International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 20s, 2025
https://theaspd.com/index.php

Neuroprotective Effects Of Teneligliptin In An Okadaic Acid-Induced Zebrafish Model Of Alzheimer's Disease

Keerthika Sundaram[1], Arunkumar Radhakrishnan[2], Saravanan Ramachandran[3], Vijayashree Raghavan[4], Caroline Sindhu Paulraj[5], Keranap James Ravichandran[6], Yamuna Vasudevan[7], Rajasekaran Subbarayan[8].

[1,5,6,7]Department of Pharmacology, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

[2]Department of Pharmacology, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

Centre for Herbal Pharmacology and Environmental Sustainability, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

[3]Native Medicine and Marine Pharmacology Laboratory, Faculty of Allied Health Sciences, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

[4]Department of Pathology, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

[8]Centre for Advanced Biotherapeutics and Regenerative Medicine, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

Centre for Herbal Pharmacology and Environmental Sustainability, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

* Corresponding author: arunkumarrvp1978@gmail.com

Abstract: *This study investigated the neuroprotective effects of Teneligliptin, a DPP-4 inhibitor, in an Okadaic Acid (OA)-induced Alzheimer's disease (AD) in zebrafish model. Zebrafish were exposed to OA to induce AD-like features, followed by treatment with Teneligliptin at concentrations of 8, 16, and 32 mg/L. Behavioral tests revealed that Teneligliptin improved anxiety-like behavior and cognitive deficits induced by OA. Antioxidant assays demonstrated that Teneligliptin restored the activities of SOD, CAT, GSH, and GPx while reducing the levels of MDA and AChE. Histopathological evaluation showed that Teneligliptin mitigated OA-induced brain tissue damage. Additionally, Teneligliptin reduced the expression of BACE1 and PSEN1, indicating its potential to regulate amyloidogenic pathways. Overall, Teneligliptin demonstrated neuroprotective effects by improving behavioral outcomes, restoring antioxidant enzyme activity, and reducing histological damage. These findings support the potential therapeutic use of Teneligliptin in neurodegenerative diseases, in addressing the pathophysiology of AD. The study suggests that Teneligliptin may be a promising agent for the treatment of AD, warranting further investigation.*

Keywords: *Teneligliptin, Okadaic Acid, Alzheimer's Disease, Zebrafish, Oxidative Stress, Neuroprotection.*

1. INTRODUCTION

Alzheimer's disease (AD) represents a chronic neurological condition characterized by a reduction in cognitive ability, memory impairments, and extensive neuronal damage (1, 2). The defining neuropathological features of Alzheimer's disease are characterized by an elevated level of amyloid-beta (Aβ) peptides in the extracellular space, leading to the formation of senile plaques, alongside the intracellular aggregation of neurofibrillary tangles (NFTs) that consist of hyperphosphorylated tau protein.

These molecular aberrations disrupt synaptic communication, precipitate neuronal apoptosis, and culminate in pronounced neurodegeneration, particularly affecting the hippocampal and cortical regions, which are critical for learning and memory. Research has linked type 2 diabetes to AD, highlighting insulin resistance, glucose dysregulation, and chronic inflammation as key factors(3, 4). Dipeptidyl peptidase-4 (DPP-4) inhibitors, commonly employed in the treatment of type 2 diabetes mellitus, have garnered attention for their specific neuroprotective properties, in addition to their function in glycemic control.

Teneligliptin is a powerful, long-lasting DPP-4 inhibitor that enhances GLP-1 bioavailability, reduces neuroinflammation and oxidative stress, and improves insulin signaling(5, 6). It is an incretin hormone recognized for its neuroprotective, anti-inflammatory, and antioxidant properties. Okadaic acid (OA) induces tau hyperphosphorylation, neuronal injury, and oxidative stress, mimicking AD pathogenesis.

(7). Zebrafish (Danio rerio) are recognized as crucial organisms for neurodegenerative disease research because of their genetic resemblance to humans, rapid developmental phases, and transparent brain structure, which enables real-time tracking of neurodegenerative processes. This study aimed to assess the neuroprotective effect of Teneligliptin in an OA-induced AD model in zebrafish, targeting neurodegeneration and oxidative stress.

2. MATERIALS AND METHODS

2.1 Zebrafish Husbandry:

Zebrafish were obtained from an L.K. fish farm in Chennai, India, and were maintained under dark and light conditions for 10 - 14 h at 28°C. The eggs were collected through natural spawning, washed, and preserved in E3 medium. Viable eggs were selected for teratogenic analysis after discarding coagulated or damaged ones. (8). The study received ethical approval from the Institutional Animal Ethics Committee (IAEC3/Proposal: 143/A. Lr:106/Dt:28.11.2023) of Chettinad Academy of Research and Education, Kelambakkam, India.

2.2 Assessment of Embryotoxicity:

Embryotoxicity of Teneligliptin was assessed at doses of 1, 2, 4, 8, 16, 32, and 64 µg/mL. The Embryos were examined at 24, 48, and 72 hours post-fertilization (hpf) under a stereomicroscope(9). Embryonic abnormalities such as bent spines, coagulation, and yolk sac edema were recorded.

2.3 Experimental Groups:

Sixty zebrafish were divided into six groups (n=10/Group): control, OA alone, OA with Teneligliptin (8, 16, and 32 mg/L), and OA with Donepezil (positive control). Behavioral assessments were conducted to evaluate the neuroprotective effects of Teneligliptin in OA-induced AD-like neurodegeneration.

2.4 Behavioral Analysis:

Behavioral assessments were conducted between 8 AM and 4 PM on the 21st day of the experiment. Daily water changes were performed according to the OECD guidelines.

2.4.1 Locomotion Activity:

Zebrafish locomotion was assessed in a tank using a GoPro Hero 10 camera. Videos were recorded for 5 min, and the distance traveled and speed were analyzed using ANY-maze software. This activity was used to evaluate the swimming behavior of zebrafish and to calculate the total distance and average speed. (10).

2.4.2 Novel Tank Test:

The Novel Tank test was used to assess fish behavior after OA exposure (11). The fish were placed in a trapezoidal tank, and their movements were recorded for 5 min. Zone duration, zone changeover frequency, and swimming behavior were analyzed from 10-minute video recordings to evaluate behavioral reactions.

2.4.3 Light/Dark Test:

The light-dark test chamber consisted of two compartments of light and dark (black painted) (12). The fish were placed in the light area, and their behavior was recorded for 5 min. Latency to enter the dark, duration in light, and compartment transitions were measured to assess fish behavior and preference.

2.4.4 T-Maze Test:

T-maze test was performed on healthy adult zebrafish in a controlled environment (25–26°C, 50 60% humidity) (13). The maze had one long arm (18 cm) and two short arms (12 cm each), with a 12×12 cm preferred habitat at one end. Fish were laid down at the starting point of the long arm and left to swim freely; food was placed in the green arm, and a continuous motion was created in the red arm. Behavior was recorded for 5 min using a GoPro Hero 10 and analyzed using ImageJ for time spent, transitions, swimming patterns, and preference, followed by statistical comparison.

2.5 Antioxidant Enzyme Level:

The Antioxidant assays were performed in the harvested brain tissue following a 21-day terminal procedure. The kit methods were utilized to study the SOD (Cat # MBS036924, MyBioSource, USA) (14), CAT (Cat # E-BC-K031-S) (15), GSH (Cat # MBS2000256, MyBioSource, USA) (16), GPx (Cat # MBS744364, MyBioSource, USA) (17), MDA (Cat # MBS2000071, MyBioSource, USA) (16) and AChE (Cat # MBS8243242, MyBioSource, USA) (18). Activity by using manufactured instruction, and absorbance was recorded to determine the antioxidant effect in the experimental groups.

2.6 Histopathology:

Zebrafish were anesthetized with 0.1% Tricaine, and the whole brain was excised and fixed in 10% neutral buffered formalin. Fixed tissues were processed using an automated system involving sequential

dehydration with graded alcohols (95% and absolute), clearing with xylene, and infiltration with liquid paraffin. Paraffin-embedded tissues were sectioned at 3 μm thickness, mounted on slides, and stained with H&E using DAKO staining kits (Denmark).

2.7 Gene Expression Analysis:

2.7.1 Brain Tissue Processing:

Zebrafish brain tissue was homogenized using liquid nitrogen and TRIzol. The homogenate was centrifuged, and the upper aqueous layer was collected into a clean tube for subsequent processing.

2.7.2 Total Ribonucleic acid Isolation:

RNA was extracted using TRIzol and chloroform, followed by centrifugation and precipitation with isopropanol. The RNA pellet was rinsed with cold ethanol, air-dried, and dissolved in RNase-free water, resulting in high-purity RNA for molecular analysis.

2.7.3 RT-PCR Analysis:

RT-PCR was performed using the Quant Studio Real-Time PCR System. RT-PCR analysis was performed on PSEN1 and BACE1. The primer sequences are presented in [Table 1]. Complementary DNA (cDNA) was synthesized from 500 ng of total RNA using a reverse transcription kit, following the manufacturer's protocol. RT-PCR reactions were prepared with SYBR Green master mix, gene-specific forward and reverse primers (optimized to a final concentration of 0.1–0.5 μM), and cDNA template in a final volume of 20 μL. Thermal cycling was conducted with a primary denaturation at 95°Celsius for 2 minutes, followed by 40 cycles of 95°Celsius for 15 seconds and 60°Celsius for 30 seconds. Specificity was confirmed through melt curve analysis. Relative gene expression was estimated using the 2^(-ΔΔCt) method, normalizing target gene expressions (PSEN1 and BACE1) with β-actin.

Table 1: Primer sequences:

Primer Name	Forward	Reverse
PSEN1	5'-GTGCTGACCGTGCTGAAGAT-3'	5'-CCAGAGGAGACCTGTGAGGA-3'
BACE1	5'-GACATGGCAGACTTTGTGGA-3'	5'-TTCAGGTGGTAGCCTTCAGC-3'
β-actin	5'-TGCCCCTCGTGCTGTTTT-3'	5'-TCTGTCCCATGCCAACCAT-3'

2.8 Statistical Analysis:

The data were gathered and analyzed using GraphPad Prism 10.4 software. A one-way ANOVA followed by post-hoc Bonferroni's multiple comparison test was performed. Statistical significance was determined as "$p^* < 0.05$, $p^{**} < 0.01$, and $p^{***} < 0.001$".

3. RESULTS AND DISCUSSION

3.1 Zebrafish Embryotoxicity:

The teratogenic effects of Teneligliptin were evaluated using zebrafish embryos at dosages of 1-64 μg/ml (Figure 1). No significant toxicity was observed up to 32 μg/ml, but substantial teratogenic effects were seen at higher doses. Adverse effects included yolk sac diffusion, embryo sac anomalies, decreased chorionic membrane size, potentially impaired development, and increased mortality.

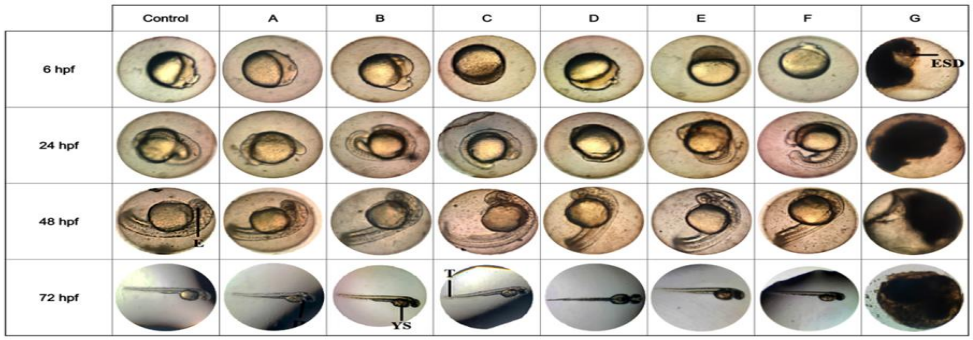

Figure 1: Morphological assessment of zebrafish embryos following exposure to varying concentrations of Teneligliptin (TGP) (1, 2, 4, 8, 16, 32, and 64 μg/mL). Embryos in the control group exhibited normal development without observable malformations. Test groups A–F displayed comparable morphology to the control, lacking any abnormalities such as notochord distortion or embryonic sac defects, indicating

group F corresponds to the LD_{50} threshold. In contrast, group G exhibited prominent embryo sac deformities. Abbreviations: E – Eye; T – Tail; YS – Yolk Sac; ESD – Embryo Sac Deformities.

3.2 Behavioral Analysis:

3.2.1 Locomotion Activity:

Adult zebrafish were utilized to evaluate Teneligliptin's impact on OA-induced locomotor deficits (Figure 2). OA exposure significantly impaired mobility (44.95 ± 22.9 cm) compared to control (302.32 ± 7.5 cm). Teneligliptin (8–32 mg/L) dose-dependently enhanced locomotion (70.07 ± 12.5, 111.08 ± 23.55, and 163 ± 14.4 cm) when compared to donepezil (178 ± 19.87 cm). The results obtained from OFT, trackplot, and heat map (Figure 2 A-F) suggested that Teneligliptin (32mg/L) effectively attenuated OA-induced locomotor impairments in zebrafish. Furthermore, Quantitative analysis of behavioral changes was represented in the bar graph (Figure 2 G).

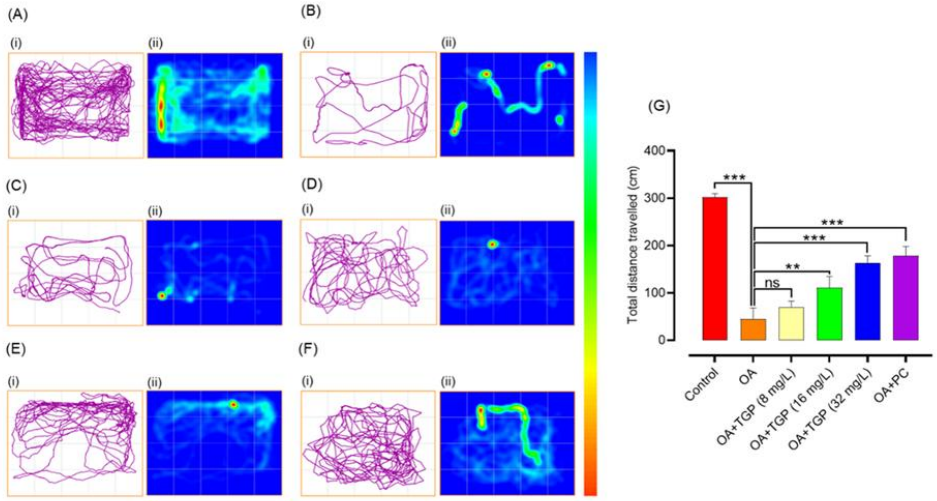

Figure 2: Locomotor activity patterns in zebrafish under different treatment condition. (A-F) Representative locomotor trajectories in the open-field test using the track plot (A-F: i) and heat map (A-F: ii): (A) Control, (B) OA, (C) OA+TGP (8 mg/L), (D) OA+TGP (16 mg/L), (E) OA+TGP (32 mg/L), and (F) OA+PC. (G) Bar graph showing total distance traveled by zebrafish across the treatment groups.

3.2.2 Novel Tank Test:

The Novel Tank Test (NTT) evaluated anxiety-like behaviors in zebrafish (Figure 3a &b). OA-treated zebrafish spent less time in the upper tank (45.66 ± 1.8 s) and more time in the lower tank (197.33 ± 4.7 s), indicating increased anxiety. Teneligliptin treatment increased the time spent by the zebrafish in the upper tank at a 32 mg/L dose (79.66 ±0.8 s) and decreased time in the lower tank (134.33 ± 1.8 s). The positive control group showed similar time spent in both upper and lower tanks as the control group. These findings suggested Teneligliptin's potential anxiolytic effects in OA-treated zebrafish.

3.2.3 Light/Dark Test:

Zebrafish behavior was assessed in a light/dark preference test. OA-treated zebrafish showed increased anxiety, spending less time in light (163.66 ± 1.1 s) and more time in dark (176.33 ± 1.2 s) (Figure 3c & d). Teneligliptin administration ameliorated the condition in a dose-dependent way by increasing the duration spent in the light zone and decreasing the time spent in the dark zone. The highest dose (32 mg/L) produced a marked effect, with zebrafish spending 241.33 ± 0.2 seconds in the light zone and 128.66 ± 0.07 seconds in the dark zone. These findings suggested Teneligliptin's potential anxiolytic effects in OA-treated zebrafish, reducing anxiety-like responses.

3.2.4 T-maze Test:

The T-maze test evaluated cognitive function and spatial memory in zebrafish (Figure 3e & f). The OA-treated group showed cognitive decline, with reduced entries into the green phase (0.33 ± 0.09) and increased entries into the red phase (9 ± 0.12). Teneligliptin treatment improved performance in a dose-dependent way. At 8 mg/L, fish made 3 ± 0.04 entries into the green phase and 6 ± 0.14 entries into the red phase. At 16 mg/L, fish made 5.33 ± 0.9 entries into the green phase and 5 ± 0.07 entries into the red phase. At 32 mg/L, Teneligliptin significantly improved performance, with 6.66 ± 0.2 entries into the green phase and 3 ± 0.04 entries into the red phase. These findings indicate that Teneligliptin exhibits dose-dependent cognitive-enhancing effects, with the highest dose showing efficacy comparable to

donepezil. Notably, the Donepezil group performed similarly to the control group, highlighting Teneligliptin's potential as a therapeutic agent for cognitive impairment.

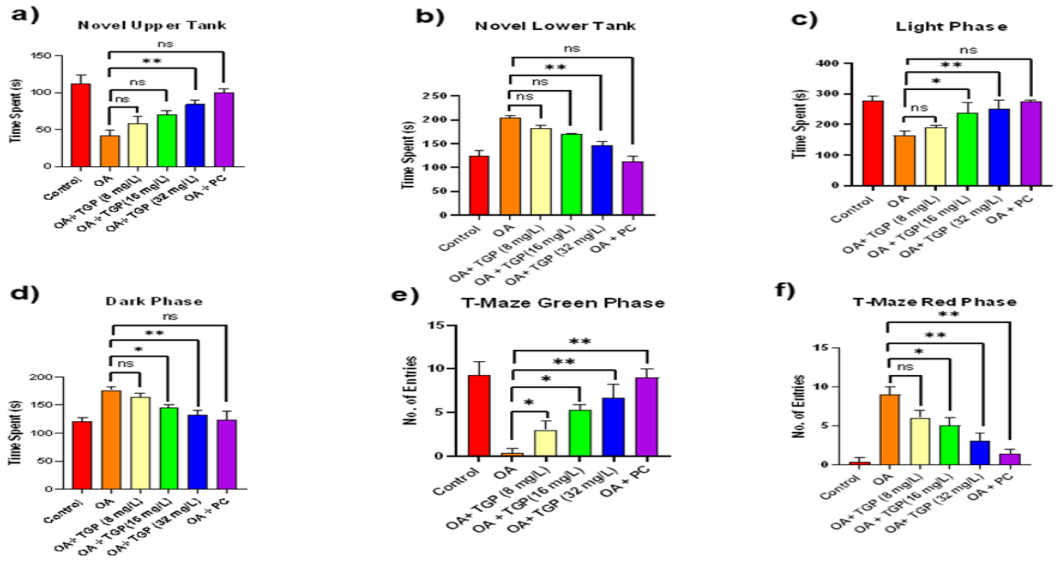

Figure 3: Behavioral analysis in different test paradigms: Novel Upper Tank (a), Novel Lower Tank (b), Light Phase (c), Dark Phase (d), T-Maze Green Phase (e), and T-Maze Red Phase (f).

3.3 Antioxidant Enzyme Level:

This study evaluated teneligliptin's impact on oxidative stress in zebrafish. OA treatment reduced SOD, CAT, GSH, and GPx levels, indicating increased oxidative stress. Teneligliptin treatment dose-dependently increased these antioxidant markers. At 32 mg/L, Teneligliptin significantly elevated SOD (1.23 ± 0.09 U/mg protein) (Figure 4 a), CAT (32.22 ± 4.9 U/mg protein) (Figure 4 b), GSH (1.38 ± 0.08 µmol/g protein) (Figure 4 c), and GPx (3.28 ± 0.12 U/mg protein) (Figure 4 d) levels, demonstrating its potential to mitigate oxidative damage. The positive control (Donepezil) showed comparable efficacy to Teneligliptin at 32 mg/L in restoring these antioxidant markers. Notably, Teneligliptin's effects on GSH and GPx levels were dose-dependent, with higher doses exhibiting more pronounced antioxidant effects.

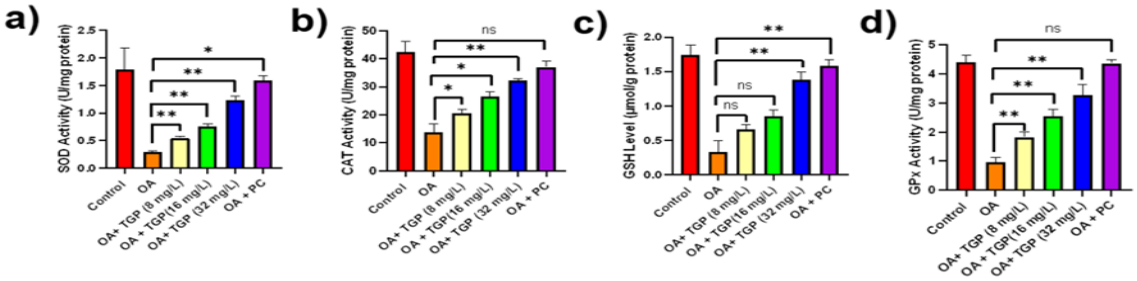

Figure 4: Quantitative assessment of antioxidant enzyme activities, including superoxide dismutase (SOD) (a), catalase (CAT) (b), reduced glutathione (GSH) (c), and glutathione peroxidase (GPx) (d).

3.4 Neurobiomarker Enzyme Level:

This study investigated the effects of Teneligliptin on AChE activity and MDA levels in OA-induced neurotoxicity in zebrafish (Figure 5a & b). OA treatment increased AChE activity (10.64 ± 0.32 U/mg protein) and MDA levels (8.06 ± 0.27 nmol/g protein), indicating cholinergic dysfunction and oxidative stress. Teneligliptin treatment dose-dependently decreased AChE activity and MDA levels. At 32 mg/L, teneligliptin significantly reduced AChE activity (4.69 ± 0.21 U/mg protein) and MDA levels (5.89 ± 0.24 nmol/g protein), demonstrating its potential to mitigate cholinergic dysfunction and oxidative damage. The positive control (Donepezil) showed comparable efficacy to Teneligliptin at 32 mg/L in reducing AChE activity (5.99 ± 0.36 U/mg protein) and MDA levels (5.69 ± 0.18 nmol/g protein). Overall, teneligliptin showed a promising therapeutic agent for mitigating neurotoxicity and oxidative stress, although its efficacy may vary compared to traditional therapies as equal of Donepezil.

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 20s, 2025
https://theaspd.com/index.php

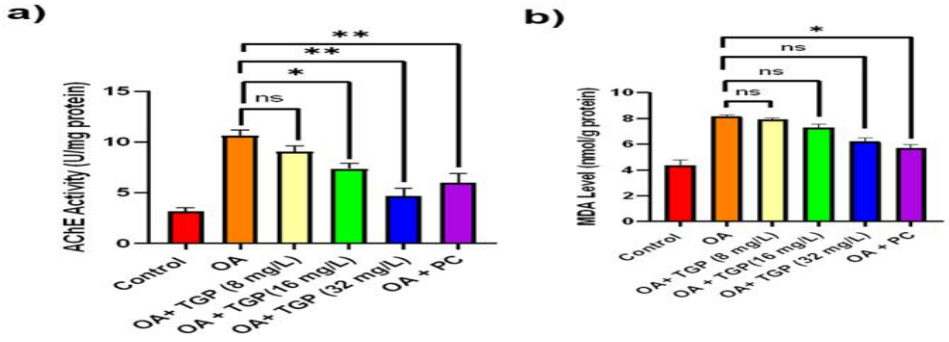

Figure 5. Quantification of Neurobiomarker enzyme levels: acetylcholinesterase (AChE) (a) and malondialdehyde (MDA) (b).

3.5 Histopathological Evaluation:

Teneligliptin treatment reduced OA-induced brain damage in zebrafish in a dose-dependent way, with the highest concentration (32 mg/L), which showed significant protection, including limited edema and cystic changes mainly in the granular layer (Figure 6).

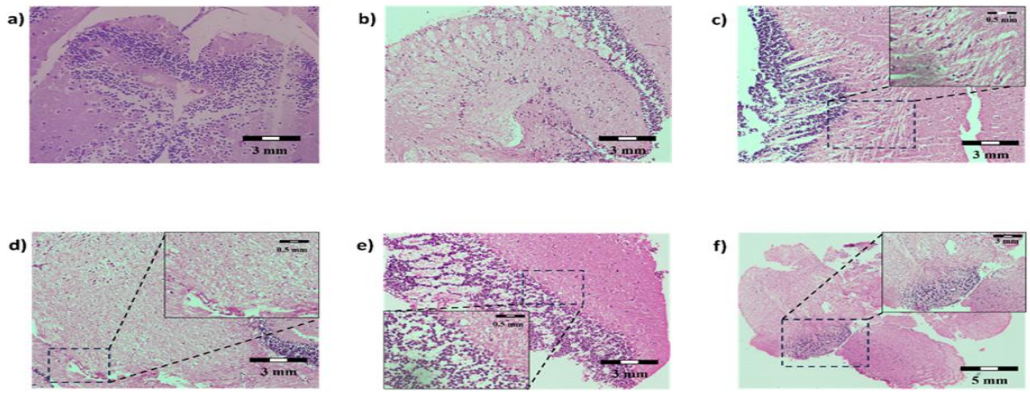

Figure 6. Representative H&E-stained sections showing histological features of brain tissue in different experimental groups: Control (a), Okadaic acid (OA)-induced group (b), OA + Teneligliptin at 8 mg/L (c), OA + Teneligliptin at 16 mg/L (d), OA + Teneligliptin at 32 mg/L (e), and OA + Positive control (Donepezil 0.046 µg/mL) (f).

3.6 Gene Expression and RT-PCR:

OA treatment increased BACE1 (2.6-fold) and PSEN1 (3.1-fold) mRNA levels, indicating amyloidogenic activation in the cells. TGP treatment decreased BACE1 and PSEN1 expression in a dose-dependent manner (Figure 7). At 32 mg/L, TGP significantly reduced BACE1 (1.3-fold) and PSEN1 (1.7-fold) expressions. The positive control group showed similar reductions in BACE1 (1.4-fold) and PSEN1 (1.3-fold) expressions. These results suggested that TGP mitigates OA-induced overexpression of AD-associated genes. TGP's effects on gene expression may contribute to its potential therapeutic benefits.

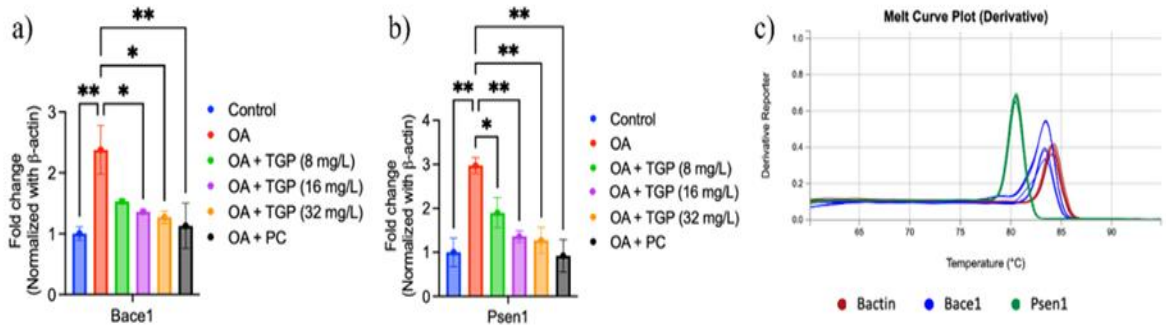

Figure 7. Gene expression analysis of Alzheimer 's-related markers: β-site amyloid precursor protein cleaving enzyme 1 (BACE1) (a), Presenilin 1 (PSEN1) (b), and corresponding melt curve analysis validating the specificity of amplification (c).

4. CONCLUSION

To sum up, Teneligliptin demonstrated significant neuroprotective potential in a zebrafish model of Okadaic acid-induced neurotoxicity. It effectively improved locomotor activity, reduced anxiety-like behavior, attenuated oxidative stress, and restored cholinergic function. Furthermore, Teneligliptin minimized neuronal damage and exhibited notable anti-apoptotic effects, with higher doses showing efficacy comparable to the standard therapeutic agent, Donepezil. These promising outcomes supported the potential repositioning of Teneligliptin for the management of neurodegenerative diseases. Future studies involving advanced molecular approaches and translational models are warranted to further elucidate its mechanisms of action and therapeutic relevance.

Ethical Approval:

The study was approved by the Institutional Animal Ethical Committee (IAEC 3/Proposal: 143 /A. Lr:106/Dt:28.11.2023) at the Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu 603 103

Conflict of Interest:

The authors declare that there are no conflicts of interest that could have appeared to influence the work reported in this manuscript.

Data Availability Statement:

On reasonable request, the data underpinning this study may be obtained from the corresponding author.

Funding:

This research was funded by the Chettinad Hospital and Research Institute, CARE, Tamil Nadu, India.

List of Abbreviations:

AD-Alzheimer Disease
Aβ-Amyloid-beta
NFT-Neurofibrillary tangle
TGP-Teneligliptin
OA-Okadaic acid
PC-Positive control
OECD-Organization for Economic Co-operation and Development
MDA-Malondialdehyde
AChE-Acetylcholinesterase
CAT-Catalase
GPx-Glutathione peroxidase
SOD-Sodium Dismutase
GSH-Glutathione reductase
H&E-Hematoxylin-eosin
RNA-Ribonucleic acid

REFERENCES

1. Safiri S, Ghaffari Jolfayi A, Fazlollahi A, Morsali S, Sarkesh A, Daei Sorkhabi A, et al. Alzheimer's disease: a comprehensive review of epidemiology, risk factors, symptoms diagnosis, management, caregiving, advanced treatments and associated challenges. Frontiers in Medicine. 2024;11:1474043. https://doi.org/10.3389/fmed.2024.1474043
2. García-Morales V, González-Acedo A, Melguizo-Rodríguez L, Pardo-Moreno T, Costela-Ruiz VJ, Montiel-Troya M, et al. Current understanding of the physiopathology, diagnosis and therapeutic approach to Alzheimer's disease. Biomedicines. 2021;9(12):1910.https://doi.org/10.3390/biomedicines
9121910
3. Michailidis M, Moraitou D, Tata DA, Kalinderi K, Papamitsou T, Papaliagkas V. Alzheimer's disease as type 3 diabetes: common pathophysiological mechanisms between Alzheimer's disease and type 2 diabetes. International journal of molecular sciences.2022;23(5):2687.https://doi.org/10.3390/
ijms23052687
4. Ramasubbu K, Devi Rajeswari V. Impairment of insulin signaling pathway PI3K/Akt/mTOR and insulin resistance induced AGEs on diabetes mellitus and neurodegenerative diseases: a perspective review. Molecular and Cellular Biochemistry. 2023;478(6):1307-24. https://doi.org/10.1007/s11010-022-04587-x
5. Alharbi SH. Anti-inflammatory role of glucagon-like peptide 1 receptor agonists and its clinical implications. Therapeutic Advances in Endocrinology and Metabolism. 2024; 15:20420188231222367. https://doi.org/10.1007/s43440-023-00500-5
6. Mouhammad ZA, Vohra R, Horwitz A, Thein A-S, Rovelt J, Cvenkel B, et al. Glucagon-like peptide 1 receptor agonists–potential game changers in the treatment of glaucoma? Frontiers in Neuroscience. 2022;16:824054. https://doi.org/10.3389/fnins.2022.824054
7. Arribas RL, Viejo L, Bravo I, Martínez M, Ramos E, Romero A, et al. C-glycosides analogues of the okadaic acid central fragment exert neuroprotection via restoration of PP2A-phosphatase activity: A rational design of potential drugs for

Alzheimer's disease targeting tauopathies. 2023. https://doi.org/
10.1016/j.ejmech.2023.115245
8. Subbarayan R, Barathidasan R, Raja ST, Arumugam G, Kuruvilla S, Shanthi P, et al. Human gingival derived neuronal cells in the optimized caffeic acid hydrogel for hemitransection spinal cord injury model. Journal of cellular biochemistry. 2020;121(3):2077-88. https://doi.org/10.1002/jcb.29452
9. Cassar S, Beekhuijzen M, Beyer B, Chapin R, Dorau M, Hoberman A, et al. A multi-institutional study benchmarking the zebrafish developmental assay for prediction of embryotoxic plasma concentrations from rat embryo–fetal development studies. Reproductive Toxicology. 2019; 86:33-44. https://doi.org/10.1016/j.reprotox.2019.02.004
10. Chen K, Wu M, Chen C, Xu H, Wu X, Qiu X. Impacts of chronic exposure to sublethal diazepam on behavioral traits of female and male zebrafish (Danio rerio). Ecotoxicology and Environmental Safety. 2021; 208:111747. https://doi.org/10.1016/j.ecoenv.2020.111747
11. Harini K, Alomar SY, Vajagathali M, Manoharadas S, Thirumalai A, Girigoswami K, et al. Niosomal bupropion: Exploring therapeutic frontiers through behavioral profiling. Pharmaceuticals. 2024;17(3):366. https://doi.org/10.3390/ph17030366
12. Rishitha N, Muthuraman A. Therapeutic evaluation of solid lipid nanoparticle of quercetin in pentylenetetrazole induced cognitive impairment of zebrafish. Life sciences. 2018; 199:80-7. https://doi.org/10.1016/j.lfs.2018.03.010
13. Amoah V, Atawuchugi P, Jibira Y, Tandoh A, Ossei PPS, Sam G, et al. Lantana camara leaf extract ameliorates memory deficit and the neuroinflammation associated with scopolamine-induced Alzheimer's-like cognitive impairment in zebrafish and mice. Pharmaceutical Biology. 2023;61(1):825-38. https://doi.org/10.1080/13880209.2023.2209130
14. Issac PK, Lite C, Guru A, Velayutham M, Kuppusamy G, Saraswathi N, et al. Tryptophan-tagged peptide from serine threonine-protein kinase of Channa striatus improves antioxidant defence in L6 myotubes and attenuates caspase 3–dependent apoptotic response in zebrafish larvae. Fish physiology and biochemistry. 2021; 47:293-311. https://doi.org/10.1007/s10695-020-00912-7
15. Janarathanam VA, Issac PK, Pan I, Kamaraj N, Ansar S, Kumar YA, et al. Investigating antioxidant effects of hamamelitannin-conjugated zinc oxide nanoparticles on oxidative stress-Induced neurotoxicity in zebrafish larvae model. Molecular Biology Reports.2024;51(1):1087.https://doi.org/10.1007/
s11033-024-09998-1
16. Vijayanand M, Issac PK, Velayutham M, Shaik MR, Hussain SA, Guru A. Exploring the neuroprotective potential of KC14 peptide from Cyprinus carpio against oxidative stress-induced neurodegeneration by regulating antioxidant mechanism. MolecularBiologyReports.2024;51(1):990.https://doi.org/
10.1007/s11033-024-09905-8
17. Brinza I, Boiangiu RS, Honceriu I, Abd-Alkhalek AM, Eldahshan OA, Dumitru G, et al. Investigating the Potential of Essential Oils from Citrus reticulata Leaves in Mitigating Memory Decline and Oxidative Stress in the Scopolamine-Treated Zebrafish Model. Plants. 2024;13(12):1648. https://doi.org/
10.3390/plants13121648
18. Amaral I, Antunes SC, Rebelo D, Carvalho AP, Rodrigues S. Biopesticide spinosad: Unraveling ecotoxicological effects on zebrafish, Danio rerio. Environmental toxicology and pharmacology. 2024; 108:104458.
https://doi.org/10.1016/j.etap.2024.104458