INTERNATIONAL JOURNAL OF SCIENTIFIC INFORMATION

Review | ISSN: 2583-8512

Acute Oral Toxicity and Anxiolytic-Like Activity of a Hydroethanolic Leaf Extract of *Apium graveolens* L. in the Light-Dark Box and Elevated Plus Maze

Purnima Tiwari[1], Sushila Kaura[2]

[1]PhD Research Scholar, Department of Pharmaceutical Sciences, Jayoti Vidyapeeth Women's University, Jaipur, Rajasthan, India

[2]Associate Professor, Department of Pharmaceutical Sciences, Jayoti Vidyapeeth Women's University, Jaipur, Rajasthan, India

Email: purnimapharmacy23@gmail.com

sushilakaura@gmail.com

Abstract

The present study evaluated the preliminary acute oral safety and anxiolytic-like activity of a hydroethanolic leaf extract of *Apium graveolens* L. in Swiss albino mice. The leaf extract was prepared with 70% ethanol and first assessed using an Organisation for Economic Co-operation and Development Guideline 423 limit-dose approach. A single oral dose of 2000 mg/kg produced no mortality or severe toxic manifestations during a 14-day observation period. Behaviour, grooming, movement, food and water intake, body weight and general appearance remained normal; tremors, convulsions and marked sedation were absent. Based on these findings, 200 and 400 mg/kg were selected as low and high pharmacological doses. Anxiolytic-like activity was assessed in the light-dark box and elevated plus maze, with vehicle as control and diazepam 2 mg/kg as standard. In the light-dark box, the extract significantly and dose-dependently increased time in the light chamber from 62.33 +/- 4.21 s in controls to 101.50 +/- 4.87 s at 200 mg/kg and 130.67 +/- 5.10 s at 400 mg/kg, while increasing light-chamber entries without marked locomotor suppression. In the elevated plus maze, open-arm time increased from 31.50 +/- 3.26 s in controls to 63.50 +/- 3.78 s and 91.83 +/- 4.12 s at 200 and 400 mg/kg, respectively; open-arm entries also increased significantly. Diazepam produced the greatest effect in both models. The consistent dose-related improvement across two validated paradigms indicates anxiolytic-like activity rather than nonspecific motor impairment. Flavonoids and phenolic compounds detected in the extract may contribute through GABAergic, antioxidant and anti-inflammatory pathways. The findings support further chemical standardization, mechanistic investigation and repeated-dose safety assessment.

KeywordsApium graveolens; acute oral toxicity; anxiolytic-like activity; light-dark box; elevated plus maze; diazepam; Swiss albino mice

Address for Correspondence
Purnima Tiwari
PhD Research Scholar
Department of Pharmaceutical Sciences
Jayoti Vidyapeeth Women's University (JVWU), Jaipur, India
purnimapharmacy23@gmail.com

Article Received on: 12.04.26

Revised on: 20.05.26

Approved for publication: 28.05.26

How to Cite this Article: Tiwari P, Kaura S. Acute Oral Toxicity and Anxiolytic-Like Activity of a Hydroethanolic Leaf Extract of Apium graveolens L. in the Light-Dark Box and Elevated Plus Maze. Int., J. Sci. Info. 2026; 4 (2): 61-71

1. Introduction

Anxiety-related disorders are characterized by excessive fear, hyperarousal, avoidance and impaired emotional regulation. Although normal anxiety can be adaptive, persistent or disproportionate anxiety reduces quality of life and may interfere with sleep, cognition, work and social functioning. Current pharmacotherapy includes benzodiazepines, selective serotonin reuptake inhibitors and related agents, but treatment may be limited by delayed onset, sedation, cognitive impairment, dependence, withdrawal and incomplete response. These limitations continue to encourage investigation of medicinal plants as sources of chemically diverse anxiolytic candidates.

Plant-derived preparations require particularly careful safety evaluation. The assumption that a natural product is automatically safe is scientifically unsound because concentrated extracts contain multiple bioactive constituents and may expose experimental animals to doses far greater than those encountered through dietary use. Acute oral toxicity testing is therefore necessary before behavioural screening. It identifies overt toxicity, supports selection of experimental doses and reduces the risk that illness, sedation or motor dysfunction will be misinterpreted as a therapeutic behavioural effect (OECD, 2001; Parasuraman, 2011).

Apium graveolens L. is an aromatic Apiaceae plant used as both food and traditional medicine. Its reported constituents include flavonoids, phenolic acids, phthalides, coumarins and volatile components (Al-Asmari et al., 2017; Makarova et al., 2022). Flavonoids and phenolic compounds are of interest in anxiety research because they may influence oxidative stress, neuroinflammation and inhibitory neurotransmission. Apigenin-related flavonoids have been discussed as ligands or modulators at GABA-A receptor-associated sites, although the activity of a crude extract is likely to result from multiple compounds acting together (Nuss, 2015; Wasowski & Marder, 2012).

Behavioural assessment of anxiety in rodents relies on their natural approach-avoidance conflicts. The light-dark box measures the conflict between exploration and aversion to a brightly illuminated compartment. An anxiolytic-like treatment generally increases time spent in the light area and the number of transitions or entries into it (Crawley & Goodwin, 1980; Bourin & Hascoet, 2003). The elevated plus maze uses the natural avoidance of open, elevated and unprotected spaces. Increased open-arm entries and increased time in open arms are accepted indicators of reduced anxiety-like behaviour (Pellow et al., 1985; Pellow & File, 1986; Walf & Frye, 2007).

Interpretation must account for locomotor effects. A sedative agent can change the distribution of time across compartments simply because the animal moves less, while a stimulant can increase entries without reducing fear. The light-dark model therefore included a locomotor activity measure, and elevated plus-maze findings were considered together with open- and closed-arm activity. Consistent improvement in two different models, in the absence of marked motor suppression, provides stronger evidence than a positive result in only one test.

This paper focuses only on the acute oral toxicity and two behavioural models specified in the study objective. It excludes the comparative plant, social interaction test and biochemical measurements. The aims were to determine whether the hydroethanolic leaf extract of *A. graveolens* was tolerated at a 2000 mg/kg limit dose, select safe doses for behavioural screening and evaluate anxiolytic-like activity at 200 and 400 mg/kg using the light-dark box and elevated plus maze, with diazepam as a standard comparator.

2. Materials and Methods

2.1 Preparation of the test extract

Authenticated *A. graveolens* leaves were cleaned, shade-dried at room temperature, coarsely powdered and extracted with 70% ethanol using a Soxhlet apparatus at approximately 60 degrees C for 24 h. The filtered extract was concentrated under controlled conditions to obtain a dark greenish-brown aromatic semisolid crude extract. The yield was 12.40 g from 100 g of dried powder (12.40%). The crude extract was freshly suspended in a suitable vehicle for oral administration.

2.2 Experimental animals and ethical considerations

Swiss albino mice were maintained under standard laboratory conditions with normal pellet diet, water ad libitum, a controlled light-dark cycle, suitable temperature and humidity and an acclimatization period before experimentation. Behavioural groups contained six animals. Procedures were performed after approval from the Institutional Animal Ethics Committee under CPCSEA Registration No. 1397/Po/Re/S/10/CPCSEA. Animals were handled gently, and the principles of replacement, reduction and refinement were followed. Testing conditions were kept consistent to reduce variation related to noise, lighting, odour, handling and time of day (Percie du Sert et al., 2020).

2.3 Acute oral toxicity study

Preliminary safety was evaluated according to the OECD Guideline 423 acute toxic class approach. Mice were fasted before dosing while retaining access to water. The hydroethanolic extract was administered orally as a single 2000 mg/kg limit dose. Animals were observed closely during the first 30 min, first 4 h and first 24 h and thereafter daily for 14 days. Recorded parameters included mortality, changes in alertness and behaviour, grooming, movement, posture, response to handling, tremors, sedation, convulsions, food intake, water intake, body-weight change and the condition of the skin, fur, eyes and general appearance.

In the absence of mortality or severe toxic signs at 2000 mg/kg, lower fractions of the safe dose were selected for behavioural testing. The selected doses were 200 mg/kg (one-tenth of the limit dose) and 400 mg/kg (one-fifth of the limit dose). These doses were intended to represent low and high screening levels while remaining well below the acute limit dose.

2.4 Experimental grouping

For each behavioural model, animals were allocated to four groups of six mice: Group I, vehicle control; Group II, diazepam 2 mg/kg; Group III, *A. graveolens* extract 200 mg/kg; and Group IV, *A. graveolens* extract 400 mg/kg. Treatments were administered orally according to the experimental protocol before testing. Diazepam served as the positive control to validate model sensitivity and provide a reference for the magnitude of the extract response.

2.5 Light-dark box model

The apparatus consisted of connected light and dark compartments that permitted free movement through a small opening. Each mouse was allowed to acclimatize to the experimental room and was then placed gently in the apparatus. The animal explored both compartments during a fixed observation period under standardized light, sound and environmental conditions. The apparatus was cleaned between trials to remove odour cues. Time spent in the light chamber, time spent in the dark chamber, number of light-chamber entries and locomotor activity were recorded. Increased light-compartment time and entries were interpreted as anxiolytic-like effects, provided locomotor activity was not markedly suppressed.

2.6 Elevated plus maze model

The elevated plus maze consisted of two open arms and two closed arms connected by a central platform and elevated above the floor. Each mouse was placed individually on the central platform facing a closed arm and allowed to explore for a fixed observation period. An arm entry was counted when all four paws entered the arm. Open-arm entries, time spent in open arms, closed-arm entries and time spent in closed arms were recorded. Increased open-arm exploration and reduced closed-arm preference were considered evidence of anxiolytic-like activity. The maze was cleaned after each trial, and all groups were tested under comparable environmental conditions.

2.7 Statistical analysis

Behavioural values were expressed as mean +/- standard error of the mean (SEM), with six animals per group. Group differences were evaluated by one-way analysis of variance followed by an appropriate multiple-comparison procedure against the vehicle control, as reported in the thesis dataset. Statistical significance was represented as $p < 0.05$, $p < 0.01$ and $p < 0.001$.

3. Results

3.1 Acute oral toxicity

No mortality occurred after oral administration of 2000 mg/kg during the first 24 h or throughout the 14-day observation period. Abnormal behavioural changes, tremors, marked sedation and convulsions were absent. Food and water intake remained normal, no marked abnormal body-weight change was observed, and the animals retained normal skin, fur, eyes, grooming, movement and response to handling. The extract was therefore considered safe up to the tested acute limit dose under the experimental conditions, and 200 and 400 mg/kg were selected for behavioural screening.

Table 1: Results of Acute Toxicity Study

Observation parameter	**Finding for *A. graveolens* extract**
Dose and route	2000 mg/kg, oral
Observation period	14 days
Mortality	Nil
Behavioural abnormality	Not observed
Tremors	Absent
Marked sedation	Absent
Convulsions	Absent
Food and water intake	Normal
Body-weight change	No marked abnormal change
General appearance/activity	Normal
Safety interpretation	Safe up to 2000 mg/kg under study conditions
Selected doses	200 and 400 mg/kg

3.2 Light-dark box

Vehicle-treated control mice spent 62.33 +/- 4.21 s in the light chamber and entered it 4.50 +/- 0.43 times. Diazepam markedly increased light-chamber exploration. The *A. graveolens* extract produced a significant, dose-dependent response. At 200 mg/kg, light-chamber time increased to 101.50 +/- 4.87 s and entries increased to 6.83 +/- 0.40. At 400 mg/kg, light-chamber time reached 130.67 +/- 5.10 s and entries reached 8.50 +/- 0.43. Correspondingly, time spent in the dark chamber declined. Locomotor activity remained close to control values, arguing against marked nonspecific sedation.

Table 2: Resuts of Light and Dark model

Treatment	Dose	Light time (s)	Dark time (s)	Light entries	Locomotor activity
Vehicle control	Vehicle	62.33 ± 4.21	237.67 ± 4.21	4.50 ± 0.43	85.33 ± 4.92
Diazepam	2 mg/kg	164.83 ± 5.62***	135.17 ± 5.62***	10.33 ± 0.49***	79.17 ± 4.36
A. graveolens extract	200 mg/kg	101.50 ± 4.87**	198.50 ± 4.87**	6.83 ± 0.40**	83.50 ± 4.11
A. graveolens extract	400 mg/kg	130.67 ± 5.10***	169.33 ± 5.10***	8.50 ± 0.43***	82.00 ± 3.95

Values are mean +/- SEM; n = 6. **p < 0.01 and ***p < 0.001 versus vehicle control.

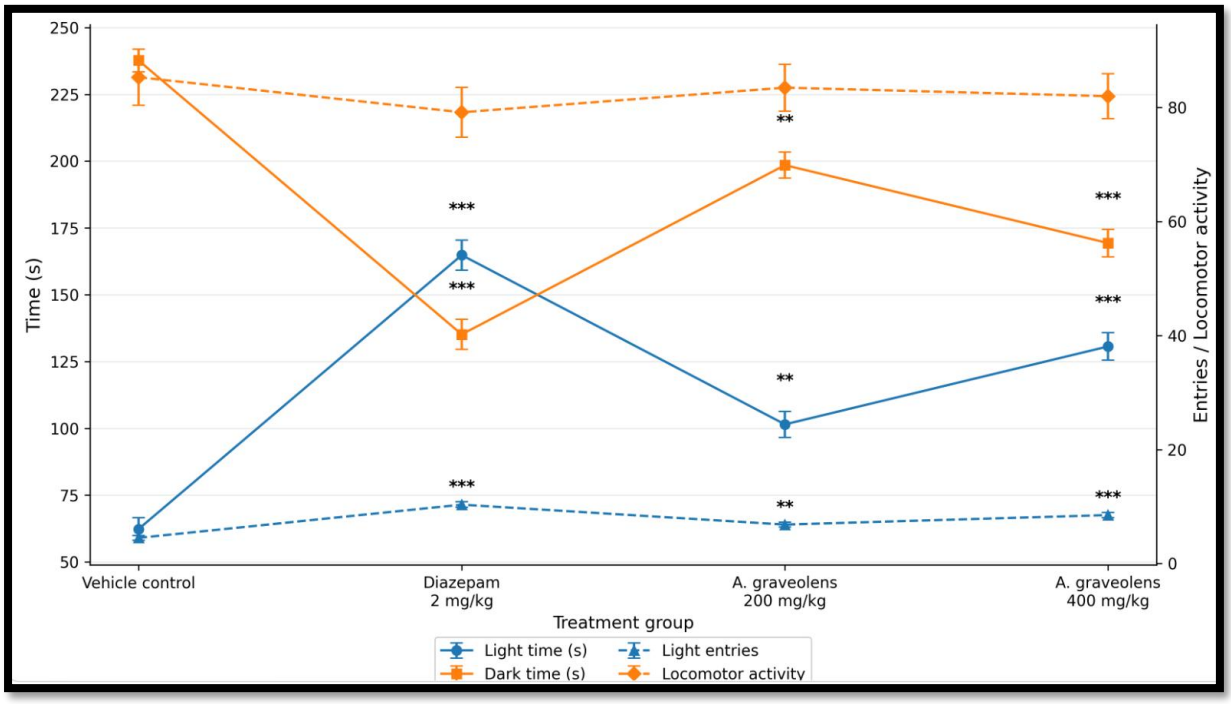

Figure 1: Combined graph of light and dark box parameters

3.3 Elevated plus maze

Control mice made 2.17 +/- 0.31 open-arm entries and spent 31.50 +/- 3.26 s in the open arms. Diazepam significantly increased both measures. *A. graveolens* increased open-arm exploration in a dose-related manner. At 200 mg/kg, open-arm entries rose to 3.83 +/- 0.31 and open-arm time to 63.50 +/- 3.78 s. At 400 mg/kg, entries increased to 5.17 +/- 0.40 and open-arm time to 91.83 +/- 4.12 s. Time spent in the closed arms decreased from 268.50 +/- 3.26 s in controls to 236.50 +/- 3.78 s and 208.17 +/- 4.12 s at the low and high doses, respectively.

Table 3: Results of Elevated Plus maze

Treatment	Dose	Open entries	Open time (s)	Closed entries	Closed time (s)
Vehicle control	Vehicle	2.17 ± 0.31	31.50 ± 3.26	8.83 ± 0.40	268.50 ± 3.26
Diazepam	2 mg/kg	6.83 ± 0.40***	118.67 ± 4.88***	5.17 ± 0.31	181.33 ± 4.88***
A. graveolens extract	200 mg/kg	3.83 ± 0.31*	63.50 ± 3.78**	7.33 ± 0.33	236.50 ± 3.78**
A. graveolens extract	400 mg/kg	5.17 ± 0.40***	91.83 ± 4.12***	6.50 ± 0.34	208.17 ± 4.12***

Values are mean +/- SEM; n = 6. *p < 0.05, **p < 0.01 and ***p < 0.001 versus vehicle control.

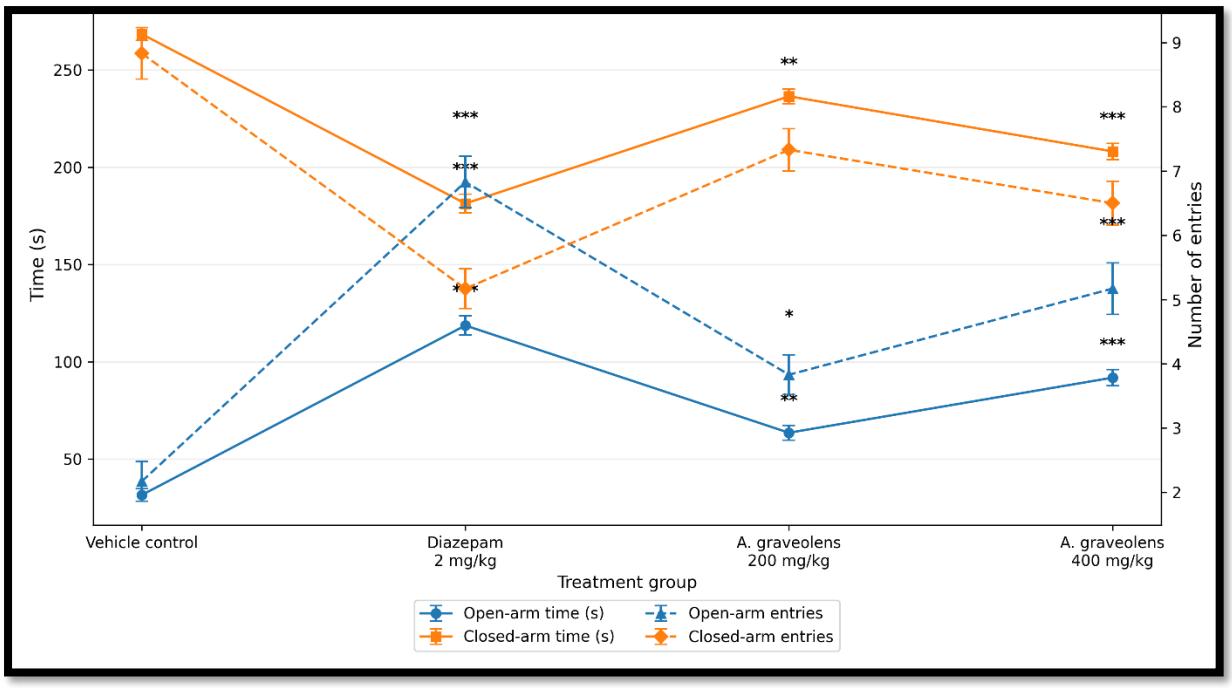

Figure 2: Combined Elevated plus maze parameters across treatment groups

4. Discussion

The acute toxicity findings provide essential context for interpreting the behavioural results. The absence of mortality and severe toxic manifestations at 2000 mg/kg indicates that the hydroethanolic leaf extract had low acute oral toxicity under the conditions of the experiment. Normal grooming, movement, food and water intake and general appearance further suggest that the animals were not experiencing overt systemic distress. Acute testing cannot establish complete safety, but it supports the use of lower doses for short-term behavioural screening and reduces the likelihood that the observed responses were produced by acute toxicosis (OECD, 2001; Parasuraman, 2011).

Selection of 200 and 400 mg/kg as one-tenth and one-fifth of the tolerated limit dose provided two separated screening levels. The behavioural effects increased from the low to the high dose in both models, which supports a dose-related pharmacological response. A clear dose-response pattern is important because it makes random variation less likely and suggests that increasing exposure to extract constituents produced progressively stronger effects. Nevertheless, the study did not determine the minimum effective dose, maximum effective dose or full therapeutic window, and additional intermediate doses would be required for formal dose-response modelling.

The light-dark box results demonstrated increased willingness to enter and remain in the illuminated compartment. Compared with controls, the 200 mg/kg dose increased light-chamber time by approximately 63%, while the 400 mg/kg dose increased it by approximately 110%. Light-chamber entries also rose in a dose-dependent manner. These changes are consistent with reduced avoidance of the brightly illuminated area, which is the principal anxiolytic-like outcome in this model (Crawley & Goodwin, 1980; Bourin & Hascoet, 2003). The effect remained lower than diazepam, as expected for a crude botanical preparation compared with a purified standard drug.

Locomotor activity remained broadly comparable with the control group. This strengthens interpretation because a marked fall in movement could produce misleading compartment times through sedation or motor impairment. The extract-treated groups showed increased light exploration without a substantial locomotor reduction, suggesting that the response was not simply caused by inability to move. However, locomotor activity in one apparatus cannot exclude all subtle sedative or stimulant effects. Dedicated open-field, rotarod or spontaneous-activity testing would provide stronger confirmation of behavioural specificity.

The elevated plus maze provided convergent evidence. The extract increased both the number of entries into open arms and the duration of open-arm exploration, while reducing time in closed arms. At 400 mg/kg, open-arm time was almost three times the control value, and open-arm entries more than doubled. Because the elevated plus maze is based on aversion to open, elevated and unprotected spaces, these findings indicate reduced anxiety-like avoidance (Pellow et al., 1985; Pellow & File, 1986; Walf & Frye, 2007). The consistency between the light-dark and elevated plus-maze results is important because the two tests use different environmental threats. Positive activity across both models is more persuasive than a result restricted to a single task.

The extract did not equal diazepam, which produced the largest behavioural changes. This should not be interpreted as failure. Diazepam is a potent, purified benzodiazepine-site modulator, whereas the hydroethanolic extract contains a complex mixture of constituents at unknown concentrations. A crude extract may have lower potency but broader biological actions. It may also contain inactive compounds that dilute the active fraction. Future bioassay-guided fractionation could determine whether a particular fraction approaches the activity of the standard at a lower dose.

The phytochemical profile offers plausible but not definitive mechanistic explanations. The extract contained alkaloids, glycosides, steroids, tannins, saponins and terpenoids, with particularly strong flavonoid and phenolic reactions. Flavonoids have been reported to interact with GABA-A receptor-associated sites and may enhance inhibitory neurotransmission, a central mechanism in anxiety regulation (Nuss, 2015; Wasowski & Marder, 2012). Phenolic compounds may reduce oxidative stress and neuroinflammatory signalling, both of which can disturb neuronal excitability. Terpenoids and volatile celery constituents may also contribute calming or neuromodulatory effects. The total response is likely to reflect synergy among multiple classes rather than a single compound.

A GABAergic interpretation is biologically reasonable because diazepam, the positive control, reduced avoidance in both models through enhancement of GABA-A receptor-mediated inhibition. Similar behavioural direction does not prove that the plant extract acts at the same receptor. Receptor-binding experiments, antagonist studies using a benzodiazepine-site blocker, measurement of brain GABA and glutamate and evaluation of stress-related hormones would be needed to establish mechanism. Chemical standardization is equally important; without quantification of marker compounds, differences between batches cannot be linked confidently to pharmacological potency.

The study has several limitations. Acute toxicity was evaluated after a single high dose and cannot predict subacute, chronic, reproductive or organ-specific toxicity. No haematological, biochemical or histopathological endpoints were included. The behavioural study used only two dose levels and did not report blinding procedures in detail. The extract was not standardized to apigenin, apiin, phenolic acids, phthalides or other marker compounds. Although locomotor activity in the light-dark box was preserved, more comprehensive motor assessment would strengthen the claim that anxiolysis was not confounded by sedation. Finally, rodent anxiety-like behaviour is a preclinical proxy and should not be translated directly into treatment recommendations for human anxiety disorders.

Despite these limitations, the results identify the hydroethanolic leaf extract of *A. graveolens* as a promising candidate for further neuropharmacological investigation. It was tolerated at a high acute limit dose and produced statistically significant, dose-dependent improvement in two validated behavioural models. The next research stage should combine repeated-dose safety assessment, quantitative phytochemical profiling and mechanism-focused experiments. Such work would determine whether the observed activity can be reproduced with standardized material and whether efficacy is separable from sedation across a wider dose range.

The relationship between safety and behavioural efficacy should be examined more deeply than the acute limit-dose result permits. A high tolerated single dose provides a preliminary margin, but repeated administration may lead to accumulation, enzyme induction or delayed hepatic and renal effects that are not visible during routine observation. Subacute studies should include haematology, liver and kidney function indices, organ weights and histopathology. Because celery contains coumarin and furanocoumarin-related constituents, possible interactions with drug-metabolizing enzymes and photosensitivity pathways should also be considered when moving beyond initial screening.

Translational interpretation should remain cautious. The behavioural models demonstrate changes in approach-avoidance behaviour in mice, not treatment of a diagnosed human anxiety disorder. Nevertheless, the convergence of two models, preserved locomotor activity and a dose-related pattern provides a rational basis for continued preclinical work. Standardized extracts should be compared with isolated flavonoids and with known receptor antagonists to determine whether the crude preparation has unique multi-target advantages. Pharmacokinetic studies will also be needed to establish which constituents reach systemic circulation and the brain at the effective doses.

A future confirmatory design should also strengthen internal validity through prospective randomization, allocation concealment and blinded behavioural scoring. Automated tracking can reduce observer bias and provide additional endpoints such as distance travelled, velocity, latency to first entry and risk-assessment behaviours. Predefined exclusion criteria and a sample-size calculation should be reported before experimentation. These measures would help distinguish a robust anxiolytic-like signal from exploratory findings and align the study more closely with contemporary standards for reproducible in vivo pharmacology.

5. Conclusion

The hydroethanolic leaf extract of *A. graveolens* produced no mortality or severe acute toxic signs after a single oral dose of 2000 mg/kg during 14 days of observation. This finding supported selection of 200 and 400 mg/kg for behavioural screening. The extract significantly increased exploration of the light compartment in the light-dark box and open arms in the elevated plus maze, with the 400 mg/kg dose consistently producing a stronger effect than 200 mg/kg. Locomotor activity was not markedly reduced, supporting an anxiolytic-like interpretation rather than nonspecific motor suppression. Although diazepam remained more effective, the consistent dose-related response across two models indicates meaningful preclinical activity. The results justify further standardization of the extract, identification of active constituents, mechanistic studies and repeated-dose toxicological evaluation; they do not constitute evidence for direct clinical use.

6. Declarations

Ethics approval: The animal work was reported as approved by the Institutional Animal Ethics Committee under CPCSEA Registration No. 1397/Po/Re/S/10/CPCSEA, with procedures conducted according to accepted animal-care principles.

Funding: No external funding was reported for this manuscript.

Conflict of interest: The author declares no conflict of interest.

Authors Contribution: Purnima Tiwari contributed to conceptualization, methodology, investigation, data collection, analysis, and preparation of the original manuscript. Sushila Kaura supervised the study, validated the methodology and findings, and critically reviewed and edited the manuscript. Both authors approved the final version.

References

- Al-Asmari, A. K., Athar, M. T., Kadasah, S. G., Al-Rahim, W. M., & Al-Shahrani, H. M. (2017). Apium graveolens Linn.: A review. Pharmacognosy Reviews, 11(21), 13-18.
- Bourin, M., & Hascoet, M. (2003). The mouse light/dark box test. European Journal of Pharmacology, 463(1-3), 55-65.
- Crawley, J. N., & Goodwin, F. K. (1980). Preliminary report of a simple animal behavior model for the anxiolytic effects of benzodiazepines. Pharmacology Biochemistry and Behavior, 13(2), 167-170.
- Makarova, E. I., Bokov, D. O., Sergunova, E. V., Chevidaev, V. V., Kakhramanova, S. D., Bessonov, V. V., Friesen, N. V., & Luferov, A. N. (2022). Apium graveolens L.: A phytochemical and pharmacological review. Research Journal of Pharmacy and Technology, 15(2), 927-934.
- Nuss, P. (2015). Anxiety disorders and GABA neurotransmission: A disturbance of modulation. Neuropsychiatric Disease and Treatment, 11, 165-175.
- Organisation for Economic Co-operation and Development. (2001). Test No. 423: Acute oral toxicity - acute toxic class method. OECD Guidelines for the Testing of Chemicals, Section 4. https://doi.org/10.1787/9789264071001-en
- Parasuraman, S. (2011). Toxicological screening. Journal of Pharmacology and Pharmacotherapeutics, 2(2), 74-79. https://doi.org/10.4103/0976-500X.81895
- Pellow, S., & File, S. E. (1986). Anxiolytic and anxiogenic drug effects on exploratory activity in an elevated plus-maze: A novel test of anxiety in the rat. Pharmacology Biochemistry and Behavior, 24(3), 525-529. https://doi.org/10.1016/0091-3057(86)90031-7
- Pellow, S., Chopin, P., File, S. E., & Briley, M. (1985). Validation of open:closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. Journal of Neuroscience Methods, 14(3), 149-167.
- Percie du Sert, N., Hurst, V., Ahluwalia, A., Alam, S., Avey, M. T., Baker, M., et al. (2020). The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLOS Biology, 18(7), e3000410.
- Walf, A. A., & Frye, C. A. (2007). The use of the elevated plus maze as an assay of anxiety-related behavior in rodents. Nature Protocols, 2(2), 322-328. https://doi.org/10.1038/nprot.2007.44
- Wasowski, C., & Marder, M. (2012). Flavonoids as GABA-A receptor ligands: The whole story? Pharmacological Reports, 64(2), 352-367.
- Tiwari, P., Kumar, B., Kaur, M., Kaur, G., & Kaur, H. (2011). Phytochemical screening and extraction: A review. Internationale Pharmaceutica Sciencia, 1(1), 98-106.
- Rios, J. L., Schinella, G. R., & Mulet, M. (2022). Flavonoids and their role in the treatment of anxiety and sleep disorders. Phytotherapy Research, 36(8), 3122-3139.