ECMC-P 2025 Conference

The 1st International Electronic Conference on Medicinal Chemistry and Pharmaceutics

01–30 November 2025 | Online

MDPI

Mansonone G as a Natural Neuroprotective Compound in a Zebrafish Model of Alzheimer's Disease

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INTRODUCTION & AIM

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that affects millions of individuals worldwide and imposes a significant socio-economic burden. The high costs of long-term care, combined with the limited efficacy and adverse effects of current treatments, have prompted increasing interest in natural compounds with therapeutic potential. Mansonone G, a bioactive compound derived from *Mansonia gagei*, has been reported to possess antioxidant and anti-inflammatory properties. This study aimed to investigate the effects of Mansonone G on memory, using zebrafish (*Danio rerio*) as a preclinical model for AD.

METHOD

To establish an Alzheimer's disease-like amnesia model, zebrafish (*Danio rerio*) were exposed to okadaic acid (OKA, 10 nM) for 4 days.

The animals were randomly assigned to six groups (n = 10 per group):

1.Control: dimethyl sulfoxide (DMSO)
2.Galantamine (1 mg/L): positive control
3.OKA (10 nM) + DMSO (6 µg/L): amnesia model
4.OKA + Mansonone G 1 (1 µg/L)
5.OKA + Mansonone G 3 (3 µg/L)
6.OKA + Mansonone G 6 (6 µg/L)

Mansonone G was administered every 3 days over a 7-day period, with regular water changes.
Cognitive function was evaluated using:
•**Y-maze test:** to assess spatial memory and locomotor activity
•**Novel Object Recognition (NOR) test:** to evaluate recognition memory
Data were analyzed using GraphPad Prism 9. Statistical significance was determined by one-way ANOVA followed by Tukey's post hoc test, with $p < 0.05$ considered significant.

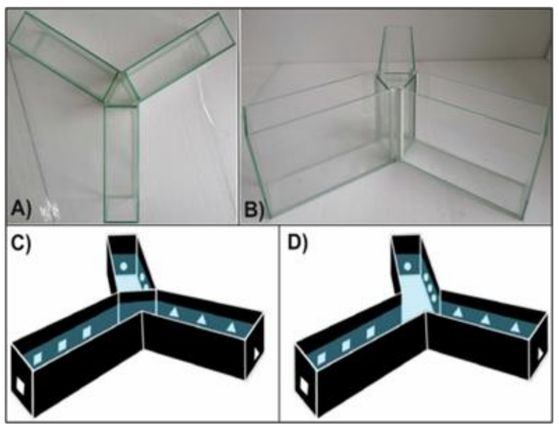

Figure 1. Diagram of the Y-maze used for behavioral testing: top view (A) and side view (B). Panels (C) and (D) depict the maze setup during the training and testing sessions, respectively. During training, the novel arm was blocked with a sliding glass plate (C), while in the testing session, the novel arm was accessible (D). Visual cues were positioned along the sides and at the end of each arm.

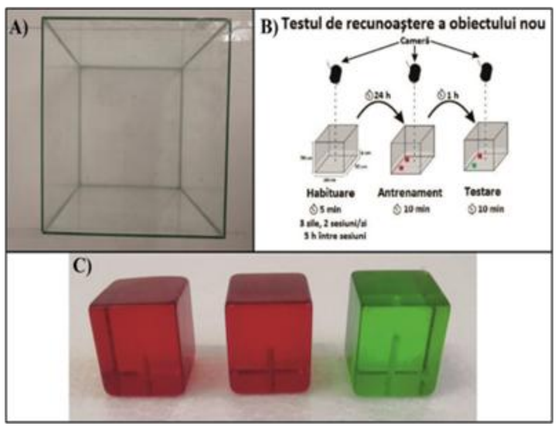

Figure 2. (A) Aquarium used for the Novel Object Recognition (NOR) test. (B) Experimental timeline: adult zebrafish were acclimated to the test aquarium for 3 consecutive days, with two sessions per day separated by a 5-hour interval. On day 4, a 10-minute training session was conducted using two identical familiar objects (F), followed one hour later by a 10-minute test session, during which one familiar object was replaced with a novel object (N). (C) Objects employed during the training and test sessions.

RESULTS & DISCUSSION

Exposure to OKA significantly impaired:

- Spatial memory (Y-maze test).
- Object recognition (NOR test) ($p < 0.0001$ vs. control group).

Treatment with Galantamine (1 mg/L) reversed these deficits, confirming the validity of the experimental model.

Mansonone G at doses of 3 and 6 µg/L:

-Significantly improved cognitive performance ($p < 0.001$–0.00001).
-Increased time spent in the novel arm (Y-maze).
-Enhanced preference for the novel object (NOR).
-Stimulated locomotor activity

The 1 µg/L dose of Mansonone G did not produce significant effects.

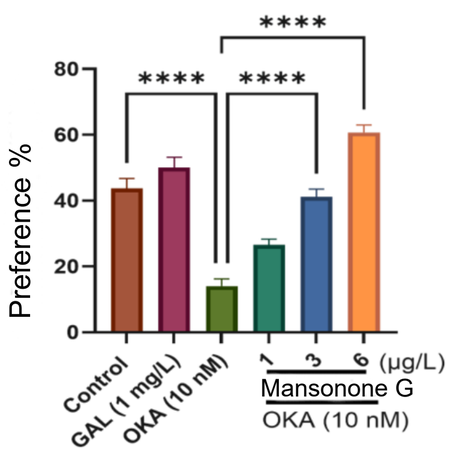

Figure 3. Effects of Mansonone G (MG; 1, 3, and 6 µg/L) on the percentage preference in the Novel Object Recognition (NOR) test in zebrafish treated with OKA (10 nM). Data are presented as mean ± SEM (n = 10 per group). ****$p < 0.00001$ versus the OKA group.

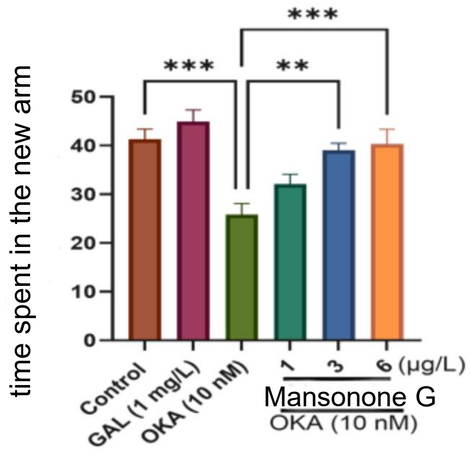

Figure 4. Effects of Mansonone G (MG; 1, 3, and 6 µg/L) on the time spent in the novel arm in the Y-maze test in zebrafish treated with OKA (10 nM). Data are presented as mean ± SEM (n = 10 per group). **$p < 0.001$; ***$p < 0.0001$ compared with the OKA group.

CONCLUSION

Mansonone G increased exploratory activity in OKA-treated zebrafish (Y-maze), enhanced memory performance in the Novel Object Recognition (NOR) test, and restored brain cholinergic function, thereby improving dementia-related symptoms.

REFERENCES

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