

Computer-Assisted Drug Repurposing And *In Vivo* Validation

Identify Doxazosin As An Anti-Alzheimer's Candidate

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Computer-assisted drug repurposing identified doxazosin as a promising candidate for Alzheimer's disease, with in vivo validation confirming its neuroprotective potential.

Problem Statement

Alzheimer's disease (AD) affects over 55 million people globally, with no curative therapy available. Current drugs like Donepezil only provide symptomatic relief, while new drug development is slow (10–15 years) and costly (> \$2 billion). Thus, there is an urgent need for faster, cost-effective, and safer therapeutic solutions.

Proposed Scientific Approach

This study employs a computer-assisted drug repurposing pipeline that combines in-silico modeling, network pharmacology, and in-vivo validation (zebrafish & mouse models) to investigate mechanistic pathways of FDA-approved drugs with potential relevance

Aim & Objectives

Scientific investigation of repurposed FDA-approved drugs for Alzheimer's disease using computational and in vivo approaches to understand mechanistic pathways

1. Computational Drug Repurposing

- Target Identification
- Ligand Selection
- Shape and Electrostatic similarity using ROCS
- Docking and MD simulations
- Network Pharmacology

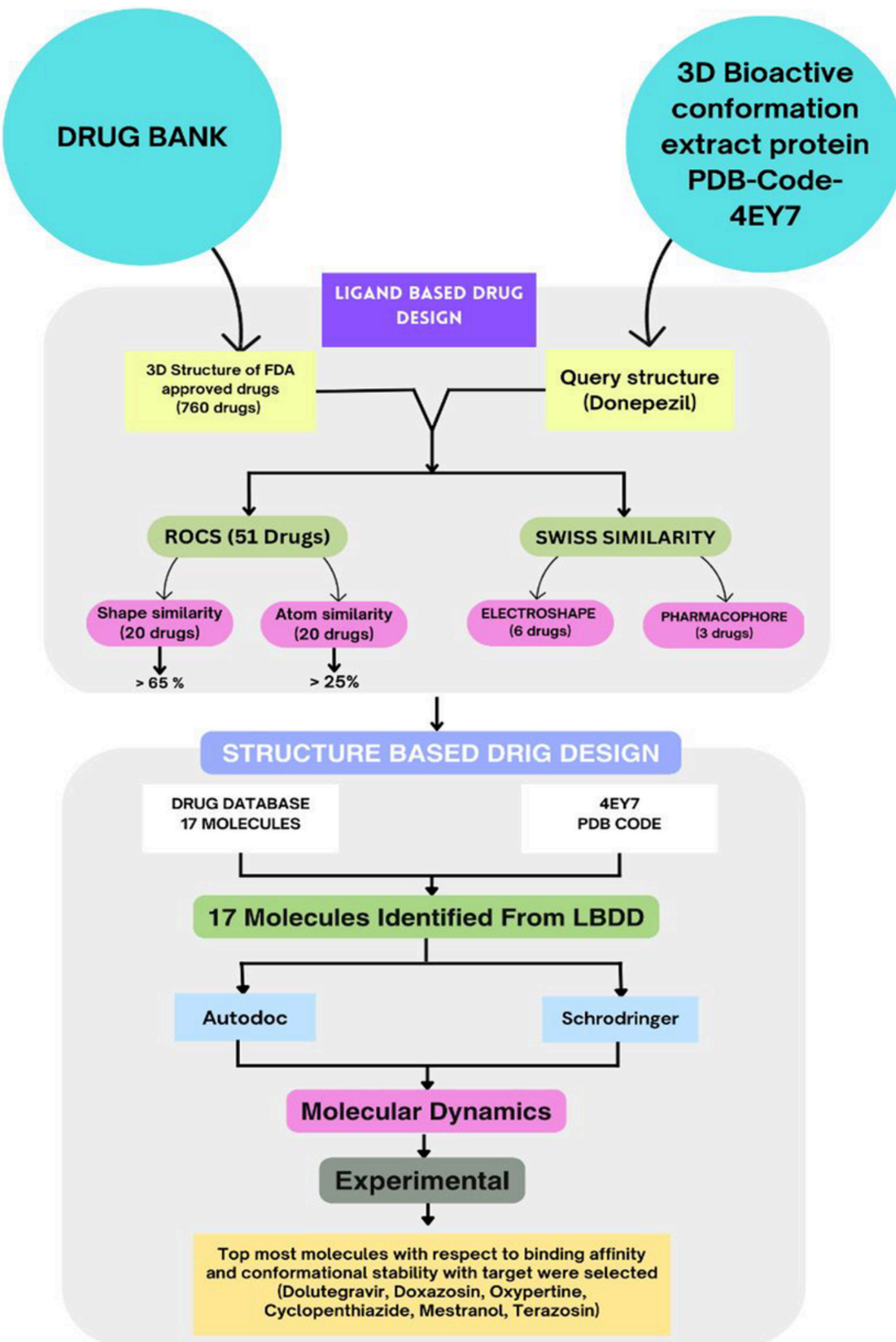
2. In-vivo Pharmacological Screening

- Evaluation of anti-Alzheimer activity using the Zebrafish Model
- Evaluation of anti-Alzheimer activity using an Animal Study

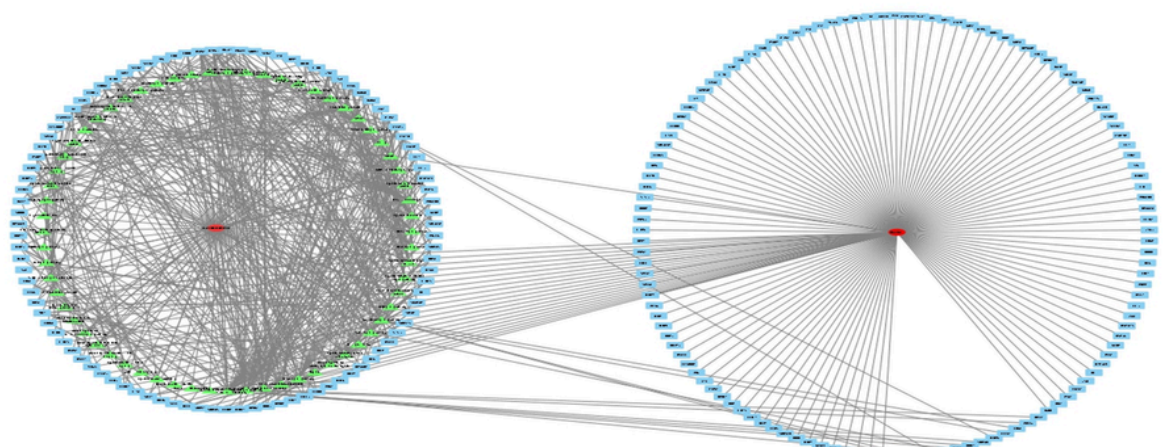
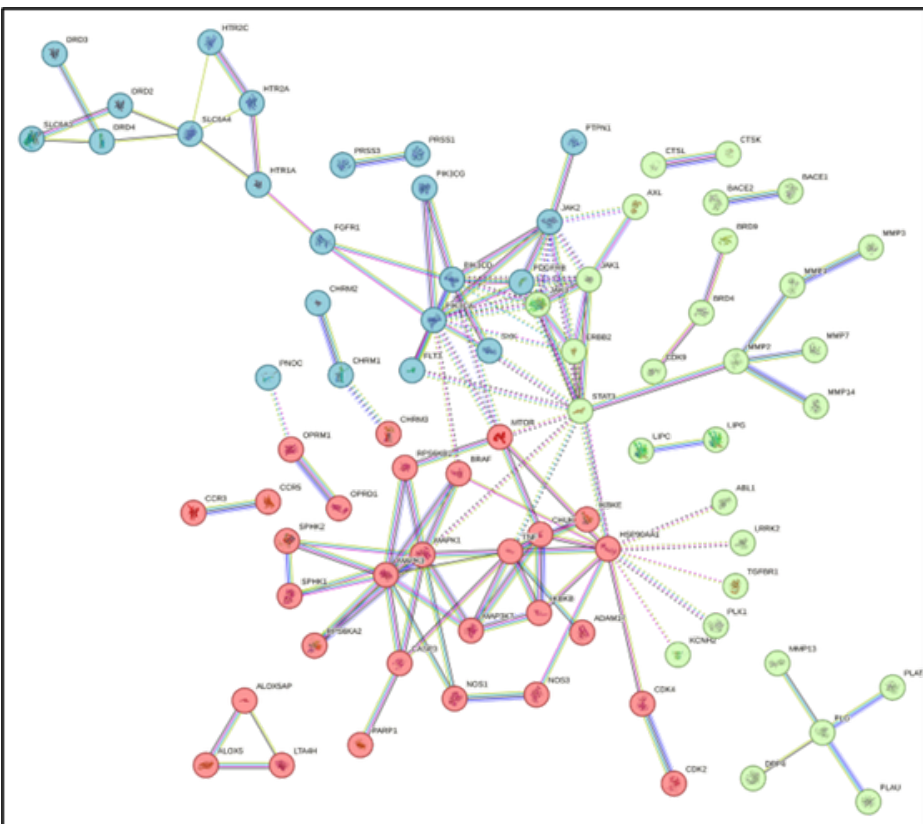
SCIENTIFIC SIGNIFICANCE

- Provides mechanistic insights into drug-target interactions in Alzheimer's disease.
- Establishes a multi-level validation approach (in-silico → zebrafish → mice).
- Demonstrates the potential of repurposed drugs in uncovering new biological mechanisms relevant to neurodegeneration

Methodology

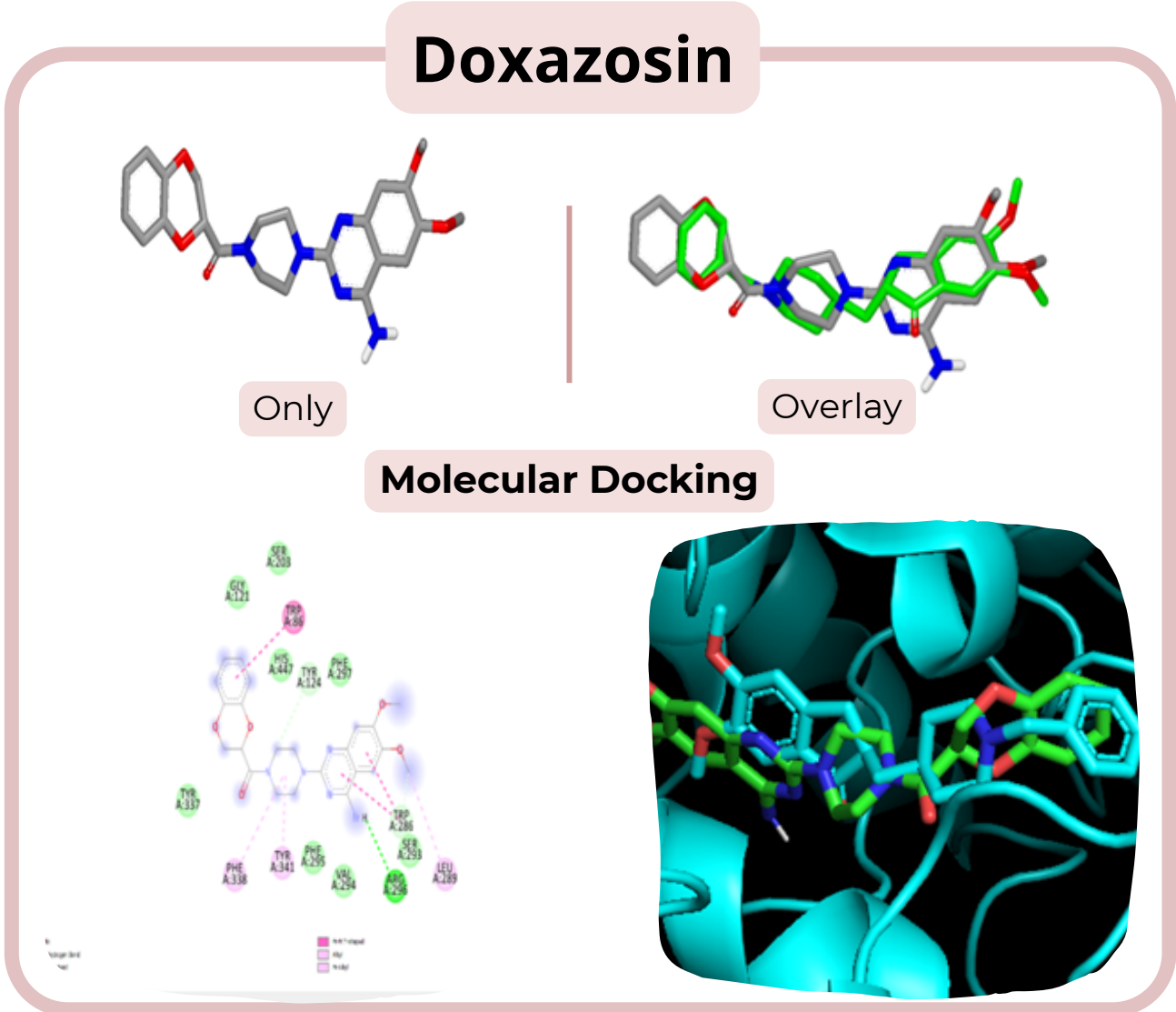


Network Pharmacology

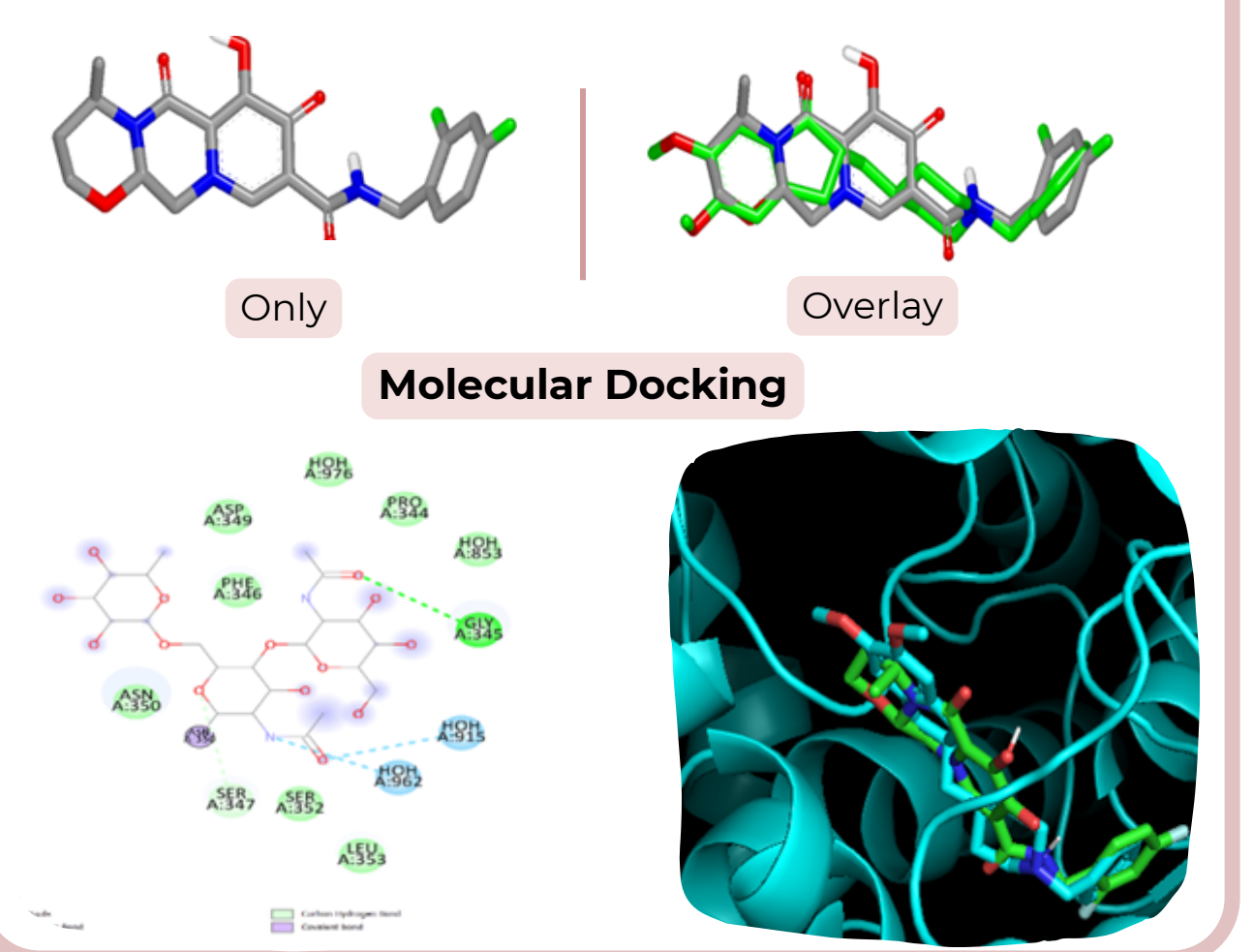


Results

Molecular Docking

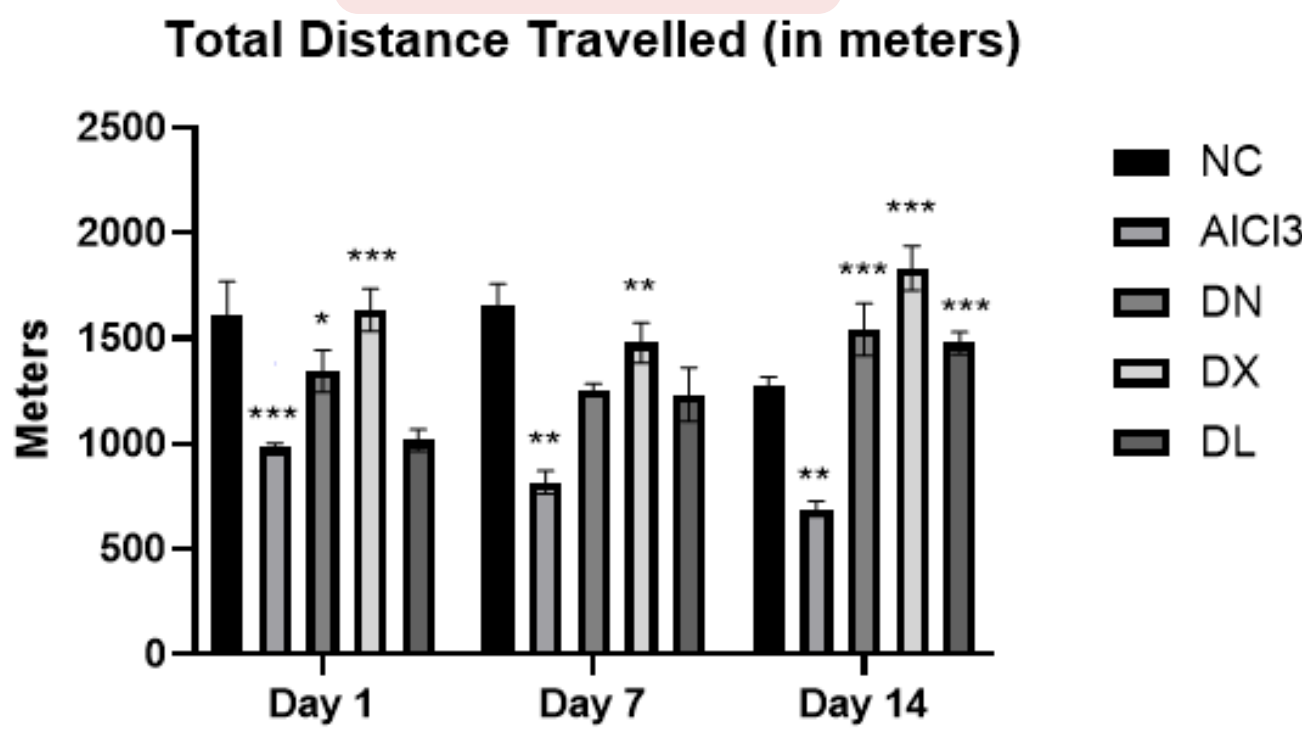


Dolutegravir

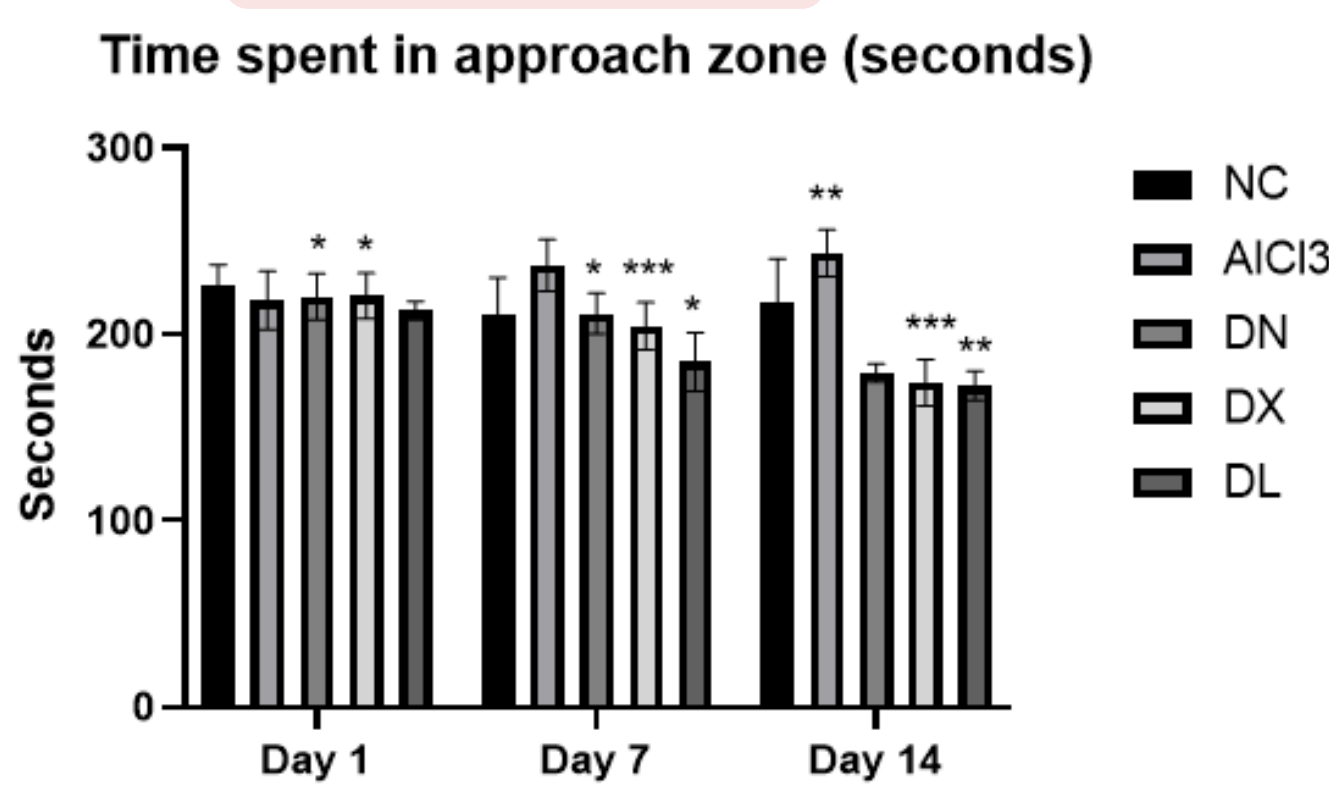


Zebra Fish Results

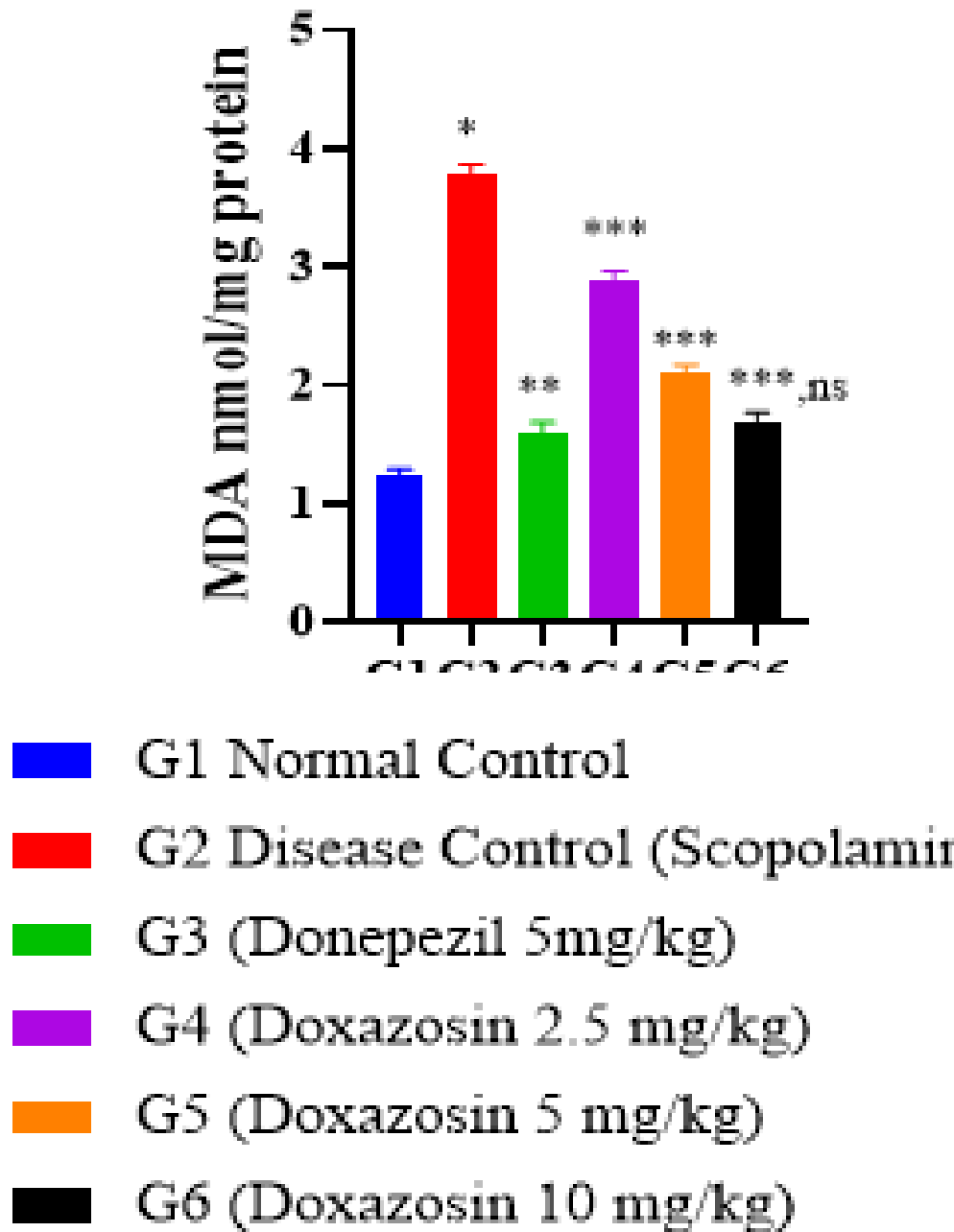
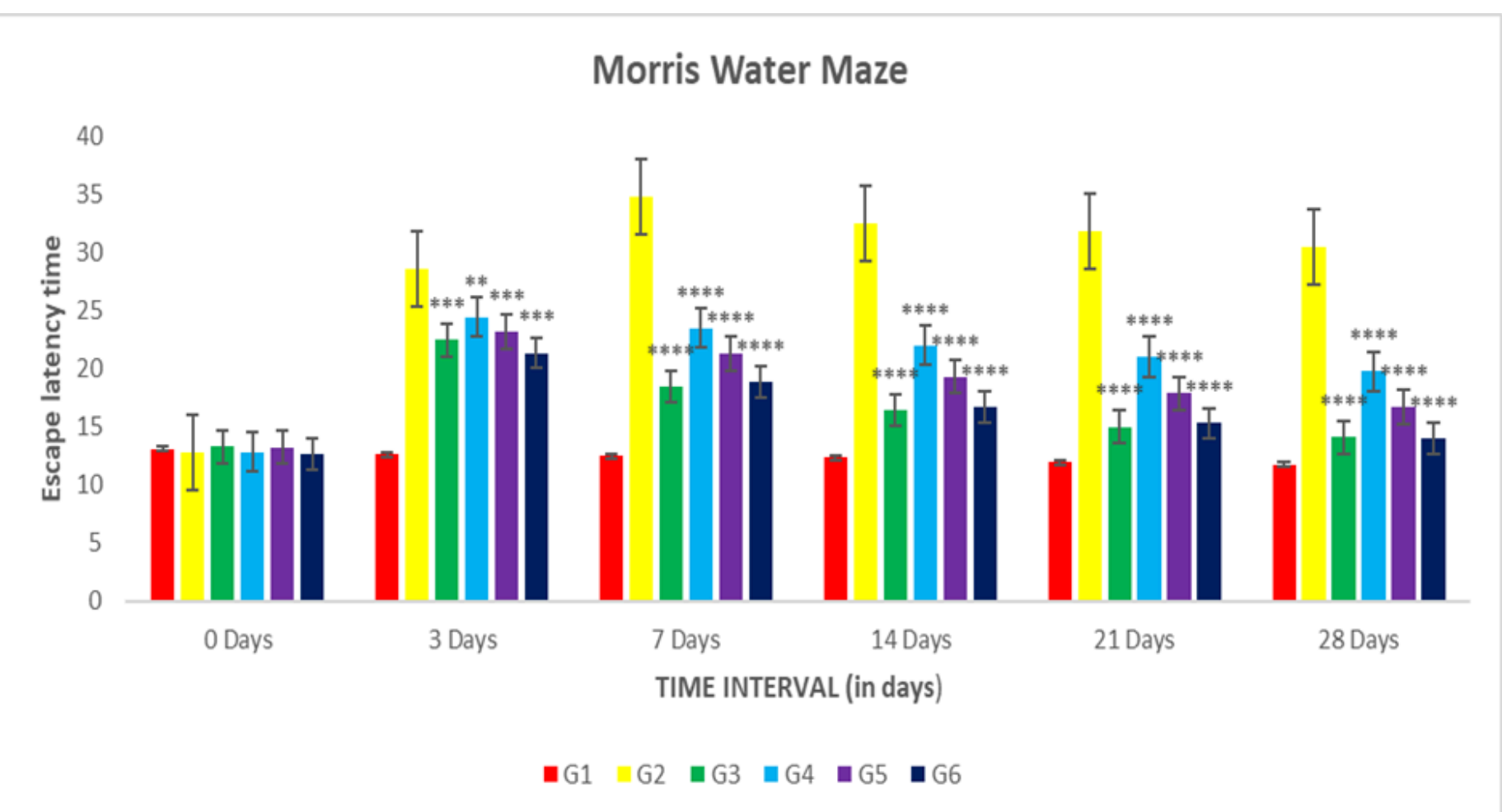
OPEN FIELD TEST



MIRROR BITING TEST



Animal Study Results



Conclusion

- This study integrates computational modelling and animal models to advance understanding of Alzheimer's pathology.
- The findings highlight how repurposed drugs can reveal new mechanistic insights into memory, oxidative stress, and neuronal integrity, contributing to fundamental neuropharmacology research

Future Scientific Directions

- Current stage: → Validated in lab and small-animal models.
- Next steps include advanced preclinical investigations to validate mechanistic findings and explore broader molecular pathways

Refrences

- Cummings JL, Zhou Y, Van Stone A, Cammann D, Tonegawa-Kuji R, Fonseca J, Cheng F. Drug repurposing for Alzheimer's disease and other neurodegenerative disorders. Nature Communications. 2025 Feb 19;16(1):1755.

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