International Journal of Engineering Sciences &Research Technology

(A Peer Reviewed Online Journal)
Impact Factor: 5.164

IJESRT

RESEARCHERID
THOMSON REUTERS

[Kumar, *et al.*, 8(12): December, 2019]
IC™ Value: 3.00

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

IJESRT

INTERNATIONAL JOURNAL OF ENGINEERING SCIENCES & RESEARCH TECHNOLOGY

ANTI-PARKINSONIAN EFFECT OF TRIGONELLA FOENUM-GRAECUM IN DRUG INDUCED CATALEPSY IN MOUSE MODEL

P. Sailaja Rao[1] & v. Ravi Kumar*[2]

[1]Assistant Professor, Department of Pharmacology, College of Pharmacy, Jazan University, Saudi Arabia

[*2]Associate Professor, M.N.R. College of Pharmacy, Sangareddy, Telangana State, India

DOI: 10.5281/zenodo.3596337

ABSTRACT

Trigonella foenum-graecum L. (Leguminoseae) is an ancient and annual legume crop mainly grown for multiple uses in many parts of the world like Asia, Europe, Africa and Australia. It possesses anticarcinogenic activities, hypocholesterolemic activities, hypoglycemic activities, antioxidant, antineoplastic agent, In the present anti-cataleptic activity of whole plant *Trigonella foenum-graecum* in Haloperidol induced and clonidine induced catalepsy in mice. Methanolic extract of whole plant *Trigonella foenum-graecum* was prepared and evaluated for anti-cataleptic property. The mice were divided into 5 groups (n=6). Group I is served as control. Group II [(haloperidol 1.0 mg/kg body weight., *i.p.* in Haloperidol induced catalepsy (HIC)]. Group III (test extract, 200 mg/kg body weight, *p.o.*). Group IV (test extract, 400 mg/kg body weight respectively.*p.o.*), Group V (levodopa and carbidopa (100mg + 25 mg/kg, *i.p.*). The anti-cataleptic effect of *Trigonella foenum-graecum*, was evaluated by locomotor activity and rota rod test using mice models. Histopathological studies of brain in mice were examined. *Trigonella foenum-graecum* extract (200 and 400 mg/kg body weight, *p.o.*) was found to decrease the duration of catalepsy significantly ($P < 0.01$) in standard bar test as compared to haloperidol group. Comparatively, METFG (400 mg/kg body weight, *p.o.*) was more potent anti-cataleptic activity than METFG (200 mg/kg body weight, *p.o.*)

KEYWORDS: Anti-cataletic activity, haloperidol, Trigonella foenum-graecum, rotarod, standard bar.

1. INTRODUCTION

Central Nervous System associated diseases are appearing as a major threat in the future because of increasing mental stress, work load and strain which seem to be absolutely necessary in day today life. In the developing world, unknowingly this inclined into a state more of CNS disorders. Some factors like atmospheric pollutants, toxins also cause neurodegenerative diseases like Parkinson's disease and Alzheimer's disease (Chanchal Raj *et al.*, 2014) As parkinsonism need a prolonged treatment with anti-parkinson's drugs, many side effects encounter including questionable efficacy in the treatment, may cause Parkinson's related movement problems like hallucinations and orthostatic hypotension. These reasons force the area of research to find new and improved treatments which will combat the adverse effects and drawbacks of the existing treatments.

In the treatment of schizophrenia and other affective disorders, Neuroleptics are extensively used. Unluckily, their use frequently is associated with upsetting side effects involving Parkinsonism and tardive dyskinesia (Dobryakova YV *et al.*, 2011). Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining the normal posture. Catalepsy is a sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain (Dhanalakshmi S *et al.*, 2004). Neuroleptic-induced catalepsy has long been used as a model for the parkinsonian‐like bradykinesia. Evidences indicate that haloperidol induces catalepsy in animals, and this behavior response has long been used as a model for EPS (extra pyramidal symptoms) effects (Datla K P *et al.*, 2007). Besides, dopamine receptor blockade and catecholamine depletion, other neurochemical hypotheses have been proposed for the development of catalepsy such as striatonigral GABAergic, cholinergic, glutamate, and serotonergic depletion, etc. Dementia has been associated with drug-induced parkinsonism and has been suggested to support the role of underlying brain damage (Humphrey PR and Maureen MD 2012). In counteracting the catalepsy induced by haloperidol Anticholinergic drugs are most effective in experimental animals. But these anti-cholinergic drugs produce

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

various side effects like dryness of mouth, constipation and urinary retention. Hence an alternate for newer drugs with fewer side effects is ongoing. In this context, an exploration to plant products which are often considered to be less toxic and free from side effects compared to synthetic drugs need importance.

Trigonellafoenum-graecum L. (commonly called as Fenugreek) is an ancient and annual legume crop belonging to family: Leguminoseae, mainly grown in many parts of the world for multiple uses. It's found in Asia, Europe, Africa and Australia. In the ancient Indian traditional system of medicine, Ayurveda, fenugreek has been suggested as an important medicine to treat a variety of digestive and mucosal conditions. The fenugreek seed has traditionally been used as a carminative, demulcent, expectorant, laxative and stomachic agent. (Jayachandra R *et al.*, 2012). Different active components of fenugreek seeds have been identified and isolated such as polyphenolic flavonoids which exhibit most common properties, that is, hypoglycemic, hypocholesterolemic, hypotriglyceridemic and antiperoxidative (Goyal et al., 2011), steroid saponins exhibiting anti-inflammatory property. Polyphenol compounds are composed of a group of substances with different chemical structures and activities and are widely present in nature. Resveratrol (3,5,4′-trihydroxy-trans-stilbene) is a well-known polyphenol compound that has widespread activities including antiobesity, antidiabetic, cardiovascular protective, and neuroprotective properties (Anuradha CV and Ravikumar P, 2001). Keeping in view of the neuroprotective property of the *Trigonellafoenum-graecum* L., the present has been designed in order to investigate the anti-cataleptic effect of the herbal drug using animal models. Histopathological studies of the brain were also examined.

2. MATERIALS AND METHODOLOGY

Collection of Plant material and extraction (Nagarjuna S et al., 2015)
The whole plant *Trigonella foenum-graecum* were collected from a local market during the month of December 2018. This material was identified and authenticated by a botanist at SV university, Tirupati, Andhra Pradesh, India. The whole plant was cleaned, reduced to small fragments, dried under shade for about 15 days and coarsely powdered in a mixer grinder. The powdered material was stored for extraction process. The powder was subjected to methanol extraction, in Soxhlet apparatus and was run about 10 cycles. After filtration through Whatman filter paper, the filtrates were dried in desiccator. The chemicals were procured from reputed companies, listed in the table 1.

Table 1 List of drugs/chemicals procured

S.No	Name of drug/chemical	Source
1	Haloperidol	RPG Life Sciences
2	Levodopa, carbidopa	Sun Pharma laboratories
3	Methanol	Unichem Laboratories
4	Hydrochloride acid	Unichem Laboratories
5	Ferric chloride	Sun Pharma laboratories

Preparation of drugs
1. Methanolic extract of Trigonellafoenu-graecum (METFG) was dissolved in saline.
2. Haloperidol was dissolved in normal saline and given orally.

Experimental animals
Swiss albino mice (20–25 g) were used for the pharmacological activities. They were kept in polypropylene cages at 25 ± 2 °C, with relative humidity 45-55 % under 12 h light and dark cycles. All the animals were acclimatized to the laboratory conditions for a week before use. They were feed with standard animal feed and water *ad libitum.*

Phytochemical screening
Methanolic extract of *Trigonellafoenum-graecum* was subjected to preliminary phytochemical investigations to identify various phytoconstituents present in whole plant according to the standard methods.

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

Preliminary Phytochemical Screening: (Khandelwal K R, 2005).
Methanolic extract of *Trigonellafoenum-graecum* (METFG) was screened for the presence of various phytoconstituents like alkaloids, flavanoids, steroids, tannins, glycosides, triterpenoids and saponins.

Tests carried out for different phytochemical constituents:
Methanolic extract of *Trigonellafoenum-graecum*was subjected to preliminary phytochemical investigations to identify various phytoconstituents present in whole plant according to the method.

1) Test for alkaloids: A small portion of crude extract was dissolved in 5 ml of 1% hydrochloric acid, filtered and tested with Dragendorff's reagent and Mayer's reagent separately. Any precipitate or turbidity with the reagents suggested the presence of alkaloids.
2) Test for flavonoids: A few drops of conc. hydrochloric acid and 1-2 magnesium turnings were added to 1 ml of methanolic extract. The presence of flavonoids was indicated by the development of pink or magenta-red colour.
3) Test for phenols (Ferric chloride test): A fraction of the extracts was treated with aqueous 5% ferric chloride and observed for formation of deep blue or black colour.
4) Test for amino acids and proteins (1 % ninhydrin solution in acetone): 2 ml of filtrate was treated with 2-5 drops of ninhydrin solution placed in a boiling water bath for 1-2 minutes and observed for the formation of purple colour.
5) Test for carbohydrates (Molisch test): To a fraction of extract α-naphthol and alcohol was added. It was mixed well and conc. sulphuric acid was added drop by drop by keeping the test tube in inclined position. Violet ring is formed at the junction of two layers which shows the presence of carbohydrates.
6) Test for saponins (Foam test): To 2 ml of extract was added 6 ml of water in a test tube. The mixture was shaken vigorously and observed for the formation of persistent foam that confirmed the presence of saponins.
7) Test for sterols (Liebermann-Burchard test): 2 ml of extract was treated with drops of chloroform, acetic anhydride and conc. H_2SO_4 and observed for the formation of dark pink or red colour.
8) Test for tannins (Braymer's test): 2 ml of extract was treated with 10% alcoholic ferric chloride solution and observed for formation of blue or greenish colour solution.

Acute Toxicity Studies of METS (OECD, 1996)
Acute toxicity studies were carried out in order to check the toxic effects for Methanolic extract of *Trigonellafoenum-graecum*. The studies were performed as per Organization for Economic Cooperation and Development (OECD). The method is used to evaluate the acute oral toxicity is up and down procedure (OECD guideline-425). Up and down procedure (OECD guideline-425) acute toxicity studies were carried out as per the OECD 425 guidelines.

Animals: Animal Protocol was approved by IAEC (Institutional Animal Ethical Committee) of CPCSEA (Committee for Purpose of Control and Supervision of Experimentation on Animals) through its reference no: IAEC/MNRCP/2018/002, Dated: 27/2/18. Male Wistar rats, weighing (180-250 gms) were obtained from NIN (National Institute of Nutrition, Hyderabad. The animals were acclimatized to the experimental room at a temperature of 23 ± 2^0 C, controlled humidity conditions (50-55%) and 12 hr light and 12 hr dark cycles. They were fed with standard food pellets (Hindustan Lever, Hyderabad) and water *ad libitum*.

Methodology (Beal M F, 2001)

Induction of Catalepsy by chronic haloperidol administration in experimental mice (Nagarjuna S et al., 2015)
Albino mice of either sex weighing 20-25 g was divided into five groups of six animals each (n=6).

Haloperidol (1.0 mg/kg, i.p) was administered daily to the mice for a period of 21 days to induce catalepsy. Plant extracts and standard drugs were administered orally 30 min before to haloperidol treatment. The animals were divided into six groups, of 6 animals (n=6).

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

3. EXPERIMENTAL PROTOCOL

Group I: The animals served as control.
Group II: The animals received haloperidol (1.0 mg/kg, i.p) and served as negative control.
Group III: The animals received haloperidol (1.0 mg/kg, i.p) and treated with METFG (200 mg/kg, p.o) suspended in vehicle.
Group IV: The animals received haloperidol (1.0 mg/kg, i.p) and treated with METFG (400 mg/kg, p.o) suspended in vehicle.
Group V: The animals received haloperidol (1.0 mg/kg, i.p) and treated with L-DOPA+ Carbidopa (100 + 25 mg/kg, p.o)

Once the animal studies are completed, on last day of the experiment, and the animals were sacrificed for histopathological examination of brain.

Cataleptic Behavior (Standard Bar Test) (Goldstein JM et al., 1975)
Catalepsy is defined as a decreased ability to initiate movement and a failure to correct the abnormal gesture. A cataleptic behaviour was measured with a "Standard bar test method". The animals were allowed to adapt to the box for 2 min. The standard (L-dopa + carbidopa) drug and test extracts were administered by oral route, half an hour prior to the haloperidol administration. Catalepsy score was measured for each hour up to 4 h after Haloperidol administration, by gently placing both the forepaws of the mouse over a wooden bar (diameter 1 cm), suspended 4 cm above the table top. The intensity of catalepsy was assessed by counting time in seconds until the mouse brought both forepaws down to the table top, with a maximum cut-off time of 180 s (Kabra MP et al., 2014). Animals would be judged to be cataleptic if they maintained this position for 30 s or more.

Estimation of Behavioural parameters by in vivo models (Hyun CK 2010)
Actophotometer (Locomotor activity)
The locomotor activity can be easily measured by using an actophotometer. It operates on photoelectric cells that were collected in circuit with a counter. When the beam of light falling on the photocell is cutoff by animal, a count is recorded. An actophotometer could have either circular or square arena in which animal moves. The animal was placed individually into a 30 cm × 30 cm black metal chamber with a screen floor and a light‑tight lid. Six beams of red light were focused 2 cm above the floor into photocells on the opposite side. Each beam interruption was registered as an event on the external counter. The effect on locomotor activity was measured for 10 min at every 30 min upto 3 hours using actophotometer. (Jayachandra Reddy P et al., 2012).

Motor coordination
Rota rod apparatus
The rotarod apparatus consists of a motor rod with a drum of 7.0 cm diameter. During the test session, it was adjusted to a speed of 20 revolutions/min. The latency to fall in a test session of 180 s was taken as a measure of motor coordination. All the animals were previously trained to remain on the rod rotating at the speed of 20 rpm for a period of 5 min. On the next day all the groups were treated with respective doses & groups were challenged with haloperidol & levodopa + carbidopa as per the treatment protocol except the normal group & the time required to fall off the rotating rod was noted for each animal.

Statistical Analysis
The statistical analysis is carried out using analysis of variance (ANOVA), followed by dunett's test. P values < 0.05 considered as significant (Jayachandra Reddy P *et al.*, 2012).

Histopathological studies

- One animal of each group was euthanized at the end of experiment.
- Brain is isolated from these animals by opening the cranium carefully.
- The isolated brains were placed in 4 % formalin & sent for histopathological studies.

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

4. RESULTS

Extractive yield of METFG obtained by Soxhlation
% Yield of extract= Amount of extract obtained/ Total amount of powder used X 100
% Yield of extract = 12.3 /200 x 100
% Yield of extract = 6.15 % w/w
Extractive value of METFG was found to be 6.15 % w/w.

The methanol extract of *Trigonella foenum-graecum* was subjected to Phytochemical screening revealed the presence of flavonoids, steroids, terpenoids, tannins and alkaloids in METFG. The results of the tests were depicted in the table no 1.

Table 1: Preliminary phytochemical investigation for methanol extract of Trigonella foenum-graecum

Phytoconstituents	METFG
Test for flavonoids	+ +
Test for terpenoids	+ +
Test for steroids	+ +
Test for alkaloids	+
Test for saponins	–
Test for carbohydrates	–
Test for amino acids and proteins	–
Test for phenols and tannins	+

Note: + indicates present; - indicates absent.

In the standard bar test,the animals treated with haloperidol (1 mg/kg, s.c.) alone for 21 days showed a significant ($P < 0.001$) increase on 21st day when tested at different time intervals. METFG was evaluated for catalytic behavior in mice using bar test on the 21st day. It was observed that there was a significant reduction ($p < 0.01$) in the cataleptic behavior between 60 and 180 min with the low dose of test extract (200 mg/kg body weight) as compared to the positive control and standard groups. METFG at high dose (400 mg/kg body weight *p.o.*) showed a significant reduction in the cataleptic behaviour between 30 to 240 mins when results were compared to standard ($p < 0.01$) and disease control ($p < 0.01$). The values were depicted in the table no 2.

Table 2: Effect of METFG on catalepsy (Standard bar test)

Grps	Cataleptic Score (in secs)					
	30 min	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**
I	16.83 ± 1.64	16.16 ± 1.99	16 ± 1.88	15.33 ± 1.77	16.33 ± 1.23	13.83 ± 1.64
II	164.66 ± 2.19	171.5 ± 1.95	174 ± 2.10**	181.83 ± 1.81*	198.66 ± 1.36*	167.5 ± 1.34*
III	148.33 ± 1.23	143 ± 1.06	136.16 ± 1.25**	125.33 ± 1.36*	124.5 ± 1.34*	144.33 ± 2.23*

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

IV	156.33 ± 1.23	160 ± 1.31	168.33 ± 1.14**	176.66 ± 1.05*	175.16 ± 1.30*	168.66 ± 1.45*
V	139.83 ± 1.42	135.66 ± 1.11	129.33 ± 1.36**	118.16 ± 1.47*	117 ± 1.53*	126.5 ± 1.52*

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** $p < 0.001$), disease control (** $p < 0.001$) and standard (**$p < 0.001$, *$p < 0.05$).

In the Actophotometer,the animals treated with haloperidol (1 mg/kg, s.c.,) alone for 21 days showed a significant ($P < 0.001$) increase in locomotor activity on 21st day when tested at different time intervals. METFG was evaluated for effect on locomotor activity in mice using bar test on the 21st day. It was observed that there was a significant reduction ($p < 0.01$) in the cataleptic behavior between 60 and 180 min with the low dose of test extract (200 mg/kg body weight) as compared to the positive control and standard groups. METFG at high dose (400 mg/kg body weight *p.o.*) showed a significant reduction in the locomotor activity between 30 to 240 min when results were compared to standard ($p < 0.01$) and disease control ($p < 0.01$). The values were depicted in the table no 3.

Table 3 Effect of METFG on locomotor activity

Grps	**Actophotometer (no. of movements/5 min)**					
	30 min	**60 min**	**90 min**	**120 min**	**150 min**	**180 min**
I	312.66 ± 1.14	318.33 ± 1.23	326 ± 1.29	330.16 ± 1.60	332.66 ± 1.23	335 ± 1.18
II	262.16 ± 1.16	258 ± 1.24	246.33 ± 1.16	227.5 ± 1.18	231.66 ± 1.23	235.66 ±1.23
III	285.83 ± 1.07	296.33 ± 1.36**	303.5 ± 1.47**	315 ± 1.31**	312.66 ± 1.36**	310.5 ± 1.61**
VI	292.33 ± 1.36	305.83 ± 1.30**	312.16 ± 1.52**	323.33 ± 1.36**	315.16 ± 1.42**	313 ± 1.24**
V	270.33 ± 1.28	284.5 ± 1.11**	294.66 ± 1.05**	312.83 ± 1.56**	308 ± 1.41**	304.16 ± 1.42**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** $p < 0.001$), disease control (** $p < 0.001$) and standard (**$p < 0.001$).

In the rotarod apparatus, the animals treated with haloperidol (1 mg/kg, s.c.,) alone for 21 days showed a significant ($P < 0.001$) decrease in fall off time on 21st day when tested. It was observed that there was a significant raise ($p < 0.01$) in fall off time with the low and high dose of test extract (200 and 400 mg/kg body weight) as compared to the positive control and standard groups. The values were depicted in the table no 4.

Table 4: Effect of METFG on muscle rigidity (Rota rod test)

Grps	**Fall- off time (in secs)**	
	0th day	**21st day**
I	115.16 ± 1.07	115.83 ± 1.13
II	116.66 ± 1.14	46.83 ± 1.35**
III	117.83 ± 1.07	85.5 ± 1.26**
IV	116.33 ± 1.23	85.16 ± 1.25**
V	114.5 ± 1.26	56.5 ± 1.26**

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** $p < 0.001$), disease control (** $p < 0.001$) and standard ($^{**}p < 0.001$).

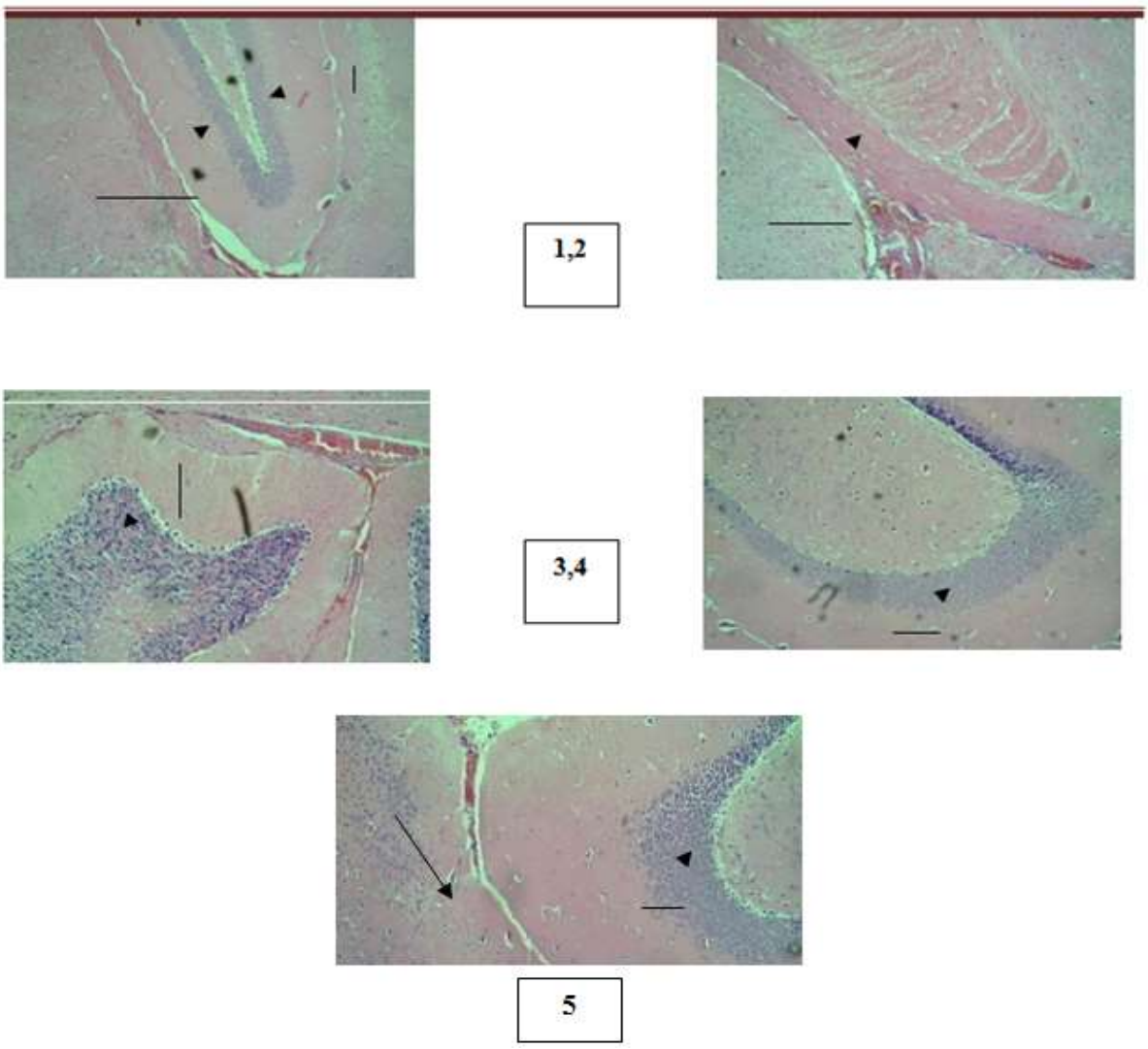

Figure 1 Histopathological studies of mice brain in haloperidol induced catalepsy mode

1) In control, the cerebellum showed the normal neuronal morphology with grey matter content
2) In disease control, the cerebellum showed the severe neuronal damage, with no grey matter content
3) In test extract (200 mg/kg body weight *p.o.*), the cerebellum showed mild neuronal damage with normal grey matter content
4) In test extract (400 mg/kg body weight, *p.o.*), the cerebellum showed moderate neuronal damage with minimal grey matter content
5) In standard, the cerebellum showed no signs of neuronal damage with optimal grey matter content

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

5. DISCUSSION

Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining the normal posture (Dunnett S B and Bjorklund A 1999. Catalepsy is a sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain (Dhanalakshmi S *et al*., 2004). Neuroleptics like haloperidol induced catalepsy in mice were used to evaluate the drugs for their anti-cataleptic activity. In the present study, the METFG was screened for its effect in haloperidol induced catalepsy in mice. The methanolic extract of whole plant *Trigonella foenum-graecum* was confirmed with the presence of phytochemical constituents such as flavonoids, steroids, terpenoids, tannins and alkaloids.

In the present study behavioural parameters were evaluated using standard bar test, actophotometer and rota rod apparatus to assess the haloperidol induced catalepsy in mice. The animals which were treated for 21 days with haloperidol showed severe cataleptic responses along with alleviated locomotor and motor coordination. The group treated with METEG at a dose 400 mg/kg showed normal locomotor activity and motor coordination without any cataleptic behavior when compared with the haloperidol-treated group. The group treated with 200 mg/kg of METEG showed some cataleptic behavior when compared to METEG at a dose of 400 mg/kg treated group. Anti cataleptic activity of METFG might be due to the action on dopaminergic transmission, and on D2 receptors and therefore increases the dopamine levels (Jayachandra Reddy P *et al*., 2012).

The previous evidences have shown beneficial effects of flavonoids on neurodegeneration in particular. Flavonoids could protect the brain by their ability to modulate intracellular signals promoting cellular survival. Alkaloids may act on the CNS, including nerve cells of the brain and spinal cord which control many direct body functions and the behavior, and may interfere or compete with the action of serotonin in the brain. One of the possible reasons for the anti-cataleptic effect could be because of the presence of flavonoids, steroids, terpenoids, tannins and alkaloids in METFG (Jayachandra Reddy P *et al*., 2012).

The histopathological results of METFG (200 mg/kg bd.wt., *p.o.*) showed mild neuronal damage with normal grey matter content in the cerebellum when compared with METFG (400 mg/kg bd.wt., *p.o*) in haloperidol induced catalepsy model, so METFG showed anti-cataleptic activity.

6. CONCLUSION

In conclusion, keeping in view of the above facts, METFG was found to be effective in reducing cataleptic scores in mice model of haloperidol induced catalepsy. Our study suggests that the test drug can be used as an alternative agent in preventing the haloperidol/neuroleptics induced extrapyramidal symptoms in parkinsonian patients. However, further investigations are required at molecular level, and also characterization of active constituents responsible for protective effect.

Conflicts of interest

The authors have no conflicts of interest with anyone.

REFERENCES

[1] Anuradha CV, Ravikumar P. (2001). Restoration on tissue antioxidants by fenugreek seeds (Trigonella foenum graecum) in alloxan-diabetic rats. Indian J Physiol Pharmacol 45:408–20.
[2] Beal MF. Experimental models of Parkinson's disease. Nat Rev Neurosci 2001; 2:325–534.
[3] Chanchal Raj N, Balasubramaniam A, Sayyed Nadeem. Effect of various extracts of *Tabernaemontanadivaricata* on haloperidol induced catalepsy in rats, *International Current Pharmaceutical Journal*, 3(3) ; 2014: 240-242.
[4] Datla KP, Zbarsky V, Rai D, Parkar S, Osakabe N, Aruoma OI. Short‐term supplementation with plant extracts rich in flavonoids protect nigrostriatal dopaminergic neurons in a rat model of Parkinson's disease. J Am Coll Nutr 2007;26:341‐9.
[5] Dhanalakshmi S, Khaserao SS, and Kasture SB. Effect of ethanolic extract of some anti asthmatic herbs on clonidine and haloperidol-induced catalepsy in mice, Orient Pharm Exp Med, 2004; 4(2):95-99.

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

[6] Dobryakova YV, Dubynin VA, Luijtelaar G V. The effect of haloperidol on maternal behavior in WAG/Rij rats and its consequences in the offspring, Acta Neurobiol Exp (Wars), 2011;71:339‑47.
[7] Dunnett SB, Bjorklund A. Prospects for new restorative and neuroprotective treatments in Parkinson's disease. Nature 1999; 399:A32–9.
[8] Goldstein JM, Barnet A, Malick JB. The evaluation of antiparkinsonian drugs on reserpine induced rigidity in rats. Eur J Pharmacol 1975;33:183‑8.
[9] Goyal M, Nagori B, Pareek A and Sasmal D. Trigonellafoenum-graecum: A review on phytochemistry and pharmacological aspects, Pharmacognosy Reviews, 2011; 5(10):195-198.
[10] Humphrey PR, Maureen MD. Rang and Dale's Pharmacology. USA: Elsevier Health; 2012.
[11] Hyun CK. Neuroprotective effect of herbal ethanol extracts from Gynostemma pentaphyllum in the 6 hydroxydopamine lesioned rat model of Parkinsonism disease. Molecules 2010;15:2814‑24.
[12] Jayachandra Reddy P, Prabhakaran V, Umasankar K, and SekarBabu M. AntiCataleptic activity of ethanol extract of *vernoniacinerea* L, Asian Journal of Pharmaceutical Science & Technology, 2012; 2(1):23-29.
[13] Khandelwal K R. Practical Pharmacognosy Techniques and Experiments. Pune: Nirali Prakashan; 2007.
[14] Nagarjuna S, Arifullah M, Sanjeeva Kumar A, Srinath B, Somasekhar Reddy K, Padmanabha Reddy. Evaluation of antioxidant and anti-parkisonian activities of Brassica oleracea in haloperidol – induced tardive dyskinesia. Intl J of Green Pharmacy, 2015; 9: 143-9.
[15] Organization for Economic Cooperation and Development. OECD Guidelines for Testing of Chemicals. Guideline 423, Acute Oral Toxicity‑Acute Toxic Class Method. Adopted March 22, 1996.