)	22.10 ± 1.16**	108.9 ± 3.96**	55.17
4.	MEVC (400 mg/kg)	15.10 ± 0.96**	133.6 ± 2.78**	69.37

All results are expressed in terms of Mean ± S.E.M., n=6, Data processed by one-way ANOVA followed by Dunnett's test, $^{*}p<0.05$, $^{**}p<0.01$ compared to vehicle treated group. MEVC-Methanolic extract of *V. capitellatum*

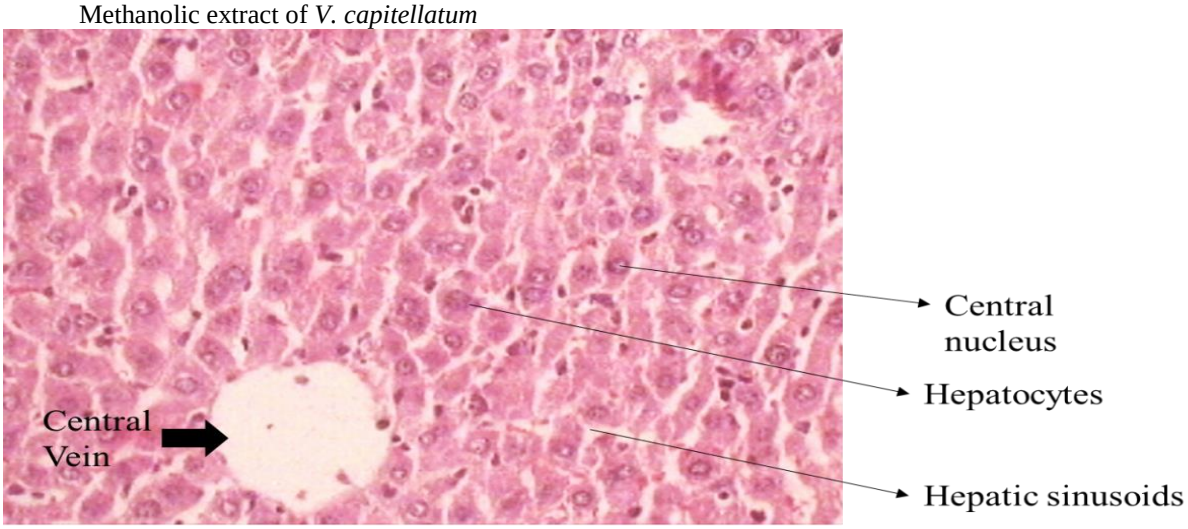

Fig. 1: Histopathological section of test extract mice.

No signs of inflammatory cell infiltration, macro and micro-vesicular steatosis necrosis with loss of radial arrangement of hepatocyte plaques, a pale eosinophilic stain, and pyknotic or absent nuclei

Discussion

Hyperparasitic plants (Mistletoes) are used in both traditional and complementary medicine to treat and control a variety of disorders. Except European mistletoe (*Viscum album),* no other mistletoe has been investigated systematically for their CNS related activities. No scientific literature is available on CNS related activities for *V. capitellatum* other species of *Viscum*. Therefore, we decided to investigate the CNS effects of *V. capitellatum* using *in-vivo* models. The present study investigated for the first time the CNS effects of a MEVC in mice. Oxidative stress is an important underlying factor in a number of neurodegenerative and psychiatric disorders.[19] Quantitative estimations revealed that MEVC contains a significant amount of antioxidants like polyphenols like polyphenols, flavonoids and proanthocyniidine. The acute oral toxicity of MEVC by cumulative dose study from 5 mg to 2000 mg/kg showed the extract was found safe up to 2000 mg/kg body weight but toxic at 5000 mg/kg. It was validated using computer software—AOT425 StatPgm. Thus, the dose for pharmacological study was selected by the up and down method as 100, 200, and 400 mg/kg bodyweight. Furthermore, liver histopathology of the test group (2000 mg/kg) does not shown signs of inflammatory cell infiltration, macro and micro-vesicular steatosis necrosis with loss of radial arrangement of hepatocyte plaques, a pale eosinophilic stain, and pyknotic or absent nuclei and showed normal articulation (Figure 1).

A reduction in locomotor activity is considered an indicator of alertness, and a decrease in it suggests a sedative effect.[20] The MEVC exhibited a decrease in locomotor score and a significant increase in the hypnotic effect. Skeletal muscle coordination and relaxant effect were monitored by the Rota rod apparatus. Diazepam significantly decreased motor activity in the rota rod performance test due to its sedative and strong neuromuscular blocking action. While, MEVC showed dose dependently increased motor coordination.

The EPM is one of the most commonly used tests, and it is very sensitive to the effects of both anxiolytic and anxiogenic drugs that act on the GABAA-benzodiazepine complex.[21] Normal mice would typically choose to spend the majority of their allotted time in the closed arms in EPM. This tendency appears to reflect an aversion to open arms caused by anxieties about open spaces. Anxiolytics are drugs that encourage open arm exploration, such as diazepam, while anxiogenics are the opposite.[22] In this study, we found that a low dose of MEVC has an anxiolytic-like effect in mice, as it enhanced open arm entries and time spent in the open arms of the EPM as compared to control animals. While, MEVC at higher doses has been found to possess anxiogenic effect.

Many neurotransmitters play a role in regulating sleep behavior. Neurons located in the anterior hypothalamus release GABA to inhibit wake-promoting areas in the hypothalamus and brainstem.[23&24] The barbiturate pentobarbital binds GABA receptors. Benzodiazepines such as diazepam enhance the affinity of GABA for its receptor and thereby increase pentobarbital-induced sleeping time.[25] Studies have revealed the hypnotic effects of a wide variety of herbal medicine components. MEVC demonstrated a dose dependent increase in pentobarbitone induced sleep ($p< 0.01$). It has been reported that flavonoids are able to cross the blood-brain barrier and induce some effects on the central nervous system, including neuroprotective and antioxidant actions.[26&27] As MEVC contains significant amount of flavonoids, dose dependent sleep potentiation may be exerted on animals.

Quantitative phytochemical estimation revealed the presence of a significant amount of flavonoids. Flavonoids are reported to possess anxiolytic effects[28&29] and antidepressant effects[30]. Therefore, it is likely that polyphenols present in this extract might be contributing to observed neuropharmacological activity.

Conclusions

V. capitellatum was found to have a substantial influence on locomotor action and sleep potentiation in the current investigation. The extract had minimal effect on spontaneous motor coordination and antianxiety activity, indicating that the extract has a selective effect in treating CNS diseases. Furthermore, it is necessary to isolate, characterise, and screen the active principles responsible for the neuropharmacological activity of *V.*

capitellatum's methanolic extract, as well as to determine the specific mechanism by which the plant exerts the above effects.

List Of Abbreviations

ATO- Acute Oral Toxicity; CNS- Central Nervous System; EPM- Eleveted Plus maze; GABA - Gamma-Amino Butyric Acid, i.p.- intra-peritoneal MEVC - methanolic extract of *Viscum capitellatum;* MeOH- Methanol; min-minute.

REFERENCE

1. W.H. Organization, Traditional medicine: Fact sheet no. 134, December 20082011.
2. W.H. Organization, "Mental health atlas 2011: resources for mental health in the Eastern Mediterranean Region", (2013).
3. M. De Souza, M. Pereira, J. Ardenghi, T. Mora, L. Bresciani, R. Yunes, F. Delle Monache, and V. Cechinel-Filho, "Filicene obtained from Adiantum cuneatum interacts with the cholinergic, dopaminergic, glutamatergic, GABAergic, and tachykinergic systems to exert antinociceptive effect in mice", ***Pharmacology Biochemistry and Behavior***, 93(1),40-46 (2009).
4. Z.-J. Zhang, "Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders", ***Life Sciences***, 75(14),1659-1699 (2004).
5. B. Barlow, "Biogeography of Loranthaceae and Viscaceae", ***The Biology of Mistletoes,*** (1983).
6. D.L. Nickrentand C.R. Franchina, "Phylogenetic relationships of the Santalales and relatives", ***Journal of Molecular Evolution***, 31(4),294-301 (1990).
7. C.N. Bambaradeniya, "The status and implications of alien invasive species in Sri Lanka". ***Zoos' Print Journal***, 17(11),930-935 (2002).
8. K. Chandra, B. Paney, and V. Lal, "Folk-lore medicinal plants of Dumka (Bihar)". ***Ancient Science of Life***, 4(3),181-185 (1985).
9. A. Szurpnicka, J. K. Zjawiony, and A. Szterk, "Therapeutic potential of mistletoe in CNS-related neurological disorders and the chemical composition of Viscum species". ***Journal of Ethnopharmacology***, 231,241-252 (2019).
10. S. McDonald, P.D. Prenzler, M. Antolovich, and K. Robards, "Phenolic content and antioxidant activity of olive extracts", ***Food Chemistry***, 73(1),73-84 (2001).
11. C.-T. Liu, C.-Y. Wu, Y.-M. Weng, and C.-Y. Tseng, "Ultrasound-assisted extraction methodology as a tool to improve the antioxidant properties of herbal drug Xiao-chia-hu-tang", ***Journal of Ethnopharmacology***, 99(2),293-300 (2005).
12. P. Deyand J. Harborne, Methods in Plant Biochemistry: Plant Phenolics. Vol. 1, Academic Press, New York 1989.
13. M. Ghosh. Fundamentals of experimental pharmacology, 2 nd edn Calcutta scientific book agency, Calcutta1984.
14. Anonymous, OECD Guidelines– "Guidance document on acute oral toxicity testing" (2001) Series on testing and assessment No24, Organization for Economic Co-operation and Development.
15. R. Turner. Neuropharmacological tests for blind screening. Screening methods in Pharmacology, Academic Press New York1965, pp. 26-32.
16. T. Okoye, P. Akah, and C. Omeke, "Evaluation of the anticonvulsant and muscle relaxant effects of the methanol root bark extracts of Annona senegalensis", ***Asian Pacific Journal of Tropical Medicine***, 3(1),25-28 (2010).
17. R.G. Lister, "The use of a plus-maze to measure anxiety in the mouse", ***Psychopharmacology***, 92,180-185 (1987).
18. E.M. Williamson, D.T. Okpako, and F.J. Evans. Selection, Preparation and Pharmacological Evaluation of Plant Material, Volume 1, John Wiley & Sons1996.
19. B. Halliwell, "Oxidative stress and neurodegeneration: where are we now?", ***Journal of Neurochemistry***, 97(6),1634-1658 (2006).
20. V. Thakurand and S. Mengi, "Neuropharmacological profile of Eclipta alba (Linn.) Hassk", ***Journal of***

Ethnopharmacology, 102(1), 23-31 (2005).
21. B.d.Á.N. Dhonnchadha, M. Bourin, and M. Hascoët, "Anxiolytic-like effects of 5-HT2 ligands on three mouse models of anxiety", ***Behavioural Brain Research***, 140(1-2), 203-214 (2003).
22. N. Subramanian, C. Jothimanivannan, R.S. Kumar, and S. Kameshwaran, "Evaluation of anti-anxiety activity of Justicia gendarussa Burm", ***Pharmacologia***, 4(5), 404 - 407 (2013).
23. E. Murillo-Rodriguez, O. Arias-Carrión, K. Sanguino-Rodríguez, M. González-Arias, and R. Haro, "Mechanisms of sleep-wake cycle modulation", ***CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders)***, 8(4), 245-253 (2009).
24. S. Datta, "Cellular and chemical neuroscience of mammalian sleep", ***Sleep Medicine***, 11(5), 431-440 (2010).
25. R. Awad, A. Muhammad, T. Durst, V.L. Trudeau, and J.T. Arnason, "Bioassay-guided fractionation of lemon balm (Melissa officinalis L.) using an in vitro measure of GABA transaminase activity", ***Phytotherapy Research***, 23,1075-1081 (2009).
26. K. A. Youdim, M. Z. Qaiser, D. J. Begley, C. A. Rice-Evans, and N. J. Abbott, "Flavonoid permeability across an in situ model of the blood–brain barrier", ***Free Radical Biology and Medicine***, 36(5), 592-604 (2004).
27. A. Paulke, M. Schubert-Zsilavecz, and M. Wurglics, "Determination of St. John's wort flavonoid-metabolites in rat brain through high performance liquid chromatography coupled with fluorescence detection", ***Journal of Chromatography B***, 832(1), 109-113 (2006).
28. M. Herrera-Ruiz, R. Román-Ramos, A. Zamilpa, J. Tortoriello, and J.E. Jiménez-Ferrer, "Flavonoids from Tilia americana with anxiolytic activity in plus-maze test", ***Journal of Ethnopharmacology***, 118(2), 312-317 (2008).
29. C. Wolfman, H. Viola, A. Paladini, F. Dajas, and J.H. Medina, "Possible anxiolytic effects of chrysin, a central benzodiazepine receptor ligand isolated from Passiflora coerulea", ***Pharmacology Biochemistry and Behavior***, 47(1),1-4 (1994).
30. V. Butterweck, G. Jürgenliemk, A. Nahrstedt, and H. Winterhoff, "Flavonoids from Hypericum perforatum show antidepressant activity in the forced swimming test", ***Planta Medica***, 66(1),3-6 (2000).

Bull. Pharm. Sci., Assiut University, Vol. 45, Issue 1, 2022, pp.129-137.

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[٢]قسم العقاقير ، كلية الصيدلة ، ماليجان ، بون ، الهند
[٣]معهد باتل للتعليم والبحوث الصيدلانية ، شيربور ، دهول ، الهند

في الدراسة الحالية ، تم فحص فيسكم كابيتالم سم. ،فرط الطفيل لمختلف الأنشطة الدوائية العصبية مثل النشاط الحركي ، نشاط استرخاء العضلات ، مضادات القلق و القدرة على النوم باستخدام الفئران السويسرية البيضاء. تم تقييم آثار مستخلص الميثانول من فيسكم كابيتالم على القلق والاكتئاب وأداء قضيب الروتا ووقت النوم الناجم عن البنتوباربيتال. تميز نشاط مستخلص الميثانول من فيسكم كابيتالم كمزيل القلق بجرعة أقل (١٠٠ مجم / كجم) بزيادة الوقت الذي يقضيه وعدد مرات الدخول في نموذج المتاهة المرتفع بالمقارنة بمجموعة المراقبة. أظهر مستخلص الميثانول من فيسكم كابيتالم (١٠٠، ٢٠٠ ، و ٤٠٠ مجم / كجم ، داخل الصفاق) زيادة كبيرة تعتمد على الجرعة في التنسيق الحركي في اختبار أداء قضيب الروتا. مستخلص الميثانول من فيسكم كابيتالم بجرعات ٥٠٠ مجم / كجم ، داخل الصفاق ادى الى الإطالة كبيرة في وقت النوم الناجم عن بنتوباربيتال. أظهر التقدير الفيتوكيميائي وجود كمية كبيرة من مادة البوليفينول. أظهرت نتائج الدراسة أن فيسكم كابيتالم تمتلك نشاطًا دوائيًا عصبيًا ، مما يؤكد الاستخدام الشعبي.