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Exploring The Anxiolytic and Neurobehavioral Benefits of Serratiopeptidase in Mice

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ABSTRACT

Serratiopeptidase exhibits therapeutic efficacy in a variety of disease models; in addition to its ability to mediate anti-inflammatory action, it is also responsible for regulating several biological activities by targeting different signaling pathways. Our study aimed to evaluate the central nervous effect of serratiopeptidase on neurobehavioral activities and to eliminate anxiety manifestations in mice. Male mice were subjected to neurobehavioral tests, including open field, negative geotaxis, head poking, and swimming tests, in addition to methods of screening for antianxiety, such as elevated pulse maze and light-dark box tests, after one hour of serratiopeptidase at 5, 10, and 20 mg/kg orally. Serratiopeptidase at 20 mg/kg produced a significant increase in the number of squares cut and rearing compared to the control group. Serratiopeptidase at 5, 10, and 20 mg/kg resulted in a decrease in the time required to correct the position of mice in comparison with the control group in negative geotaxis, and there was an increase in the number of stockings compared with the control group. Serratiopeptidase (20 mg/kg) significantly increased the duration of time spent in the open arm and significantly decreased the amount of time spent in the closed arm compared with the control group and the light-dark box test. Serratiopeptidase at 20 mg/kg significantly increased the time spent on the light side of mice and significantly decreased the time spent on the dark side. Serratiopeptidase at 20 mg/kg demonstrated superior effects to the group treated with sertraline in reducing anxiety-like behavior in both tests. In conclusion, serratiopeptidase has a stimulatory effect on the central nervous system, and a high dose may produce anxiolytic-like effects.

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INTRODUCTION

Serratiopeptidase is a nonspecific proteolytic enzyme produced by the Gram-negative gut bacteria Serratia sp. E-15. It is already an established anti-inflammatory, analgesic, and mucolytic agent and has therefore been the subject of immense attention from pharmaceutical organizations **(Naser and Albadrany, 2024).** Apart from that, serratiopeptidase also exhibits therapeutic efficacy in a variety of disease models, ranging from clinical trials and animal pathological studies to preliminary clinical evaluations **(Hosseini *et al.*, 2024).** In addition to its anti-inflammatory action, it is also responsible for regulating several biological activities by targeting different signaling pathways **(Saha *et al.*, 2020; Albadrany *et al.*, 2021; Bashar and Albadrany, 2022).** Since several studies have confirmed the biological effect of serratiopeptidase at the molecular level, it appears that serratiopeptidase also mediates neurobehavioral activities as well as abolishing anxiety manifestations **(Bhalla *et al.*, 2022).**

Numerous models and experimental paradigms have been designed to explore anxiety behavior in rodents and construct new therapeutic strategies inspired by these models in a variety of anxiety disorders **(La-Vu *et al.*, 2020).** There is no doubt that many aspects are correlated with human anxiety, confirming the value of such behavior paradigms in dissecting the anxiolytic and allied mechanisms of action associated with newer molecule discovery **(Bashar and Albadrany, 2022; Kenwood *et al.*, 2022).** Serrapeptidase modulates the employment of a variety of neuronal machinery such as the dopamine transporter, leading to alterations in concentration levels of critical monoaminergic neurotransmitters such as

dopamine, noradrenaline, and serotonin. This means that it seems to be able to regulate neurotransmitter release from presynaptic vesicles and affect the intraneuronal reuptake of the major neurotransmitters with possible benefit from a synaptic re-equilibration of neurotransmitter presence **(Azzam *et al.*, 2023)**.

Laboratory animals have been part of scientific research for a long time. It was once believed that medical practice would collapse if laboratory animals were banned. Most of our biological, medical, environmental, and developmental studies today have utilized laboratory animals **(Albadrany and Naser, 2020; Naser and Albadrany, 2021; Naser *et al.*, 2021; Al-Jumaa *et al.*, 2024).** As a result, identifying a potential molecule using a sound experimental approach is of critical importance. Given the scarcity of research on serratiopeptidase's effects on the central nervous system. This study aims to evaluate its influence on locomotor activity, cognitive behavior, and muscle strength, as well as to evaluate the potential anti-anxiety effects in mice.

MATERIALS AND METHODS

Ethical approval

All experimental techniques followed the International Association for the Study of Pain criteria and were authorized by the University of Mosul/College of Veterinary Medicine committee with approval number UM.VET.2024.006. The welfare of the animals was prioritized.

Animals

The study employed forty-five male albino mice weighing between 30 and 40grammes. The animals were kept and acclimated at the Faculty of veterinary medicine, University of Mosul, Iraq. The animals had access to both food and water.

Drugs

Serratiopeptidase (somazin-Bio) was obtained from Bioactive T Pharma, United Kingdom. Sertraline (Sertra TAO® 50 mg film-coated tablets) was obtained from TAD Pharma GmbH, Heinz-Lohmann-StraBe, Germany. The two drugs were dissolved in distilled water for oral administration, and the volume of administration was 2 ml/kg of body weight.

Experiments

Experiment 1: Neurobehavioral tests

Study design

20 male mice were randomly allocated into the following groups:

- Control group receive distilled water orally
- Serratiopeptidase 5mg/kg orally
- Serratiopeptidase 10mg/kg orally
- Serratiopeptidase 20mg/kg orally

An hour after the mice were given the drug, the following tests were performed on them:

Open filed test

The open-field box (50 x 50 cm) was divided into twenty-five (25) equal squares with side boundaries of considerable height (30 cm) to prevent the mice from escaping. A camera was used to capture activity for three minutes after mice were placed in the open field arena's middle square. Number of squares or lines that the animal crosses with all its limbs., rearing, frequency of defecation, and urination **(Stanford, 2007).**

Swimming test

The swimming test, which relies on the neurological and functional integration of multiple brain regions, was used to quantify muscular strength and exhaustion. To prevent the impact of water temperature on performance, a unique plastic swimming pool measuring 60 x 30 x 40 cm was utilized, filled with water to a depth of 30 cm at room temperature(Mohammad, 1986; Schapiro et al., 1970). Every animal spent three minutes in the pool. The following ranks were part of the test's scoring system:

0: Underwater nose.

1.Nose above or above the water's surface number one.

2. The head and nose are at or above the water line, and the ears are buried.

3: Similar to 2, but with mid-ear water level.

4.The water level at the base of the ear is the same as in step three.

Behavioral Tests for Measuring Cognitive Impairment

Negative Geotaxis

The negative geotaxis test is an important neurobehavioral test in rodents as it evaluates the efficiency of the vestibular system and neuromuscular activity. The device consisted of a wooden surface inclined at a 45-degree angle. The mouse was placed with its head facing downwards, and the time required to correct its position was calculated. If it did not correct its position within 60 seconds, the animal was excluded **(Motz and Alberts, 2005).**

Head Pocking Test

This test measures the efficiency of cognitive function in an animal's exploration of the environment. A plastic surface with a diameter of 60 cm and a height of 20 cm was used, containing 10 regularly distributed circular holes. The mouse was observed for three minutes and the number of times the head was inserted into the mentioned holes was counted **(Al-Shalchi and Mohammad, 2024).**

Experiment 2

Behavioral test for detection antianxiety effect

Study design

25 male mice were randomly allocated into the following groups :

Group 1: negative control group receive distilled water orally

Group 2: Positive control sertraline 10mg/kg orally

Group 3: Serratiopeptidase 5mg/kg orally

Group 4: Serratiopeptidase 10mg/kg orally

Group 5: Serratiopeptidase 20mg/kg orally.

The second group was tested four hours after taking sertraline, because at this time it reaches its highest concentration in the rodent's brain **(Tremaine *et al.*, 1989)**. while the other groups were tested one hour after taking it.

1. Elevated plus maze

It was composed of two open arms (35×5 cm2) with two opposite closed arms of the same size and a small middle square (5×5 cm2) between the arms**(Rodgers and Dalvi, 1997; Naser and Alberifkani, 2023)**. In a dim area, the maze was elevated 50 cm above the ground. Each mouse was positioned at the center of the elevated plus maze with its head facing the open arm, and a video camera filmed the mice's free exploration for 5 minutes, and the following were recorded within 5 minutes:

1- Time spent in the open arm.

2- Time spent in closed arm.

3- Number of times entering the open arm.

4. Number of times entering the closed arm.

2. The dark and light box test

This test was performed to assess anxiety-related behaviors in the mice. A mobile phone stand was placed 50 cm above the box for video recording, with an opening (6 × 6 cm^2) between the two compartments. The experiment used two compartments: a light side 40 × 30 × 20 cm^3 (white walls and highly lit with a 100 W bulb) and a dark side 40 × 30 × 20 cm^3 (opaque black walls and dark) **(Bourin and Hascoët, 2003).** After five minutes of exploration, the mouse was placed on the dark side with its head facing the light side, and the following were noted:

1. Number of times the dark side was entered
2. Number of times the light side was entered
3. Duration of staying on the dark side.
4-Duration of Staying on the bright side.

Statistical analysis

The Kruskal-Walli's test and Dunn's test were used to statistically analyze non-parametric data, whereas analysis of variance and the least significant difference test were used to analyze parametric data with multiple means. A significance level of $p < 0.05$ was established.

RESULTS

Neurobehavioral tests

The outcome of the open field experiment showed that one hour after dosing male mice with serratiopeptidase at 5 ,10 and 20 mg/kg of body weight, there was a significant increase in the number of squares cut and the number of times standing on the hind legs compared to the control group **(Table 1).**

Table1: The effect of administration of serratiopeptidase on mice behavior in open field test**.**

Parameters / Groups	Squares or lines crossed	Rearing	Number of fecal balls	Number of times urinate
First group (Control)	13.2 ± 1.71	3.6 ± 2.61	0 ± 0	0 ± 0
Serratiopeptidase (5mg/kg)	90.4 ±12.32*	20.40 ± 2.06 *	0.4 ± 0.24	0.2 ± 0.2
Serratiopeptidase (10mg/kg)	89.8 ± 14.74*	27.0 ± 3.11*	0.2 ± 0.20	0 ± 0
Serratiopeptidase (20mg/kg)	93.6 ± 3.52*	22.0 ±2.48*	0.2 ± 0.20	0 ± 0

The data are mean ± SE of 5 mice/group. * Significantly different from the data of control group, at ($p \leq 0.05$).

The outcome of the negative geotaxis experiment showed that one hour after dosing male mice with serratiopeptidase at 5 ,10 and 20 mg/kg of body weight, there was a decrease in the time required to correct the position of mice in comparison with the control group furthermore, in the head pocking test there were increased in numbers of pocking in compared with control group.

In the swimming experiment, there were no significant differences in swimming scores in the groups dosed with serratiopeptidase compared to the control group **(Fig.1).**

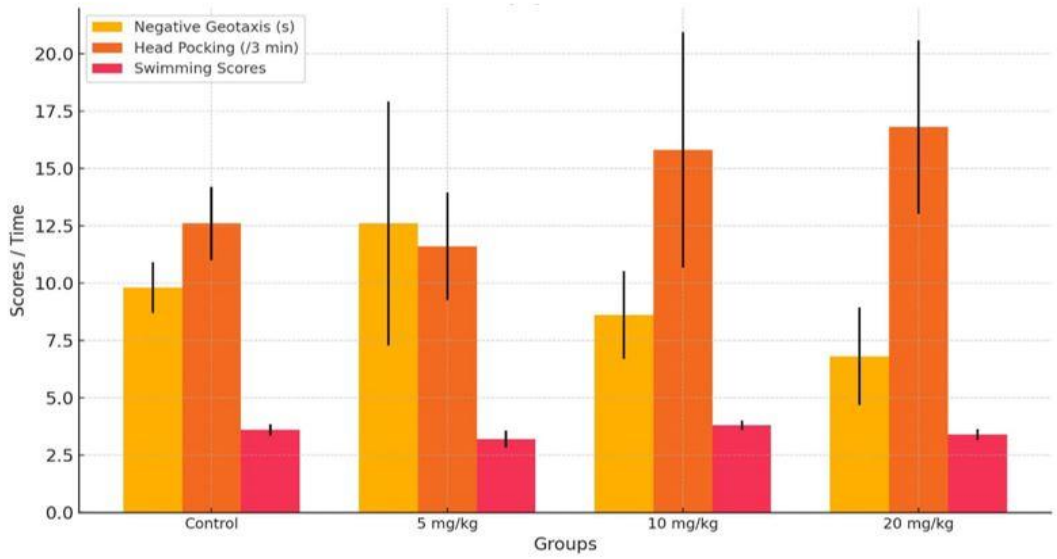

Fig. 1: The effect of serratiopeptidase on mice behavior in negative geotaxis test, head pocking test and swimming test after one hour.

In the elevated maze test, serratiopeptidase significantly increased the duration of time spent in the open arm and significantly decreased the amount of time spent in the closed arm compared to the control group an hour after administration of 20 mg/kg. and the light-dark box test, serratiopeptidase at the same dose revealed anxiolytic effects, represented by a significant increase in the time spent in the light side of mice and a significant decrease in the time spent in the dark side. Serratiopeptidase at 20 mg/kg demonstrated significant effects on the group treated with sertraline at 10 mg/kg in reducing anxiety-like behavior in both tests (**Table 2).**

Table 2: Effect of administration of serratiopeptidase on the mice behaviour in elevated pulse maze and light-dark box test.

Parameters / Groups	Elevated pulse maze		Light -Dark box test	
	Time spent in open arm(second)	Time spent in closed arm(second)	Duration of staying on the dark side(second)	Duration of Staying on the bright side (second)
Negative control	111.40 ± 5.97	188.60 ± 5.97	143.00 ± 19.69	157.00 ± 19.69
Positive control 10mg/kg of sertraline	146.40 ± 17.13	153.60 ± 17.13	180.60 ± 16.93*	119.40 ± 16.93*
Serratiopeptidase (5mg/kg)	134.60 ± 16.69*	165.40 ± 16.69*	141.60 ± 29.59	158.40 ± 29.59
Serratiopeptidase (10mg/kg)	137.00 ± 15.10*	163.00 ± 15.10*	147.80 ± 29.50	152.20 ± 29.50
Serratiopeptidase (20mg/kg)	187.40 ± 23.92*	112.60 ± 23.92*	101.60 ± 26.23*	198.40 ± 26.23*

The data are mean ± SE of 5 mice/group. * Significantly different from the data of control group, at ($p \leq 0.05$).

DISCUSSION

There has been increasing interest in serratiopeptidase's central nervous effects over the last few years. Recent research has unveiled a putative role for serratiopeptidase in ameliorating neuroinflammation-mediated transient or chronic pain and associated neurological disorders **(Tiwari, 2017; Jadhav *et al.*, 2020).**

In this study, serratiopeptidase had a stimulating effect on the nervous system by increasing locomotor activity, the number of head poking, and the speed of body correction in the negative geotaxis test, in

addition to not affecting the mice in the swimming test, as there were no significant differences between the groups. To our knowledge, our study is the first conducted on mice to evaluate serratiopeptidase at the nervous system level.

To circumvent the limitations of in vitro studies, various animal models are often employed to assess the efficacy of serratiopeptidase to improve motor function in response to insult in a clinically relevant paradigm **(Al-awadhi *et al.*, 2024; FC *et al.*, 2024).** Attenuating motor deficits in animals represents a direct behavior of the enzyme, thereby indicating a lesser degree of subjectivity than the pain/discomfort threshold **(Jadhav *et al.*, 2020).** Several animal behavioral paradigms have been employed to evaluate motor enhancements, including motor coordination-improving tests such as rotarod, staircase, and horizontal/vertical grip strength, as well as tests to indicate improvements in fine and gross motor function **(Crawley, 1999).** Therefore, the use of various animal models in this section might not only underscore the translation potential of serratiopeptidase in clinical applications but also its beneficial effects on diverse motor activities. Furthermore, the discussions in this section also provide insight into the biological relevance of employing these in vivo models.

Findings in these in vivo animal behavioral studies corroborate the beneficial effects of serratiopeptidase administration by improving motor function. For instance, oral administration of serratiopeptidase to arsenic-exposed rats improved locomotor activity, increased the number of rearings, and decreased immobility time in open-field test measurements. In sciatic nerve crush-induced neuropathic pain in rats, oral administration of serratiopeptidase increased coordination and muscle power in a dose-dependent manner **(Firdaus *et al.*, 2022; Saxena *et al.*, 2022; Naik *et al.*, 2023).** The intracerebroventricular injection of serratiopeptidase restored grip strength and prolonged the retention time and latency to lift in comparison with the group in rats, thereby enhancing the fine motor activities in these rats in the training and on the first day of the memory assessment **(Naik *et al.*, 2023).**

The increase in motor activity and neurobehavioral of mice treated with serratiopeptidase in our study may be due to its mechanisms in the brain through inhibition of the brain cholinesterase and thus an increase in the concentration of acetylcholine, which has stimulating effects for the central nervous system and memory. In the central nervous system, acetylcholine acts as a fast synaptic neurotransmitter to create direct and indirect excitatory effects on postsynaptic neurons as well as on presynaptic neurons **(Ohkuma and Katsura, 2001; Teleanu *et al.*, 2022).**

A major strength of our study is that the dose of serratiopeptidase that is therapeutically effective against experimentally induced anxiety has been demonstrated. The anxiolytic effects of protease enzymes have been investigated using various experimental models. In this regard, several researchers have reported the antianxiety effects exhibited by it. The anxiolytic potential of serratiopeptidase has been demonstrated in an acute restraint stress-induced anxiety test in rats **(Bakare and Owoyele, 2021).** The anti-inflammatory aspect appears to be the most likely candidate. Serratiopeptidase minimizes discomfort and probable anxiousness by interacting with neurons and perhaps also some neuroprotective chemicals in the brain. It features extremely strong inhibitory potential, is biologically available in the peripheral framework, and quickly crosses the blood-brain barrier **(Dhiman and Purohit, 2023).** However, the increase of serotonin and dopamine in the brain brought on during a low dose of serratiopeptidase suggests modulation in the levels of these key neurotransmitters, which might be the reason for the anti-anxiety action. The concentration of 5-HT and the metabolite of dopamine, 5-HIAA, significantly increased in the cortex and hypothalamus of mice **(Yardimci *et al.*, 2023).**

CONCLUSIONS

In conclusion, the administration of serratiopeptidase at doses of 5, 10, and 20 mg/kg demonstrated significant anxiolytic effects in mice, as evidenced by the improvement in neurobehavioral parameters across various tests, including the elevated plus maze and light-dark box test. These findings suggest the potential of serratiopeptidase as a therapeutic agent for managing anxiety-related behaviors.

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Conflict of interest

The authors declare they have no competing interest.

REFERENCES

AL-AWADHI, R. M., KILANY, O. E., ABDALLAH, O. M., NAGUIB, F. M., and NAGEH, H., 2024. Neuroprotective Effects of Grape Seed Extract against Cadmium Toxicity in Broilers. Journal of Applied Veterinary Sciences, 9(3), 86–101. DOI: 10.21608/javs.2024.293367.1344

AL-JUMAA, Z. M., AL-TAEE, S. K., JABER, M. T., and RAHHAWI, A. M., 2024. Histopathological Alteration and Molecular Detection of Gills Rot Fungus in Carp Fish. Journal of Applied Veterinary Sciences, *9*(4), 54–59. DOI: 10.21608/javs.2024.301499.1373

AL-SHALCHI, R. F., and MOHAMMAD, F. K., 2024. Adverse neurobehavioral changes with reduced blood and brain cholinesterase activities in mice treated with statins. Veterinary World, 17(1), 82. https://doi.org/10.14202/vetworld.2024.82-88

ALBADRANY, Y. M., NASER, A. S., and HASAN, M. M., 2021. Study the analgesic effect of diclofenac and silymarin coadministration in chicks. Iraqi Journal of Veterinary Sciences, 35(5), 25-31. https://doi.org/10.33899/ijvs.2021.127065.1453

ALBADRANY, Y., and NASER, A., 2020 . Coenzyme Q10 coadministration with diclofenac augmented impaired renal function in broiler chickens (Gallus gallus domesticus). Veterinary World, 13(4), 642. https://doi.org/10.14202/vetworld.2020.642-648

AZZAM, S. M., RAHMAN, A. A. S. A., AHMED-FARID, O. A., EL-WAFA, W. M. A., and SALEM, G. E. M., 2023 . Lipopolysaccharide induced neuroprotective effects of bacterial protease against Alzheimer's disease in male Wistar albino rats. International Journal of Biological Macromolecules, 230, 123260. https://doi.org/10.1016/j.ijbiomac.2023.123260

BAKARE, A. O., and OWOYELE, B. V., 2021. Bromelain reduced pro-inflammatory mediators as a common pathway that mediate antinociceptive and anti-anxiety effects in sciatic nerve ligated Wistar rats. Scientific Reports, 11(1), 289. https://doi.org/10.1038/s41598-020-79421-9

BASHAR, Q. M., and ALBADRANY, Y. M., 2022. Evaluation of the Antipyretic, Analgesic, and Anti-inflammatory Effects of Pregabalin in Chicks. Egyptian Journal of Veterinary Sciences, 53(3), 323–328. https://doi.org/10.21608/ejvs.2022.131986.1336

BHALLA, S., MEHAN, S., KHAN, A., and REHMAN, M. U., 2022. Protective role of IGF-1 and GLP-1 signaling activation in neurological dysfunctions. Neuroscience and Biobehavioral Reviews, 142, 104896. https://doi.org/10.1016/j.neubiorev.2022.104896

BOURIN, M., and HASCOËT, M., 2003. The mouse light/dark box test. European Journal of Pharmacology, 463(1–3), 55–65. https://doi.org/10.1016/S0014-2999(03)01274-3

BURNE, T. H. J., JOHNSTON, A. N. B., MCGRATH, J. J., and MACKAY-SIM, A., 2006. Swimming behaviour and post-swimming activity in Vitamin D receptor knockout mice. Brain Research Bulletin, 69(1), 74–78. https://doi.org/10.1016/j.brainresbull.2005.10.014

CRAWLEY, J. N. 1999. Behavioral phenotyping of transgenic and knockout mice: experimental design and evaluation of general health, sensory functions, motor abilities, and specific behavioral tests. Brain Research, 835(1), 18–26. https://doi.org/10.1016/S0006-8993(98)01258-X

DHIMAN, A., and PUROHIT, R., 2023. Targeting tachykinin peptides involved in viral infections through in silico approach: Screening the unforeseen potency of serratiopeptidase. Journal of Molecular Liquids, 392, 123504. https://doi.org/10.1016/j.molliq.2023.123504

FC, F., KJP, M., MMM, C., TL, F., BBI, T., and BN, V., 2024. Effects of Aqueous and Ethanolic Extracts of Ginger (Zingiber Officinale) Rhizome on Serum Progesterone Level and Markers of Oxidative Stress in African Giant Rat (Cricetomys Gambianus) in Captivity. Journal of Applied Veterinary Sciences, 9(3), 11-18. DOI: 10.21608/javs.2024.278828.1326

FIRDAUS, Z., KUMAR, D., SINGH, S. K., and SINGH, T. D., 2022. Centella asiatica alleviates AlCl3-induced cognitive impairment, oxidative stress, and neurodegeneration by modulating cholinergic activity and oxidative burden in rat brain. Biological Trace Element Research, 200(12), 5115–5126. https://doi.org/10.1007/s12011-021-03083-5

HOSSEINI, S. B., AZIZI, M., NOJOUMI, S. A., and VALIZADEH, V., 2024. An up-to-date review of biomedical applications of serratiopeptidase and its biobetter derivatives as a multi-potential metalloprotease. Archives of Microbiology, 206(4), 180. https://doi.org/10.1007/s00203-024-03889-6

JADHAV, S. B., SHAH, N., RATHI, A., RATHI, V., and RATHI, A., 2020. Serratiopeptidase: Insights into the therapeutic applications. Biotechnology Reports, 28, e00544. https://doi.org/10.1016/j.btre.2020.e00544

JAGANNATHAN, H., THOTA, A., B. KUMARAPPA, A. K., and KISHORE, G., 2020. A comparative study of aceclofenac versus etoricoxib in the management of acute low back pain in a tertiary care hospital. Journal of Drug Assessment, 9(1), 60–65. https://doi.org/10.1080/21556660.2020.1734008

KENWOOD, M. M., KALIN, N. H., and BARBAS, H., 2022. The prefrontal cortex, pathological anxiety, and anxiety disorders. Neuropsychopharmacology, 47(1), 260–275. https://doi.org/10.1038/s41386-021-01109-z

LA-VU, M., TOBIAS, B. C., SCHUETTE, P. J., and ADHIKARI, A., 2020. To approach or avoid: an introductory overview of the study of anxiety using rodent assays. Frontiers in Behavioral Neuroscience, 14, 145. https://doi.org/10.3389/fnbeh.2020.00145

MOHAMMAD, F. K. 1986. Assessment Of Behavioral, Neurochemical And Developmental Effects In Developing Rats Following In Utero Exposure To Non-Teratogenic Levels Of 2, 4-D And 2, 4, 5-T (Herbicides, Ontogeny). 8(5):551-60. PMID: 3785517

MOTZ, B. A., and ALBERTS, J. R., 2005. The validity and utility of geotaxis in young rodents. Neurotoxicology and Teratology, 27(4), 529–533. https://doi.org/10.1016/j.ntt.2005.06.005

NAIK, S., KATARIYA, R., SHELKE, S., PATRAVALE, V., UMEKAR, M., KOTAGALE, N., and TAKSANDE, B., 2023. Nattokinase prevents β-amyloid peptide (Aβ1-42) induced neuropsychiatric complications, neuroinflammation and BDNF signalling disruption in mice. European Journal of Pharmacology, 952, 175821. https://doi.org/10.1016/j.ejphar.2023.175821

NASER, A. S., and ALBADRANY, Y. M., 2024. Evaluation of the therapeutic effects of serratiopeptidase in chicks. Macedonian Veterinary Review, 47(2), 115-122.https://doi.org/10.2478/macvetrev-2024-0021

NASER, A. S., and ALBERIFKANI, N. M., 2023. Assessment of anxiolytic-like effects of acute and chronic treatment of flurbiprofen in murine. Journal of Ideas in Health, 6(1), 814–819. https://doi.org/10.47108/jidhealth.Vol6.Iss1.268

NASER, A., ALBADRANY, Y., and SHAABAN, K. A., 2021 . Methods of Pain Assessment in Chicks as a

Model. Egyptian Journal of Veterinary Sciences, *52*(2), 241–249. https://doi.org/10.21608/ejvs.2021.64605.1219

OHKUMA, S., and KATSURA, M., 2001. Nitric oxide and peroxynitrite as factors to stimulate neurotransmitter release in the CNS. Progress in Neurobiology, 64(1), 97–108. https://doi.org/10.1016/S0301-0082(00)00041-1

RODGERS, R. J., and DALVI, A., 1997. Anxiety, defence and the elevated plus-maze. Neuroscience and Biobehavioral Reviews, 21(6), 801–810. https://doi.org/10.1016/S0149-7634(96)00058-9

SAHA, S., BUTTARI, B., PANIERI, E., PROFUMO, E., and SASO, L., 2020. An overview of Nrf2 signaling pathway and its role in inflammation. Molecules, 25(22), 5474. https://doi.org/10.3390/molecules25225474

SAXENA, P., SELVARAJ, K., KHARE, S. K., and CHAUDHARY, N., 2022. Superoxide dismutase as multipotent therapeutic antioxidant enzyme: Role in human diseases. Biotechnology Letters, 1–22. https://doi.org/10.1007/s10529-021-03200-3

SCHAPIRO, S., SALAS, M., and VUKOVICH, K., 1970. Hormonal effects on ontogeny of swimming ability in the rat: assessment of central nervous system development. Science, 168(3927), 147–151. https://doi.org/10.1126/science.168.3927.147

STANFORD, S. C. 2007. The open field test: reinventing the wheel. Journal of Psychopharmacology, 21(2), 134–135. https://doi.org/10.1177/0269881107073199

TELEANU, R. I., NICULESCU, A.-G., ROZA, E., VLADÂCENCO, O., GRUMEZESCU, A. M., and TELEANU, D. M., 2022. Neurotransmitters—key factors in neurological and neurodegenerative disorders of the central nervous system. International Journal of Molecular Sciences, 23(11), 5954. https://doi.org/10.3390/ijms23115954

TIWARI, M. 2017. The role of serratiopeptidase in the resolution of inflammation. Asian Journal of Pharmaceutical Sciences, 12(3), 209–215. https://doi.org/10.1016/j.ajps.2017.01.003

YARDIMCI, A., ERTUGRUL, N. U., OZGEN, A., OZBEG, G., OZDEDE, M. R., ERCAN, E. C., and CANPOLAT, S., 2023. Effects of chronic irisin treatment on brain monoamine levels in the hypothalamic and subcortical nuclei of adult male and female rats: An HPLC-ECD study. Neuroscience Letters, 806, 137245. https://doi.org/10.1016/j.neulet.2023.137245

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