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NEUROBEHAVIOURAL AND ANALGESIC EFFECT OF OCIMUM GRATISSIMUM LINN. LEAVES ESSENTIAL OIL IN WISTAR ALBINO MICE

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Studies have shown that pain relieving medications may be neuroprotective. *Ocimum gratissimum* Linn. that is widely used in traditional medicine for debility and many other illnesses neuropharmacologically related has not been fully explored.

Aim. This study was designed to investigate the safety of intake, neurobehavioral and analgesic effects of the Essential Oil of *Ocimum gratissimum* Linn leaves (EOOG) in mice.

Methods. Acute toxicity of EOOG was determined following standard method while the neurobehavioural properties were assessed using the open field for Novelty-Induced Rearing (NIR), Novelty-Induced Grooming (NIG) and locomotor activity in mice. The hole board apparatus was used for the frequency of head dips. The Y-maze was used for short- working memory. Mechanistic studies were conducted with Atropine (muscarinic blocker, 0.5 mg/kg), Propanolol (non-selective β-adrenoceptor blocker, 0.2 mg/kg), Haloperidol (dopamine receptor blocker, 0.2 mg/kg), Cyproheptadine (Serotoninergic antagonist, 0.5 mg/kg) and Yohimbine (α-$_2$ adrenergic blocker, 1 mg/kg). The analgesic activity of *Ocimum gratissimum* was investigated using acetic acid writhing test and thermally-induced pain.

Results. The median lethal dose (LD_{50}) of *Ocimum gratissimum* was 2449 mg/kg. The EOOG significantly reduced novelty-induced behaviour in a dose-dependent manner. The exploratory activity of animals treated with the EOOG was observed to decrease non-dose dependently with the highest dose (40 mg/kg) showing no activity on the hole board apparatus. The EOOG produced a significant reduction in locomotor activity in all the doses in a non-dose dependent manner but at the lowest dose. In the Y-maze, EOOG did not produce any significant effect on working memory as the percentage alternation produced was not significantly different from the control. The EOOG in hot plate analgesic assay showed increased reaction time suggesting central nervous system analgesic property.

Conclusions. The results of the investigation showed that EOOG might possess sedative properties due to its ability to inhibit NIR and NIG, head dips, and locomotor activity. Furthermore, the inhibition of nociception marked in this research advocates antinociceptive activity which might be through the peripheral or central opioid receptor.

Key words: Ocimum gratissimum; neuroprotective; pain; sedative; medicinal plants.

Central Nervous System (CNS) diseases are complex, with multiple symptoms, like the negative symptoms of Schizophrenia, which tend to be resistant to treatment. Furthermore, the complexity of the brain and its neuronal pathways result in a significant risk of side effects, even when the most-biochemically selective agent is administered. The lack of disease-modifying treatments for CNS diseases represents a very significant unmet medical need, and of a high priority. These failures of synthetic drugs and their side effects have necessitated looking into ancient healing methods for alternatives [1].

Pain causes a lot of suffering and discomfort to the victims, lowering the quality

of life and therefore needs to be carefully managed. To suppress pain, non-steroidal anti-inflammatory drugs (NSAIDs) are mostly prescribed [2, 3]. For severe or chronic malignant pain, opioid analgesics are drugs of choice [4]. However, due to adverse side effects like gastric lesions, caused by NSAIDs and tolerance and dependence induced by opiates, the use of these drugs as analgesic agents have not been successful in all cases. Therefore, analgesic drugs lacking those effects are being searched all over the world as alternatives to NSAIDs and opiates.

Many of the thousands of plant species growing throughout the world have a direct pharmacological action on the body [5], and many native African plants are rich in medicinal properties that are well documented in folkloric medicine as a potential source for novel compounds with beneficial therapeutic effects and fewer side effects being natural products. However, we must not assume that since a plant has been used for thousands of years, it is therefore safe and truly effective for its claimed indications, thus, they must be scientifically investigated [6]. *Ocimum gratissimum* Linn. is a native African plant widely used in traditional medicine for health and healings. Pre-clinical studies of brain injuries in experimental rodent animal models have shown neurobehavioral and neurodegenerative abnormalities [7]. Currently, there are only a few literature available for neuropharmacological profile of *Ocimum gratissimum* leaf. Thus, this study aimed to evaluate the safety of consumption, neurobehavioral and analgesic effect of essential oil of *Ocimum gratissimum* leaf (EOOG) in mice.

Material and Methods

Toxicity Assay

The method described by OECD (2002) was used to determine the LD_{50}, which is the index of acute toxicity. Male Swiss Albino mice (20–25 g) were used. This method involved an initial dose-finding procedure, in which the animals were divided into three groups of five animals. Doses of 10, 100, and 1000 mg/kg were administered intra-peritoneally (*i.p.*) for each mouse per group. The treated animals were monitored for 24 hours for mortality and general behaviour. Likewise, four different doses of (500, 1000, 2000, and 3000 mg/kg) were chosen and administered intra-peritoneally respectively to four groups of one mouse per group. The treated animals were monitored for 24 hours. The LD_{50} was then calculated as the geometric mean of the highest dose showing no death and the lowest dose showing death.

Novelty-induced rearing (NIR) and grooming (NIG) in mice

The behavioural parameters employed in this observational analysis were rearing and grooming [8, 9]. The frequency of rearing and grooming episode was quantified using a manual counter and a stopwatch. The total frequency was summed up for each animal for 30 minutes of observation time. Rearing was taken as the number of times the mouse stood on its hind limbs or with its forelimbs against the wall of the observation cage or in the free air. Grooming was taken as the number of body cleaning with paws, picking of the body, and pubis with mouth and face washing actions.

Exploratory behaviour on hole-board apparatus

The effect of the EOOG on the frequency of head dipping was determined in the hole-board with 16 equidistant holes in the floor through which the animal can poke its head. The test is a measure of exploratory behavior that reveals the sedative activity of agents. Thirty animals were divided into six groups (n = 5). Group 1 was given distilled water (10 mL/kg, i.p), while group 2–5 received EOOG (5, 10, 20, and 40 mg/kg, i.p.) respectively and group 6 received Diazepam (2 mg/kg). The animals were placed on top of the wooden board 30 minutes after treatment administration. The number of times that each animal dipped its head into the holes was counted for 5 min [10].

Locomotor activity in the open field

Motor activity was measured in an open field apparatus consisting of a white Plexiglas box (28 × 28 × 25 cm) with a painted black grid dividing the floor into 16 (7×7 cm) equal squares. The animals were divided into six groups (n = 5). Group 1 was given the vehicle (10 mL/kg distilled water), while group 2–5 received EOOG (5, 10, 20, and 40 mg/kg, i.p), respectively and group 6 received Diazepam (2 mg/kg). Thirty minutes after a single intraperitoneal (i.p.) injection of EOOG or standard drug, the animals were placed singly in the center of the box; the number of squares crossed with all four paws was counted for 5 min. The cage was cleaned with 70% ethanol at a 5-minute interval when the animal was removed [11].

Y-maze test

The animals were divided into six groups (n = 5). Group 1 was given distilled water (10 mL/kg, *i.p*), group 2 - 5 received EOOG (5, 10, 20, and 40 mg/kg, *i.p*) respectively, and group 6 received diazepam (2 mg/kg), all administered 30 minutes before the observation. Each mouse was placed in one of the arm compartments usually arm A for consistency and was allowed to move freely through the maze, and the series of arm entries were recorded for 5 min. An arm entry is defined as the body of a mouse (except for its tail) completely entering into an arm compartment and the sequence of arm entries is manually recorded. An alternation is defined as an entry into all three arms on consecutive devices. The alternation behavior was defined by the successful entry into the three arms, an overlapping triplet sets, and such behaviour (in percentage) was expressed as the ratio of actual alternations to possible alternation (defined as the total number of arm entries minus two) multiplied by 100. Seventy percent (70%) ethanol was used to clean the Y-maze at intervals [12].

Mechanistic Studies

Mice were pre-treated (intraperitoneally) with neurotransmitter blockers 15 min before administration of EOOG (10 mg/kg i.p) to evaluate the possible mode of actions of the extracts on novelty-induced rearing behaviours in mice. The following transmitter receptor blockers were used: Atropine (muscarinic blocker, 0.5 mg/kg), Propanolol (non-selective β-adrenoceptor blocker, 0.2 mg/kg), Haloperidol (dopamine receptor blocker, 0.2 mg/kg), Cyproheptadine (Serotoninergic antagonist, 0.5 mg/kg) and Yohimbine (α_2 -adrenergic blocker, 1 mg/kg) [30]

Acetic Acid-Induced Writhing Test

The method described by [14] was employed. Acetic acid (0.7%) was injected intra-peritoneally and the animal was observed for a specific contraction of the body referred to as writhing. A comparison of writhing was made between positive control (Diclofenac), control, and test sample, given orally 30 minutes before acetic acid injection. Each experimental group consisted of five mice. The animals were divided into five groups, Group 1 received distilled water (10 mL/kg, i.p), Group 2–4 received EOOG (2.5, 5, and 10 mg/kg, *i.p*) respectively while group 5 received Diclofenac (2 mg/kg).

Hot Plate Latency Assay

The method described by [15] as modified by [16] was used for this study. Animals were divided into five experimental groups consisting of five mice each: control (10 mL/kg distilled water, *i.p.*), EOOG (2.5, 5, and 10 mg/kg, *i.p.*), and pethidine (10 mg kg, *i.p.*). Animals were fasted for 12 hours with adequate clean water provided *ad libitum*. Each of the mice was placed on a hot plate maintained at the temperature of 55 ± 1 °C and the Pain Reaction Time (PRT) or latency period determined with a stopwatch was recorded which represents the time taken for the mice to react to the pain stimulus. The response to pain stimulus considered included; jumping, raising, and licking of the hind foot. The cut off time was fixed for 20 s.

Results and Discussion

The Essential Oil of *Ocimum graissimum* (EOOG) leaves did not produce any sign of toxicity until the intra-peritoneal dose of 3000 mg/kg. The median lethal dose (LD_{50}) of EOOG in mice was found to be 2449 mg/kg (*i.p.*) body weight. The administration of EOOG (5–40 mg/kg, *i.p.*) reduced novelty induced rearing in mice. A significant [$F(5, 24) = 4.85$, $P < 0.001$] reduction in the frequency of rearing episodes was observed at doses 5 mg/kg and 10 mg/kg when compared to the vehicle (Fig. 1). However, EOOG doses showed significant differences ($P < 0.05$) in the depression of novelty induced rearing, compared to the reference drug (Diazepam, 2 mg/kg).

The administration of EOOG (5–40 mg/kg, *i.p.*) reduced novelty induced rearing in mice. A significant [$F(5, 24) = 4.051$, $P < 0.001$] reduction in the frequency of grooming episodes was observed at doses 5 mg/kg and 10 mg/kg when compared to the vehicle (Fig. 2). Also the studied plant (5–40 mg/kg, *i.p.*) showed a significant reduction [$F(5, 24) = 137.7$, $P < 0.001$] in the locomotor activity of mice at all doses when compared to vehicle (Fig. 3). The EOOG (5–40 mg/kg, i.p.) reduced significantly [$F(5, 24) = 5.71$, $P < 0.001$] entrance of mice in Y-maze which is an indication of a reduction in locomotor activity when compared to control.

The extract shows no percentage alteration at lower doses (5–20 mg/kg, *i.p.*) when compared to the control, hence, has no impairment effect on learning and memory (Fig.4). A significant [$F(5, 24) = 26.50$, $P < 0.001$] reduction in head dips was observed at

lower doses, however, a U-shaped pattern was observed with dose (10 mg/kg, *i.p.*) showing the highest significant reduction in head dips when compared to vehicle (Fig. 5). Pre-treatment with Propranolol, Yohimbine, and Cyproheptadine reversed the inhibitory effect of EOOG on novelty-induced rearing (Table 1). One-way analysis of variance (ANOVA) showed a significant difference [F (7, 34) = 115.0, $P < 0.0001$ (NIR)] and [F (6, 28) =133.5, $P < 0.0001$(NIG)] between EOOG + Antagonists and EOOG alone.

The antagonists alone showed significant ($P < 0.001$) difference in NIR and NIG as compared to EOOG (10 mg/kg), but when administered with EOOG (10 mg/kg after 15 minutes), only Propranolol showed significant ($P < 0.001$) increase in NIR, indicating a reversal of EOOG activity. Pre-treatment with Cyproheptadine and Yohimbine showed no significant effect on the activity of EOOG, but pre-treatment with Atropine and Haloperidol showed significant ($P < 0.001$) further depression activity. As revealed in Table 2, the vehicle-treated animals administered acetic acid showed marked writhing; however, the administration of EOOG 2.5–10 mg/kg significantly antagonized this symptom. At the same time, Diclofenac antagonized these effects.

The result revealed marked writhing count with vehicle-treated animals administered acetic acid; however, the administration of EOOG 2.5–10 mg/kg significantly antagonized the symptoms. As shown in Table 3, the administration of EOOG 2.5–10 mg/kg significantly [F (5, 24) = 12.85, $P < 0.0001$ (NIR)] protect against thermal stimulus compared to vehicle-treated animals. Pethidine also exhibited similar activity.

This work was undertaken to study the neurobehavioural and analgesic effect of essential oil of *Ocimum gratissimum* Linn. leaf in Swiss mice. Some of the neurobehaviour explored in this work are novelty-induced rearing, and grooming, locomotor activity in the open field, percentage correct alternations in the Y-maze, and head dips in the hole board. Mechanistic studies were also carried out to ascertain the pathway through which these effects are been elicited. Afterward, analgesic studies were carried out using the thermal hot plate, and acetic acid methods.

The acute toxicity of EOOG was established by the determination of LD_{50}. The LD_{50} is the dose required to cause mortality in half the members of the tested population of the experimental animals. The higher the value of the LD_{50} is for an extract, the relatively safe the extract is assumed to be. The median lethal dose (LD_{50}) of EOOG in mice was found to be 2449 mg/kg (i.p., body weight).

A compound is considered to have CNS activity if it crosses the blood-brain barrier and modulates the neurotransmitters in the CNS,

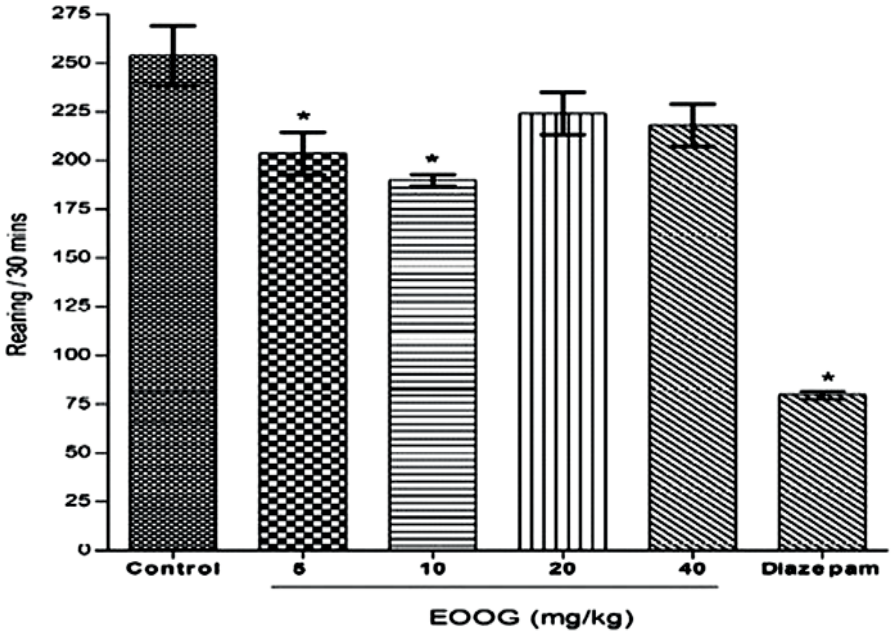

Fig. 1. **Effect of EOOG (Essential oil of *Ocimum gratissimum* Leaves) on Novelty-induced rearing behaviour in Swiss mice (*$P < 0.05$)**

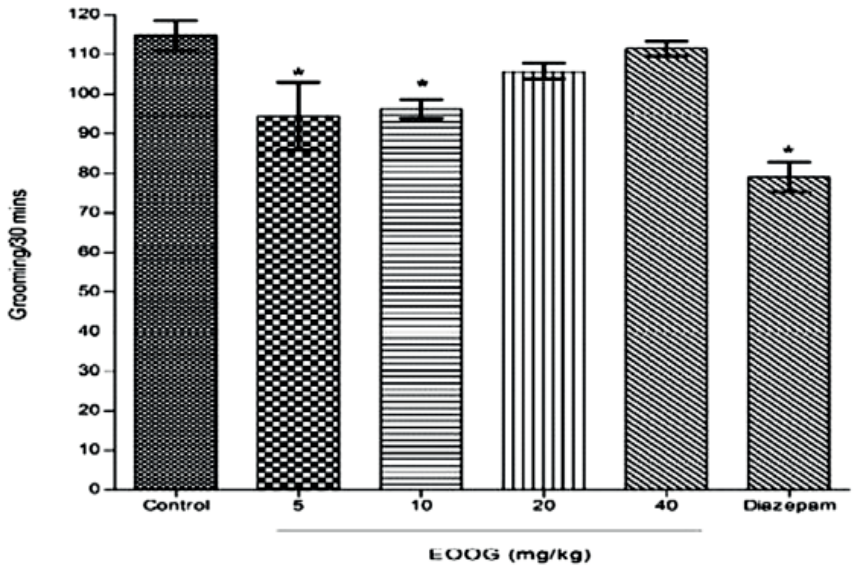

Fig. 2. **Effect of EOOG (Essential oil of *Ocimum gratissimum* Leaves) on Novelty-induced grooming behaviour in Swiss mice (*$P < 0.05$)**

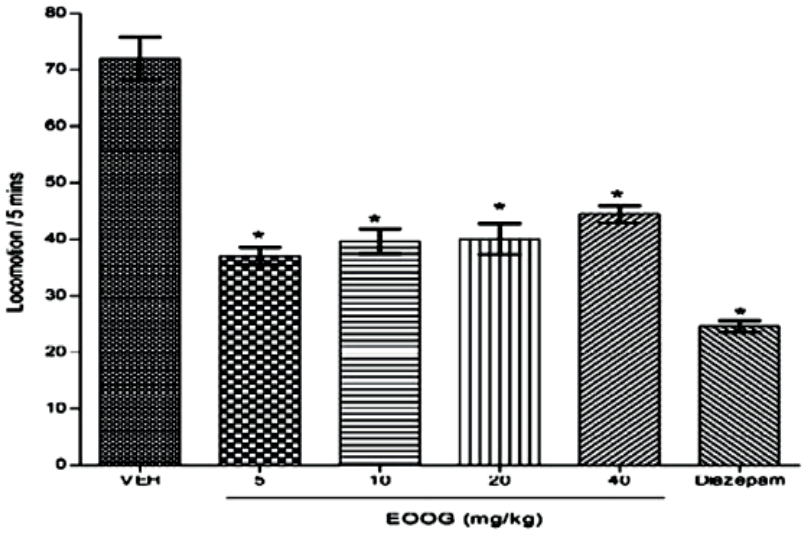

Fig 3. **Effect of EOOG (Essential oil of Ocimum gratissimum Leaves) on locomotor activity in the open field in Swiss mice (*$P < 0.001$)**

which eventually causes changes in behavioural expressions in the mice. Neurobehavioural effects of *Ocimum gratissimum* on Novelty-Induced Behaviours (NIB) (rearing, grooming, and locomotor activity) in mice were observed. Rearing is a vertical locomotor activity that involves an animal standing on its hind limbs while raising its forearms in the air or placed on the wall of the cage [8]. It is an indication of explorative behaviour which measures central nervous system excitation [16]. This behaviour has been used to classify test drugs/substances as sedatives or stimulants [17]. The results obtained showed that (EOOG) in 5 and 10 mg/kg inhibited/attenuated the novelty-induced rearing (NIR) behavior in a statistically significant manner comparable to the standard drug diazepam dose-dependently. The ability of an extract to inhibit rearing suggests its sedative effect. This is in agreement with [12],

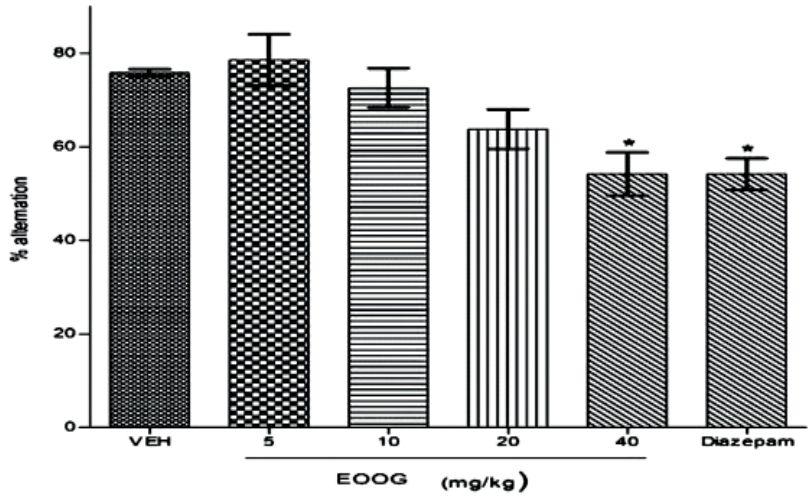

Fig. 4. **Effect of EOOG (Essential oil of *Ocimum gratissimum* Leaves) on learning and memory in the Y-maze in Swiss mice (*$P < 0.05$)**

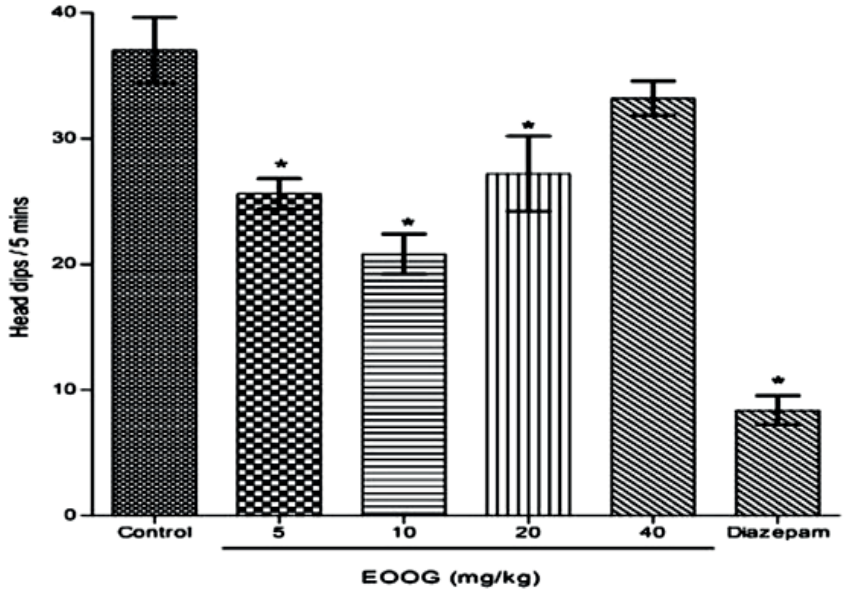

Fig. 5. **Effect of EOOG (Essential oil of *Ocimum gratissimum* leaves) on the frequency of head dips in Swiss mice (*$P < 0.05$)**

which reported that CNS stimulants increased rearing while [18], submitted that CNS depressants inhibited this behaviour.

Grooming is a "maintenance" behaviour that is specifically elicited in a situation in which an animal is in stress-induced frustration [10]. It is described as a face or head-important behavioural component in animals, and that plays a deactivating role in restoring homeostasis under stressful situation [19]. The inhibitory effect of an extract on Novelty-Induced Grooming (NIG) suggests its stress-attenuating role in a novel environment. The EOOG at 5 and 10 mg/kg also inhibited novelty-induced grooming behaviour significantly in a dose-dependent manner. At the highest doses (20 and 40 mg/kg), EOOG did not demonstrate any inhibitory activity of the extract compared to the standard drug, Diazepam. This inhibitory effect observed in both Novelty-Induced Rearing (NIR) and Novelty-Induced Grooming (NIG) behaviours suggest the EOOG possess a sedative or central nervous system depression activity at 5 and 10 mg/kg. This is in agreement with some plants that have shown to possess strong

Table 1. **Effects of Antagonists on Novelty-induced rearing and Novelty-induced grooming in Swiss mice**

Treatment group	Rearing (NIR)	Grooming (NIG)
VEH (10ml/kg)	225.80 ± 5.74	114.80 ± 3.72
EOOG (10 mg/kg)	189.80 ± 2.81	96.20 ± 2.39
Haloperidol (0.2 mg/kg)	107.06 ± 11.64	46.00 ± 0.70
Haloperidol (0.2 mg/kg) + EOOG	13.00 ± 3.08#	23.80 ± 1.35#
Cyproheptadine (0.5 mg/kg)	103.00 ± 3.97	17.20 ± 1.36
Cyproheptadine (0.5 mg/kg) + EOOG	171.20 ± 10.07	30.20 ± 2.05
Yohimbine (1 mg/kg)	127.20 ± 14.39	38.20 ± 7.94
Yohimbine (1 mg/kg) + EOOG	153.20 ± 8.68	71.60 ± 1.96
Propranolol (0.2 mg/kg)	96.00 ± 4.03	42.60 ± 5.41
Propranolol (0.2 mg/kg) + EOOG	222.00 ± 9.00**	59.20 ± 6.33
Atropine (0.5 mg/kg)	128.80 ± 8.42	40.60 ± 2.56
Atropine (0.5mg/kg) + EOOG	77.20 ± 8.20#	70.00 ± 2.30

$^{\#}P < 0.001$ (significant further depression), $^{**}P < 0.001$ (significant reversal) between EOOG + Antagonists and EOOG alone

Key: VEH= Vehicle; EOOG = Essential Oil of *Ocimum gratissimum*

Table 2. **Effect of Essential Oil of *Ocimum gratissimum* on Acetic Acid-induced Writhing in Swiss mice**

Treatment ($n = 5$)	Dose (mg/kg)	Writhing Counts (per 30 min)	% inhibition
Control	10 mL/Kg	42.67 ± 7.49	-
Diclofenac sodium	2 mg/kg	15.00 ± 2.91*	64.84
EOOG	2.5 mg/kg	21.67 ± 3.19*	49.21
	5.0 mg/kg	18.50 ± 1.69*	56.64
	10.0 mg/kg	16.67 ± 1.26*	60.93

$^{*}P < 0.001$ as compared to vehicle control is significant.

Key: EOOG = Essential Oil of *Ocimum gratissimum*

sedative effects such as *Cissus quadrangularis, Spondias mombin, Ficus thoningii, Stachys lavandulifolia, Nigella sativa*, and *Cryptolepsis sanguinolenta* [20–25].

The exploratory activity test is a measure of exploratory behaviour in rodents [26, 27] and has been employed to screen sedative agents. 26 reported that reduction in the frequency of head dips depicts CNS depression. The method has been used also to measure anxiety and test anxiolytic agents. The exploratory test carried out in this study is based on assumption that the head-dipping of animals is inversely proportional to their anxiety state in a moderately aversive environment. Therefore, an increased number of head dips on the hole board means reduced anxiety state [28]. In more aversive situations, when the anxiety level of the animals is high, the holes may represent a possible way to escape from the aversive environment instead of an explorable object. The exploratory activity of animals treated with the EOOG was observed to decrease non-dose dependently with the highest dose (40 mg/kg) showing no activity on the hole board apparatus. In a moderate condition, anxiolytics increase the frequency of head poking, while sedative agents decrease the frequency of head poking. Since a decrease in the frequency of head dips in the hole board

Table 3. **Effect of Essential Oil of *Ocimum gratissimum* on Thermally-induced Pain in mice**

Treatment (n =5)	Dose (mg/kg)	Mean Latency of Response	% Protection against thermal stimulus
Control	10 mL/Kg	4.54 ± 0.34	–
EOOG	2.5 mg/kg	6.00 ± 0.05*	32.21
	5.0 mg/kg	6.04 ± 0.21*	33.00
	10.0 mg/kg	6.34 ± 0.22*	39.60
Pethidine	10.0 mg/kg	21.74 ± 0.56*	379.10

*$P < 0.001$ as compared to Vehicle treated mice.

by the EOOG was observed in all (but not 40 mg/kg) the doses used for this experiment, it is therefore suggested that EOOG has sedative properties; in accordance with (29).

Spontaneous motor activity is a parameter used to measure central nervous system excitability in animals. However, this behaviour (motor activity) has been shown to be mainly governed by motor area of frontal cortex, corpus striatum and brainstem. Any morphological changes or change in the level of brain amines in these areas is expected to cause neurotoxicity which may be in the form of motor deficit. Dopamine is one of the main amines found in the substantial nigra, ventral tegmental area, and hypothalamus of the brain, and has been implicated in the locomotor and exploratory activity. Drugs that enhance dopaminergic transmission produce increased locomotor activity (10), and are said to be stimulants, while agents that reduce dopaminergic transmission suppress locomotor activity. The EOOG produced a significant reduction in locomotor activity in all the doses in a non-dose dependent manner, but at the lowest dose, the reduction was more significant. This decrease in locomotor activity marked in the entire doses buttresses the fact that EOOG may be an index of the central nervous system depressant effect.

Spontaneous alternation is a behavioural test for measuring the willingness of rodents to explore new environments. Rodents typically prefer to explore a new arm of the Y-maze rather than returning to one that was previously visited. The EOOG at the three lower doses used for this experiment has no effect on working memory as the percentage alternation produced was not significantly different from the control. Conversely, at the highest dose (40 mg/kg), a statistically significant reduction in percentage correct alternation was marked, advocating the point that EOOG may have a memory impairing effect as the dose is increased.

In this study, the neural mechanism of action of the extract was investigated by interacting EOOG with the antagonists of the systems that regulate neurobehaviours in rodents. The administration (intraperitoneally, 15 minutes prior) of atropine and haloperidol did not reverse the inhibitory effect of the extract on rearing and grooming, rather propanolol, potentiated the effect of the EOOG, thus excluding involvement of cholinergic, dopaminergic, and α-adrenergic systems. In another experiment, pre-treatment with β-adrenergic and serotonergic antagonists reversed the inhibitory effect of the extract on the observed parameters. This shows that the EOOG may contain a compound(s) that has an affinity for β-adrenergic and serotonergic receptors, thus suggesting the participation of β-noradrenergic and serotonergic systems in the inhibitory effect of the EOOG on novelty-induced behaviours.

The thermally-induced pain (hot plate) test responses are believed to be spinally and supra-spinally mediated reflex and are to assess centrally acting analgesics. The effectiveness of analgesics agents in the hot plate pain model is highly correlated with the relief of human pains (30). In this investigation, EOOG significantly increased reaction time to pain stimuli at all the doses in the 30^{th} minute compared to the normal control, similar to pethidine. These results are indicative that thermal stimulation is associated with central neurotransmission. The result further confirms the central analgesic effect of EOOG since the test is predominantly spinal reflex mediated and is considered to be selective for opioids like and centrally acting analgesics. Janssen et al. [31] and [32] submitted that peripheral analgesics are known to be inactive on thermal stimuli,

and the receptors are mostly implicated in central mediation of anti-nociceptive response are the opioid receptors.

In the acetic acid-induced abdominal constriction test, EOOG dose-dependently and significantly reduced the abdominal writhing level, which was comparable with the standard drug diclofenac sodium at 2 mg/ kg in this investigation. Inhibition of abdominal constrictions by EOOG is thus suggestive of its anti-nociceptive action, which may be due to inhibitory action against the synthesis and release of inflammatory mediators. Although this test of nociception has been successfully employed to screen peripheral acting analgesics, centrally acting analgesics (such as opioid agonists without peripheral action) have effectively attenuated nociception in this model. This phenomenon is attributed to a lack of specifics between peripheral and central pain effects [33]. Hence, the need for a model that can discriminate pains in the peripheral components from pains in the central components.

Conclusion

The acute toxicity test showed that the essential oil of *Ocimum gratissimum* leaves could be utilized as documented in traditional use. The inhibitory effects demonstrated on neurobehavioural parameters suggest that essential oil possesses a sedative or central nervous system depressant activity. The mechanistic study indicates that the β-adrenoceptors and serotonergic systems may be responsible for the inhibitory effects observed.

The essential oil of *Ocimum gratissimum* produced a significant reduction in locomotor activity in all the doses in a non-dose dependent manner but at the lowest dose. In the Y-maze, oil did not produce any significant effect on working memory as the percentage alternation produced was not significantly different from the control. The oil in hot plate analgesic assay showed increased reaction time suggesting central nervous system analgesic property. In conclusion, the results of the investigation showed that essential oil of *Ocimum gratissimum* might possess sedative properties due to its ability to inhibit NIR and NIG, head dips, and locomotor activity. Furthermore, the inhibition of nociception marked in this research advocates antinociceptive activity which might be through the peripheral or central opioid receptor.

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НЕЙРОПОВЕДІНКОВИЙ І ЗНЕБОЛЮЮЧИЙ ЕФЕКТ *Ocimum gratissimum* Linn. ЕФІРНА ОЛІЯ ЛИСТЯ У МИШЕЙ Wistar albino

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Дослідження показали, що знеболюючі препарати можуть бути нейропротекторними. *Ocimum gratissimum* Linn. який широко використовується в традиційній медицині для лікування слабкості та багатьох інших нейрофармакологічно пов'язаних захворювань, до кінця не вивчений.

Мета. Це дослідження було розроблено з метою вивчення безпечності споживання, нейроповедінкових і знеболювальних ефектів ефірної олії листя *Ocimum gratissimum* Linn (EOOG) у мишей.

Методи. Гостру токсичність EOOG визначали за стандартним методом, тоді як нейроповедінкові властивості оцінювали за допомогою відкритого поля для виховання, викликаного новизною (NIR), догляду, викликаного новизною (NIG) і рухової активності мишей. Для визначення частоти падіння голови використовувався апарат hole board. Y-подібний лабіринт використовувався для короткочасної пам'яті. Механічні дослідження проводили з атропіном (мускариновий блокатор, 0,5 мг/кг), пропанололом (неселективний блокатор β-адренорецепторів, 0,2 мг/кг), галоперидолом (блокатор дофамінових рецепторів, 0,2 мг/кг), ципрогептадином (серотонінергічний антагоніст, 0,5 мг/кг). і йохімбін (α-2-адреноблокатор, 1 мг/кг). Анальгетичну активність *Ocimum gratissimum* досліджували за допомогою тесту на звивання з оцтовою кислотою та термічного болю.

Результати. Середня летальна доза (LD_{50}) *Ocimum gratissimum* становила 2449 мг/кг. EOOG значно зменшив поведінку, спричинену новизною, залежно від дози. Спостерігалося, що дослідницька активність тварин, які отримували EOOG, зменшувалася незалежно від дози, причому найвища доза (40 мг/кг) не виявляла активності на апараті з отворами. EOOG викликав значне зниження рухової активності у всіх дозах незалежно від дози, але при найнижчій дозі. У Y-лабіринті EOOG не справляв жодного суттєвого впливу на робочу пам'ять, оскільки вироблена зміна у відсотках істотно не відрізнялася від контролю. EOOG в анальгетичному аналізі на гарячій пластині показав збільшення часу реакції, що свідчить про аналгетичну властивість центральної нервової системи.

Висновки. Результати дослідження показали, що EOOG може мати седативні властивості завдяки своїй здатності пригнічувати NIR та NIG, падіння голови та рухову активність. Крім того, інгібування ноцицепції, відзначене в цьому дослідженні, свідчить про антиноцицептивну активність, яка може здійснюватися через периферичний або центральний опіоїдний рецептор.

Ключові слова: *Ocimum gratissimum*; нейропротектор; болезаспокійливий; лікарські рослини.