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An Investigation of the Effects of Mansorin on Memory Processes in a Zebrafish (*Danio rerio*) Animal Model

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INTRODUCTION & AIM

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that affects millions of people worldwide, with a major socio-economic impact.

The high costs associated with long-term patient care, together with the limited efficacy and adverse effects of current therapies, stimulate interest in natural compounds with therapeutic potential. Mansorine (MA), a coumarin compound extracted from *Mansonia gagei*, is known for its antioxidant and anti-inflammatory properties. The aim of this study was to evaluate the effects of MA on memory, using zebrafish (*Danio rerio*) as a preclinical model for AD.

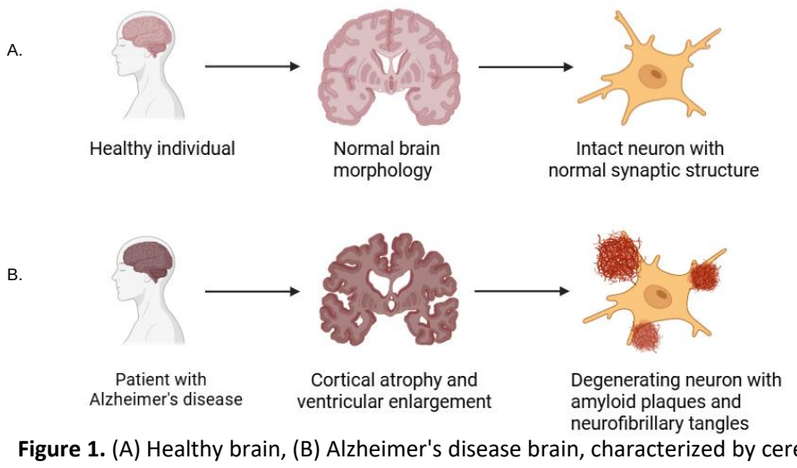

Figure 1. (A) Healthy brain, (B) Alzheimer's disease brain, characterized by cerebral atrophy, accumulation of extracellular β-amyloid plaques, and neurofibrillary tangles formed by hyperphosphorylated tau protein. These changes lead to synaptic dysfunction, neuronal loss, and impaired cognitive function. Figure created with BioRender.com.

METHOD

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

Animals were divided into 6 groups (n = 10/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 + MA 1 (1 µg/L)
5. OKA + MA 3 (3 µg/L)
6. OKA + MA 6 (6 µg/L)

MA was administered every 3 days during a 7-day period, with water changes accordingly.

Cognitive function was assessed by:

- Y-maze – spatial memory and locomotor activity
- NOR (Novel Object Recognition) – recognition of novel objects

Statistical analysis was performed in GraphPad Prism 9, using ANOVA followed by Tukey's test, with a significance threshold of $p < 0.05$.

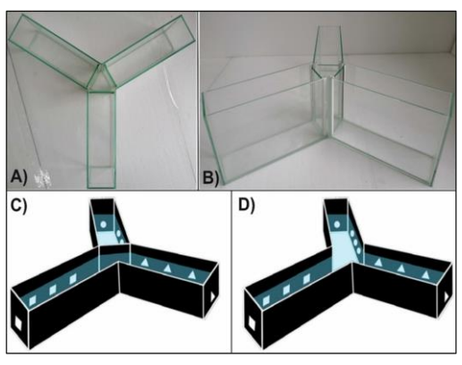

Figure 2. Illustration of the Y-maze used in testing: top view (A) and side view (B). The schematic representation shows the maze configuration during the training session, when the novel arm was blocked with a sliding glass plate (C), and during the testing session, when the novel arm was open (D). Visual cues were placed on the sides and behind each arm.

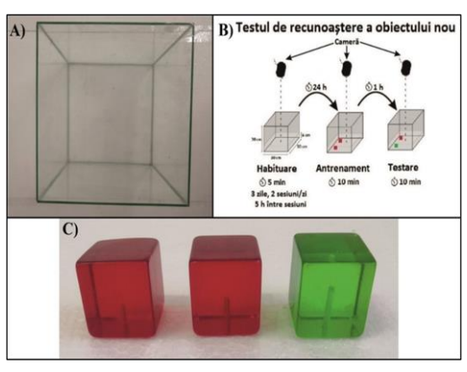

Figure 3. (A) Aquarium used for the novel object recognition (NOR) test. (B) Experimental design: adult zebrafish were housed in the test aquarium for 3 consecutive days (2 sessions per day, with a 5-hour interval between sessions). On the fourth day, they were subjected to a training session (10 minutes, with two familiar objects – F), followed, after one hour, by a test session (10 minutes), in which one of the familiar objects was replaced by a novel object (N). (C) Objects used in the training and test sessions.

RESULTS & DISCUSSION

OKA significantly affected:

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

Galantamine (1 mg/L) reversed these deficits, validating the experimental model.

MA at doses of 3 and 6 µg/L:

- significantly improved cognitive performance ($p < 0.001 – 0.00001$)
- increased time exploring the novel arm (Y-maze)
- increased preference for the novel object (NOR)
- stimulated locomotor activity
- The 1 µg/L MA dose did not produce significant effects.

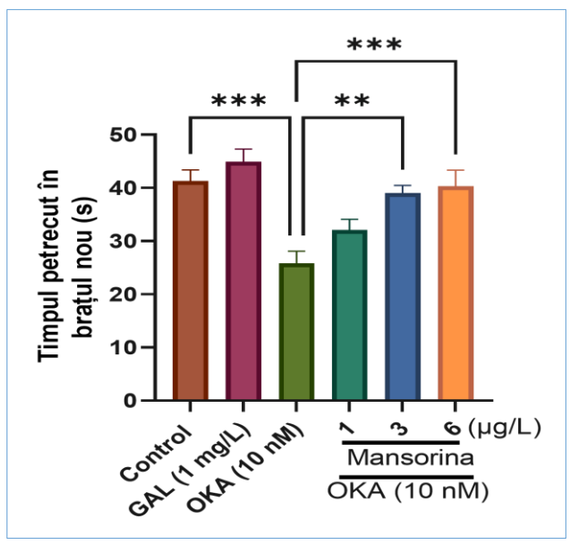

Figure 4. Effects of MA (1, 3 and 6 µg/L) on the time spent in the novel arm in the Y-maze test in fish treated with OKA (10 nM). Values are expressed as mean ± SEM, n = 10 animals/group. **p < 0.001; ***p < 0.0001 versus OKA group.

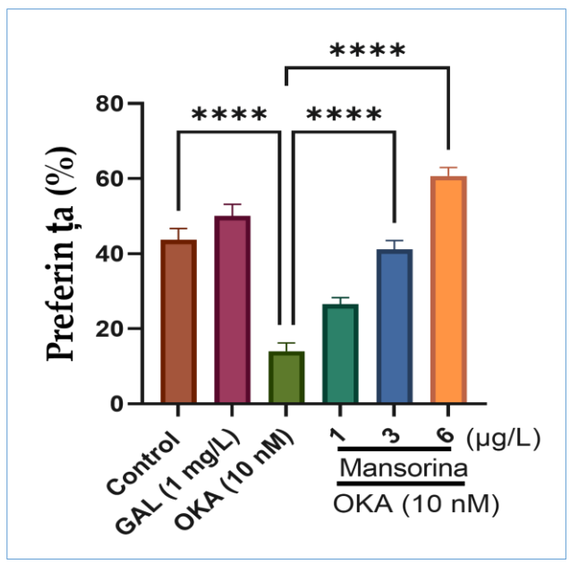

Figure 5. Effects of MA (1, 3 and 6 µg/L) administration on the percentage of preference in the novel object recognition (NOR) test in fish treated with OKA (10 nM). Values are expressed as mean ± SEM, n = 10 animals/group. ****p < 0.00001 compared to the OKA group.

CONCLUSION

- MA increased exploratory activity in OKA-treated animals (Y-maze).
- MA enhanced memory performance in the NOR test.
- MA restored brain cholinergic function and improved dementia symptoms.

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